Official Journal of Korean College of Rheumatology

pISSN 2093-940X
eISSN 2233-4718

JRD Journal of Rheumatic Diseases

Vol. 29, Suppl. 1, May, 2022

KCR 2022
42nd KCR Annual Scientific Meeting and The 16th International Symposium

Date | May 19(Thu) – 21(Sat), 2022
Vanue | Seoul Dragon City, Seoul, Korea

대한류마티스학회
Korean College of Rheumatology

SCAN ME

KCR 2022

42nd Korean College of Rheumatology Annual Scientific Meeting &
16th International Symposium

May 19 (Thu) - 21 (Sat), 2022

Day 2 May 20 (Fri)

Sponsored Symposium 1

The Role of Baricitinib in the Treatment of RA

Lecture Title: **Baricitinib in the real-world data**

DATE **12:00-13:00, May 20 (Fri)**

CHAIR **Yong-Beom Park**
Yonsei Univ., Korea

SPEAKER **Yun-Hong Cheon**
Gyeongsang Nat'l Univ., Korea

Day 3 May 21 (Sat)

Sponsored Symposium 2

Ixekizumab : Recent updates on the treatment of Spondyloarthritis

Lecture Title: **IL-17 inhibition in spondyloarthritis: The efficacy of Ixekizumab and clinical relevance**

DATE **08:00-09:00, May 21 (Sat)**

CHAIR **Seong-Ho Kim**
Inje Univ., Korea

SPEAKER **Yeon-Ah Lee**
Kyung Hee Univ., Korea

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1일 1회 복용하는 젤잔즈 XR 11mg이 RA 치료에 승인되었습니다.[3]

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(as of 2020.12.07)

MTX 포함 2가지 csDMARDs-IR RA 환자에게 젤잔즈 5mg과 약동학적으로 동등한, 하루 한 번 복용하는 젤잔즈 XR 11mg을 고려해주세요![3]

[References] 1. Data on file. Pfizer Inc, New York, NY. 2. Lamba M, et al. Extended-release once-daily formulation of tofacitinib: evaluation of pharmacokinetics compared with immediate-release tofacitinib and impact of food. J Clin Pharmacol. 2016;56(11):1362-1371. 3. 젤잔즈 XR 11 mg 제품설명서(최초품목허가일: 2020.12.07).

Abbreviations. RA, rheumatoid arthritis; XR, extended release

[주요 안전성 정보[3] Version 2020.12.07] 젤잔즈 투여 환자에서 중대한 감염, 악성 종양, 정맥혈전색전증이 보고되었습니다. 한국 화이자는 국내에서 허가 받지 않은 용법, 용량으로 젤잔즈를 투여하는 것을 권장하지 않습니다.

[제품요약정보] 젤잔즈정 5 mg 전문의약품 [원료약품 분량] 1정(206.00 mg) 중 토파시티닙시트르산염(토파시티닙으로서 5 mg) (별규) 8.078 mg [성상] 흰색의 원형 필름코팅정제 [효능·효과] 1. 류마티스 관절염: 메토트렉세이트에 적절히 반응하지 않거나 내약성이 없는 성인의 중등증 내지 중증의 활동성 류마티스관절염의 치료. 이 약은 단독투여 또는 메토트렉세이트나 다른 비생물학적 류마티스제제(DMARDs)와 병용투여 할 수 있다. 이 약은 생물학적 항류마티스제제 또는 아자티오프린 및 사이클로스포린과 같은 강력한 면역억제제와 함께 사용해서는 안 된다. 2. 건선성 관절염: 이전 항류마티스제제(DMARDs)에 적절히 반응하지 않거나, 내약성이 없는 성인의 활동성 건선성 관절염의 치료. 이 약은 메토트렉세이트나 다른 비생물학적 항류마티스제제 (DMARDs)와 병용투여 한다. 건선성 관절염 환자에 대한 이 약 단독요법의 유효성은 연구되지 않았다. 이 약을 생물학적 항류마티스제제 또는 아자티오프린 및 사이클로스포린과 같은 강력한 면역억제제와 함께 사용해서는 안 된다. 3.궤양성 대장염: 코르티코스테로이드, 아자티오프린, 6-메르캅토푸린(6-MP)을 포함한 통상적인 치료제 또는 생물학적 제제에 적절히 반응하지 않거나, 반응이 소실되거나 또는 내약성이 없는 성 인의 중등도-중증 활동성 궤양성 대장염의 치료. 이 약을 생물학적 제제나 아자티오프린 및 사이클로스포린과 같은 강력한 면역억제제와 함께 사용해서는 안된다. [용법·용량] 1. 투여시 주의사항 1) 절대림프구수(ALC)가 500 cells/㎣ 미만, 절대호중구수(ANC) 1,000 cells/㎣ 미만, 또는 헤모글로빈 수치 9 g/dL 미만인 환자에게는 이 약의 투여를 시작하지 않는다. 2) 이 약의 투여 전, 투여 중 및 투여 후 결핵을 포함한 감염에 대해 면밀히 모니터링해야 하며, 중대한 감염이 발생한 환자는 감염이 조절될 때까지 이 약의 투여를 중단해야 한다. 3) 림프구 감소, 호중구 감소 및 빈혈의 조절을 위해 일시적으로 이 약의 투여를 중단하는 것이 필요할 수 있다. 4) 이 약은 음식물 섭취와 상관없이 경구 투여할 수 있다. 2. 류마티스 관절염 및 건선성 관절염의 권장용량: 이 약의 권장용량은 1회 5 mg, 1일 2회 투여이다. 다음의 환자에서 이 약의 용량은 1일 1회, 1회 5 mg으로 감량해야 한다: 강력한 CYP3A4 억제제(예. 케토코나졸)를 투여 중인 환자, 중등도의 CYP3A4 억제제 및 강력한 CYP2C19 억제제(예. 플루코나졸)를 투여 중인 환자, 중등증 또는 중증의 신장애 환자, 중등증의 간장애 환자. 림프구 감소, 호중구 감소 및 빈혈의 조절을 위해 일시적으로 이 약의 투여를 중단하는 것이 필요할 수 있다. 3. 궤양성 대장염의 권장용량: 1회 10 mg 1일 2회로 최소 8주 동안 투여 후, 치료 반응에 따라 5 mg 또는 10 mg을 1일 2회 투여한다. 유지용량으로 최소 유효용량을 사용한다. 이 약 1회 10 mg을 1일 2회로 16주 동안 투여한 후에도 적절한 치료적 유익성을 보이지 않으면 투여를 중단한다. 다음의 환자에서 이 약 1회 10 mg을 1일 2회로 투여 중인 경우 1회 5 mg 1일 2회로 또는 이 약 1회 5 mg 1일 2회로 투여 중인 경우 1일 1회 5 mg으로 감량해야 한다: 강력한 CYP3A4 억제제(예. 케토코나졸)를 투여 중인 환자, 중등도의 CYP3A4 억제제 및 강력한 CYP2C19 억제제(예. 플루코나졸)를 투여 중인 환 자, 중등증 또는 중증의 신장애 환자, 중등증의 간장애 환자. 절대림프구수(ALC) 500 cells/㎣ 미만인 환자에서 이 약의 투여를 중단한다. 절대호중구수(ANC) 500-1,000 cells/㎣인 환자에서 이 약 1회 10 mg을 1일 2회 투여한 경우 1회 5 mg 1일 2회로 감량한다. 절대호중구수(ANC)가 1,000 cells/㎣ 초과가 되면, 임상적 반응에 따라 이 약 1회 10 mg 1일 2회로 다시 증량한다. 기존에 이 약 1회 5 mg을 1일 2회로 투여한 경우 투여를 잠정 중단한다. 절대호중 구수(ANC)가 1,000 cells/㎣ 초과가 되면, 이 약 1회 5 mg 1일 2회로 다시 투여한다. 절대호중구수(ANC) 500 cells/mm3 미만인 환자에서 이 약의 투여를 중단한다. 헤모글로빈 수치가 2 g/dL 초과의 감소 또는 8.0 g/dL 미만인 환자에서는 헤모글로빈 수치가 정상이 될 때까지 투여 잠정 중단할 수 있다. [사용상의 주의사항] 1. 경고 : 1) 중대한 감염: 이 약을 투여하는 환자들은 입원 또는 사망으로 이어질 수 있는 중대한 감염이 나타날 위험이 높다. 이러한 감 염이 나타난 대부분의 환자들은 메토트렉세이트 혹은 코르티코스테로이드 같은 면역억제제를 병용 투여하고 있었다. 중대한 감염이 나타난 경우, 감염이 조절될 때까지 이 약의 투여를 중단해야 한다. 보고된 감염은 다음을 포함한다: 폐질환 혹은 폐 이외의 질환이 있는 활성결핵. 환자들은 이 약을 투여하기 전 및 투여 중에 잠복결핵검사를 받아야 한다. 잠복결핵의 치료는 이 약 투여 전에 선행되어야 한다. 효모균증 및 간질성 형질세포폐렴을 포함한 침습적 진균 감염. 침습적 진균감염 환자는 국소보다는 전신으로 확산되는 질환으로 나타난다. 기회 감염성 병원체에 기인한 세균성, 바이러스성(헤르페스 바이러스 포함) 및 기타 감염 만성 또는 재발성 감염환자는 이 약의 투여를 시작하기 전 치료의 위험성 및 유익성에 대해 주의 깊게 고려해야 한다. 이 약 투여 중 또는 투여 이후 환자들은 감염 징후 및 증상의 발현을 주의 깊게 관찰해야 하며, 치료 시작 전 잠복 결핵에 음성반응을 보인 환자에서 결핵 발현 가능성 에 대하여도 주의 깊은 관찰이 필요하다. 2) 악성종양: 이 약을 투여한 환자들에게서 림프종 및 기타 악성 종양이 관찰되었다. 이 약과 면역억제제를 병용투여받은 신장이식 환자에서 엡스테인-바 바이러스(Epstein Barr Virus)와 관련이 있는 이식 후 림프세포 증식성 질환이 증가하는 것으로 관찰되었다. 3) 정맥혈전색전증: 임상시험 및 시판 후 보고의 이 약을 투여한 환자들에게서 정맥혈전색전증이 관찰되었다. 적어도 1 개 이상의 심혈관계 위험 요인이 있는 만 50 세 이상의 류마티스관절염 환자를 대상으로 진행중인 한 건의 대규모, 무작위배정, 허가 후 안전성감시(PASS) 연구에서 환자들은 토파시티닙 5 mg 1 일 2 회, 토파시티닙 10 mg 1 일 2 회또는 TNF 억제제를 투여받았다. TNF 억제제에 비해 토파시티닙을 투여받은 환자들에서 폐색전증(PE)의 용량 의존적 증가가 관찰되었다. 이러한 폐색전증 사례들 대부분은 중증이었고, 일부에서 사망을 초래했다. 이 연구에서 토파시티닙 투여군의 폐색전증 사례는 다른 토파시티닙 임상시험들에 비해 더 빈번하게 보고되었다. 이 연구의 세 개 투여군 모두에서 심부정맥혈전증 사례가 관찰되었다. 환자들에 대해 투여시작 전과 투여 중 주기적으로 정맥혈전색전증 위험요인을 평가한다. 위험 요인이 있는 환자는 이 약을 주의하여 사용한다. 정맥혈전색전증의 징후 및 증상이 있는 환자는 긴급히 평가한다. 용법·용량 또는 효능·효과에 관계없이, 정맥혈전색전증이 의심되면 이 약을 중단한다. 2. 다음 환자에는 투여하지 말 것 : 1) 이 약 또는 이 약의 구성성분에 과민증이 있는 환자 2) 중대한 감염(예. 패혈증) 또는 국소 감염을 포함한 활성 감염이 있는 환자 3) 활동성 결핵이 있는 환자 4) 중증 간장애 환자 5) 절대호중구수(ANC) 500 cells/㎣ 미만인 환자 6) 절대림프구수(ALC) 500 cells/㎣ 미만인 환자 7) 헤모글로빈 수치 8 g/dL 미만인 환자 8) 임부 또는 임신가능성이 있는 여성 9) 이 약은 유당을 함유하고 있으므로 갈락토오스 불내성(galactose intolerance), Lapp 유당분해효소 결핍증(Lapp lactase deficiency)또는 포도당-갈락토오스 흡수장애(glucose-galactose malabsorption) 등의 유전 적인 문제가 있는 환자에게는 투여하면 안 된다. 3. 다음 환자에는 신중히 투여할 것 1) 감염이 의심되는 환자 2) 결핵 병력이 있는 환자 3) 면역력이 약화된 환자 4) 고령자 5) 당뇨병 환자 6)위장관 게실환자(위장관 천공가능성이 있다.) 7) 호중구수 또는 림프구수 감소 환자, 헤모글로빈 수치 감소 환자 8) 경증 또는 중등도의 간 장애 환자 9) 신장애 환자 10) 간질성폐렴 병력이 있는 환자 4. 이상반응 1) 이상반응 : 기관계 및 CIOMS 빈도 분류에 따른 이상반응으로 폐렴, 인플루엔자, 대상포진, 요로감염, 부비동염, 기관지염, 코인두염, 인두염, 빈혈, 고지혈증, 두통, 고혈압, 기침, 복통, 구토, 설사, 구역, 위염, 소화불량, 발진, 관절통, 발열, 말초부종, 피로, 감마 글루타밀 전달효소 증가, 혈중 콜레스테롤 증가, 체중증가, 혈중 크레아틴 인산활성효소 증가가 흔하게 보고되었다. 2) 류마티스 관절염에 대한 임상시험: (상기도 감염, 코인두염 및 요로감염을 포함한) 전반적인 감염, (폐렴, 대상포진, 요로감염, 연조직염, 위장염, 게실염을 포함한) 중대한 감염, 결핵, 기회 감염, 바이러스 재활성화, 정맥혈전색전증 (비흑색종피부암[non-melanoma skin cancer] 제외한) 악성 종양, 간 효소 상승, 림프구 수 및 호중구 수 감소, 용량-관련 지질 및 혈청크레아티닌 증가가 보고되었다. 3) 건선성 관절염에 대한 임상시험: 이 약을 투여받은 활동성 건선성 관절염 환자에서 관찰된 안전성 프로파일은 류마티스 관절염환자에서 관찰된 안전성 프로파일과 유사하였다. 5. 일반적 주의: 이 약은 류마티스 관절염의 치료에 사용시, 류마티스전문의 또는 류마티스 관절염 치료에 전문 지식이 있는 의사에 의해 투여가 시작되고 모니터링 되어야한다. 설명서개정년월일: 2020.10.28

[제품요약정보] 젤잔즈 XR 서방정 11 mg 전문의약품 [원료약품 분량] 1정(225.400 mg) 중 토파시티닙시트르산염(토파시티닙으로서 11 mg) (별규) 17.771 mg [성상] 분홍색의 한쪽 옆면에 구멍이 있는 타원형 정제 [효능효과] 메토트렉세이트에 적절히 반응하지 않거나 내약성이 없는 성인의 중등증 내지 중증의 활동성 류마티스 관절염의 치료. 이 약은 단독투여 또는 메토트렉세이트나 다른 비생물학적 항류마티스제제(DMARDs)와 병용투여 할 수 있다. 이 약은 생물학적 항류마티스제제제 또는 아자티오프린 및 사이클로스포린과 같은 강력한 면역억제제와 함께 사용해서는 안된다. [용법용량] 정확한 용량 투여를 위해, 이 약은 통째로 삼켜야 하며, 으깨거나 쪼개거나 씹어서는 안된다. 1. 투여시 주의사항 1)~4) : 5mg과 상동. 5) 젤잔즈정과 젤잔즈 XR 서방정의 상호전환 : 젤잔즈정 5 mg 을 1 일 2 회 투여하는 환자는 젤잔즈정 5 mg 을 마지막으로 복용한 다음날부터 젤잔즈 XR 서방정 11 mg 1 일 1 회 용법으로 전환할 수 있다. 젤잔즈 XR 서방정 11 mg 을 1 일 1 회 투여하는 환자는 젤잔즈 XR 서방정 11 mg 을 마지막으로 복용한 다음날부터 젤잔즈정 5 mg 을 1 일 2 회 용법으로 전환할 수 있다. 젤잔즈 XR 서방정 11 mg 1 일 1 회는 젤잔즈정 5 mg 을 1 일 2 회 투여와 약동학적 동등성이 입증되었다. 2. 류마티스 관절염의 권장용량 : 이 약의 권장용량은 1일 1회 11 mg 투여이다. CYP2C19 및/또는 CYP3A4 억제제를 투여중인 환자, 중등도 및 중증 신장애 환자, 중등도 간장애 환자에서는 젤잔즈정 5mg 1일 1회 투여로 감량하는 것이 권장된다. [사용상의 주의사항] 1. 경고 : 5mg과 상동. 2. 다음 환자에는 투여하지 말 것 : 유당 관련 내용 제외하고 5mg과 상동3. 다음 환자에는 신중히 투여할 것 : 5mg과 상동. 4. 이상반응 1) 이상반응 : 5mg과 상동. 2) 류마티스 관절염에 대한 임상시험: 5mg과 상동. 5. 일반적 주의: 1)~12) : 5mg과 상동. 13) 젤잔즈XR 서방정에만 해당되는 사항(1) 다른 비변형제제와 마찬가지로, 중증의(병리적 또는 의인성) 위장관 협착이 있는 환자에게 젤잔즈 XR 서방정을 투여 시 주의해야 한다. 협착이 있는 환자들에서 다른 비변형서방제형 약물의 소화과정 중, 폐쇄성 증상이 드물게 보고되었다. (2) 정제 껍질 젤잔즈 XR 서방정을 투여한 환자는 비활성 정제껍질이 변 또는 인공항문을 통해 배설되는 것을 발견할 수 있다. 정제 껍질이 발견되더라도, 이 약의 활성성분은 이미 흡수되었다는 것을 환자에게 알려야 한다. (3) 젤잔즈 XR 서방정은 소르비톨을 함유하고 있다. 소르비톨(또는 과당)을 함유한 제품을 병용 투여하거나 소르비톨(또는 과당)을 섭취하는 경우, 상가적인 영향에 대해 고려해야 한다.: 설명서개정년월일: 2020.12.07 * 제품에 대한 자세한 정보는 최신의 제품설명서를 참고하시기 바라며, 홈페이지(www.pfizer.co.kr)를 통해 확인하실 수 있습니다. 제품 의학정보 문의: Website: www.pfizermedicalinformation.co.kr /Tel: 080-210-2114/E-mail: mis.korea@pfizer.com

PP-XXR-KOR-0010-20JAN2023

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[제품명] 휴미라펜주 40mg/0.4ml, 휴미라프리필드시린지주 40mg/0.4ml, 휴미라프리필드시린지주 20mg/0.2ml (아달리무맙, 유전자재조합) **[효능・효과]** 성인 1. 류마티스 관절염: 메토트렉세이트를 포함한 DMARDs(disease-modifying anti-rheumatic drugs)에 대한 반응이 적절하지 않은 성인의 중등도에서 중증의 활동성 류마티스 관절염의 치료. 이전에 메토트렉세이트로 치료받지 않은 성인의 중증의 활동성 및 진행성 류마티스 관절염의 치료. 이 약은 단독투여 또는 메토트렉세이트나 다른 DMARDs와 병용 투여할 수 있다. 메토트렉세이트에 내약성이 없거나 지속적인 병용투여가 부적절한 경우에는 단독 투여한다. 이 약과 메토트렉세이트와의 병용투여는 관절손상 진행속도를 감소시키고(X-선측정 결과) 신체활동기능을 향상시킨다. 2. 건선성 관절염: 이전에 DMARDs(disease-modifying anti-rheumatic drugs)에 대한 반응이 적절하지 않은 성인의 활동성 및 진행성 건선성 관절염의 치료. 이 약은 다발성, 대칭성 아형을 지닌 환자의 말초 관절손상 진행속도를 감소시키고(X-선측정 결과), 신체활동기능을 향상시킨다. 3. 축성 척추관절염: (1)강직성 척추염: 기존 치료에 대한 반응이 적절하지 않은 성인의 중증의 강직성 척추염의 치료, (2)방사선학적으로 강직성 척추염이 확인되지 않는 중증 축성 척추관절염: 방사선학적 검사에서 강직성 척추염이 확인되지 않으나, 상승된 CRP 수치 및/또는 MRI상 객관적인 염증의 징후를 보이는 중증 축성 척추관절염의 치료. 이 약은 비스테로이드성 항염증제(NSAIDs) 약물에 대한 반응이 적절하지 않거나, 불내성인 환자에 사용한다. 4. 성인 크론병(만 18세 이상): 코르티코스테로이드제나 면역억제제 등의 치료에 반응을 나타내지 않거나, 내약성이 없는 경우 또는 이러한 치료방법이 금기인 중등도에서 중증의 활성 크론병의 치료. 유도 요법의 경우 이 약은 코르티코스테로이드제와 병용투여한다. 코르티코스테로이드제에 내약성이 없거나, 지속적인 병용투여가 부적절한 경우 단독투여할 수 있다. 5. 건선: 전신치료 또는 광선요법이 필요한 성인의 중등도에서 중증의 만성 판상 건선의 치료. 6. 궤양성 대장염: 코르티코스테로이드 및 6-MP(6-mercaptopurine) 또는 AZA(azathioprine)를 포함한 통상적인 치료에 대해 반응이 적절하지 않거나 내약성이 없는 경우 또는 이러한 치료방법이 금기인 성인의 중등도에서 중증의 활성 궤양성 대장염의 치료. 7. 베체트 장염: 스테로이드 또는 면역억제제 등의 통상적인 치료에도 적절한 반응이 나타나지 않는 베체트 장염의 치료. 8. 화농성 한선염: 기존의 전신 요법에 적절한 반응을 나타내지 않는 중등도에서 중증의 활성 화농성 한선염의 치료. 9. 포도막염: 코르티코스테로이드에 적절한 반응을 나타내지 않은 성인의 비-감염성 중간 포도막염, 후포도막염 및 전체포도막염의 치료. 소아 1. 소아 크론병(만 6~만 17세): 일차 영양요법, 코르티코스테로이드, 면역조절제 등의 치료에 적절한 반응을 나타내지 않거나, 내약성이 없는 경우 또는 이러한 치료방법이 금기인 소아 환자(만 6~만 17세)에서 중등도에서 중증의 활성 크론병의 치료. 2. 소아 특발성 관절염: (1) 다관절형 소아 특발성 관절염: 하나 이상의 DMARDs(disease-modifying anti-rheumatic drugs)에 대해 부적절한 반응을 보인 만 2세 이상의 소아 및 청소년에서 활성 다관절형 소아 특발성 관절염의 치료. (2) 골부착부위염 관련 관절염: 기존 치료에 적절한 반응을 나타내지 않거나 내약성이 없는 만 6세 이상 어린이 및 청소년의 활성 골부착부위염 관련 관절염의 치료. 3. 소아 판상 건선: 국소 치료 및 광선요법에 적절한 반응을 나타내지 않거나 해당 치료가 부적절한 만 4세 이상의 어린이 및 청소년의 중증 만성 판상 건선의 치료. **[용법・용량]** 환자가 자가 주사하는 것이 적절하며 필요시 치료 추적이 가능하다고 의사가 판단하는 경우, 환자는 주사방법에 대한 교육을 받은 후 이 약을 자가 주사할 수 있다. 80 mg의 투여는 하루에 40 mg을 2 번 주사한다. 160 mg의 투여는 하루에 40 mg을 4 번 주사하거나, 이틀에 걸쳐 40 mg을 2 번씩 주사할 수 있다. 성인 1. 류마티스 관절염: 성인 류마티스 관절염 환자에 대한 이 약의 권장 용량은 아달리무맙 40 mg을 2주에 1회 피하 주사한다. 이 약을 투여하는 동안 메토트렉세이트의 병용투여를 유지한다. 글루코코르티코이드, 살리실산염, 비스테로이드성항염증제(NSAIDs), 진통제, 다른 DMARDs의 병용투여를 유지할 수 있다. 단독요법의 경우 이 약에 대한 반응이 감소한 환자는 40 mg 매주 투여 또는 80mg 격주 투여로 증량하면 유용한 효과를 얻을 수 있다. 2. 건선성 관절염, 강직성 척추염 및 방사선학적으로 강직성 척추염이 확인되지 않는 중증 축성 척추관절염: 건선성 관절염, 강직성 척추염 및 방사선학적으로 강직성 척추염이 확인되지 않는 중증 축성 척추관절염 환자에 대한 이 약의 권장 용량은 아달리무맙 40 mg을 2주에 1회 피하 주사한다. 상기 효능효과에 대해 임상적인 반응은 보통 치료 12주 이내에 나타나며, 이 기간 내에 반응을 나타내지 않는 환자의 경우에는 투여 지속여부를 신중히 재고한다. 3. 성인 크론병: 성인 중등도에서 중증 크론병에 대한 이 약의 권장 용량은 첫 주에 아달리무맙 80 mg을 투여하고 첫 투여 후 2주 후에 40 mg을 투여한다. 빠른 효과를 얻어야 할 필요가 있는 경우에는, 유도 요법동안 이상 반응에 대한 위험성이 증가한다는 것을 알리고, 첫 주에 160 mg을 투여하고 첫 투여 후 2주 후에 80 mg을 투여할 수 있다. 유도요법의 경우 이 약은 코르티코스테로이드제와 병용 투여한다. 코르티코스테로이드제에 내약성이 없거나, 지속적인 병용투여가 부적절한 경우 단독 투여할 수 있다. 유도 요법 후, 아달리무맙 40 mg을 2주에 1회 피하 주사한다. 만약 투여를 중지하고 재발의 증상과 징후가 나타나면 이 약을 재투여 할 수 있다.

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아달로체® 프리필드시린지주 40mg / 아달로체® 프리필드펜주 40mg

[효능·효과] • **성인** 1. 류마티스 관절염 2. 건선성 관절염 3. 축성 척추관절염 (강직성 척추염, 방사선학적으로 확인되지 않는 축성 척추관절염) 4. 성인 크론병(18세 이상) 5. 건선 6. 궤양성대장염 7. 베체트 장염 8. 화농성 한선염 • **소아** 1. 소아 크론병(6세~17세) 2. 소아 특발성 관절염 (다관절형 소아 특발성 관절염, 골부착부위염 관련 관절염) 3. 소아 판상 건선 **[용법·용량]** • **성인 (18세 이상)** 1. 류마티스 관절염: 40mg 2주에 1회 피하주사. 반응 감소 시 40mg 매주 또는 80mg 2주에 1회. 2. 건선성 관절염, 강직성 척추염 및 방사선학적으로 강직성 척추염이 확인되지 않는 중증 축성 척추관절염: 40mg 2주에 1회. 3. 성인 크론병: (유도) 첫 주 80mg, 2주 후 40mg 또는 첫 주 160mg, 2주 후 80mg. (유지) 40mg 2주에 1회. 반응 감소 시 40mg 매주 또는 80mg 2주에 1회. 4. 건선: (유도) 첫 주 80mg. (유지) 40mg 2주에 1회. 반응 감소 시 40mg 매주 또는 80mg 2주에 1회. 5. 궤양성 대장염: (유도) 첫 주 160mg, 2주 후 80mg. (유지) 40mg 2주에 1회. 반응 감소 시 40mg 매주 또는 80mg 2주에 1회. 6. 베체트 장염: 첫 주 160mg, 2주 후 80mg, 첫 투여 4주 후 40mg 2주에 1회. 7. 화농성 한선염: 첫 주 160mg, 2주 후 80mg, 첫 투여 4주 후 40mg 매주 또는 80mg 2주에 1회. 치료 중단 시 40mg 매주 또는 80mg 2주에 1회로 재투여. • **소아** 1. 소아 크론병 (6세~17세) (40kg 이상) 성인과 동일. 2. 소아 특발성 관절염 (다관절형 소아 특발성 관절염, 골부착부위염 관련 관절염) (30kg 이상) 40mg 2주에 1회. 3. 소아 판상 건선 (30kg 이상) 처음 2회 매주 40mg, 이후 40mg 2주에 1회. **[사용상의 주의사항]** 이 약은 휴미라주40밀리그램(아달리무맙, 유전자재조합)을 대조약으로 한 동등생물의약품이다. • **금기** 1.아달리무맙 또는 이 약의 성분에 과민증인 환자 2. 활동성 결핵 또는 패혈증, 기회감염과 같은 다른 중증 감염이 있는 환자 (경고항 참조) 3. 중등도 내지 중증의 심부전 (NYHA class III/IV) 환자 **[포장단위]** 프리필드시린지(0.8mL), 프리필드펜주(0.8mL) x 1개 / Box **[사용기간]** 제조일로부터 36개월 **[저장방법]** 밀봉용기, 냉장(2~8℃)보관, 차광보관 **[수입자, 제조의뢰자]** 삼성바이오에피스(주), 인천광역시 연수구 첨단대로 107 **[제조자]** Biogen(Denmark) Manufacturing ApS (원료의약품), 삼성바이오로직스주식회사, 대한민국, 인천광역시 연수구 송도바이오대로 300 (송도동, 삼성바이오로직스) (원료의약품) **[판매자]** ㈜유한양행, 서울특별시 동작구 노량진로 74 (대방동), 전화: 080-024-1188 **[개정연월일]** 프리필드시린지: 2021.07.20 프리필드펜: 2021.07.20 ※ 자세한 허가사항은 식약처 의약품통합정보시스템 홈페이지(https://nedrug.mfds.go.kr/)를 참조하여 주시기 바랍니다. 요약 허가사항에 반영되지 않은 허가 변경이 상기일자 이후에 있을 수도 있습니다.

1. 의약품 안전나라 의약품통합정보시스템(http://nedrug.mfds.go.kr/index)

ADC-A1.1-172-20210

YUHAN

SAMSUNG BIOEPIS

BELIEF IN RELIEF

Cosentyx® secukinumab

Here with you

코센틱스®는 AS로 고통받고 있는 환자들에게 RELIEF, 그 이상의 가치를 제공합니다[1-6]

FAST & LONG LASTING RELIEF[3,6]

* The proportions of patients achieving ASDAS-CRP inactive disease were 25.8% and 16.8% at week 52 and 25.0% and 18.4% at week 156 with secukinumab 300 and 150 mg, respectively.

† Cosentyx® Patient Numbers From Launch Until October 2020. This numbers included patients with PsO, PsA, and AS.

Study design[1]: 4-year results from the MEASURE 1 study; Patients opting to enroll had completed 2 years' treatment in the MEASURE 1 core study with s.c secukinumab 150 or 75mg every 4weeks , following IV loading to Week 4, or placebo treatment to week 16/24. Up-titration from secukinumab 75-150mg q4week was permitted following a protocol amendment. Efficacy is reported for patients originally randomized to secukinumab. Radiographic changes were assessed using the mSASSS and changes in MRI measures of inflammation using the Berlin scoring method. Safety and tolerability were evaluated. Among 274 extension study participants, 89.7% (78/87) and 93.0% (93/100) originally randomized to secukinumab 150 and 75 mg, respectively, completed 208 weeks.

Study design[2]: 3-year long-term end of study results; Randomized, double blinded, parallel group, placebo-controlled phase 3 study. A total of 226 patients were randomized to IV secukinumab 10 mg/kg (baseline, weeks 2 and 4) followed by s.c. secukinumab 300 mg (IV-300 mg) or 150 mg (IV-150 mg) every 4 weeks, or a matched placebo. Patients in the placebo group were re-randomized to s.c. secukinumab at a dose of 300 or 150 mg at week 16. Analysis at week 156 included patients initially randomized to secukinumab and those who switched from placebo to secukinumab at week 16 (any secukinumab 300 or 150 mg). Outcome measures at week 156 included ASAS 20/40, BASDAI, ASAS PR, ASAS 5/6, and ASDAS-CRP inactive disease.

Study design[3]: After the 2-year MEASURE 1 trial, 274 patients receiving s.c. secukinumab 150 or 75 mg (following IV loading or initial placebo treatment to 16/24 weeks) every 4 weeks were invited to enter the 3-year extension study. Dose escalation from 75 to 150 mg (approved dose) was allowed at or after week 156 based on the judgement of the treating physician. Assessments at week 260 (5 years) included ASAS 20/40 and other efficacy outcomes. Data are presented as observed. Safety assessment included all patients who received ≥1 dose of study treatment.

Study design[4]: Randomized, double blinded, parallel group, placebo-controlled phase 3 study. A total of 226 patients were randomized to IV secukinumab 10 mg/kg (baseline, weeks 2 and 4) followed by s.c secukinumab 300 mg (IV-300 mg) or 150 mg (IV-150 mg) every 4 weeks, or a matched placebo. Patients in the placebo group were re-randomized to s.c. secukinumab at a dose of 300 or 150 mg at week 16. The primary endpoint was ASAS20 response rate at week 16 in the IV-300 mg or IV-150 mg versus placebo. Other endpoints assessed through week 52 included improvements in ASAS40, ASAS 5/6, BASDAI, and ASAS PR, as well as the change from baseline in hsCRP levels.

AS, ankylosing spondylitis; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C-Reactive Protein; PsO, psoriasis; PsA, psoriatic arthritis; s.c., subcutaneous; IV, intravenous; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; MRI, magnetic resonance imaging; ASAS20, Assessment of SpondyloArthritis international Society criteria for 20% improvement; ASAS40, Assessment of SpondyloArthritis international Society criteria for 40% improvement; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASAS PR, Assessment of SpondyloArthritis international Society partial remission; ASAS, Assessment in SpondyloArthritis international Society; hsCRP, high-sensitivity C-reactive protein

References 1. Braun J, et al. Rheumatology (Oxford). 2018. doi: 10.1093/rheumatology/key375 **2.** Pavelka K, et al. ACR Open Rheumatol. 2020 Feb;2:119-127. **3.** Baraliakos X, et al. RMD Open. 2019 Sep 3;5:e001005. **4.** Data on file. COSENTYX® access. Novartis Pharmaceuticals Corp; October 2020. **5.** Marzo-Ortega H, et al. Arthritis Rheumatol. 2020; 72 (suppl 10). **6.** Pavelka K, et al. Arthritis Res Ther. 2017 Dec 22;19(1):285.

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서울시 영등포구 국제금융로10 Three IFC 49층

Product Information

처방하시기 전 QR 코드 또는 식품의약품안전처 의약품통합정보시스템(https://nedrug.mfds.go.kr)을 통해 상세 제품정보를 참조하시기 바랍니다.

코센틱스센소레디펜 (세쿠키누맙,유전자재조합)

prolia® denosumab

처음부터 끝까지 이유있는 자신감 프롤리아

Help her move forward with the relentless protection of **Prolia**®[1-2]

Reference 1. Camacho PM, *et al. Endocr Pract.* 2016;22(Suppl 4):1-421. **2.** Bone HG, *et al. Lancet Diabetes Endocrinol.* 2017;5(7):513-523.

PROLIA® Product Information **[제품명]** 프롤리아프리필드시린지(데노수맙) **[효능·효과]** 1. 폐경 후 여성 골다공증 환자의 치료 2. 남성 골다공증 환자의 골밀도 증가를 위한 치료 3. 글루코코르티코이드 유발성 골다공증의 치료 4. 안드로겐 차단요법을 받고 있는 비전이성 전립선암 환자의 골 소실 치료 5. 아로마타제 저해제 보조요법을 받고 있는 여성 유방암 환자의 골 소실 치료 **[용법·용량]** 이 약은 보건의료 전문가에 의해 투여되어야 한다. 이 약 1시린지(데노수맙 60mg)을 매 6개월마다 상완, 허벅지 위쪽 또는 복부에 피하 주사한다. 모든 환자는 칼슘 1000mg과 비타민D 400IU 이상을 매일 복용해야 한다. 정기 투여일에 이 약을 투여하지 못했을 경우, 가능한 빨리 투여한다. 그 후, 마지막 투여일자로부터 매 6개월마다 투여한다. **[경고]** 턱뼈 괴사가 보고되었다. **[다음 환자에게는 투여하지 말 것]** 1. 저칼슘혈증이 있는 환자는 이 약의 투여를 시작하기 전에 저칼슘혈증을 치료해야 한다. 2. 임부 3. 과민반응 **[약물유해반응]** 폐경 후 골다공증 환자에서 보고된 가장 흔한(≥5%이며 위약군보다 흔한) 약물이상반응은 등 통증, 팔다리 통증, 근골격통, 고콜레스테롤혈증 및 방광염. 남성 골다공증 환자에서 보고된 가장 흔한(≥5%이며 위약군보다 흔한) 약물이상반응은 등 통증, 관절통, 비인두염. 글루코코르티코이드 유발성 골다공증 환자에서 보고된 가장 흔한(>3%이며 활성대조군보다 흔한) 약물이상반응은 등 통증, 고혈압, 기관지염 및 두통. 안드로겐 차단요법을 받고 있는 전립선암 환자 또는 아로마타제 저해제 보조요법을 받고 있는 유방암 환자의 골 소실에 대하여 보고된 가장 흔한(10%) 약물이상반응은 관절통, 등 통증. **[일반적 주의]** 이 약 투여 중 엑스지바주를 투여하면 안 된다. 과민반응, 저칼슘혈증 및 무기질 대사, 턱뼈 괴사, 비정형 전자하부 및 골간 대퇴골 골절, 이 약의 치료 중단 후 다발성 척추 골절, 심각한 감염, 피부 유해사례, 골격근 통증, 골 교체 억제의 가능성이 있으므로 환자를 모니터링하고 필요시 치료 중단 등의 의학적 조치를 고려한다. **[적응상의 주의]** 우발적으로 주사침에 찔리는 것을 최소화하기 위하여, 이 약에는 녹색의 보호대가 장착되어 있다. 투여하기 전에 주사침 앞쪽으로 녹색 보호대를 밀어서는 안된다. **[보관 및 취급상의 주의사항]** 동결을 피하여 차광, 냉장 (2-8℃) 보관. **[수입판매원]** 암젠코리아유한회사 (서울특별시 중구 을지로5길 19, 20층 (수하동, FERRUM TOWER)). **※제품을 처방하시기 전 상세 제품설명서를 참고하여주시기 바랍니다.**

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For further medical information, please contact : | 수신자 부담 : 00798 611 3554 | e-mail : medinfo.JAPAC@amgen.com

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KR-03518-PRO-2019-Oct

† 65세 이상 RA 환자의 경우 동반질환 및 감염 위험이 높아질 수 있으므로 치료에 주의를 요합니다. † 오렌시아는 연령에 관계없이 remission rate, EULAR 반응율, DAS28-ESR 감소율이 모두 비슷하게 나타났습니다.[1] * 오렌시아는 65세 이상 RA 환자에서 효과 부족으로 인한 치료 중단 및 안전성 문제로 인한 치료 중단이 낮았으며 이로 인한 높은 persistence를 확인하였습니다.[2]
RA, rheumatoid arthritis; DAS28, 28-joint disease activity score; ESR, erythrocyte sedimentation rate

오렌시아®주 250mg(아바타셉트)

[효능 · 효과] 1. 성인 류마티스 관절염: 중등증-중증의 활동성 류마티스 관절염을 가진 성인 환자 2. 소아 특발성 관절염: 중등증-중증의 활동성 류마티스 관절염을 가진 6세 이상의 소아 환자 **[용법 · 용량]** 1. 성인 류마티스 관절염: 오렌시아®는 표1에 제시한 체중 범위별 투여량을 참고하여 30분간 정맥 내 주입으로 투여해야 합니다. 첫 투여 이후에, 오렌시아®는 첫 주입 이후 2주 및 4주 후, 그리고 그 이후에는 매 4주마다 투여해야 합니다. 오렌시아®는 단독치료제로 사용하거나 또는 TNF길항제를 제외한 DMARDs와 병용으로 투여할 수 있습니다. 소아 특발성 관절염 환자에는, 각 환자의 체중을 기준으로 계산 용량을 사용합니다. 2. 소아 특발성 관절염: 75kg 미만의 체중인 6 내지 17세의 소아 특발성 관절염 환자에의 오렌시아®의 권장용량은 매 투여시 환자의 체중을 기초로 10mg/kg을 투여합니다. 75kg 이상의 체중인 소아 환자에게는 성인의 권장 용량을 따라 오렌시아®를 투여해야하며, 최고 1000mg을 초과하지 않습니다. 오렌시아®는 30분간의 정맥 주입으로 투여해야 합니다. 첫 투여 이후에, 오렌시아®는 첫 투여후 2주 및 4주 후에 투여하고 그 이후 매 4주마다 투여합니다. 오렌시아®는 단독요법 또는 메토트렉세이트(MTX)와 병용하여 사용할 수 있습니다. **[사용상의 주의사항]** 다음 환자에는 투여하지 말 것: 이 약은 주성분(아바타셉트)이나 또는 이외의 구성 성분에 과민반응을 나타내는 것으로 알려진 환자에게 투여해서는 안 됩니다. *최신 제품정보는 (주)한국BMS제약 홈페이지(bms.com/kr) 또는 식약처 홈페이지 의약품정보란에서 확인하실 수 있습니다. **[제조회사]** BMS Company **[판매회사]** 한국BMS제약

표1. 정맥 투여 시 오렌시아® 주 250mg(아바타셉트)의 용량

환자 체중	용량	바이알 개수[a]
< 60kg	500mg	2
60 내지 100kg	750mg	3
> 100kg	1g	4

[a] 각 바이알에는 아바타셉트 250mg이 들어있다.

오렌시아® 서브큐 프리필드시린지 125mg(아바타셉트)

[효능 · 효과] 성인 류마티스 관절염: 중등증에서 중증의 활동성 류마티스 관절염을 가진 성인 환자. **[용법 · 용량]** 성인 류마티스 관절염: 아바타셉트는 단독치료제로 사용하거나 또는 TNF 저해제를 제외한 DMARDs와 병용으로 투여할 수 있습니다. 1. 피하 투여 요법: 이 약은 일주일에 한 번 피하 투여용으로만 사용해야 합니다. 이 약은 오렌시아® 주 250mg(아바타셉트) 정맥 부하 용량 투여 없이 시작할 수 있습니다. 의사가 필요하다고 판단하는 경우, 정맥 부하 용량 투여로 치료를 시작하는 환자는 표 1의 체중에 따른 분류에 따라 한 번의 정맥 주입으로 시작하여야 합니다. 정맥 투여 후 하루 이내에 이 약의 첫 피하 투여를 실시해야 합니다. 오렌시아® 정맥 투여를 받고 있던 환자가 피하 투여로 변경하는 경우에는 다음에 계획된 정맥 투여 용량 대신에 첫 피하 투여 용량을 적용합니다. 2. 정맥 투여 요법: 부하 용량으로서 오렌시아® 주 250mg(아바타셉트)을 이용한 정맥 투여는 표 1에 제시한 체중 범위별 투여량을 참고하여 30분간 정맥 내 주입으로 투여해야 합니다. **[사용상의 주의사항]** 다음 환자에는 투여하지 말 것: 이 약은 주성분(아바타셉트)이나 또는 이외의 구성성분에 과민반응을 나타내는 것으로 알려진 환자에게 투여해서는 안 됩니다. *최신 제품정보는 (주)한국BMS제약 홈페이지 의약품정보란에서 확인하실 수 있습니다. **[제조회사]** BMS Company **[판매회사]** 한국BMS제약

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427KR20PR01605-01/Nov2020

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ORENCIA® (abatacept)

astellas

Prograf Tacrolimus

국내에서 수행된 MTX에 반응하지 않는
75명의 RA환자를 대상으로 한 4상 임상시험에서

TAC 병용은 LEF 병용에 비해 **비열등한 DAS28 개선 효과**를 보였으며, **양호한 내약성**을 나타냈습니다.[1]

24주 시점에서 **DAS28 score**를 보았을 때 TAC+MTX군은
LEF+MTX군에 비해 **비열등 하였습니다.**[1]

mean difference of DAS28: −0.1812, 95% CI: −0.8073, 0.4450

TAC+MTX 군의 경우 37명 중 18명, LEF+MTX 군의 경우
38명 중 27명에서 **이상사례가 보고**되었습니다.[2]

프로그람 캡슐 제품설명서

프로그람 주사 제품설명서

[Study information] A 24-week multi-center, double-blind, randomized, non-inferiority study in 75 rheumatoid arthritis(RA) patients with inadequate response to methotrexate (MTX) to investigate the efficacy and safety of tacrolimus(TAC) versus leflunomide(LEF) when combined with MTX in RA patients. Initial add-on dose: 1 capsule/day (TAC 1.5 mg/day) or LEF (10 mg/day) for 4 weeks(If tolerable, doses were then increased to 2 capsules/day until the end of the study).

[References] 1. Shin, K, et al. Efficacy and safety of add-on tacrolimus versus leflunomide in rheumatoid arthritis patients with inadequate response to methotrexate. *Int J Rheum Dis.* 2019 Jun;22(6):1115-1122. 2. Shin, K, et al. Efficacy and safety of add-on tacrolimus versus leflunomide in rheumatoid arthritis patients with inadequate response to methotrexate. *Int J Rheum Dis.* 2019 Jun;22(6):1115-1122. Supplementary Table 2.

류마티스 관절염 환자에서 TAC 와 MTX, 기타항류마티스제(DMARD) 또는 항 TNF알파제제를 병용했을 때의 유효성 및 안전성은 확립되어 있지 않습니다. 또한 면역억제작용을 가진 약물(면역억제제: 부신피질호르몬 등, 항류마티스제(DMARD): MTX 등) 과의 병용 시, 둘 다 면역억제작용을 가지므로 과도한 면역 억제가 일어날 수 있으므로 병용에 주의 해야 합니다.(Ref: 사용상의 주의사항 5. 일반적 주의 및 6-2) 병용주의 항 참고)

※ 보다 자세한 안전성 정보는 제품설명서를 참고해 주십시오.

한국아스텔라스제약(주) (06164) 서울특별시 강남구 테헤란로 521 파르나스타워 7층, Tel. 02-3448-0504

AKR-PRGAI-202201-01

JW 중외제약

ACTEMRA®
tocilizumab

Act your life!

악템라®는 DMARD 병용요법 뿐만 아니라 단독요법에서도 유효성이 입증된 생물학적 제제입니다.

- 악템라 단독요법과 adalimumab 단독요법의 head-to-head 임상에서 우위적 유효성을 입증하였습니다.[1]
- 방사선학적 평가를 통해 단독요법, DMARDs 병용요법에서 관절손상 억제효과를 확인하였습니다.[2-3]
- 5년 장기투여시에도 관해율(ACR70, DAS28<2.6)이 유의하게 유지되었습니다.[4]
- IV제제와 SC제제의 비열등성 시험에서 두 제제의 동등한 유효성 및 내약성을 입증하였습니다.[5]
- 이상 반응 발현율은 타 생물학적 제제의 류마티스 관절염 환자 대상 임상시험과 유사한 수준이었습니다.[6]

Reference. 1. Gabay C et al, Lancet. 2013 May 4;381 (9877):1541-50. 2. Yamanaka H et al, Mod Rheumatol. 2011;21(2):122-33. 3. Dougados M et al, Ann Rheum Dis. 2013 Jan;72(1):43-50. 4. Nishimoto N et al, Ann Rheum Dis. 2009 Oct;68(10):1580-4. 5. Ogata A et al, Arthritis Care Res (Hoboken). 2014 Mar;66(3):344-54. 6. Schiff MH et al, Arthritis Res Ther. 2011;13(5):R141.

[제품요약정보] 악템라®주, 악템라® 피하주사 162mg [전문의약품] ■**주성분** 토실리주맙(Tocilizumab) • IV : 80mg/4ml, 200mg/10ml, 400mg/20ml • SC(PFS/AI) : 162mg/0.9ml ■**효능·효과** [류마티스 관절염(성인)]: 메토트렉세이트(MTX)를 포함한 이전에 한 가지 이상의 DMARDs (Disease-Modifying anti Rheumatic Drug)에 대한 반응이 적절하지 않거나 불내성인 성인의 중등도 내지 중증의 활동성 류마티스 관절염의 치료, 메토트렉세이트와의 병용투여 시 관절손상 진행속도의 감소(X-선 측정결과)와 신체 기능의 향상 [전신형 소아 특발성 관절염]: 비스테로이드성 소염진통제(NSAID) 및 전신성 코르티코스테로이드(Corticosteroid)에 대한 반응이 적절하지 않은 2세 이상의 전신형 소아 특발성 환자의 치료 [다관절형 소아 특발성 관절염]: 메토트렉세이트(MTX)에 대한 반응이 적절하지 않은 2세 이상의 다관절형 소아 특발성 환자의 치료 ■**용법·용량** [IV] [류마티스 관절염(성인)] • 이 약은 단독 투여 또는 메토트렉세이트나 다른 DMARD와 병용 투여할 수 있다. 메토트렉세이트에 내약성이 없거나 지속적인 병용 투여가 부적절한 경우에는 단독 투여할 수 있다. • 성인의 활동성 류마티스 관절염에 대해, kg(몸무게)당 8 mg을 4주 1회 정맥 투여하며, 100 kg 이상의 환자에 대해서는 정맥 투여 시 800 mg을 초과해서는 안 된다. • 간 효소의 상승, 호중구감소증 및 혈소판감소증 등의 실험실적 검사치 이상이 발생한 경우 용량 조절이 권장된다. • 투여 시 생리식염 주사액으로서 최종 100 mL가 되도록 희석하고, 1시간 이상 점적정주 한다. [전신형 소아 특발성 관절염(2세이상)] • 이 약은 메토트렉세이트와 병용 투여한다. 메토트렉세이트에 내약성이 없거나 지속적인 병용 투여가 부적절한 경우에는 단독 투여할 수 있다. • 몸무게 30kg미만 : 전신형 소아 특발성 관절염에 대해, kg(몸무게)당 12mg을 2주 1회 정맥 투여한다. • 몸무게 30kg이상 : 전신형 소아 특발성 관절염에 대해, kg(몸무게)당 8mg을 2주 1회 정맥 투여한다. • 100 kg 이상의 환자에 대해서는 정맥 투여 시 800 mg을 초과해서는 안 된다. • 간 효소의 상승, 호중구감소증 및 혈소판감소증 등의 실험실적 검사치 이상이 발생한 경우 용량 조절이 권장된다. • 투여 시 생리식염 주사액으로서 최종 100 mL(몸무게가 30kg 미만인 경우 50mL)가 되도록 희석하고, 1시간 이상 점적정주 한다. [다관절형 소아 특발성 관절염(2세이상)] • 이 약은 메토트렉세이트와 병용 투여한다. 메토트렉세이트에 내약성이 없거나 지속적인 병용 투여가 부적절한 경우에는 단독 투여할 수 있다. • 몸무게 30kg미만 : 다관절형 소아 특발성 관절염에 대해, kg(몸무게)당 10mg을 4주 1회 정맥 투여한다. • 몸무게 30kg이상 : 다관절형 소아 특발성 관절염에 대해, kg(몸무게)당 8mg을 4주 1회 정맥 투여한다. • 100 kg 이상의 환자에 대해서는 정맥 투여 시 800 mg을 초과해서는 안 된다. • 간 효소의 상승, 호중구감소증 및 혈소판감소증 등의 실험실적 검사치 이상이 발생한 경우 용량 조절이 권장된다. • 투여 시 생리식염 주사액으로서 최종 100 mL가 되도록 희석하고(몸무게가 30kg 미만인 경우 50mL), 1시간 이상 점적정주 한다. [SC] [류마티스 관절염(성인)] • 이 약은 단독 투여 또는 메토트렉세이트나 다른 DMARD와 병용 투여할 수 있다. 메토트렉세이트에 내약성이 없거나 지속적인 병용 투여가 부적절한 경우에는 단독 투여할 수 있다. • 이 약은 1회 162 mg을 2주 간격으로 피하 투여한다. • 4주 간격으로 '악템라주(토실리주맙)(유전자재조합)'를 정맥 투여받고 있던 환자가 이 약으로 변경하고자 할 경우에는 다음에 계획된 정맥 투여 일정부터 이 약 162 mg을 2주 간격으로 피하 투여한다. ■**주요 사용상의 주의사항** [다음 환자에는 투여하지 말 것] 1) 심각한 감염증이 있는 환자(감염증이 악화될 우려가 있다) 2) 활동성 결핵 환자(증세를 악화시킬 우려가 있다) 3) 이 약 및 이 약의 성분에 과민증 환자 [다음 환자에는 신중히 투여할 것] 1) 감염 합병증이 있는 환자 또는 감염증이 의심되는 환자 2) 결핵의 기감염자(특히 결핵의 과거 병력이 있는 환자 및 흉부 X선상 결핵 치유소견이 있는 환자) 3) 감염 감수성 증가 상태에 있는 환자 4) 간질성 폐렴의 기왕력이 있는 환자 5) 위장 궤양이나 장관 게실이 있는 환자 6) 백혈구 감소, 호중구 감소, 혈소판 감소가 있는 환자 7) 활동성 간 질환이나 간 장애가 있는 환자

※자세한 제품정보는 제품설명서 및 회사홈페이지(http://www.jw-pharma.co.kr)를 참조하여 주십시오. 또한 문의사항이 있으실 경우 고객만족팀(1588-2675)으로 문의 주시기 바랍니다.

Simple dosing[1]

Proven persistence[2-6]

주사 한 번을 한 달에 한 번만[1]

신뢰할 수 있는 치료 유지율[2-6]

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심퍼니®프리필드시린지주(골리무맙)

【원료약품 및 분량】 1 프리필드시린지(0.5 mL) 중 골리무맙 50 mg / 1 프리필드시린지(1.0 mL) 중 골리무맙 100 mg **【성상】** 무색투명한 유리용기에 무색~담황색 액이 충전되어 있는 주사침이 부착된 프리필드시린지 **【효능효과】** 1. 류마티스 관절염: 이 약은 메토트렉세이트와 병용하여 다음과 같은 적응증에 투여한다. 1) 메토트렉세이트를 포함한 질환완화약제(DMARD) 치료에 불충분한 반응을 보인 성인 환자에서 중등도에서 중증의 활성 류마티스 관절염의 치료 및 신체활동 기능(Physical function)의 향상 2) 기존에 메토트렉세이트로 치료받은 적이 없는 성인 환자에서 중등도에서 중증의 활성 류마티스 관절염의 치료 3) X선으로 측정했을 때 질환과 관련된 구조적 손상 진행의 지연 2. 건선성 관절염: 이 약은 단독 또는 메토트렉세이트와 병용하여 다음과 같은 적응증에 투여한다. 1) 기존의 질환완화약제(DMARD) 치료에 불충분한 반응을 보인 성인 환자에서 활성 건선성 관절염의 치료 2) X선으로 측정했을 때 질환과 관련된 구조적 손상 진행의 지연 및 신체활동 기능(Physical function)의 향상 3. 축성 척추관절염: 1) 강직성 척추염: 보편적인 치료에 불충분한 반응을 보인 성인 환자에서 중등도에서 중증의 활성 강직성 척추염의 치료 2) 방사선학적으로 강직성 척추염이 확인되지 않는 축성 척추관절염: 방사선학적 검사에서 강직성 척추염이 확인되지 않으나, 상승된 CRP 수치 및/또는 MRI상 객관적인 염증의 징후를 보이는 성인의 중증 활성 축성 척추관절염의 치료. 이 약은 비스테로이드성항염증제(NSAID)s 약물에 대한 반응이 적절하지 않거나, 불내성인 환자에 사용한다. 4. 궤양성 대장염: 코르티코스테로이드나 6-머캅토퓨린 또는 아자티오프린 등 보편적인 치료법에 불충분한 반응을 보이거나, 그러한 치료에 내약성이 없거나 또는 금기인 성인의 중등도에서 중증의 활성 궤양성 대장염**【용법용량】** 이 약의 투여는 류마티스 관절염, 건선성 관절염, 강직성 척추염, 방사선학적으로 강직성 척추염이 확인되지 않는 축성 척추관절염 및 궤양성 대장염을 진단 및 치료했던 경험이 있는 숙련된 의사에 의해 실시 및 감독되어야 한다. 피하 주사 방법에 대하여 적절히 훈련받은 다음, 담당의사가 적합하다고 판단하는 경우에 환자는 이 약을 자기 주사할 수 있다. 이 때 필요하면 의학적 추적조사도 동반될 수 있다. 다회 투여가 필요한 경우에는 이미 주사된 부위를 피하여 주사한다. 1. 류마티스 관절염: 이 약 50 mg을 월 1회로 매월 정기적인 날짜에 피하주사한다. 이 약은 메토트렉세이트와 병용 투여한다. 2. 건선성 관절염: 이 약 50 mg을 월 1회로 매월 정기적인 날짜에 피하주사한다. 3. 강직성 척추염 및 방사선학적으로 강직성 척추염이 확인되지 않는 축성 척추관절염: 이 약 50 mg을 월 1회로 매월 정기적인 날짜에 피하주사한다. 이 약은 류마티스 관절염 환자에게 메토트렉세이트와 병용 투여해야 하며, 건선성 관절염이나 강직성 척추염 환자에게 단독 또는 메토트렉세이트나 다른 비생물학적 질환완화약제(DMARD)와 병용 투여할 수 있다. 현재까지의 자료를 바탕으로 보면 일반적으로 투여 12~14주 이내(3~4회 투여 후)에 임상 반응을 나타내는 것으로 보인다. 이 기간 내에 치료적 유익성을 보이지 않는 환자는 투여 지속 여부를 재고해야 한다. 류마티스 관절염, 건선성 관절염, 강직성 척추염 환자 및 방사선학적으로 강직성 척추염이 확인되지 않는 축성 척추관절염 환자에서 3~4회 투여 이후 적절한 임상반응을 달성하지 못한 체중 100 kg 이상의 환자에서 이 약 50 mg 용량과 100 mg 용량에서 특정한 중대한 약물유해반응의 증가하는 위험을 비교하여 월 1회 100 mg까지 이 약을 증량하는 것이 고려될 수 있다. 100 mg 용량을 3~4회 추가 투여한 후에 치료적 유익성을 보이지 않는 환자는 투여 지속 여부를 재고해야 한다. 4. 궤양성 대장염: 이 약 200 mg을 치료 첫 주에, 그로부터 2주 뒤에 100 mg을 피하주사한다. 이후에 4주에 한번 100 mg을 피하주사한다.**【사용상의주의사항 요약】** 1. 경고 1) 심각한 감염 · 이 약을 투여 받은 환자에서 결핵, 세균성 패혈증, 침습성 진균, 기타 기회감염을 포함한 입원 또는 사망이 발생하였다. · 심각한 감염이나 패혈증이 발생한 경우 이 약의 투여를 중단해야 한다. · 잠복성 결핵 검사 결과 양성인 경우, 이 약을 투여하기 전에 결핵 치료를 시작해야 한다. · 잠복 결핵 감염 검사 결과 음성인환자를 포함하여 투약 중 결핵의 징후 및 증상에 대한 면밀한 모니터링을 해야 한다. 2) 악성 종양 · 이 약을 포함한 종양괴사인자 알파(TNFα) 저해제를 투여 받은 어린이 및 청소년에서 림프종 및 다른 악성 종양이 보고되었으며, 일부는 치명적이었다. 2. 다음 환자에는 투여하지 말 것 · 이 약의 주성분 또는 부형제에 과민성의 병력이 있는 환자 · 활성 결핵 패혈증과 같은 중증의 다른 감염 기회감염이 있는 환자 · 중등도에서 중증의 심부전이 있는 환자 3. 다음 환자에는 신중히 투여할 것 · 간질성 폐렴의 기왕력이 있는 환자는 투여 중 주기적인 모니터링이 필요하며 재발 시에는 투여를 중단하고 적절한 조치를 취할 것 **【저장방법】** 냉장(2~8℃) 보관, 밀봉용기, 동결을 피할 것, 차광보관 **【수입 및 판매원】** ㈜한국얀센 **【제품설명서 개정년월일】** 2021-03-02 ※ 기타 상세한 내용은 제품설명서를 참고하시기 바랍니다.

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JRD

Journal of Rheumatic Diseases

Vol. 29, Suppl. 1, May, 2022

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	이승근 (부산의대)	임미진 (인하의대)	정재현 (고려의대)
	채지영 (분당제생병원)		
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간사	이주하 (가톨릭의대)	이창훈 (원광의대)	
위원	김근태 (고신의대)	김상현 (계명의대)	김재훈 (고려의대)
	성윤경 (한양의대)	송　란 (경희의대)	엄완식 (한양류마엄완식내과)
	이상원 (연세의대)	이윤종 (서울의대)	천윤홍 (경상의대)
	최상태 (중앙의대)		
연구위원회			
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간사	한승우 (경북의대)		
위원	고정희 (가톨릭의대)	구본산 (인제의대)	김진현 (충남의대)
	김태종 (전남의대)	김해림 (건국의대)	김현아 (아주의대)
	문수진 (가톨릭의대)	박동진 (전남의대)	오지선 (서울아산병원)
	이상엽 (동아의대)	이상진 (경북의대)	이재준 (성균관의대)
	이화정 (대구가톨릭의대)	주지현 (가톨릭의대)	최인아 (충북의대)
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정보위원회			
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간사	채지영 (분당제생병원)		
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	박성훈 (대구가톨릭의대)	손창남 (계명의대)	이상엽 (동아의대)
	이상원 (연세의대)	장성혜 (순천향의대)	정상윤 (차의대)
	정주양 (아주의대)	정종혁 (원광의대)	최윤정 (전북의대)

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간사	이은봉 (서울의대)	최병용(서울의료원)	
위원	강은하 (서울의대)	김건우 (대구파티마병원)	김형진 (성균관의대)
	문기원 (강원의대)	박은정 (국립의료원)	서미령 (가천의대)
	엄완식 (한양류마엄완식내과)	윤종현 (가톨릭의대)	이광훈 (동국의대)
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법제윤리위원회			
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간사	최상태 (중앙의대)		
위원	박희진 (가톨릭관동의대)	방소영 (한양의대)	이광훈 (동국의대)
	이창훈 (원광의대)	정재현 (고려의대)	정주양 (아주의대)
	표정윤 (연세의대)		

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	Jung Yoon Pyo (Yonsei Univ.)	

Program at a Glance

Day 1: May 19(Thu), 2022

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(Shilla Room, 3F)</th></tr>
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Advanced Course</td></tr>
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(Clinical)</td><td>Year in Review
(Basic)</td><td></td></tr>
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Pfizer Korea</td><td>Luncheon Symposium II
ACTEMRA tocilizumab</td><td>Luncheon Symposium III
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(Clinical)</td><td>Basic Research Workshop for Rheumatologist
Animal Models of Key Arthropathies</td><td></td></tr>
<tr><td>16:00 - 16:30</td><td colspan="3">Coffee Break</td></tr>
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(Basic)</td><td>Clinical Research Workshop for Rheumatologist
Planning and Conducting Clinical Research</td><td>Editorial Committee Workshop</td><td></td></tr>
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Day 2: May 20(Fri), 2022

Time	Room A (Grand Ballroom Hanra A & B, 3F)	Room B (Grand Ballroom Baekdu A & B, 5F)	Room C (Grand Ballroom Hanra C, 3F)
08:00 - 09:00	**Breakfast Symposium I** abbvie	**Breakfast Symposium II** CELLTRION PHARM CELLTRION	**Breakfast Symposium III** Pfizer Korea
09:00 - 10:00	**Keynote Lecture**		
10:00 - 10:30	**Coffee Break**		
10:30 - 12:00	**International Symposium** Recent Advances in Pathogenesis of Systemic Lupus Erythematosus	**Free Paper Session** Epidemiology & Health Services Research	**Free Paper Session** Sjögren's Syndrome, Systemic Sclerosis, and Inflammatory Myositis
12:00 - 13:00	**Luncheon Symposium IV** Lilly	**Luncheon Symposium V** Bristol Myers Squibb™	**Luncheon Symposium VI** YUHAN SAMSUNG BIOEPIS
13:00 - 14:30	**International Symposium** 2022 Clinical Research Update of Sjögren's Syndrome	**KCR-KAI Joint Symposium**	**Free Paper Session** Osteoarthritis and Orthopedics
14:30 - 15:30	**Poster Viewing and Coffee Break**		**Medical Humanities** Work Ethics and Labor Relation in the COVID-19 Era
15:30 - 17:00	**International Symposium** Vasculitis Session	**Free Paper Session** Rheumatoid Arthritis Clinical Research	
17:00 - 17:30	**Academic Awards**		
17:30 - 18:00	**General Assembly**		

Program at a Glance

Day 3: May 21(Sat), 2022

Time	Room A (Grand Ballroom Hanra A & B, 3F)	Room B (Grand Ballroom Baekdu A & B, 5F)	Room C (Grand Ballroom Hanra C, 3F)
08:00 - 09:00	**Breakfast Symposium IV** YUHAN SAMSUNG BIOEPIS	**Breakfast Symposium V** Lilly	**Breakfast Symposium VI** janssen | Johnson & Johnson
09:00 - 10:00	**Keynote Lecture**		
10:00 - 10:30	**Coffee Break**		
10:30 - 12:00	**International Symposium** Treatment of Osteoarthritis: To be Used and Abused?	**Free Paper Session** Spondyloarthritis	**Free Paper Session** Systemic Lupus Erythematosus
12:00 - 13:00	**Luncheon Symposium VII** NOVARTIS	**Luncheon Symposium VIII** AMGEN	**Luncheon Symposium IX** astellas
13:00 - 14:30	**International Symposium** Synovial Macrophage and Fibroblast in RA	**KCR-KSBMR Joint Symposium**	**Free Paper Session** Vasculitis and Metabolic Bone Disease
14:30 - 15:30	**Poster Viewing and Coffee Break**		
15:30 - 17:00	**International Symposium** New Horizon of Systemic Sclerosis	**Free Paper Session** Rheumatoid Arthritis Basic Research	**Coding and Insurance Guideline in Rheumatic Disease**
17:00 - 17:30	**Presentation Awards Session**		
17:30 - 18:00	**Closing Remark**		

Day 1. May 19(Thu)

10:00 - 12:00	[Symposium] **Year in Review (Clinical)**	**Room A** Korean
Chairs	**Won Park** *(Inha Univ., Korea)* **Sung Soo Kim** *(Univ. of Ulsan, Korea)*	
10:00 - 10:30	**Clinical update of systemic lupus erythematosus** Seung-Ki Kwok *(The Catholic Univ. of Korea, Korea)*	
10:30 - 11:00	**Idiopathic inflammatory myositis** Jinhyun Kim *(Chungnam Nat'l Univ., Korea)*	
11:00 - 11:30	**Update of IgG4 related disease** Yong Gil Kim *(Univ. of Ulsan, Korea)*	
11:30 - 12:00	**Behçet's disease** Sang-Won Lee *(Yonsei Univ., Korea)*	

10:00 - 12:00	[Symposium] **Year in Review (Basic)**	**Room B** Korean
Chairs	**Sung-Hwan Park** *(The Catholic Univ. of Korea, Korea)* **Sang-Hyon Kim** *(Keimyung Univ., Korea)*	
10:00 - 10:30	**Emerging concepts of endotypes/phenotypes in osteoarthritis** Gunil Im *(Dongguk Univ., Korea)*	
10:30 - 11:00	**Gout: Basic science of gout** Seokchan Hong *(Univ. of Ulsan, Korea)*	
11:00 - 11:30	**SpA: Insight into the pathogenesis of SpA** Tae-Jong Kim *(Chonnam Nat'l Univ., Korea)*	
11:30 - 12:00	**Update in the pathogenesis of Sjögren's syndrome** Jennifer Jooha Lee *(The Catholic Univ. of Korea, Korea)*	

09:00 - 12:00	[Workshop] **Musculoskeletal US Workshop I -Advanced Course**	**Room D** Korean
Chair	**Chong-Hyeon Yoon** *(The Catholic Univ. of Korea, Korea)*	

Session 1 : Practical Applications of Musculoskeletal Ultrasound in Rheumatology Clinic

09:00 - 09:30	**How to use ultrasonic equipment settings** Hyun Ok Kim *(Gyeongsang Nat'l Univ., Korea)*
09:30 - 10:00	**Ultrasonographic perspectives in giant cell arteritis, polymyalgia rheumatica and Sjögren's syndrome** Hyun-Sook Kim *(Soonchunhyang Univ., Korea)*
10:00 - 10:30	**Assessment of rheumatoid arthritis disease activity with ultrasound** Ran Song *(Kyung Hee Univ., Korea)*

Day 1. May 19(Thu)

Chair	Hye-Soon Lee *(Hanyang Univ., Korea)*

Session 2 : Ultrasound-guided Injection

10:30 - 11:00	**Ultrasound-guided intra-articular injection** Hyoun-Ah Kim *(Ajou Univ., Korea)*
11:00 - 11:30	**Ultrasound-guided extra-articular injection** Chang Hoon Lee *(Wonkwang Univ., Korea)*
11:30 - 12:00	**The tips and considerations for ultrasound-guided injection** Jae Hoon Kim *(Korea Univ., Korea)*

12:00 - 13:00	[Luncheon Symposium I – Pfizer] **Recent Update of Advanced RA Treatment**	**Room A** Korean
Chair	**Sung-Hwan Park** *(The Catholic Univ. of Korea, Korea)*	
12:00 - 12:40	**The role of tofacitinib as a JAK pioneer** Hyoun-Ah Kim *(Ajou Univ., Korea)*	

12:00 - 13:00	[Luncheon Symposium II - JW Pharmaceutical] **IL-6R Inhibition: Transforming People's Lives, for a Future on Their Term**	**Room B** Korean
Chair	**Chang Keun Lee** *(Univ. of Ulsan, Korea)*	
12:00 - 12:40	**Evolution of tocilizumab: From rheumatoid arthritis to CAR T cell therapy and COVID-19** Seung-Ki Kwok *(The Catholic Univ. of Korea, Korea)*	

12:00 - 13:00	[Luncheon Symposium III – AbbVie] **Strategies to Solve the Problem of Ankylosing Spondylitis with AbbVie's Assets**	**Room C** Korean
Chair	**Sung Won Lee** *(Dong-A Univ., Korea)*	
12:00 - 12:40	**The present and future of ankylosing spondylitis treatments** Tae-Jong Kim *(Chonnam Nat'l Univ., Korea)*	

13:10 - 14:00	[Special Lecture] **Presidential Plenary Session**	**Room A, B, C** Korean
Chairs	**Tae-Hwan Kim** *(Hanyang Univ., Korea)* **Sang-Heon Lee** *(Konkuk Univ., Korea)*	
13:10 - 13:35	**Changing role of rheumatologist in Korea** Sang-Heon Lee *(Konkuk Univ., Korea)*	
13:35 - 14:00	**Past, present and future of rheumatology in Korea** Yeong-Wook Song *(Song Rheumatology Clinic., Korea)*	

14:00 - 16:00	[Free Paper Session] **International Free Paper Session (Clinical)**	**Room A** English
Chairs	**Dae Hyun Yoo** *(Hanyang Univ., Korea)* **Chan Hong Jeon** *(Soonchunhyang Univ., Korea)*	
IO-01	**Risk of venous thromboembolism in Korean patients with rheumatoid arthritis treated with JAK inhibitors : A nationwide population-based study** Yeo-Jin Song *(Hanyang Univ., Korea)*	
IO-02	**Increased thromboembolic risk of JAK inhibitors after switching from biologic DMARDs in patients with rheumatoid arthritis** Yeonghee Eun *(Sungkyunkwan Univ., Korea)*	
IO-03	**Gut microbiome in patients with established rheumatoid arthritis: Factors associated with the composition, and its value of predicting treatment response** Jung Hee Koh *(The Catholic Univ. of Korea, Korea)*	
IO-04	**Time-averaged DAS28 and HAQ predict cardiovascular disease in patients with rheumatoid arthritis: Data from KORONA registry** Hong Ki Min *(Konkuk Univ., Korea)*	
IO-05	**Increased cardiovascular risk in patients with systemic lupus erythematosus: population-based Cohort Study in Korea** Jungyong Han *(Hanyang Univ., Korea)*	
IO-06	**Long-term exposure to PM10 and systemic-lupus-erythematosus-related mortality in the Korean population** Ji-Hyoun Kang *(Chonnam Nat'l Univ., Korea)*	
IO-07	**Neutralizing antibody formation after COVID-19 vaccination in elderly patients with rheumatoid arthritis** Eunsong Kang *(Asan Medical Center, Korea)*	
IO-08	**Immunogenicity and safety of inactivated and mRNA COVID-19 vaccines in patients with systemic lupus erythematosus** Ho So *(The Chinese Univ. of Hong Kong, Hong Kong)*	
IO-09	**Clinical characteristics and prognosis of patients with anti-melanoma differentiation-related gene 5 (MDA5) related diseases** Chen Yu *(Peking Union Medical College Hosp., China)*	
IO-10	**Three-dimensional analysis of the trapezium subchondral bone and its association with trapeziometacarpal joint osteoarthritis** Ji Sup Hwang *(Seoul Nat'l Univ., Korea)*	

Day 1. May 19(Thu)

14:00 - 16:00	[Workshop] **Basic Research Workshop for Rheumatologist: Animal Models of Key Arthropathies**	**Room B** Korean
Chairs	**Young Mo Kang** *(Kyungpook Nat'l Univ., Korea)* **Jun-Ki Min** *(The Catholic Univ. of Korea, Korea)*	
14:00 - 14:30	**Animal models of osteoarthritis (OA)** Je-Hwang Ryu *(Chonnam Nat'l Univ., Korea)*	
14:30 - 15:00	**Experimental procedures of mouse OA research** Gyuseok Lee *(Chonnam Nat'l Univ., Korea)*	
15:00 - 15:30	**Animal models of rheumatoid arthritis** Seung-Ah Yoo *(The Catholic Univ. of Korea, Korea)*	
15:30 - 16:00	**Experimental procedures of mouse arthritis models** Saseong Lee *(The Catholic Univ. of Korea, Korea)*	

13:30 - 16:30	[Workshop] **Musculoskeletal US Workshop II -Basic Course**	**Room D** Korean
Chair	**Hae-Rim Kim** *(Konkuk Univ., Korea)*	

Session 1: Introduction to Musculoskeletal Ultrasound in Rheumatology

13:30 - 14:00	**Musculoskeletal ultrasound in rheumatology – Upper extremities** Jae Hyun Jung *(Korea Univ., Korea)*
14:00 - 14:30	**Musculoskeletal ultrasound in rheumatology – Lower extremities** Ju-Yang Jung *(Ajou Univ., Korea)*
14:30 - 15:30	**Workshop – Upper extremities** **Tutors** **Wrist & elbow** : Yun Sung Kim *(Chosun Univ. Hosp., Korea)*, Jin Su Park *(NHIS Ilsan Hosp., Korea)* **Shoulder** : Young Bin Joo *(Hanyang Univ., Korea)*, Yune-Jung Park *(The Catholic Univ. of Korea, Korea)*
15:30 - 16:30	**Workshop – Lower extremities** **Tutors** **Knee** : Min Kyung Chung *(Ewha Womans Univ., Korea)*, Jinhee Lee *(The Catholic Univ. of Korea, Korea)* **Ankle & Foot** : In Ah Choi *(Chungbuk Nat'l Univ., Korea)*, Young Sun Suh *(Gyeongsang Nat'l Univ., Korea)*

16:30 - 18:30	[Free Paper Session] **International Free Paper Session (Basic)**	**Room A** English
Chairs	**Yeong-Wook Song** *(Song Rheumatology Clinic., Korea)* **Jason Jungsik Song** *(Yonsei Univ., Korea)*	
IO-11	**Identification of a key regulator of MYH9 for synoviocyte migration and invasion through secretome profiling** Saseong Lee *(The Catholic Univ. of Korea, Korea)*	
IO-12	**Multi-omics identifies S100 proteins as biomarkers of RA progression which can be regulated by epigenetic drugs** Marzena Ciechomska *(Nat'l Institute of Geriatrics, Poland)*	
IO-13	**Dysfunction of parkin increases osteoclast activity linking to bone erosion of inflammatory arthritis** Ji-Eun Kim *(Univ. of Ulsan, Korea)*	
IO-14	**Cell-specific activation of PADI4 promoter in human fibroblast-like synoviocytes from patients with rheumatoid arthritis** Khrystyna Malysheva *(S. Gzhytskyi Nat'l Univ. of Veterinary Medicine and Biotechnologies, Ukraine)*	
IO-15	**Effect of disease-modifying anti-rheumatic drugs on lung microenvironment of SKG mice** Sung Hae Chang *(Soonchunhyang Univ., Korea)*	
IO-16	**Peptoniphilus gorbachii ameliorates collagen-Induced arthritis in mice by improving intestinal homeostasis and immune regulation** Young Sun Suh *(Gyeongsang Nat'l Univ., Korea)*	
IO-17	**The immune mechanism of Janus kinase inhibitors on Shingles in rheumatoid arthritis patients** Hong Ki Min *(Konkuk Univ., Korea)*	
IO-18	**Identification of the HLA-B*51:01 immunopeptidome in Behçet's disease** Ye-Ji Lee *(Seoul Nat'l Univ., Korea)*	
IO-19	**Inhibition of NADPH oxidases prevent the development of osteoarthritis** Jin Han *(Kyungpook Nat'l Univ., Korea)*	

Day 1. May 19(Thu)

16:30 - 18:30	[Workshop] **Clinical Research Workshop for Rheumatologists: Planning and Conducting Clinical Research**	**Room B** Korean
Chairs	**Gwan Gyu Song** *(Korea Univ., Korea)* **Kichul Shin** *(Seoul Nat'l Univ., Korea)*	
16:30 - 17:00	**Setting up a prospective cohort** Sang-Cheol Bae *(Hanyang Univ., Korea)*	
17:00 - 17:30	**Conducting a retrospective clinical study using Korea National Health Insurance data** Hyun Jung Kim *(Korea Univ., Korea)*	
17:30 - 18:00	**How to start IITs from scratch** Howard Lee *(Seoul Nat'l Univ., Korea)*	
18:00 - 18:30	**e-CRF tools for Investigator Initiated Trial** Soo-Hwan Kim *(Dt&CRO, Korea)*	

16:30 - 18:30	[Workshop] **Editorial Committee Workshop**	**Room C** Korean
Chairs	**Young Ho Lee** *(Korea Univ., Korea)* **Seong-Kyu Kim** *(Daegu Catholic Univ., Korea)*	
16:30 - 17:00	**Suggestions to be indexed in SCIE and get high impact factor** Hyun Jun Park *(Pusan Nat'l Univ., Korea)*	
17:00 - 17:30	**Successful submission strategy on SCI journal** Hwichool Kim *(Editage, Korea)*	
17:30 - 18:00	**Biostatistics for clinical researchers** Hyonggin An *(Korea Univ., Korea)*	
18:00 - 18:30	**New PubMed: Searching tips & more!** Sung Ae Park *(Korea Univ. Medical Library, Korea)*	

Day 2. May 20(Fri)

The Session with the icon provides English-Korean translation
통역 아이콘이 표시된 세션은 한-영 동시통역을 제공합니다.

08:00 - 09:00	[Breakfast Symposium I – AbbVie] **Strategies to Solve the Problem of Rheumatoid Arthritis with AbbVie's Assets**	**Room A** Korean
Chair	**Seung-Jae Hong** *(Kyung Hee Univ., Korea)*	
08:00 - 08:40	**Management of rheumatoid arthritis considering safety** Ki-Jo Kim *(The Catholic Univ. of Korea, Korea)*	

08:00 - 09:00	[Breakfast Symposium II – Celltrion] **Real-world Switching Case of CT-P17**	**Room B** English
Chair	**Shin-Seok Lee** *(Chonnam Nat'l Univ., Korea)*	
08:00 - 08:40	**Clinical data and real-world switching case of CT-P17** Hubert Marotte *(Centre Hospitalier Universitaire(CHU) de Saint-Étienne, France)*	

08:00 - 09:00	[Breakfast Symposium III – Pfizer] **Real-World Perspectives of Ankylosing Spondylitis Management**	**Room C** Korean
Chair	**Eun Young Lee** *(Seoul Nat'l Univ., Korea)*	
08:00 - 08:40	**Insights from real-world: Practical approach to anti TNF therapy for AS treatment** Jun Won Park *(Seoul Nat'l Univ., Korea)*	

09:00 - 10:00	[Keynote Lecture] **Keynote Lecture**	**Room A, B, C** English
Chair	**Tae-Hwan Kim** *(Hanyang Univ., Korea)*	
09:00 - 10:00	**Current threats to the specialty of rheumatology in the US and internationally: A call to action** Kenneth Saag *(The Univ. of Alabama at Birmingham, USA)*	

Day 2. May 20(Fri)

10:30 - 12:00	[International Symposium] **Recent Advances in Pathogenesis of Systemic Lupus Erythematosus**	**Room A** English
Chairs	**Sang-Cheol Bae** *(Hanyang Univ., Korea)* **Seung-Cheol Shim** *(Chungnam Nat'l Univ., Korea)*	
10:30 - 11:00	**New concepts on the pathogenesis of lupus nephritis** George Tsokos *(Harvard Medical School, Beth Israel Deaconess Medical Center, USA)*	
11:00 - 11:30	**New insights into the role of antinuclear antibodies in systemic lupus erythematosus** Peter E. Lipsky *(AMPEL BioSolutions, USA)*	
11:30 - 12:00	**ETV5 promotes Tfh cell differentiation and the pathogenesis of systemic lupus erythematosus** Yoontae Lee *(POSTECH, Korea)*	

10:30 - 12:00	[Free Paper Session] **Epidemiology & Health Services Research**	**Room B** Korean
Chairs	**Choong-Ki Lee** *(Yeungnam Univ., Korea)* **Jinseok Kim** *(Jeju Nat'l Univ., Korea)*	
O-01	**Safety and clinical influences of COVID-19 vaccination in patients with autoimmune rheumatic diseases** Youngjae Park *(The Catholic Univ. of Korea, Korea)*	
O-02	**Autoantibody profiles in patients with COVID-19 infection** Hyemin Jeong *(Soonchunhyang Univ., Korea)*	
O-03	**Association between cardiovascular outcome and rheumatoid arthritis : nationwide population- based cohort study** Seonyoung Kang *(Sungkyunkwan Univ., Korea)*	
O-04	**Increased risk of malignancy in patients with Takayasu's arteritis: A population-based cohort study in Korea** Seulkee Lee *(Sungkyunkwan Univ., Korea)*	
O-05	**Increased risk of herpes zoster in patients with rheumatoid arthritis using tofacitinib compared with tumor necrosis factor inhibitor** Yeo-Jin Song *(Hanyang Univ., Korea)*	
O-06	**Clinical course and risk factors for development and progression of interstitial lung disease in primary Sjögren's syndrome: a single centered, retrospective, observational study** Kyung-Ann Lee *(Soonchunhyang Univ., Korea)*	
O-07	**Comparison of prescription drug use patterns during pregnancy and postpartum in Korean women with rheumatic conditions: A national population-based study** Jin Su Park *(Nat'l Health Insurance Service Ilsan Hosp., Korea)*	
O-08	**Multidimensional correlates to chronic pain among patients with musculoskeletal pain in different rheumatic diseases: Based on the Biopsychosocial approach** Hyoun-Ah Kim *(Ajou Univ., Korea)*	

10:30 - 12:00	[Free Paper Session] **Sjögren's Syndrome, Systemic Sclerosis, and Inflammatory Myositis**	**Room C** English & Korean
Chairs	**Seong Wook Kang** *(Chungnam Nat'l Univ., Korea)* **Myeung Su Lee** *(Wonkwang Univ., Korea)*	
O-09	**IL-17 and CCR9+α4β7– Th17 cells promote salivary gland inflammation, dysfunction, and cell death in Sjögren's syndrome** Jin-Sil Park *(The Catholic Univ. of Korea, Korea)*	
O-10	**Correlations between salivary scintigraphic and histopathologic data of salivary glands in patients with Sjögren's syndrome** Ji-Won Kim *(Ajou Univ., Korea)*	
O-11	**Impact of age on the diagnostic performance of unstimulated salivary flow rates and salivary gland ultrasound for primary Sjögren's syndrome** Kyung-Ann Lee *(Soonchunhyang Univ., Korea)*	
O-12	**Reduced Rxr-α signaling increases dry eye disease inducing γδ T17 cells in the conjunctiva** Jehan Alam *(Baylor College of Medicine, USA)*	
O-13	**Angiographic characteristics of vasculopathy in patients with idiopathic inflammatory myopathies and systemic sclerosis** Jina Yeo *(Gachon Univ., Korea)*	
O-14	**The association of anti-cyclic citrullinated peptide antibody with interstitial lung disease in systemic sclerosis: a retrospective analysis** Jangwoo Ha *(Yonsei Univ., Korea)*	
O-15	**Ultrasound may detect subclinical interstitial lung disease in systemic sclerosis** MARWIN Gutierrez *(Instituto Nacional de Rehabilitacion, Italy)*	
O-16	**Expressions of CCR2 and CCL2, and association between their expression and NET stimulation in adult-onset Still's disease** Ju-Yang Jung *(Ajou Univ., Korea)*	
O-17	**Increased expression of receptor for advanced glycation end-products in sarcopenic patient skeletal muscle** Ji Sup Hwang *(Seoul Nat'l Univ., Korea)*	

12:00 - 13:00	[Luncheon Symposium IV - Lilly] **The Role of Baricitinib in the Treatment of RA**	**Room A** Korean
Chair	**Yong-Beom Park** *(Yonsei Univ., Korea)*	
12:00 - 12:40	**Baricitinib in the real-world data** Yun-Hong Cheon *(Gyeongsang Nat'l Univ., Korea)*	

Day 2. May 20(Fri)

12:00 - 13:00	[Luncheon Symposium V – BMS] **Real World Evidences in Long-term RA Treatment with Biologics**	**Room B** Korean
Chair	**Wan-Uk Kim** *(The Catholic Univ. of Korea, Korea)*	
12:00 - 12:20	**Real world evidences and considerations for long-term persistence of biologics in RA** Sang-Hyon Kim *(Keimyung Univ., Korea)*	
12:20 - 12:40	**Real world evidences of RA treatment with biologics in Korea** Jennifer Jooha Lee *(The Catholic Univ. of Korea, Korea)*	

12:00 - 13:00	[Luncheon Symposium VI – Yuhan] **The New Adalimumab Option in Rheumatic Diseases Treatment**	**Room C** English
Chair	**Seung-Cheol Shim** *(Chungnam Nat'l Univ., Korea)*	
12:00 - 12:40	**ADALLOCE®(SB5) adalimumab in rheumatic diseases: Data from clinical trials and the real world** Carlo Selmi *(Humanitas Univ., Italy)*	

13:00 - 14:30	[International Symposium] **2022 Clinical Research Update of Sjögren's Syndrome**	**Room A** English
Chairs	**Shin-Seok Lee** *(Chonnam Nat'l Univ., Korea)* **Yun Jong Lee** *(Seoul Nat'l Univ., Korea)*	
13:00 - 13:30	**Big data Sjögren project consortium** Manuel Ramos-Casals *(Univ. of Barcelona, Spain)*	
13:30 - 14:00	**ESSPRI, a single term with multiple meanings: A consideration based on Korean studies** Yun Jong Lee *(Seoul Nat'l Univ., Korea)*	
14:00 - 14:30	**Current and future treatment of primary Sjögren's syndrome** Xavier Mariette *(Hôpitaux Universitaires Paris-Sud Bicêtre, France)*	

13:00 - 14:30	[Symposium] **KCR-KAI Joint Symposium**	**Room B** Korean
Chairs	**Tae-Hwan Kim** *(Hanyang Univ., Korea)* **Wan-Uk Kim** *(The Catholic Univ. of Korea, Korea)*	
13:00 - 13:30	**Role of bystander T cells in autoimmune diseases** Je-Min Choi *(Hanyang Univ., Korea)*	
13:30 - 14:00	**Exploration of the key driving molecules in systemic sclerosis-associated interstitial lung disease by the advanced bioinformatic analysis** Ki-Jo Kim *(The Catholic Univ. of Korea, Korea)*	
14:00 - 14:30	**ZIP8 exacerbates collagen-induced arthritis by increasing pathogenic T cell responses** Sung-Gyoo Park *(Seoul Nat'l Univ., Korea)*	

13:00 - 14:30	[Free Paper Session] **Osteoarthritis and Orthopedics**	**Room C** English & Korean
Chairs	**Sung Won Lee** *(Dong-A Univ., Korea)* **Hyun Sik Gong** *(Seoul Nat'l Univ., Korea)*	
O-18	**Sodium chloride affects cartilage associated marker expression during in vitro chondrogenesis from induced pluripotent stem cell** Kijun Lee *(The Catholic Univ. of Korea, Korea)*	
O-19	**Immunomodulation by mesenchymal stromal cell exosomes in osteoarthritis** Kristeen Ye Teo *(Nat'l Univ. of Singapore, Singapore)*	
O-20	**Mitochondrial transplantation ameliorates the development and progression of osteoarthritis** A Ram Lee *(The Catholic Univ. of Korea, Korea)*	
O-21	**Soluble CCR2 gene therapy controls joint inflammation, cartilage damage, and the progression of osteoarthritis by targeting MCP-1 in a monosodium iodoacetate (MIA)-induced OA rat model** Hyun Sik Na *(The Catholic Univ. of Korea, Korea)*	
O-22	**The potential role of SIRT1 in osteoarthritis pain treatment by blocking the nerve growth factors** Sang Yeob Lee *(Dong-A Univ., Korea)*	
O-23	**Coenzyme Q10 encapsulated in micelles ameliorates osteoarthritis by inhibiting inflammatory cell death** Hyun Sik Na *(The Catholic Univ. of Korea, Korea)*	
O-24	**Associations between body composition measurements of obesity and the radiographic progression of hand osteoarthritis: Data from the Dong-gu Study** Sung-Eun Choi *(Chonnam Nat'l Univ., Korea)*	
O-25	**Association of serum uric acid level with bone mineral density in peri-menopausal and postmenopausal Korean women: A single-center study of 3566 cases** Seongmin Kang *(Univ. of Ulsan, Korea)*	
O-26	**The relationship between the osteoporosis and cortial index of the mandibular bone in rheumatoid arthritis** Gürkan Iden *(Dr. Yaşar Eryılmaz Doğubeyazıt Devlet Hastanesi, Turkey)*	

15:30 - 17:00	[International Symposium] **Vasculitis Session**	**Room A** English
Chairs	**Bin Yoo** *(Univ. of Ulsan, Korea)* **Chan-Bum Choi** *(Hanyang Univ., Korea)*	
15:30 - 16:00	**Somatic mutations in rheumatologic diseases: VEXAS syndrome and beyond** Peter C. Grayson *(Nat'l Institutes of Health, USA)*	
16:00 - 16:30	**Recent basic studies in ANCA-associated vasculitis** Akihiro Ishizu *(Hokkaido Univ., Japan)*	
16:30 - 17:00	**Systemic vasculitis in Korea** Chan-Bum Choi *(Hanyang Univ., Korea)*	

Day 2. May 20(Fri)

15:30 - 17:00	[Free Paper Session] **Rheumatoid Arthritis Clinical Research**	**Room B** English & Korean
Chairs	**Jung-Yoon Choe** *(Daegu Catholic Univ., Korea)* **Jung Soo Song** *(Chung-Ang Univ., Korea)*	
O-27	**Comparative effectiveness of janus kinase inhibitors and biologic disease-modifying antirheumatic drugs in Korean patients with rheumatoid arthritis; an interim analysis of the real-world study** Soo-Kyung Cho *(Hanyang Univ., Korea)*	
O-28	**Comparative Effectiveness and Safety profiles of baricitinib and tofacitinib in Rheumatoid arthritis: A Real-World, Single Center Study** Bong-Woo Lee (*The Catholic Univ. of Korea, Korea)*	
O-29	**Comparative efficacy and safety of IL-6/JAK/STAT pathway inhibitors in rheumatoid arthritis: systematic review and network meta-analysis** Rudra Goswami *(AIIMS, India)*	
O-30	**Impact of early age at menopause on disease outcomes in postmenopausal women with rheumatoid arthritis: Results from a large observational cohort of Korean patients with rheumatoid arthritis** Eun Hye Park *(Chung-Ang Univ., Korea)*	
O-31	**The implication of persistent pain in patients with rheumatoid arthritis albeit in DAS28-remission: data from the KOBIO registry** Hyoun-Ah Kim *(Ajou Univ., Korea)*	
O-32	**Increased risk of dementia in patients with rheumatoid arthritis: a nationwide population-based cohort study** Younghee Eun *(Sungkyunkwan Univ., Korea)*	
O-33	**Retention rate and safety of biologics or targeted synthetic disease modifying anti-rheumatic drugs in patients with rheumatoid arthritis associated with interstitial lung disease: Results from the KOBIO registry** Sun-Kyung Lee *(Hanyang Univ., Korea)*	
O-34	**Tumor Necrosis Factor (TNF) inhibitors does not accelerate the progression of RA-ILD: results from the KORAIL cohort** Sang Wan Chung *(Kyung Hee Univ., Korea)*	

15:00 - 17:00	[Symposium] **Medical Humanities: Work Ethics and Labor Relation in the COVID-19 Era**	**Room C** Korean
Chairs	**Yong-Beom Park** *(Yonsei Univ., Korea)* **Geun-Tae Kim** *(Kosin Univ., Korea)*	
15:00 - 16:00	**The ethics of hospital human resource development during the pandemic: Ethical principles** Ilhak Lee *(Yonsei Univ., Korea)*	
16:00 - 17:00	**Labor issues in the COVID-19 situation: Cases and alternatives** Dong Wook Yun *(Law Firm Seo-Hee, Korea)*	

Day 3. May 21(Sat)

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08:00 - 09:00	[Breakfast Symposium IV – Yuhan] **Valuable Options for Treatment Rheumatic Disease**	**Room A** Korean
Chair	**Jinseok Kim** *(Jeju Nat'l Univ., Korea)*	
08:00 - 08:40	**Biosimilar: Past, present and future** Seung-Jae Hong *(Kyung Hee Univ., Korea)*	

08:00 - 09:00	[Breakfast Symposium V – Lilly] **Ixekizumab: Recent Updates on the Treatment of Spondyloarthritis**	**Room B** Korean
Chair	**Seong-Ho Kim** *(Inje Univ., Korea)*	
08:00 - 08:40	**IL-17 inhibition in spondyloarthritis: The efficacy of Ixekizumab and clinical relevance** Yeon-Ah Lee *(Kyung Hee Univ., Korea)*	

08:00 - 09:00	[Breakfast Symposium VI – Janssen] **Redefine Persistence in AS Management**	**Room C** Korean
Chair	**Chang-Hee Suh** *(Ajou Univ., Korea)*	
08:00 - 08:40	**Long-lasting Golimumab in AS: Learnings from real-world evidence** Bon San Koo *(Inje Univ., Korea)*	

09:00 - 10:00	[Keynote Lecture] **Keynote Lecture**	**Room A, B, C** English
Chair	**Sang-Heon Lee** *(Konkuk Univ., Korea)*	
09:00 - 10:00	**The future of rheumatology** Antony Rosen *(The Johns Hopkins Univ. School of Medicine)*	

Day 3. May 21(Sat)

10:30 - 12:00	[International Symposium] **Treatment of Osteoarthritis: To be Used and Abused?**	Room A English
Chairs	**Han Joo Baek** *(Gachon Univ., Korea)* **Hyun Ah Kim** *(Hallym Univ., Korea)*	
10:30 - 11:00	**Hype and truth - treatment paradigm of osteoarthritis** David Hunter *(Univ. of Sydney, Australia)*	
11:00 - 11:30	**Addicted to prescription, medical abuse of osteoarthritis** Yuqing Zhang *(Massachusetts General Hosp., USA)*	
11:30 - 12:00	**Use or abuse? APM for degenerative meniscus in osteoarthritis** Hyun Ah Kim *(Hallym Univ., Korea)*	

10:30 - 12:00	[Free Paper Session] **Spondyloarthritis**	Room B Korean
Chairs	**Hoon-Suk Cha** *(Sungkyunkwan Univ., Korea)* **Eun Young Lee** *(Seoul Nat'l Univ., Korea)*	
O-35	**Physical trauma exacerbates arthritis and enthesitis in curdlan-administered SKG mice model** Seung Hoon Lee *(Hanyang Univ., Korea)*	
O-36	**PPM1A promotes matrix mineralization of osteoblasts differentiation via FOXO1A-RUNX2 pathway in ankylosing spondylitis** Subin Weon *(Hanyang Univ., Korea)*	
O-37	**A pilot study on deep learning-based grading of the corner of vertebral body for the assessment of radiographic progression in patients with ankylosing spondylitis** Bon San Koo *(Inje Univ., Korea)*	
O-38	**Analysis of radiographic progression in patients with ankylosing spondylitis: Using group-based trajectory modeling and decision trees** Juyeon Kang *(Inje Univ., Korea)*	
O-39	**The spinal radiographic change correlates with past alkaline phosphatase levels in patients with ankylosing spondylitis** Bon San Koo *(Inje Univ., Korea)*	
O-40	**CCL20 inhibition for treating inflammation in ankylosing spondylitis** Hui-Ju Kim *(Chonnam Univ., Korea)*	
O-41	**Metagonimus yokogawai-derived protein attenuates inflammation in ankylosing spondylitis** Moon-Ju Kim *(Chonnam Univ., Korea)*	
O-42	**Long-term treatment with ixekizumab in patients with axial spondyloarthritis: Two-year results from COAST-Y** Young In Eom *(Lilly Korea Ltd, Korea)*	

10:30 - 12:00	[Free Paper Session] **Systemic Lupus Erythematosus**	**Room C** English & Korean
Chairs	**Jisoo Lee** *(Ewha Womans Univ., Korea)* **Chang-Hee Suh** *(Ajou Univ., Korea)*	
O-43	**B cell-specific deletion of Crif1 drives lupus-like autoimmunity by activation of IL-17, IL-6, and pathogenic Tfh cells** Jin-Sil Park *(The Catholic Univ. of Korea, Korea)*	
O-44	**Biological insights into systemic lupus erythematosus through an immune cell-specific transcriptome-wide association study** Xianyong Yin *(Univ. of Michigan, USA)*	
O-45	**The association between CD40 rs4810485 polymorphism and susceptibility of systemic lupus erythematosus: Systematic review and meta analysis** Rizki Febriawan *(Utama Hosp Belitung, Indonesia)*	
O-46	**The role of sphingolipids in patients with systemic lupus erythematosus** Ji-Won Kim *(Ajou Univ., Korea)*	
O-47	**Combined model of renal histopathology and clinical parameters better predict one year renal outcomes in lupus nephritis: Analysis of 334 kidney biopsies** Aishwarya Gopal *(Jawaharlal Institute of Postgraduate Medical Education and Research, India)*	
O-48	**Coexisting tubulointerstitial inflammation and damage is a risk factor for chronic kidney disease in patients with lupus nephritis: Results from the KORNET registry** Dong-Jin Park *(Chonnam Nat'l Univ., Korea)*	
O-49	**Subtherapeutic hydroxychloroquine concentration is associated with increased disease activity and greater organ damage during 5-year follow-up in patients with systemic lupus erythematosus** Ji-Hyoun Kang *(Chonnam Nat'l Univ., Korea)*	
O-50	**Effect of smoking on thrombotic events in antiphospholipid syndrome: A large prospective cohort study** Hui Jang *(Chinese Academy of Medical Sciences & Peking Union Medical College, China)*	
O-51	**Efficacy of rivoraxaban in patients with antiphospholipid syndrome** Zumrad Ubaydullaeva *(Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Uzbekistan)*	

12:00 - 13:00	[Luncheon Symposium VII – Novartis] **Understanding IL-17 Inhibition in SpA**	**Room A** English
Chair	**Hoon-Suk Cha** *(Sungkyunkwan Univ., Korea)*	
12:00 - 12:40	**The role of IL-17A in Ankylosing spondylitis and axial PsA** Matthew Brown *(King's College London, UK)*	

Day 3. May 21(Sat)

12:00 - 13:00	[Luncheon Symposium VIII – Amgen] **Move Forward with the Long-term Protection of Prolia**	Room B Korean
Chair	**Dae Hyun Yoo** *(Hanyang Univ., Korea)*	
12:00 - 12:40	**Denosumab key clinical questions** Sung-Soo Kim *(Univ. of Ulsan, Korea)*	

12:00 - 13:00	[Luncheon Symposium IX – Astellas] **Tacrolimus**	Room C Korean
Chair	**Jung-Yoon Choe** *(Daegu Catholic Univ., Korea)*	
12:00 - 12:40	**Tacrolimus in rhematoid arthritis** Chan-Bum Choi *(Hanyang Univ., Korea)*	

13:00 - 14:30	[International Symposium] **Synovial Macrophage and Fibroblast in RA**	Room A English
Chairs	**Yong-Wook Park** *(Chonnam Nat'l Univ., Korea)* **Seungwoo Han** *(Kyungpook Nat'l Univ., Korea)*	
13:00 - 13:30	**Synovial macrophages as gatekeepers of inflammation** Gerhard Krönke *(Univ. of Erlangen, Germany)*	
13:30 - 14:00	**Cellular deconstruction of inflamed synovium defines diverse inflammatory phenotypes in rheumatoid arthritis** Soumya Raychaudhuri *(Brigham & Women's Hosp., Harvard Medical School, USA)*	
14:00 - 14:30	**Roles of stromal cells and potential significance for future therapy in RA** Sang-il Lee *(Gyeongsang Nat'l Univ., Korea)*	

13:00 - 14:30	[Symposium] **KCR-KSBMR Joint Symposium**	Room B Korean
Chairs	**Sang-Heon Lee** *(Konkuk Univ., Korea)* **Yong-Chan Ha** *(Seoul Bumin Hosp., Korea)*	
13:00 - 13:30	**Anabolic therapy for osteoporosis** Ha Young Kim *(Univ. of Ulsan, Korea)*	
13:30 - 14:00	**Ideal sequential therapy in osteoporosis management** Kyoung Min Kim *(Yonsei Univ., Korea)*	
14:00 - 14:30	**Prevention and treatment of fracture in RA** Jun-Ki Min *(The Catholic Univ. of Korea, Korea)*	

13:00 - 14:30	[Free Paper Session] **Vasculitis and Metabolic Bone Disease**	**Room C** English & Korean
Chairs	**Soo Kon Lee** *(CHA Univ., Korea)* **Chang Keun Lee** *(Univ. of Ulsan, Korea)*	
O-52	**Update on comparative cardiovascular safety of febuxostat versus allopurinol among patients with gout** Se Rim Choi *(Seoul Nat'l Univ., Korea)*	
O-53	**The utility of dual-energy computed tomography in predicting gout flares in gout patients after discontinuing colchicine prophylaxis** Min Jung Kim *(Seoul Nat'l Univ., Korea)*	
O-54	**Effects of long-term febuxostat or allopurinol on the progression of chronic kidney disease** Byeongzu Ghang *(Jeju Nat'l Univ., Korea)*	
O-55	**A cross-sectional internet survey of gout management and outcomes during established COVID-19 pandemic in 2020-2021** Jasvinder Singh *(Univ. of Alabama at Birmingham, USA)*	
O-56	**The effect of Behçet's disease on carotid intima media thickness and its relationship with disease activity** Merve Polat *(Karadeniz Technical Univ., Turkey)*	
O-57	**Reclassification of patients with previously diagnosed GPA according to both the 2012 CHCC definitions and the 2007 EMA algorithm using the 2022 ACR/EULAR criteria** Jung Yoon Pyo *(Yonsei Univ., Korea)*	
O-58	**Patterns of coronary involvement of antineutrophil cytoplasmic antibody (ANCA) -associated vasculitis in Korean patients** Jinseok Kim *(Yonsei Univ., Korea)*	
O-59	**Comparison of ultrasound-guided trigger-point needling and blinded needling for myofascial pain syndrome** Recep Sade *(Ataturk Univ., Turkey)*	

15:30 - 17:00	[International Symposium] **New Horizon of Systemic Sclerosis**	**Room A** English
Chairs	**Jae-Bum Jun** *(Hanyang Univ., Korea)* **Eun Bong Lee** *(Seoul Nat'l Univ., Korea)*	
15:30 - 16:00	**Update in the pathogenesis of systemic sclerosis** Christopher Denton *(Royal Free Hosp., UK)*	
16:00 - 16:30	**Update in interstitial lung disease in SSc** Oliver Distler *(Univ. Hosp. Zurich, Switzerland)*	
16:30 - 17:00	**Update in pulmonary arterial hypertension in SSc** Eun Bong Lee *(Seoul Nat'l Univ., Korea)*	

Day 3. May 21(Sat)

15:30 - 17:00	[Free Paper Session] **Rheumatoid Arthritis Basic Research**	**Room B** English & Korean
Chairs	**Ho-Youn Kim** *(Ho-Youn Kim's Clinic for Arthritis-Rheumatism, Korea)* **Sang-il Lee** *(Gyeongsang Nat'l Univ., Korea)*	
O-60	**Orosomucoid acid-2, an acute phase reactant, promotes rheumatoid inflammation** Kimyo Kim *(The Catholic Univ. of Korea, Korea)*	
O-61	**LKB1 regulates the migration of fibroblast-like synoviocytes via oxidative stress-induced inflammatory cytokines in patients with rheumatoid arthritis** Ha-Reum Lee *(Chungnam Nat'l Univ., Korea)*	
O-62	**Postranslational modification in mammals protects citrullinated MCP1/CCL2 chemokine from partial degradation** Nataliia Korchynska *(Rzeszow Univ., Poland)*	
O-63	**Assessment of disease activity in patients with rheumatoid arthritis utilizing plasma tumor M2-pyruvate kinase test** Sung Soo Ahn *(Yonsei Univ., Korea)*	
O-64	**Association analysis of a MUC5B promoter variant rs35705950 with rheumatoid arthritis-interstitial lung disease in Korea** Young Bin Joo *(Hanyang Univ., Korea)*	
O-65	**Therapeutic effect of folic acid in collagen-induced arthritis mouse model** Kijun Lee *(The Catholic Univ. of Korea, Korea)*	

15:30 - 17:00	[Symposium] **Coding and Insurance Guideline in Rheumatic Disease**	**Room C** Korean
Chairs	**Young Il Seo** *(Hallym Univ., Korea)* **Seung-Jae Hong** *(Kyung Hee Univ., Korea)*	
15:30 - 16:00	**Rheumatic diseases and KCD 8th revision** Sukil Kim *(The Catholic Univ. of Korea, Korea)*	
16:00 - 16:30	**Principles and future prospects of insurance benefits in rheumatoid diseases** Gihyeon Seo *(Health Insurance Review and Assessment Service, Korea)*	
16:30 - 17:00	**Insurance guideline and tips for treatment of rheumatic disease** Seung-Jae Hong *(Kyung Hee Univ., Korea)*	

E-poster Presentation

No.	Title	Presenter
	RA-pathogenesis and animal model & Cytokines and mediators	
P-001	Anti-arthritic activities of the Eleutherococcus senticosus, Achyranthes japonica, and Atractylodes japonica mixed extract fermented with nuruk in a type II collagen-induced arthritis mouse model	Chong Hyuk Chung *(School of Medicine, Wonkwang Univ., Korea)*
P-002	A green-lipped mussel prevents rheumatoid arthritis via regulation of inflammatory response and osteoclastogenesis	Hong Ki Min *(Department of Internal Medicine, Konkuk Univ. Medical Center, Korea)*
P-003	HLA-DRB1 non-SE fine specificity associations with anti-RA33 autoantibody positivity in rheumatoid arthritis patients stratified by different serological phenotypes	Nurul Aain Ahmad fauzi *(Institute for Medical Research, Nat'l Institutes of Health Complex, Ministry of Health Malaysia, Malaysia)*
P-004	Precision nanomedicine in rheumatoid arthritis: customized multifunctional polymeric nanocarriers for alleviation of inflammation severity in rheumatoid arthritic rats	ANAS Ahmad *(Cumming School of Medicine, Univ. of Calgary, Canada)*
P-005	APE1 inhibits the inflammation of fibroblast-like synoviocytes via oxidative stress regulation in patients with rheumatoid arthritis	Ha-Reum Lee *(Chungnam Nat'l Univ. School of Medicine, Korea)*
P-006	A novel cytokine consisting of p40 and EBI3 subunits suppresses experimental autoimmune arthritis via reciprocal regulation of Th17 and Treg cells	Seon-Yeong Lee *(The Catholic Univ. of Korea, Korea)*

No.	Title	Presenter
	RA-clinical aspects	
P-007	Seasonal analysis of relative search volume of rheumatoid arthritis in Korea	Eunsung Kim *(Bumin Hosp., Korea)*
P-008	Cardiac hydatid cyst in a patient with rheumatoid arthritis	Giorgi Apkhazava *(Tbilisi City Medical, Georgia)*
P-009	Course of COVID-19 in patients with rheumatoid arthritis (own data)	Eugenia Aronova *(V.A. Nasonova Research Institute of Rheumatology, Russian Federation)*
P-010	Study of the features of post-covid syndrome in patients with rheumatoid arthritis	Eugenia Aronova *(V.A. Nasonova Research Institute of Rheumatology, Russian Federation)*
P-011	Ultrasound as a potential tool to detect interstitial lung disease in daily clinical setting of patients with rheumatoid arthritis	MARWIN Gutierrez *(Instituto Nacional de Rehabilitacion, Mexico)*
P-012	Rheumatoid factor (RF) and anti-cyclic citrullinated protein autoantibodies (ACPA) seroconversion and seroreversion in rheumatoid arthritis patients between 2005 and 2021	Chun Lai Too *(Immunogenetic Unit. Allergy and Immunology Research Center. Institute for Medical Research. MOH, Malaysia)*
P-013	Autoantibodies sustainability in rheumatoid arthritis (RA) patients and their clinical characteristics: Malaysian real-world data between 2005 and 2021	Chun Lai Too *(Immunogenetic Unit. Allergy and Immunology Research Center. Institute for Medical Research. MOH, Malaysia)*
P-014	Use of disease-modifying anti-rheumatic drugs after cancer diagnosis in rheumatoid arthritis patients	Kyung-Su Park *(Catholic Univ. St. Vincent's Hosp., Korea)*
P-015	The relationship between Anti-CCP, C-reactive protein in serum and rheumatoid factor in synovial fluid in patients with rheumatoid arthritis in the Kyrgyz Republic	Nazgul Omurzakova *(Nat'l Center of Cardiology and Internal Medicine, Kyrgyzstan)*
P-016	Impact of comorbidity on disease activity and functional status in patients with rheumatoid arthritis receiving biologic DMARDs, a longitudinal analysis of the KOBIO-RA	Ju Yeon Kim *(Seoul Nat'l Univ. Hosp., Korea)*

E-poster Presentation

No.	Title	Presenter
	RA-treatment	
P-017	Is a cumulative dose of methotrexate important for rapid remission in rheumatoid arthritis?	Galina Gridneva *(V.A.Nasonova Rheumatology Research Institute, Russian Federation)*
P-018	Clinical predictors of inadequate response to conventional synthetic and biologic DMARDs in Chinese patients with rheumatoid arthritis	Hui Zhong *(Peking Union Medical College Hosp., China)*
P-019	"Stereotypical" adverse reactions to non-biologic Disease Modifying Anti-Rheumatic Drugs in patients with rheumatoid arthritis requiring biological therapy	Elena Matianova *(V.A.Nasonova Rheumatology Research Institute, Russian Federation)*
P-020	The efficacy and safety of biologic DMARDs on progression of RA-ILD	Sang Wan Chung *(Kyung Hee Univ. Medical Center, Korea)*
P-021	Management of rheumatoid arthritis in China: a study of the implementation of 2021 ACR guideline	Shangyi Jin *(Peking Union Medical College Hosp., China)*
P-022	Study of methotrexate metabolism in patients taking statins	Galina Gridneva *(V.A.Nasonova Rheumatology Research Institute, Russian Federation)*
P-023	Digital aging and mental health deteriorations: how can we mitigate the risk among the elderly with rheumatoid arthritis disease in Indonesia?	Rosinta Hotmaida Pebrianti Purba *(Bappenas, Indonesia)*
P-024	Comparison of drug persistence between tumor necrosis factor-α inhibitors and tocilizumab in patients as first-line treatment with rheumatoid arthritis using the Korean Health Insurance Review and Assessment Service database	Byung Wook Song *(Pusan Nat'l Univ. Hosp., Korea)*
P-025	Impact of Korean red ginseng on fatigue in patients with rheumatic disease: A randomized, double-blind study	Soo-Kyung Cho *(Hanyang Univ. Hosp. for Rheumatic Diseases, Korea)*
P-026	The Preoperative Patient's Expectations and It's Clinical Outcomes After Rheumatoid Forefoot Deformity Surgery	Dong Hong Kim *(Hanyang Univ. Hosp., Korea)*

No.	Title	Presenter
	SLE-clinical aspects, APS	
P-027	Effect of systemic lupus erythematosus on carotid intima media thickness and its relationship with disease activity	Gökhan Polat *(Atatürk Univ., Turkey)*
P-028	Wernicke encephalopathy secondary to systemic lupus erythematosis enteropathy	Arzu Shahveranova *(Adana Çukurova University, Turkey)*
P-029	Prognostic factors for the development of systemic lupus erythematosus in patients with immune thrombocytopenia	Soo Min Ahn *(Asan Medical Center, Korea)*
P-030	A case of portal and hepatic vein occlusion in systemic lupus erythematosis	Mehmet Selim Kan *(Atatürk Univ., Turkey)*
P-031	Disease flare of systemic lupus erythematosus in patients with end-stage renal disease on dialysis	Young-Eun Kim *(Asan Medical Center, Univ. of Ulsan College of Medicine, Korea)*
P-032	Clinical relevance according to staining patterns and titers of antinuclear antibody	Mi Ryoung Seo *(Gil Medical Center, Gachon Univ. College of Medicine, Korea)*
P-033	Long-term renal outcomes of patients with non-proliferative lupus nephritis	Eunsong Kang *(Asan Medical Center, Korea)*

No.	Title	Presenter
	SLE-clinical aspects, APS	
P-034	Computer aided detection of the white matter lesions associated with systemic lupus erythematosus in cranial magnetic resonance imaging	Ahmet Yalcin *(Ataturk Univ., Faculty of Medicine, Turkey)*
P-035	Internuclear ophthalmoplegia in lupus cerebritis: double jeopardy	Paul Shiu *(St Joseph's Medical Center - Graduate Medical Education, USA)*
P-036	Working memory and processing speed in systemic lupus erythematosus: Correlation with disease activity	Rudrani Chatterjee *(Clinical Psychologist, India)*
P-037	Etiology of raised serum creatinine in patients with systemic lupus erythematosus at presentation and association of number of crescents in renal biopsy with rapidly progressive renal failure	RAJAT Kharbanda *(Senior Resident, India)*
P-038	CRP elevation in SLE pericarditis: Not all patients with SLE pericarditis have an elevated CRP value	Hyunsue Do *(Severance Hosp., Yonsei Univ. College of Medicine, Korea)*
P-039	Prevalence of latent tuberculosis infection and its associations with clinical and serological parameters in systemic lupus erythematosus	Gayathri Ms *(Jawaharlal Institute of Postgraduate Medical Education and Research, India)*
P-040	Comparison of physical functions of systemic lupus erythematosis and healthy persons and their relationship with disease activity	Yasin Baki Baydas *(Bezmialem Univ., Turkey)*

No.	Title	Presenter
	SLE-pathogenesis and animal model	
P-041	Vitronectin, a novel urinary proteomic biomarker, promotes cell pyroptosis in juvenile systemic lupus erythematosus	Zhe Cai *(Guangzhou Women and Children's Medical Center, China)*
P-042	Effect of tumor necrosis factor-α gene polymorphisms in risk of systemic lupus erythematosus patients susceptibility: Update meta-analysis	Steven Irving *(Faculty of Medicine, Univ. of Sebelas Maret, Indonesia)*

No.	Title	Presenter
	SLE-treatment	
P-043	A retrospective single center study of the clinical response of tacrolimus treatment in patients with lupus nephritis	Ji-Won Kim *(Ajou Univ. School of Medicine, Korea)*
P-044	Acute pancreatitis after corticosteroid pulse therapy in rheumatic disease: Acute pancreatitis is common adverse reaction after corticosteroid pulse therapy	Jinseok Kim *(Yonsei Univ. College of Medicine, Korea)*
P-045	Myelodysplastic syndrome occurrence in post-therapeutic systemic lupus erythematosus patients	Ninda Devita *(Faculty of Medicine Public Health and Nursing, Universitas Gadjah Mada, Indonesia)*

E-poster Presentation

No.	Title	Presenter
	Spondyloarthropathies and psoriatic arthritis	
P-046	Vitronectin-derived bioactive peptide prevents spondyloarthritis by modulating Th17/Treg imbalance in mice with curdlan-induced spondyloarthritis	Hong Ki Min *(Konkuk Univ. Medical Center, Korea)*
P-047	The relationship between the osteoporosis and cortial index of the mandibular bone in psoriatic arthritis	Viliam Gasanova *(Bahçeşehir İstinye Univ., Turkey)*
P-048	Evaluation of the relationship between ankylosing spondylitis and its inflammation indicator calprotectin and its relationship with disease activity	Mehmet Alperen Tezcan *(Ataturk Univ., Turkey)*
P-049	Investigation of the relationship of ankylosing spondylit and varicocele	Muhammed Emre Isıktas *(Atatürk Univ., Turkey)*
P-050	The effect of ankylosing spondylitis on carotis intima media thickness and its relationship with disease activity	Elshad İsmailov *(Atatürk Univ., Turkey)*
P-051	Predictive role of neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio and platelet-to-lymphocyte ratio in the assessment of clinical response and drug persistence of tumor necrosis factor-alpha inhibitors in patients with ankylosing spondylitis	Dong Hyuk Moon *(Pusan Nat'l Univ. School of Medicine, Pusan Nat'l Univ. Hosp., Korea)*
P-052	A deep-learning-based approach for automated assessment of modified Stoke ankylosing spondylitis spine score (mSASSS) on spine radiographs: a preliminary study	Sun Yeop Lee *(Deepnoid, Inc., Korea)*
P-053	Intra-articular corticosteroids for sacroiliitis in treatment of spondyloarthritis	Pallavi Vij *(All India Institute of Medical Sciences, India)*
P-054	Drug retention of biologic agents in Korean patients with psoriatic arthritis	Ju Yeon Kim *(Seoul Nat'l Univ. Hosp., Korea)*
P-055	Safety profile of ixekizumab for the treatment of psoriatic arthritis and axial spondyloarthritis up to 3 years: An updated integrated safety analysis	Young In Eom *(Lilly Korea Ltd, Korea)*
P-056	A comparison of physical functions and its relationship with disease activity of persons with ankylosing spondilitis	Aysenur Kara *(Atatürk Univ., Turkey)*

No.	Title	Presenter
	Behçet's disease & Vasculitis	
P-057	Diagnostic value of 3D T1-weighted sampling perfection with application optimized contrast evolution (SPACE) magnetic resonance imaging in patients with giant cell arteritis	Recep Sade *(Ataturk Univ., Turkey)*
P-058	Determination of the frequency of entositis and its relationship with disease activity in Behçet's disease by ultrasonography	Serhat Kaya *(Tunceli Devlet Hastanesi, Turkey)*
P-059	NeuroBehçet with spinal leptomeningeal involvement	Oğuzhan mete *(Atatürk Univ., Turkey)*
P-060	Investigation of the frequency of varicocele in Behçet's disease	Cafer Koçak *(Atatürk Univ., Turkey)*
P-061	The relationship of venous involvement with disease activity in Behçet's syndrome	Muhammed Halid Yener *(Atatürk Univ., Turkey)*
P-062	Serum albumin, prealbumin, and ischemia-modified albumin levels in patients with ANCA-associated vasculitis: A prospective cohort study	Sung Soo Ahn *(Yongin Severance Hosp., Yonsei Univ. College of Medicine, Korea)*

No.	Title	Presenter
	Behçet's disease & Vasculitis	
P-063	Comparison of physical functions of people with Behçet's disease and healthy and their relationship with disease activity	Yusuf Geylani *(Bitlis State Hosp., Turkey)*
P-064	COVID-19 vaccination related small vessel vasculitis with multi-organ involvement	Yunkyung Kim *(Department of Internal Medicine, Kosin Univ. College of Medicine, Korea)*
P-065	BVAS version 3 and BVAS/GPA	Jangwoo Ha *(Yonsei Univ. College of Medicine, Korea)*
P-066	Application of the 2022 new criteria for microscopic polyangiitis to patients with previously diagnosed microscopic polyangiitis	Jung Yoon Pyo *(Yonsei Univ. College of Medicine, Korea)*
P-067	Effect of the number of metabolic syndrome components on all-cause mortality in patients with antineutrophil cytoplasmic antibody-associated vasculitis	PIL GYU Park *(Severance Hosp., Korea)*
P-068	Aortic involvement as a rare complication of granulomatosis with polyangiitis: A case report	Su Jin Choi *(Ulsan Univ. Hosp., Univ. of Ulsan College of Medicine, Korea)*
P-069	ANCA sero-positivity and AAV occurrence after SARS-CoV-2 infection	Eunju Lee *(Yonsei Univ. College of Medicine, Korea)*
P-070	New-onset IgA vasculitis in adult patients following SARS-CoV-2 vaccines	Yunjung Choi *(Jeonbuk Nat'l Univ. Hosp., Korea)*
P-071	A case of microscopic polyangiitis with periaortitis treated with cyclophosphamide	Seoung Wan Nam *(Wonju Severance Christian Hosp., Korea)*
P-072	Churg-strauss syndrome presenting as acute abdomen- A case report	Subbarayudu Boda *(GITAM Institute of Medical Sciences and Research (GIMSR), India)*

No.	Title	Presenter
	Crystal induced arthropathies	
P-073	Identification of tofuses and diagnosis of gout disease with dual-energy CT	Iraklı Tortladze *(TSSU First Univ. Clinic, Georgia)*
P-074	Spondylodiscitis and paravertebral abscess associated with calcium pyrophosphate dihydrate deposition disease	Burak Sarılar *(Pamukkale Univ., Turkey)*
P-075	Urate-lowering efficacy and renal safety of febuxostat in patients with advanced chronic kidney disease not yet on dialysis: A meta-analysis of observational studies	Changnam Son *(Keimyung Univ. School of Medicine, Korea)*
P-076	A rare coexistence of quadriceps tendon calcification and patellar tendon calcification	Muhammed Eyyüp Çelik *(Atatürk Univ., Turkey)*
P-077	Diagnosis and treatment of gout patients at emergency room	Mi Ryoung Seo *(Gil Medical Center, Gachon Univ. College of Medicine, Korea)*
P-078	Genetic analysis for inflammasome genes polymorphisms in the gout susceptibility	Denise Clavijo-cornejo *(Instituto Nacional de Rehabilitación, Mexico)*
P-079	Depletion, activation, and stimulation of bone destruction of innate and innate-like immune cells in gout	Ki-Jeong Park *(Chonnam Nat'l Univ. Hosp., Korea)*

E-poster Presentation

No.	Title	Presenter
	Crystal induced arthropathies	
P-080	Gout disease modification: Proposal for a definition	Jasvinder Singh *(Univ. of Alabama at Birmingham, USA)*
P-081	Predictors of increased vascular stiffness in gout patients	Wooseong Jeong *(Division of Rheumatology, Jeju Nat'l Univ. School of Medicine, Korea)*
P-082	Clinical features of Korean patients with calcium pyrophosphate crystal deposition disease: A retrospective multicenter study	Eun Hye Park *(Chung-Ang Univ. College of Medicine, Korea)*
P-083	Effect of lifestyle change on incident gout: a nationwide population-based cohort of young men	Yeonghee Eun *(Kangbuk Samsung Hosp., Sungkyunkwan Univ. School of Medicine, Korea)*
P-084	Gout is associated with the risk of osteoporosis: a population-based study	Jihyoun Kim *(Department of internal medicine, Chungbuk Nat'l Univ. Hosp., Korea)*

No.	Title	Presenter
	Pediatric rheumatology	
P-085	Vascular imaging findings with high-pitch low-dose dual-source CT in atypical Kawasaki disease	Recep Sade *(Ataturk Univ., Turkey)*
P-086	Bilateral calcification of ear cartilage	Gökhan Polat *(Atatürk Univ., Turkey)*
P-087	The treatment effect of tofacitinib on Blau syndrome: A case series of Chinese pediatric patients	Zhe Cai *(Guangzhou Women and Children's Medical Center, China)*
P-088	The evaluation of MRI findings of sacroiliitis in patients with juvenile idiopathic arthritis for detection of active and structural damage lesions according to updated preliminary OMERACT pediatric JAMRIS scoring system	Berhan Pirimoglu *(Ataturk Univ. School of Medicine, Turkey)*
P-089	The clinical characteristics of 15 IgG4 related disease in pediatric patients	Zheng Liu *(Peking Union Medical College Hosp., China)*
P-090	Predictors of long-term functional outcomes of enthesitis related arthritis (ERA) category of juvenile idiopathic arthritis (JIA) in adulthood: A single centre experience from a tertiary care hospital	Naveen R *(Sanjay Gandhi Postgraduate Institute of Medical Sciences, India)*
P-091	Secondary hemophagocytic lymphohistiocytosis: Overwhelming clinical manifestations may cause more chemotherapy than necessary	Soo-Young Lee *(College of Medicine, The Catholic Univ. of Korea, Korea)*
P-092	Interstitial lung disease in pediatric systemic lupus erythematosus: A case report	Soo-Young Lee *(College of Medicine, The Catholic Univ. of Korea, Korea)*
P-093	A20 Haploinsufficiency identified in a girl presented with systemic juvenile idiopathic arthritis: A case report	Jung-Woo Rhim *(College of Medicine, The Catholic Univ. of Korea, Korea)*
P-094	Withdrawn	-
P-095	Flare-up of juvenile idiopathic arthritis (JIA) the day after receiving a booster shot of BNT162b2 mRNA vaccine	Hyong Suk Park *(Myongji Hosp., Korea)*
P-096	Challenges and management for pediatric rheumatology patient's in the COVID-19 era: Perspectives from several countries	Putri Ayu *(Andalas Univ., Indonesia)*

No.	Title	Presenter
	Fibromyalgia and soft tissue disorders	
P-097	The use of shear-wave elastography for myofascial pain syndrome's severity	Recep Sade *(Ataturk Univ., Turkey)*
P-098	Amigos de fibro (Fibro Friends): Validation of an educational program for health promotion in fibromyalgia	Mateus Antunes *(Univ. of São Paulo (USP), Brazil)*
P-099	Amigos de fibro (Fibro Friends): Validation of an educational e-book to promote the health of patients with fibromyalgia in Brazil	Mateus Antunes *(Univ. of São Paulo (USP), Brazil)*

No.	Title	Presenter
	Idiopathic inflammatory myositis and muscle biology	
P-100	Withdrawn	-
P-101	Erdheim-Chester disease mimicking coronary artery disease in a systemic lupus erythematosus patient	Grigol Nemsadze *(TSSU First Univ. Clinic, Georgia)*
P-102	New onset clinically amyopathic dermatomyositis following SARS-CoV-2 vaccine: A case report	Eric Ranniel Guevarra *(Univ. of Santo Tomas Hosp., Philippines)*
P-103	Rare case of dermatomyositis following SARS-CoV-2 vaccination	Mark Andrian Yano *(Philippine General Hosp., Philippines)*
P-104	Clinical characteristics and outcomes of adult patients with anti-MDA5 dermatomyositis- A single centre experience from South India	Shivraj Padiyar *(Christian medical College, India)*
P-105	Changes in quantitative interstitial lung disease scores on high-resolution CT in idiopathic inflammatory myositis	Jina Yeo *(Gil Medical Center, Gachon Univ. College of Medicine, Korea)*
P-106	Time-dependent changes in rapidly progressive-interstitial lung disease and mortality risk in anti-MDA5 antibody positive dermatomyositis patients: A cohort study of 272 cases in China	Hanxiao You *(The First Affiliated Hosp. of Nanjing Medical Univ., China)*
P-107	Coexisting of anti-Ro52 autoantibodies on anti-MDA5 autoantibodies-positive dermatomyositis is highly associated with rapidly progressive interstitial lung disease and mortality risk	Hanxiao You *(The First Affiliated Hosp. of Nanjing Medical Univ., China)*
P-108	Galectin-9 and CXCL-10 as biomarkers in assessing disease activity in Dermatomyositis and Polymyositis - A single centre cohort study	SAI KUMAR Dunga *(Jawaharlal institute of postgraduate medical education and research, India)*
P-109	Role of semiquantitative thigh magnetic resonance imaging (tMRI) in determining skeletal muscle outcomes at baseline and on follow up in idiopathic inflammatory myopathies (IIMs)	Mamatha Gorijavolu *(Jawaharlal institute of postgraduate medical education and research, India)*

E-poster Presentation

No.	Title	Presenter
	Sjögren's syndrome	
P-110	Hyperglobulinemia in primary Sjögren's syndrome predicts the poor outcome: From multicenter registration study	Hui Zhong *(Peking Union Medical College Hosp., China)*
P-111	Primary Sjögren's syndrome is associated with increased risks of not just lymphoma: a systematic review and meta-analysis	Hui Zhong *(Peking Union Medical College Hosp., China)*
P-112	Salivary ultrasonography and histopathologic evaluation of secondary Sjögren's syndrome in rheumatoid arthritis patients	Minae Oh *(Seoul St. Mary's Hosp., The Catholic Univ. of Korea, Korea)*
P-113	STAT4 gene polymorphisms in risk of Sjögren's syndrome patients susceptibility: Update systematic review and meta-analysis	Rendra Ristian wibowo *(Sebelas Maret Univ., Indonesia)*
P-114	Interstitial lung disease in Sjögren's syndrome: Prevalence, patterns, treatment, and prognosis	Jung Hee Koh *(College of Medicine, The Catholic Univ. of Korea, Korea)*
P-115	Distinct metabolic biomarkers to distinguish immunoglobulin G4-related disease from Sjögren's syndrome and pancreatic cancer and predict disease prognosis	Yu Peng *(Peking Union Medical College Hosp., China)*
P-116	Predictors of the future development of systemic lupus erythematosus (SLE) in Korean primary Sjögren's syndrome (pSS) patients with anti-DNA antibody (+) by the Farr method.	Bong-Woo Lee *(Yeouido St. Mary's Hosp., College of Medicine, The Catholic Univ. of Korea, Korea)*

No.	Title	Presenter
	Systemic sclerosis and Raynaud's phenomenon	
P-117	Analysis of clinical features of myocardial involvement in systemic sclerosis	Huilin He *(Peking Union Medical College Hosp., China)*

No.	Title	Presenter
	Miscellaneous rheumatic and inflammatory diseases	
P-118	Brain magnetic resonance imaging finding in autoimmune rheumatic disease	Recep Sade *(Ataturk Univ., Turkey)*
P-119	Spontaneous knee hemarthrosis associated with enoxaparin treatment in a post COVID-19 patient	Mark Andrian Yano *(Philippine General Hosp., Philippines)*
P-120	Clinical profile and outcome of adult Filipino patients with septic arthritis in a tertiary hospital in the Philippines	Mark Andrian Yano *(Chong Hua Hosp., Philippines)*
P-121	Tuberculosis fasciitis of the neck in Behçet's patient	Yunus Fersan *(Atatürk Univ., Turkey)*
P-122	Chronic inflammatory demyelinating polyneuropathy (CIDP) in polyangiitis granulomatosis with cyclophosphamide	Kadem tüysüz *(Atatürk Univ., Turkey)*
P-123	A rare combination of autoimmune pancreatitis and focal cranial eosinophilic granuloma	Tamar Melkadze *(TSSU First Univ. Clinic, Georgia)*
P-124	Diagnostic value of the inflammatory scores in polymyalgia rheumatica	Ji-Won Kim *(Ajou Univ. School of Medicine, Korea)*
P-125	A short long way from juvenile idiopathic arthritis to pachydermoperiostosis (Touraine–Solente–Gole syndrome)	Bogdan Ion Gavrila *(Univ. of Medicine and Pharmacy, Carol Davila, Romania)*

No.	Title	Presenter
	Miscellaneous rheumatic and inflammatory diseases	
P-126	Allopurinol and febuxostat hypersensitivity in a patient with young onset gout	Mark Andrian Yano *(Philippine General Hosp., Philippines)*
P-127	Curative-intent resection is a strong indicator of steroid-free remission in IgG4-related disease	Jung Gon Kim *(Division of Rheumatology, Seoul St. Mary's Hosp., College of Medicine, Korea)*
P-128	Application of HScore and MS score in diagnosis of macrophage activation syndrome associated with adult onset Still's disease	Zhao Peng *(Chinese Academy of Medical Sciences & Peking Union Medical College, China)*
P-129	The role of interleukin-18 as a diagnostic biomarker to differentiate active adult-onset Still's diseas from COVID-19	Roland Helmizar *(Indonesian Univ., Indonesia)*
P-130	Cancer-associated vasculitis: A single-centre pilot study	Hyunsue Do *(Severance Hosp., Yonsei Univ. College of Medicine, Korea)*
P-131	Withdrawn	-
P-132	Cerebellar infarction as the initial presentation of IgG4-Related Disease	Gaurav Nepal *(Tribhuvan Univ. Institute of Medicine, Nepal)*

No.	Title	Presenter
	Epidemiology & Public health	
P-133	Relationship between Lung Involvement and Gout in COVID-19 disease	Fatih ışık *(Atatürk Univ., Turkey)*
P-134	Post-COVID mesial temporal sclerosis	Megi Kurtanidze *(Tbilisi City Medical, Georgia)*
P-135	Incidence of rheumatic diseases during the COVID-19 pandemic in Korea: A nationwide claims study	Soo Min Ahn *(Asan Medical Center, Korea)*
P-136	Changes in the lungs that develop with COVID-19 in patients with rheumatoid arthritis	Eugenia Aronova *(V.A. Nasonova Research Institute of Rheumatology, Russian Federation)*
P-137	Incidence, prevalence, and clinical characteristics in ANCA-associated vasculitis: A National Health Insurance Service Database (2002-2018)	Jinsu Park *(Nat'l Health Insurance Service Ilsal Hosp., Korea)*
P-138	Association between sarcopenia and rheumatoid arthritis in the Korean population: a nationwide cross-sectional study	Jae Hyun Jung *(Korea Univ. College of Medicine, Korea)*
P-139	Psychometric properties of the PHQ-8 in individuals with osteoarthritis	Patrick Brzoska *(Witten/Herdecke Univ., Faculty of Health, School of Medicine, Germany)*
P-140	The Barriers Of Patients With Osteoporosis In Various Countries During The COVID-19 Pandemic	NURALIAH Nuraliah *(West Sulawesi Research and Empowerment Center, Indonesia)*
P-141	Use of telemedicine for follow-up of lupus nephritis in the COVID-19 outbreak: A randomized controlled trial	Ho So *(The Chinese Univ. of Hong Kong, Hong Kong)*

E-poster Presentation

No.	Title	Presenter
	Epidemiology & Public health	
P-142	Immunopathological process in the Chronic arthritis and Rheumatic Heart Diseases caused by streptococcus of Group A	Nazgul Omurzakova *(Nat'l Center of Cardiology and Internal Medicine, Kyrgyzstan)*
P-143	Comparison of renal outcomes and mortality in early and delayed onset lupus nephritis	Soo-Kyung Cho *(Hanyang Univ. Hosp. for Rheumatic Diseases, Korea)*
P-144	Level of knowledge on systemic lupus erythematosus among nursing students in selected universities in the Philippines	Cherry Ann Garcia Durante *(Emilio Aguinaldo College - Manila, Philippines)*
P-145	Comparative safety of tofacitinib and TNF inhibitor in Korean patients with rheumatoid arthritis: A prospective, single-center cohort study	Yeo-Jin Song *(Hanyang Univ. Hosp. for Rheumatic Diseases, Korea)*
P-146	A tale of three paths: singaporean patient journeys from initial symptoms of gout to presentation for health care	Aloysius Chow *(Lee Kong Chian School of Medicine, Nanyang Technological Univ., Singapore)*

No.	Title	Presenter
	Osteoporosis and metabolic bone diseases	
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P-148	Relationship between Vitamin D, Body mass index with Bone mineral density of Mongolian miners	Garamjav Khishigdavaa *(Medipas Hosp., Mongolia)*
P-149	Application of Machine Learning to identify osteoporosis based on the extreme learning machine (ELM) model algorithm	Rifaldy Fajar *(Univ. of L'Aquila, Italy)*
P-150	FRAX model is useful for prediction of major fractures in RA patients with glucocorticoid-induced osteoporosis	Yoon-Kyoung Sung *(Hanyang Univ. Hosp. for Rheumatic Diseases, Korea)*
P-151	Genetic variation of susceptibility gene of osteoporosis, measuring method of osteoporosis risk	Ahmad Ahmad *(Universitas Al Asyariah Mandar, Indonesia)*
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P-154	Serum, synovial visfatin level during flare-up and remission of primary knee OA	Haytham Abd elaal *(MOH, Egypt)*
P-155	Influence of metabolic syndrome in patients with knee osteoarthritis	Jamol Uzokov *(Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Uzbekistan)*

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P-157	Detection of the sesamoid bone of the metacarpal joint in patients with osteoarthritis using the deep learning model	Bon San Koo *(Inje Univ. Seoul Paik Hosp., Inje Univ. College of Medicine, Korea)*
P-158	Blood D-dimer level after COVID-19 in patients with knee osteoarthritis	Zumrad Ubaydullaeva *(Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Uzbekistan)*
P-159	Lactobacillus (LA-1) and butyrate inhibit osteoarthritis by controlling autophagy and inflammatory cell death of chondrocytes	JooYeon Jhun *(The Catholic Univ. of Korea, Korea)*

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KCR 2022

42nd Korean College of
Rheumatology Annual Scientific Meeting
and the 16th International Symposium

May 19(Thu) - 21(Sat), 2022

Seoul Dragon City, Seoul, Korea

DAY 01

PROGRAM

May 19(Thu)

Symposium

Year in Review (Clinical)

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Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Clinical update of systemic lupus erythematosus

Seung-Ki Kwok
The Catholic Univ. of Korea, Korea

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of diverse autoantibodies and immune complex deposit in target tissues. It affects multiple organs and has significant morbidity and mortality. Identification and development of new treatment strategy for SLE is currently an area of intense investigation. This talk will include the general update of SLE in clinical aspect. It will also provide recent clinical updates in SLE including novel treatments such as Anifrolumab which binds to the type I interferon receptor, blocking the activity of type I interferons (interferon-α and interferon-β) as well as Volcosporin, a new calcineurin inhibitor.

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Idiopathic inflammatory myositis

Jinhyun Kim
Chungnam Nat'l Univ., Korea

Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune muscle diseases with systemic involvement. Based on the different clinical features and pathologic findings, they are classified into five subtypes: dermatomyositis, polymyositis, immune-mediated necrotizing myositis, inclusion-body myositis and antisynthetase syndrome. Several other organs may be affected, particularly lungs, heart, skin, gastrointestinal tract and joints, often determining the morbidity and mortality associated with these autoimmune disorders. Due to clinical heterogeneity, patients with IIM present with varying degrees of muscle disease, cutaneous manifestations, and internal organ involvement. The diagnosis and classification of IIM is based primarily on the classification system composed of clinical features, laboratory value and muscle biopsy. The course is generally chronic and variable. Recently, many studies have also demonstrated that the physician can define the clinical syndromes, establish treatment strategy and predict outcomes based on the patients myositis-specific autoantibodies and myositis-associated antibodies profiles.

To control IIMs and prevent disease complication, high-dose corticosteroids in combination with immunosuppressant has been the mainstay of treatment. With the rarity of these conditions, diagnosis and management of patients can be a clinical challenge for the physician. The scientific research makes continuous advances in the understanding of these diseases, in particular with regards to the serological findings, diagnostic strategies and therapeutic approaches. The aim of this review is to highlight the most relevant literature contributions focused on the clinical aspects of IIMs.

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Vol. 29, Suppl. 1, May, 2022
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Update of IgG4 related disease

Yong Gil Kim
Univ. of Ulsan, Korea

Immunoglobulin G4-related disease (IgG4-RD) is a systemic fibro-inflammatory condition of unknown etiology. This disorder is characterized by lymphoplasmacytic tissue infiltration with IgG4-positive plasma cells and elevation of serum IgG4 levels. Diffuse swelling or mass formation can occur in most organs, and the pancreas, biliary tree, lacrimal gland, salivary glands, and retroperitoneum/aorta are frequently involved. The mainstay treatment for the achievement of remission is a glucocorticoid, and most patients respond well to the initial treatment. However, patients often experience relapses during glucocorticoid tapering or maintenance therapy. In patients with a high risk of relapse, more stringent treatment and follow-up strategies may be considered to prevent frequent relapse, organ damage, and additional glucocorticoid use. Therefore, I have reviewed interesting results published after 2021 including the clinical parameters associated with prognosis and diagnostic algorithms.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Behçet's disease

Sang-Won Lee
Yonsei Univ., Korea

Behcet syndrome (BS), which has been widely used instead of Behcet disease by the European Alliance of Associations for Rheumatology (EULAR) since 2018, is a variable vessel vasculitis affecting from capillaries to the aorta. According to the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides, BS is characterised by recurrent oral and/or genital Aphthous ulcers accompanied by cutaneous, ocular, articular, gastrointestinal, and/or central nervous system inflammatory lesions. In addition, BS may exhibit small vessel vasculitis, thromboangiitis, thrombosis, arteritis and arterial aneurysms. BS occurs in Mediterranean basins, Middle East and Far East Asia more often than in Europe and North America. The prevalence of BS in Turkey, Iran, Saudi Arabia and Japan was 370, 80, 20 and 11.9, respectively, whereas that in overall Europe and the United States was 7.1 and 5.2. The genetic factors of BS include HLA-B*51, ERAP1 variations, IL10, IL23-IL12RBs, STAT4, NF-kB, and IFNGR1, which may enhance the susceptibility of individuals. The environmental aetiology is comprised of three categories such as infectious factors, microbiome and additional trigger factors. Also, the immunological aetiology consists of two important mechanisms: neutrophil mediated mechanism of damage including neutrophil extracellular traps (NETs), and other immunological mechanisms including Th1/Th17 expansion, JAK/STAT and NF-kB pathways, Treg downregulation, and NK and gamma delta T cells dysregulation. Since BS exhibits various organ-specific manifestations and the laboratory, radiologic and histologic evidence for the diagnosis still remains insufficient, the classification criteria for BS have been modified and supplemented very slowly to date. The criteria for diagnosis of Behcet's disease proposed by the international study group in 1990 are currently used and the revised criteria proposed by the International Criteria for Behçet's Disease (ICBD) in 2014 are also used. In particular, the 2014 ICBD criteria are composed of the scoring system in which different weights are assigned to organ-based lesions and put an item of ocular lesions on top of the algorithm. The latest version of the treatment guidelines is the 2018 update of the EULAR recommendation for the management of Behcet's syndrome. A review paper published in 2021 classified the 2018 recommendations by organ and listed the drugs to be applied, which made it easy to understand. Finally, during the COVID-19 pandemic, BS was reported to not affect the symptoms or outcomes due to COVID-19.

Symposium

Year in Review (Basic)

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May 19(Thu) - 21(Sat), 2022

Emerging concepts of endotypes/phenotypes in osteoarthritis

Gunil Im
Dongguk Univ., Korea

Osteoarthritis (OA) has been investigated as one of important target diseases for regenerative medicine. The concept of early OA has recently emerged under the assumption that if OA is detected and intervened early, progression of OA might be arrested or delayed before irreversible destruction of the joint occurs. This concept also matters in regenerative medicine for OA because new regenerative technologies can work better when joint damage is minimal.

Diagnostic criteria for early OA have been suggested in this background to find a group of patients who have a higher possibility of developing full-blown OA. However, as currently suggested criteria of early OA are mostly expert opinions lacking higher level of evidence, clinical validations are necessary to prove their value in patient care. While new treatment methods that can suppress or prevent symptoms at an early stage of OA before progressive and irreversible changes occur are being developed, detailed definition and classification of early OA agreed upon by major stakeholders in OA field and validated by prospective studies are necessary to prove the efficacy of these methods.

As clinical outcome of regenerative treatment is related to patient characteristics and the status of the whole joint, it is of critical significance to predict which patient will progress and who will be responsive to regenerative treatment. While diagnostic criteria for early OA should be highly sensitive and applicable without employing biomarkers or magnetic resonance imaging, a subclassification and comprehensive endotyping /phenotyping using these techniques might be needed to detect the population who would be responsive to regenerative medicine.

JRD Journal of Rheumatic Diseases
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Gout: Basic science of gout

Seokchan Hong
Univ. of Ulsan, Korea

Gouty arthritis is a type of inflammatory arthritis characterized by the deposition of monosodium urate (MSU) crystals in the joints and/or various tissues. This disorder presents as painful acute inflammatory arthritis, usually affecting the big toe and foot. A key pathogenic factor in gout is hyperuricemia, which promotes the precipitation of MSU crystals. MSU crystals elicit acute and chronic inflammatory responses, mainly through activation of NLRP3 inflammasome complex, leading to the secretion of pro-inflammatory cytokines, IL-1β and IL-18. Although, the underlying mechanism of MSU crystals driven inflammation for the development of gouty arthritis has been studied, further studies are still needed. Thus, studies investigating the role of MSU crystals in the various immune system are ongoing.

JRD Journal of Rheumatic Diseases
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SpA: Insight into the pathogenesis of SpA

Tae-Jong Kim
Chonnam Nat'l Univ., Korea

Spondyloarthritis (SpA) comprises a group of inflammatory diseases of the joints and spine, with various clinical manifestations. The group includes ankylosing spondylitis, reactive arthritis, psoriatic arthritis, arthritis associated with inflammatory bowel disease, and undifferentiated spondyloarthritis. The exact etiology and pathogenesis of spondyloarthritis are still unknown, but several hypotheses explaining the pathogenesis exist. These hypotheses suggest that spondyloarthritis is caused by arthritogenic peptides, an unfolded protein response, HLA-B*27 homodimer formation, malfunctioning endoplasmic reticulum aminopeptidases, and, last but not least, gut inflammation and dysbiosis. The gut–joint axis of inflammation in SpA is further reinforced by similarities in immunopathogenesis at both anatomical sites and by the clinical success of therapies blocking TNF and IL-23 in IBD and in some forms of SpA.

This review addresses these two critical pathways of inflammation, discussing their nature and these factors that may activate or enhance the pathways in patients with SpA. In addition, genetic and other markers important to the inflammatory pathways implicated in SpA are explored.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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KCR 2022
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Update in the pathogenesis of Sjögren's syndrome

Jennifer Jooha Lee
The Catholic Univ. of Korea, Korea

Primary Sjogren's syndrome (pSS) is a chronic systemic autoimmune disease of the exocrine glands characterized by primarily immune-mediated pathological features. Various immune cells are infiltrated in the glands resulting in glandular dysfunction. The presence of autoantibodies - anti SSA/Ro and SSB/La is characteristic which suggests that T cell-mediated initial inflammation subsequently invokes B cell activation and production of autoantibodies.

The initial event of this immune dysregulation involves activation of plasmacytoid dendritic cell (pDC) resulting in type I interferons. Interferon signature genes (ISGs) are highly expressed in some of the patients and the ISG score is usually correlated with systemic disease activity of pSS. B cell activating factor (BAFF) secreted from DCs contributes to B cell activation and production of autoantibodies. The epithelial cells in the gland have been considered as the target of the dysregulated immune cells. However, at the same time, they are not innocent targets but they are actively involved with inflammation in the gland acting as antigen presenting cells and producing inflammatory cytokines.

Genetic predisposition is one of the explanations for the susceptibility of the disease. There was a large scale GWAS study that delineate susceptible genes including non-HLA genes such as STAT4, IRF5, CXCR5 and IL12. Further a recent study found 10 novel genes that had mutations in European pSS patients. In addition to genetic risk, epigenetic modification such as methylation profile or non-coding RNA expression affect the gene expressions in pSS. Further, integrative analyses combining genetic, epigenetic, transcriptive information suggest the potential biomarker and key pathways of the pSS. Those analyses are performed not only with peripheral blood data but also salivary glands data.

Another approach to explain the pathogenesis of the disease is to suggest the role of microbiome. The role of gut microbiome was reported in many autoimmune diseases in regulating immune cells especially Th17/Treg cells. In line with this, strategies using gut microbiome or metabolites to alleviate the manifestations of pSS have been reported. Oral microbiome also affects the local environment of the target organ and is thought to contribute to salivary gland inflammation.

In this update, recent studies of the pathogenesis regarding aspects mentioned above will be addressed.

Luncheon Symposium I
Pfizer

Recent Update
of Advanced RA Treatment

KCR 2022 May 19(Thu) - 21(Sat), 2022
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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

The role of tofacitinib as a JAK pioneer

Hyoun-Ah Kim
Ajou Univ., Korea

Rheumatoid arthritis (RA) is a chronic inflammatory arthritis characterized by destruction of synovial joints and systemic inflammation. In recent years, there have been many improvements in treatment of RA with the emergence of biologics or targeted synthetic disease modifying anti-rheumatic drugs (tsDMARDs). Novel small molecule JAK inhibitors that are orally administered have challenged the treatment of RA by providing evidence of superiority to first- and second-line standards-of-care through innovative head-to-head clinical trials. RA treatment recommendations have evolved over the years and currently focus on a treating to a target (T2T) approach. The guidelines recommend initiations of treatment with DMARDs as soon as the disease is confirmed, and the treatment should be adjusted at least every 3 months to reach a targeted, sustained remission or low disease activity. This lecture addresses the major clinical studies and long-term outcomes of tofacitinib. Tofacitinib demonstrated significant reduction in the signs and symptoms of RA vs. placebo, as measured by ACR20, as early as week 2. Tofacitinib with and without MTX improved signs and symptoms of RA in adults with moderate to severe RA. Drug persistence over 8.5 years was similar for tofacitinib with and without MTX. Tofacitinib demonstrated a consistent safety profile (as monotherapy or combination therapy) in open-label long-term extension data reported up to 9.5 years. Tofacitinib provided improvement in RA signs and symptoms over 24 months in patients from the Asia-Pacific region. Frequency of AEs and SAEs in the Asia-Pacific patient population over 92 months was generally consistent with that reported in global studies.

Tofacitinib may be an effective treatment option to consider for long- term treatment in RA.

Luncheon Symposium II
JW Pharmaceutical

IL-6R Inhibition:
Transforming People's Lives,
for a Future on Their Term

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Evolution of tocilizumab: From rheumatoid arthritis to CAR T cell therapy and COVID-19

Seung-Ki Kwok
The Catholic Univ. of Korea, Korea

Interleukin 6 (IL-6) is an interleukin that acts as both a pro-inflammatory cytokine and an anti-inflammatory myokine. IL-6 has pleotrophic activities in diverse biologic processes and has been deeply implicated in the pathogenesis of various immune-mediated inflammatory diseases. Tocilizumab, a humanized anti-IL-6 receptor antibody, has shown remarkable efficacy in rheumatoid arthritis (RA), juvenile idiopathic arthritis, and adult-onset Still's disease. Emerging evidence has demonstrated the benefit of tocilizumab for several types of acute inflammatory diseases, including cytokine storms induced by chimeric antigen receptor (CAR) T cell therapy and coronavirus disease 19 (COVID-19). This talk will include a brief introduction of the development of tocilizumab. In addition, it will summarize not only the pivotal clinical trials which play major roles in the approval by regulatory agencies but also real word data of tocilizumab in the treatment of RA. Finally, this lecture will also include the clinical study results of tocilizumab in diverse acute inflammatory diseases, especially cytokine storms induced by CAR T cell therapy and COVID-19.

Luncheon Symposium III
AbbVie

Strategies to Solve the Problem of Ankylosing Spondylitis with AbbVie's Assets

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Vol. 29, Suppl. 1, May, 2022
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The present and future of ankylosing spondylitis treatments

Tae-Jong Kim
Chonnam Nat'l Univ., Korea

Axial spondyloarthritis is a chronic, progressive rheumatic disease characterised by inflammatory back pain, limited spinal mobility, enthesitis, and peripheral articular and extra-articular manifestations. With limited treatment options in the past, the need for early diagnosis and treatment was less crucial, but with the availability of new effective treatment options (biologic agents blocking tumor necrosis factor alpha (TNF-a), interleukin (IL)-17, JAKi) and with the evidence that early treatment may retard the radiological progression, it becomes imperative that we make efforts to identify these patients and institute treatments as early as possible after the onset of symptoms.

In 2002, Humira, the originator adalimumab, became the third TNFi to be approved in the USA after infliximab and etanercept. Adalimumab significantly reduced the signs and symptoms of active AS and established a sustained clinical response in patients who had an inadequate response or intolerance to NSAID therapy in ATLAS study. The ABILITY study was developed to further evaluate the efficacy and safety of adalimumab in the treatment of patients with nr-axSpA. This represented the first randomised controlled clinical trial to use the ASAS axial SpA criteria in classifying patients with nr-axSpA.

The unmet medical need for treatment remains high, especially in patients who have an inadequate response to biological disease-modifying antirheumatic drugs. JAK inhibitors have emerged as a new therapeutic class for immune-mediated inflammatory diseases and have received marketing approval by regulatory agencies for rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis. SELECT-AXIS 1 is a multi-centre, randomised, double blind, parallel-group, placebo-controlled, phase 2/3, two-period study of upadacitinib. oral upadacitinib 15 mg once daily significantly improved disease activity, function, and MRI-detected axial inflammation in patients with active ankylosing spondylitis after 14 weeks of treatment.

Special Lecture

Presidential Plenary Session

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Vol. 29, Suppl. 1, May, 2022
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Changing role of rheumatologist in Korea

Sang-Heon Lee
Konkuk Univ., Korea

A rheumatologist is an internal medicine doctor who specializes in diagnosing and treating inflammatory conditions that affect the joints, tendons, ligaments, bones, and muscles. Rheumatologists diagnose and treat musculoskeletal conditions, but they do not perform surgery.

Since rheumatology was introduced in mid 1980s in Korea, rheumatology has been established as an important subspecialty in internal medicine. When I started rheumatology fellowship in 1992, there were few hospitals that can train and run the rheumatology training program. At that time, role of rheumatology in tertiary hospital was mainly focused on consulting physician, when the diagnosis and management of systemic autoimmune disease was neglected for long time. Pioneers of Korean rheumatology did hard work to develop the diagnosis and treatment of systemic rheumatic diseases, which was barren land in Korean medical society. Since 1990s, the number of rheumatology fellow was rapidly increasing supported by medical needs for rheumatic diseases, especially in university hospital. Now, all university hospitals have rheumatology subspecialty as a division of internal medicine, most of which have 2 to 4 staffs in one center. I am highly confident that Korean rheumatology is the top specialty in terms of growing up fast for basic research and clinical practice for past decades. With the rapid growing immunological sciences, rheumatology is now equipped with excellent medicine to treat refractory rheumatic diseases, which lead to remarkable treatment outcome. Currently, rheumatology subspecialty board members reach around 460, which is still not enough to satisfy medical needs. However, we are faced with grim prediction for the rheumatology workforce, suggested by rapid drop in applicant of rheumatology fellowship. To maintain and develop the rheumatology in the future, we have to pay attention to the role of rheumatologist. I suggest that the future rheumatology should be developed in parallel in basic research and clinical practice. The tertiary hospital or center should concentrate on basic research and refractory systemic autoimmune disease. Private clinic should expand the spectrum of musculoskeletal problems. Since aging society continues to accelerate, the medical needs for musculoskeletal disease, including degenerative joint diseases, soft tissue pain are expected to increase year by year. We have superior advantages over other musculoskeletal specialists such as orthopaedic surgeon, anesthesiologist in term of treating combined medical comorbidities. The main reason for unpopularity to apply rheumatology among internal medicine residency, is the grim position and uncertainty in rheumatology prospect. Since the number of rheumatology staffs in tertiary hospital remain plateau, we should make steady and persistent effort to expand the clinical spectrum covering most of musculoskeletal problems in private clinic base. To achieve this goal, we do more pay attention to promote the role of rheumatologist to the public, and concentrate on the development of better clinical practice program in KCR.

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Past, present and future of rheumatology in Korea

Yeong-Wook Song
Song Rheumatology Clinic., Korea

Rheumatology was first recognized as a distinct clinical specialty in Korea 41 years ago. Young physicians who were trained in rheumatology in the USA and afterwards returned to Korea contributed substantially to advances in rheumatology clinical practice, educational programs and research activities. They also established the Korean Rheumatism Association, later renamed the Korean College of Rheumatology. Rheumatologists had a major role not only in raising the level of clinical and scientific activities, but also in promoting academic exchanges around the Asia–Pacific region, the USA and Europe. Today, continued efforts are required to raise the standard of clinical and basic research, to optimize clinical practice in the translational era in medicine, to exploit personalized and targeted therapies for the rheumatic diseases. Approach to rheumatic disease need to be multi-disciplinary and patient centered. Clinical examination of the patients should not be neglected.

Free Paper Session

International Free Paper Session (Clinical)

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

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Vol. 29, Suppl. 1, May, 2022
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IO-01

Risk of venous thromboembolism in Korean patients with rheumatoid arthritis treated with JAK inhibitors : A nationwide population-based study

Yeo-Jin Song[1,2], Soo-Kyung Cho[1,2], Seung-Hun You[3], Jeong-yeon Kim[3], Hyoungyoung Kim[1,2], Sun-Young Jung[3], Yoon-Kyoung Sung[1,2]

[1] Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea
[2] Hanyang University Institute for Rheumatology Research, Seoul, Republic of Korea
[3] College of Pharmacy, Chung-Ang University, Seoul, Republic of Korea

Background

There has been a safety concern about an increased risk of thromboembolic events in patients with rheumatoid arthritis (RA) treated with Janus kinase inhibitors (JAKis). In this study, we aimed to determine the risk of venous thromboembolism (VTE) in Korean patients with RA treated with JAKis compared with tumor necrosis factor (TNF) inhibitors.

Methods

Using the National Health Insurance Service database between 2015 and 2019, patients with prevalent RA who started JAKi or TNF inhibitor were selected as study population. All participants were naïve to targeted therapy, and those who ever experienced any VTE event; or used anticoagulant agents within 30 days were excluded. Demographic and clinical characteristics were all balanced by stabilized inverse probability of treatment weighting (IPTW) using propensity score. Then, cox proportional hazard model with considering death as competing risk was used to evaluate the risk of VTE in JAKi users compared with TNF inhibitor users.

Results

A total of 4,178 patients were included: 871 JAKi users and 3,307 TNF inhibitor users followed up for 1,029.2 person-years (PYs) and 5,940.3 PYs, respectively. The crude incidence rate of VTE were 0.29 per 100 PYs (95% confidence interval [CI] 0.09–0.90) in JAKi users and 0.35 per 100 PYs (CI 0.23–0.54) in TNF inhibitor users. After stabilized IPTW, weighted hazard ratio (HR) by cox proportional hazard model was 0.55 (CI 0.09–3.21). When additionally adjusting imbalanced variables even after stabilized IPTW, HR was 0.54 (CI 0.09–3.15).

Conclusions

There was no increased risk of VTE in RA patients treated with JAKis compared with TNF inhibitors in Korea.

Keywords

thromboembolism, rheumatoid arthritis, Janus kinase inhibitor

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IO-02

Increased thromboembolic risk of JAK inhibitors after switching from biologic DMARDs in patients with rheumatoid arthritis

Yeonghee Eun[1], Gi Hyeon Seo[2], Seonyoung Kang[3], Seulkee Lee[3], Hyungjin Kim[3,4], Hoon-Suk Cha[3], Eun-Mi Koh[3], Jaejoon Lee[3]

[1] Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Republic of Korea
[2] N/A, Health Insurance Review and Assessment Service, Republic of Korea
[3] Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea
[4] Department of Medical Humanities, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea

Background

Safety concerns regarding JAK inhibitors have grown since the ORAL surveillance trial reported that their use was associated with an increase in major adverse cardiovascular events compared to TNF inhibitors. However, real-world data on the association between JAKi and thromboembolic events are sparse. We compared the incidence of thromboembolic events (TEs) before and after switching to Janus kinase inhibitors (JAKi) from biologic disease-modifying anti-rheumatic drugs (bDMARDs) in patients with rheumatoid arthritis (RA).

Methods

Among patients with a diagnostic code for RA taking bDMARDs, patients who switched to JAKi or another bDMARD between March 2015 and December 2020 were included in this self-controlled case series study. The outcome was the occurrence of TEs. The incidence rate ratios (IRRs) for TEs in the period after switching to JAKi or another bDMARD compared with the period before switching were calculated based on an assumed Poisson distribution.

Results

There were 1,150 and 2,254 patients who switched to JAKi and another bDMARD, respectively. The mean follow-up duration was 4.5 ± 1.8 years. In the JAKi group, the IRR for TE after drug switching was 1.56 (95% confidence interval [CI] 1.22–1.98, P < 0.001) compared with the period before the drug switch; in the bDMARD group, the IRR was 1.16 (95% CI 0.98–1.38, P = 0.079).

Conclusions

Switching from bDMARDs to JAKi was associated with an increase in TE incidence in RA patients in a real-world

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IO-03

Gut microbiome in patients with established rheumatoid arthritis: Factors associated with the composition, and its value of predicting treatment response

Jung Hee Koh[1,2], Dong-Hyun Kim[3], Wan-Uk Kim[1,2]

[1] Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Republic of Korea
[2] Center for Integrative Rheumatoid Transcriptomics and Dynamics, College of Medicine, The Catholic University of Korea, Republic of Korea
[3] Biomedical Sciences, Seoul National University College of Medicine, Republic of Korea

Background

The gut microbiota has been proposed to be an important environmental factor in the development of rheumatoid arthritis (RA). However, changes in the gut microbiome of RA patients who were already treated with disease-modifying anti-rheumatic drugs (DMARDs) have not been studied well. The aim of the present study was to characterize the gut microbiota profile of patients with established RA and to investigate its association with certain characteristics of RA. Especially, we focused on whether the abundance and composition of gut microbiota were influenced by biological DMARDs (bDMARDs). In addition, pretreatment gut microbial community can differentiate clinical response to the additional conventional synthetic DMARDs (csDMARDs) treatment in patients already treated with csDMARDs and responded inadequately.

Methods

A total of 99 patients with RA and 30 healthy participants were recruited. The microbiome composition was assessed using 16S rRNA amplificon sequencing. For RA patients with moderate-to-high disease activity, treatment change after stool collection and treatment response in 6 months follow-up were further observed.

Results

The diversity of gut microbiota was not different between established RA and healthy participants, regardless of disease activity. Young (<45 years), hypertensive, and anti-citrullinated protein antibody (ACPA) negative patients showed less diversity of gut microbiota. Patients treated with tumor necrosis factor α inhibitors had an overabundance of genera Bifidobacterium, Anaerostipes, Blautia, Subdoligranulum, and Lachnospiraceae ND3007 group, among other bDMARDs users. Gut microbiota including genera Subdoligranulum and Fusicantenibacter were associated with future clinical response of additional csDMARDs therapy in patients who had been treated with csDMARDs.

Conclusions

Patients with established RA appear to have a distinct gut microbiota composition, which is influenced by age, comorbidity, ACPA, and DMARDs. In addition, our results support the value of the gut microbiome as a possible prognostic tool in RA therapeutics.

Keywords

Rheumatoid arthritis, Microbiota, treatment

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IO-04

Time-averaged DAS28 and HAQ predict cardiovascular disease in patients with rheumatoid arthritis: Data from KORONA registry

Hong Ki Min[1], Seung-Ki Kwok[2], Hae-Rim Kim[3], Sang-Heon Lee[3], Kwi Young Kang[2], Sung-Hwan Park[2]

[1] Rheumatology, Konkuk University Medical Center, Republic of Korea
[2] Rheumatology, College of Medicine, The Catholic University of Korea, Republic of Korea
[3] Rheumatology, Konkuk University School of Medicine, Republic of Korea

Background

To evaluate the predictive role of time-averaged disease activity score (DAS)28 and Health Assessment Questionnaire (HAQ) on cardiovascular disease (CVD) events in patients with rheumatoid arthritis (RA).

Methods

Patients with RA were recruited from 23 tertiary hospitals. Baseline and annual follow-up data of demographic, laboratory, questionnaire, RA-associated parameters, and occurrence of CVD were collected. Patients were divided into three groups according to time-averaged DAS28: 1) low (<3.2), 2) moderate (3.2 – 5.1), and 3) high (>5.1). Kaplan–Meier curves was performed to compare the cumulative probability of CVD. Hazard ratios of each factor on the occurrence of CVD were obtained using univariate and multivariate Cox regression analyses.

Results

A total of 4034 RA patients with 1764 for low, 2002 for moderate, and 268 for high time-averaged DAS28 groups were included. Baseline age, disease duration, ESR, CRP, DAS28, and HAQ scores were higher in the high time-averaged DAS28 group. The incidence rate of CVD was 2.78, 3.53, and 8.13 events per 1000 person-years for the low, moderate, and high time-averaged DAS28 groups, respectively. The incidence rate ratio of CVD in the high time-averaged DAS28 group was 2.194 (95% confidence interval 1.142 – 5.111). The cumulative hazard for CVD in the high time-averaged DAS28 group was significantly high (log-rank p = 0.04). In multivariate Cox regression analysis, age, high time-averaged DAS28, and time-averaged HAQ >0.5, were positively associated with CVD events in RA patients.

Conclusions

In patients with RA, time-averaged DAS28 and HAQ could predict the occurrence of CVD.

Figure & Table

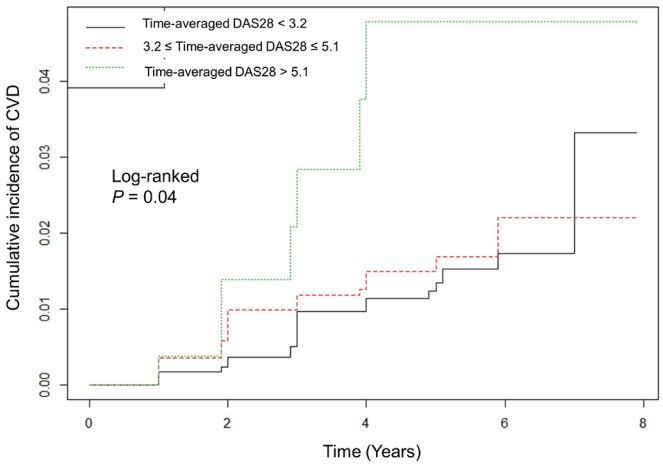

Figure. Cumulative incidence rates of CVD in RA patients

Keywords

cardiovascular disease, DAS28, Rheumatoid arthritis

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IO-05

Increased cardiovascular risk in patients with systemic lupus erythematosus: Population-based Cohort Study in Korea

Jungyong Han[1,2], Hyoungyoung Kim[1,2], Yena Jeon[3], Gaeun Kang[3], Sun-Young Jung[4], Eun Jin Jang[5], Soo-Kyung Cho[1,2], Yoon-Kyoung Sung[1,2]

[1] Rheumatology, Hanyang University Seoul Hospital, Republic of Korea
[2] Rheumatology, Hanyang University Institute for Rheumatology Research, Republic of Korea
[3] Statistics, Kyungpook National University, Republic of Korea
[4] Pharmacy, Chung-Ang University, Republic of Korea
[5] Information Statistics, Andong National University, Republic of Korea

Background

Patients with systemic lupus erythematosus (SLE) have a higher frequency of traditional cardiovascular risk factors and cardiovascular disease (CVD) is known to be one of major causes of mortality. This study aimed to investigate the risk of CVD in SLE patients compared to general population in Korea.

Methods

We identified incident SLE patients and age- and sex-matched control group (1:4 ratio) from National Health Insurance Service (NHIS) database in Korea between 2008 and 2018. The incidence rates of CVD (ischemic heart disease, stroke, and cardiac arrest) and major adverse cardiac event (MACE, myocardial infarction, stroke, and sudden cardiac death) were calculated and increased risk of CVD and MACE in SLE patients compared to general population were estimated using cox proportional hazard models.

Results

We analyzed 8,568 SLE patients, and age- and sex-matched 34,272 controls. The incident rate ratios (IRRs) for CVD and MACE of SLE patients compared to general population were 3.77 (95% confidence interval [CI] 3.33-4.26), and 3.14 (95% CI 2.58-3.81), respectively. After adjusting for the confounders, the CVD risk of SLE patients was remained higher than general population (hazard ratio [HR] 1.49, 95% CI 2.58-3.42), while the HR of MACE was decreased to 1.15 (95% CI 0.87-1.51).

Conclusions

In Korea, SLE patients have significant increased cardiovascular risk compared to general population.

Figure & Table

	SLE patients (n=8,568)		General population (n=34,272)		IRR (95% CI)	HRsd (95% CI) *
	No. of cases	Incidence per 1,000 PYs	No. of cases	Incidence per 1,000 PYs		
CVD events	477	11.16	536	2.96	3.77 (3.33, 4.26)	1.49 (1.25, 1.76)
Ischemic heart disease	295	6.84	375	2.07	3.31 (2.84, 3.86)	1.43 (1.16, 1.77)
Cardiovascular mortality	75	1.70	13	0.07	23.92 (13.28, 43.11)	5.02 (2.48, 10.15)
Stroke	140	3.21	191	1.05	3.06 (2.46, 3.80)	1.09 (0.79, 1.49)
MACE	178	4.08	237	1.30	3.14 (2.58, 3.81)	1.15 (0.87. 1.51)
Myocardial infarction	40	0.91	51	0.28	3.25 (2.15, 4.92)	1.37 (0.81, 2.33)
Cardiac sudden death	0	NC	0	NC	NC	NC
Stroke	140	3.21	191	1.05	3.06 (2.46, 3.80)	1.09 (0.79, 1.49)

PY, person-year; IRR, incidence rate ratio; HR, hazard ratio; sd, subdistribution; CI, confidence interval; CVD, cardiovascular disease; MACE, major adverse cardiovascular event; NC, not calculated

*HR adjusted for age, sex, insurance, comorbidities (hypertension, diabetes mellitus, and hyperlipidemia), Charlson comorbidity index, and medication history (e.g., antiplatelet agents, cholesterol lowering agents, ACE inhibitor, ARB, beta-blocker, calcium-channel blocker, diuretics, NSAIDs, and steroid)

Table. The incidence rate ratio and adjusted hazard ratio of CVD risk in SLE patients compared to general population

Keywords

Systemic lupus erythematosus, Cardiovascular risk, Hazard ratio

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IO-06

Long-term exposure to PM10 and systemic-lupus-erythematosus-related mortality in the Korean population

Ji-Hyoun Kang[1], Chang Kyun Choi[2], Sung-Eun Choi[1], Dong-Jin Park[1], Shin-Seok Lee[1]

[1] Division of Rheumatology, Department of Internal Medicine, Chonnam National University Medical School and Hospital, Republic of Korea
[2] Department of Preventive Medicine, Chonnam National University Medical School, Republic of Korea

Background

The effect of air pollutants on the risk or progression of systemic lupus erythematosus (SLE) has been evaluated in several studies. However, their results were inconsistent and large-scale investigations are lacking. We evaluated the effect of particulate matter (PM) 10 on the risk or prognosis of SLE in a cohort drawn from a very large number of SLE cases registered in a nationwide database.

Methods

A case-cohort study consisting of 23,511 SLE cases and 204,521 cohorts was conducted using NHIS customized data. The district-specific annual average PM10 concentration for the year 2004 was estimated using a land-use regression model. A mixed Cox proportional hazard regression with random intercepts for districts was performed to evaluate the association between PM10 and the SLE risk for the general population and between PM10 and mortality for SLE patients.

Results

There was no significant association between PM10 exposure and SLE risk. However, the plot of the association between PM10 exposure and mortality in male SLE patients followed an inverted U-shape. Compared to the first quintile, the hazard ratios of mortality for the second, third, fourth, and fifth quintiles were 1.541 (95% confidence interval [CI]: 1.049–2.185), 1.278 (95% CI: 0.893–1.829), 1.395 (95% CI: 0.972–2.002), and 1.266 (95% CI: 0.881–1.818). Those associations were not significant in females.

Conclusions

A past PM10 exposure was associated with high mortality in male SLE patients. Further studies of the risk associated with a higher than average PM exposure level are needed.

Keywords

PM10, mortality, systemic lupus erythematosus

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IO-07

Neutralizing antibody formation after COVID-19 vaccination in elderly patients with rheumatoid arthritis

Eunsong Kang[1], Yong Gil Kim[1], Ji Seon Oh[2], Seokchan Hong[1], Soomin Ahn[1], Chang Keun Lee[1], Bin Yoo[1]

[1] Rheumatology, Asan medical center, Republic of Korea
[2] Department of Information Medicine, Asan medical center, Republic of Korea

Background

The guidelines of COVID-19 vaccination in patients with rheumatoid arthritis (RA) have been continuously updated concerning whether disease modifying anti-rheumatic drugs (DMARDs) need to be discontinued before vaccination. Furthermore, there is great discussion on the effectiveness of COVID-19 booster vaccine. We investigated the differences in antibody production between patients who received two doses of ChAdOx1-S nCoV-19 and those who received the third dose of mRNA vaccine. Also, antibody production under different medication scenarios and clinical parameters was analysed.

Methods

From October 14, 2021 to January 21, 2022 at a tertiary referral center, two patient groups diagnosed with RA were studied prospectively; one group that completed two doses of ChAdOx1-S nCoV-19 vaccine, second group that completed mRNA 3rd vaccine.

SARS-CoV-2 antibody titres were determined by semi-quantitative anti-SARS-CoV-2 S enzyme immunoassay. Differences in antibody titres were analysed in patients who received corticosteroid and different DMARDs. The results were expressed as box and whisker plots and statistical analysis with a multivaiate logistic regression model was performed.

Results

In a total of 261 patients, 153 patients had completed two doses of ChAdOx1-S nCoV-19, 108 patients had completed mRNA 3rd vaccine. The positive rates of anti-SARS-CoV-2 neutralizing antibody (titre > 0.8U/mL) were 97% (149/153) and 99% (107/108) respectively. However, regarding acquisition of high antibody titre (> 250U/mL), the positive rates were found to be only 31% (47/153) for group 1 but 94% (102/108) for group 2. Multivariate analysis revealed that corticosteroid use (OR 0.35;95% CI:0.16-0.75), older age (OR 0.91;95% CI:0.86-0.98), and male (OR 0.23;95% CI:0.07-0.74) were associated with low rate of high antibody titres after two doses of ChAdOx1-S nCoV-19.

Conclusions

We can support the suggestion that a third dose of mRNA vaccine might be required in RA patients who have already received two doses of ChAdOx1-S nCoV-19, especially older male patients treated with corticosteroid.

Figure & Table

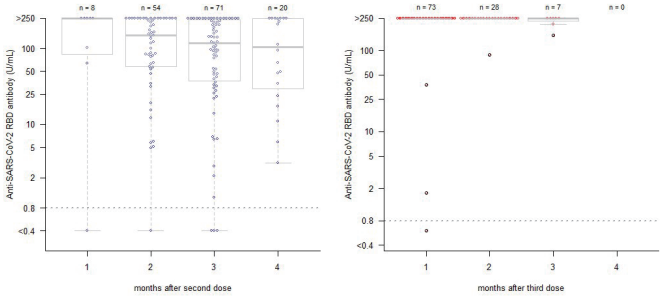

Figure. Anti-SARS-CoV RBD antibody titre in RA patients who received two doses of ChAdOx1-S nCoV-19 (A) and in patients who received an additional mRNA vaccine after two doses of ChAdOx1-S nCoV-19 (B)

Keywords

Rheumatoid Arthritis, COVID-19 vaccination, antibody formation

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IO-08

Immunogenicity and safety of inactivated and mRNA COVID-19 vaccines in patients with systemic lupus erythematosus

Ho So[1], Tena Li[1], Vivien Chan[1], Lai Shan Tam[1], Paul Chan[2]

[1] Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong
[2] Microbiology, The Chinese University of Hong Kong, Hong Kong

Background

Vaccination against SAR-CoV-2 is believed to be the key to end the pandemic. Currently, there are two COVID-19 vaccines available in Hong Kong - they are the inactivated virus vaccine CoronaVac® (Sinovac) and the mRNA-based vaccine Comirnaty® (BioNTech/Fosun). However, the efficacy and safety of COVID-19 vaccines in patients with SLE is uncertain due to a complex interplay of underlying autoimmunity and immunosuppressive therapies used.

Methods

This was a prospective, case-control study. Patients with SLE planning to receive COVID-19 vaccines were recruited and matched 1:1 with healthy controls. The immunogenicity of the COVID-19 vaccines was assessed by a surrogate neutralization assay at 28 days after the second dose. The main outcomes included the antibody response and adverse effects comparing SLE patients and controls. Predictors of responses in SLE patients were analyzed. The change of SLE disease activity was evaluated.

Results

Sixty-five SLE patients received 2 doses of COVID-19 vaccines (Comirnaty: 38; CoronaVac: 27) were recruited. Many of them were on systemic glucocorticoids (75.8%) and immunosuppressants (54.5%). At day 28 after the second dose of vaccines, 92.3% (Comirnaty: 100%; CoronaVac: 81.5%, p=0.01) had positive neutralizing antibody. However, compared to the age, gender, vaccine type matched controls, the level was significantly lower (p<0.001) in patients with SLE (figure). The self-reported side-effects of the vaccines in lupus patients were common but mild, and were more frequent in the Comirnaty group. There was no significant change in lupus disease activity up to 28 days after vaccination. The independent predictors of neutralizing antibody level included the dosage of systemic glucocorticoids, use of mycophenolate and type of vaccines (table).

Conclusions

COVID-19 vaccines produced satisfactory but impaired serological response in SLE patients compared to controls which was dependent on the immunosuppressive medications use and type of vaccines received. There was no new safety signal. Booster dose is encouraged.

Figure & Table

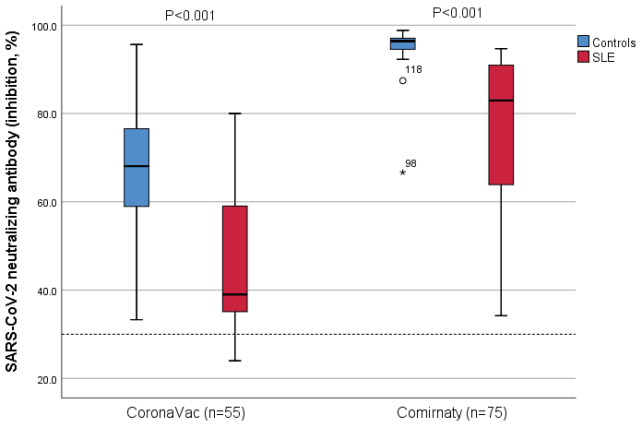

Figure. Distribution of neutralizing antibody levels after COVID-19 vaccines comparing (A) SLE patients and matched controls, (B) SLE patients and matched controls in two vaccine subgroups, and (C) two vaccine types in SLE patients. Data for each group are presented as box plots: central values within boxes correspond to median; the range between the lower (Q1) and upper (Q3) bounds of the boxes is the IQR. Whiskers represent scores outside IQR and ends in maximum (higher "calculated value" = Q3 + 1.5 x IQR) and minimum (lower "calculated value" = Q1 − 1.5 x IQR). Spots are outliers above the maximum or under the minimum values. Data regarding were analyzed using Mann-Whitney-U test. Dotted line denotes the cut-off level for positivity (30%).

Keywords

SLE, COVID, vaccine

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IO-09

Clinical characteristics and prognosis of patients with anti-melanoma differentiation-related gene 5 (MDA5) related diseases

Chen Yu[1], Luwei Yang[2], Li Zhang[1], Shuang Zhou[1], Chaojun Hu[1], Jiuliang Zhao[1], Dong Xu[1], Mengtao Li[1], Chanyuan Wu[1], Qian Wang[1], Lindi Jiang[2], Zuojun Xu[3], Xiaofeng Zeng[1]

[1] Department of Rheumatology, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences & Peking Union Med, China
[2] Department of Rheumatology, Zhongshan Hospital, Fudan University (Xiamen Branch), China
[3] Department of Pulmonary and Critical Care Medicine, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences & Peking Union Med, China

Background

Idiopathic inflammatory myopathy (IIM) is a group of heterogeneous systemic autoimmune diseases, of which patients with anti-melanoma differentiation-associated gene 5 (MDA5) antibody are of specific clinical characteristics. Our study is aimed to propose the concept of patients with anti-MDA5 related diseases (Anti-MDA5-RD), and to describe the clinical characteristics and prognosis of these patients.

Methods

Patients with anti-MDA5 admitted to Peking Union Medical College Hospital from November 2015 to December 2018 were retrospectively studied. Patients were divided into either remission or progression group according to their prognosis. Demographic data and clinical outcomes were compared between the two groups. A multivariate Logistic regression model was applied to explore independent risk factors for poor prognosis. Furthermore, the clinical manifestations and prognosis of patients with both anti-MDA5 and anti-Ro-52 were compared with patients with only anti-MDA5.

Results

A total of 126 patients were included. Rash is the most common initial symptom (65.1%) and clinical amyopathic dermatomyositis (CADM) is the most common clinical subtype (74.8%). Logistics analysis showed anti-Ro-52 (OR 9.17, 95%CI 1.97-42.62, P = 0.005), serum ferritin > 1000ng/ml (OR 2.91, 95%CI 1.03-8.21, P = 0.044), age > 50 (OR 7.78, 95%CI 1.75-34.66, P = 0.007) and hypoxemia at diagnosis (PaO2 < 60 mmHg) (OR 30.68, 95%CI 6.48-145.33, P < 0.001) were independent risk factors for poor prognosis. Patients with anti-MDA5 combined with anti-Ro-52 had a higher risk of rapidly progressive interstitial lung disease (RP-ILD) (42.0% vs 24.6%, P = 0.04) and a worse response to intensive immunosuppressive therapy.

Conclusions

Anti-MDA5 related disease is a high-risk clinical subtype. Patients with anti-Ro-52 are prone to RP-ILD and have a poor response to traditional immunosuppressive therapy. Early combination therapy with biologics may improve the prognosis of these patients.

Figure & Table

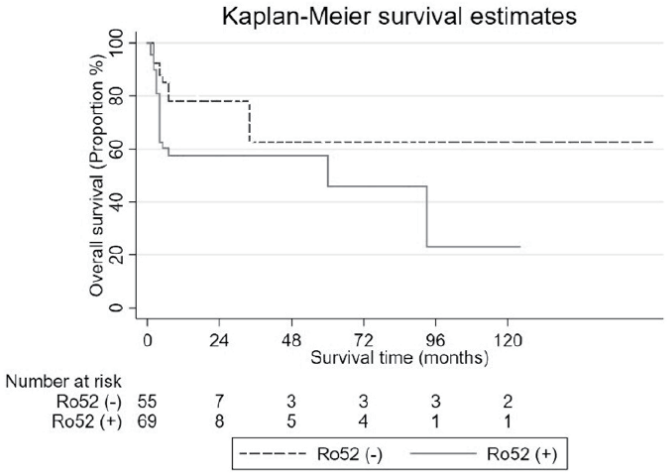

Figure. Kaplan-Meier survival estimates based on patients combined with anti-Ro-52 antibody

Keywords

inflammatory myopathy, anti-melanoma differentiation associated gene 5, interstitial lung disease

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IO-10

Three-dimensional analysis of the trapezium subchondral bone and its association with trapeziometacarpal joint osteoarthritis

Ji Sup Hwang[1], Hyun Sik Gong[1]

[1] Department of Orthopedic Surgery, Seoul National University Bundang Hospital, Republic of Korea

Background

Studies suggest that subchondral bone properties are associated with the pathogenesis of osteoarthritis (OA), but this relationship has not been confirmed in the trapeziometacarpal joint (TMCJ). The purposes of this study are (1) to evaluate the thickness and density of three-dimensional (3D) trapezium subchondral bone models derived from conventional computed tomography (CT) images, and (2) to evaluate the relationship between subchondral bone properties and early stage TMCJ OA.

Methods

We reviewed patients with a distal radius fracture who underwent conventional CT scans and such osteoporosis evaluations as bone mineral density (BMD) and bone turnover markers (BTMs). From 3D trapezium subchondral bone models, we measured SBT and SBD according to the OA stage and performed multivariate analyses to evaluate their associations with age, gender, body mass index, BMD, and BTMs.

Results

Out of the 156 patients (78 men and 78 age-matched women; mean age, 67±10 years) , there were 30 (19%) with grade 0 TMCJ OA, 71 (45%) with grade 1, 13 (8%) with grade 2, and 42 (27%) with grade 3. The average SBT and SBD were 1.84 ± 0.41 mm and 568.4 ± 69.0 Hounsfield units (HU), respectively. In the multivariate analysis, SBT was significantly lower in patients with grade 1 OA than those with grade 0 or grade 3 OA, but SBD generally increased according to the OA severity. Low SBT was associated with female sex and low hip BMD, and low SBD was associated with female sex, low hip BMD, and high osteocalcin.

Conclusions

Patients with early-stage radiographic TMCJ OA have a lower SBT at the trapezium, which may support the potential role of subchondral bone in OA pathogenesis. This study also shows that subchondral bone properties are associated with BMD and osteocalcin levels. Further studies are necessary to determine whether patients with early OA can benefit with osteoporosis therapies.

Figure & Table

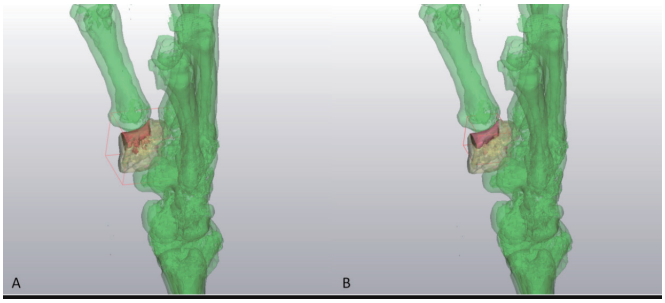

Figure. The subchondral bone thickness and density were measured from the three-dimensional trapezium models.

Keywords

Trapeziometacarpal joint, Osteoarthritis, Subchondral bone

Workshop

Basic Research Workshop for Rheumatologist: Animal Models of Key Arthropathies

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

Animal models of osteoarthritis (OA)

Je-Hwang Ryu
Chonnam Nat'l Univ., Korea

Osteoarthritis (OA), which is the most common chronic degenerative joint disorder worldwide, is characterized primarily by cartilage degradation and narrowing of the joint spaces. Both genetic and acquired factors, such as obesity, mechanical influences and age, are involved in the complex pathogenesis of OA, whereby cartilage homeostasis is disrupted by biophysical factors (for example, mechanical stress) and biochemical factors (for example, proinflammatory cytokines). The chondrocyte is a unique resident cell that synthesizes cartilage-specific extracellular matrix (ECM) components as well as various catabolic and anabolic factors. The pathogenesis of OA activates various biochemical pathways in chondrocytes, leading to proinflammatory cytokine production, inflammation, degradation of the ECM by matrix metalloproteinases (MMPs) and a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS), and cessation of ECM synthesis via the dedifferentiation and apoptosis of chondrocytes. The culture of chondrocytes is one of the most powerful tools for exploring the intracellular and molecular features of chondrocyte differentiation and activation. However, chondrocytes tend to dedifferentiate into fibroblasts when they are subcultured, which is a major problem. Here we introduce the method of primary culture and phenotyping of murine chondrocytes. In addition to in vitro cell culture, various in vivo studies are currently ongoing to understand OA pathophysiology and develop successful treatment regimens based on this knowledge. Animal models have played a key role in achieving this goal. Experimental animal models currently used to study OA can be classified based on the etiology under investigation.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

Experimental procedures of mouse OA research

Gyuseok Lee
Chonnam Nat'l Univ., Korea

Disease animal models that accurately reflect disease progression and symptoms are essential for further elucidation of disease pathogenesis and the development of treatments. Currently, various animal models are used to study osteoarthritis (OA), which is one of the most common degenerative diseases in the world.

Based on disease etiology, OA can be classified into primary (idiopathic) and secondary OA. Primary OA is a disease that occurs naturally due to degenerative changes (dedifferentiation) in chondrocytes. Secondary OA is an inducible disease associated with some causes and risk factors, including trauma, congenital causes, obesity, or bone deformities. According to this classification of OA, animal models have been categorized into spontaneous and induced OA models. However, the causes of OA are not completely understood and recent studies have proposed novel OA-inducing pathways related to adipokines or metabolic disorders such as hypercholesterolemia. The diverse etiology of OA has raised the need for a new classification of OA based on clinical phenotype. Five OA phenotypes have been proposed to replace the conventional primary and secondary classifications with disease features. These include post-traumatic, metabolic, aging, genetic, and pain phenotypes.

In this lecture, OA animal models which reflect these five OA phenotypes will be introduced and detailed experimental processes will be explained. Surgically induced OA models such as destabilized media meniscus (DMM) surgery or anterior cruciate ligament transection (ACLT) on mice reflect post-traumatic phenotype. Metabolic OA models including high-fat diets or high cholesterol diets showed metabolic phenotypes of OA. Spontaneous OA models such as STR/ort mouse strain or aged mice and senescent cell transplantation model have aging phenotypes of OA. Intra-articular (IA) injection models of adenovirus expressing the gene of interest have been used to study the genetic phenotype of OA. Monoiodoacetate (MIA) IA injection models with pain assay such as the von Frey test or hot plate test have been used to study pain phenotypes of OA.

Furthermore, the analytic method for assessment of disease progression of OA animal models including histological analysis of cartilage damage, osteophyte maturation, and subchondral bone thickening will be explained and the microCT-based knee joint imaging method using a contrasting agent will be introduced in this lecture.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Animal models of rheumatoid arthritis

Seung-Ah Yoo
The Catholic Univ. of Korea, Korea

Rheumatoid arthritis (RA) is a common autoimmune disorder that afflicts ~1% of the population. Despite the advent of anticytokine therapies that ameliorate the inflammatory manifestations of disease, there is no cure, and the pathogenesis of RA is not fully understood. In RA joints, various inflammatory cells, including innate immune cells, adaptive immune cells, endothelial cells, and fibroblast-like synoviocytes (FLSs), are activated. To understand the pathogenic processes of RA in humans, animal models are helpful and essential tools. These are also important for testing the novel and existing drugs for their potency, efficacy and safety. The rodent models are used widely because of low cost, homogeneity of the genetic background, ease of handling. In this presentation, we focus on animal models of arthritis induced in various species along with the genetic models.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

Experimental procedures of mouse arthritis models

Saseong Lee
The Catholic Univ. of Korea, Korea

Collagen induced arthritis (CIA) is an essential experimental tool for pre-clinical research on rheumatoid arthritis. Using lyophilized bovine collagen and Freund's adjuvant, DBA-1 mice are immunized to acquire an autoimmune response on collagen to get inflamed in articular joints. The procedure in this model requires multiple steps that need to be performed properly, from initial collagen emulsification with adjuvants before immunization to clinical assessment and histological analysis of the affected joint, making this experimental arthritis model complicated and difficult to replicate the same results. In this lecture, we will look at specific materials and methods for accurately performing CIA model without omitting crucial details including dissolving collagen adequately, injecting the collagen-adjuvant emulsion in the right position, and animal facility issues, etc., which will be of practical help to the performers in deriving successful results.

Free Paper Session

International Free Paper Session (Basic)

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JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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IO-11

Identification of a key regulator of MYH9 for synoviocyte migration and invasion through secretome profiling

Saseong Lee[1], Eunbyeol Choi[1], Sehyun Chae[2], Seung-Ah Yoo[1,3], Daehee Hwang[4], Wan-Uk Kim[1,5]

[1] Center for Integrative Rheumatoid Transcriptomics and Dinamics, The Catholic University of Korea, Republic of Korea
[2] Department of Developmental Disorders & Rare Diseases Research Group, Korea Brain Research Institute, Republic of Korea
[3] Department of Medical Life Sciences, The Catholic University of Korea, Republic of Korea
[4] Department of Biological Sciences, Seoul National University, Republic of Korea
[5] Department of Internal Medicine, The Catholic University of Korea, Republic of Korea

Background

Invasive pannus, mainly composed of fibroblast-like synoviocytes (FLSs), is a hallmark of rheumatoid arthritis (RA) pathology. In the present study, we sought to present a pannus-derived secretome profile in rheumatoid synovium in an unbiased manner and reveal a pathogenic mechanism of a newly identified secretome protein.

Methods

The secreted proteins from RA-FLSs were identified through a proteomics approach using liquid chromatography-mass spectrometry (LC-MS). To further narrow into a group of proteins that are increased in RA synovial fluid (SF) when compared to osteoarthritis (OA) SF, the SFs were proceeded with parallel reaction monitoring (PRM), a quantitative proteomics method. In vitro migration and invasion assays were performed under MYH9 deficient or blebbistatin-treated conditions in RA-FLSs.

Results

The 843 secretory proteins from RA-FLSs treated with TNFα and IL-1β were profiled by using LC-MS/MS analysis. Gene ontology analysis revealed that 493 proteins were involved in pannus-driven RA pathologies. Among these, 151 proteins were selected to be further quantitatively analyzed in 117 RA and 45 OA SFs using PRM method. Total 16 differentially expressed proteins (DEPs) were selected according to whether it was significantly higher in RA compared to OA SF, and whether it was correlated with synovial hyperplasia, articular vascularity, or inflammatory levels of RA patients. Among the DEPs, MYH9 has met all the criteria for the DEPs and is a novel factor in terms of RA pathogenesis. MYH9 levels were increased in RA-FLSs under disease-aggravating conditions. RA-FLSs depleted with MYH9 gene expression or molecular function significantly defected in cell migration and invasion.

Conclusions

The present study clearly suggested a pannus-derived secretome profile of RA synovium through a stepwise approach starting from RA-FLS-secreted proteins to synovial fluids that were under a series of disease severity in inflammatory arthritis and proposed a pathogenic role of a newly discovered molecular player, MYH9, in RA-FLS-driven articular tissue destruction.

Keywords

Secretome, Pannus, Fibroblast-like Synoviocytes

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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IO-12

Multi-omics identifies S100 proteins as biomarkers of RA progression which can be regulated by epigenetic drugs

Marzena Ciechomska[1], Leszek Roszkowski[1], Dominik Cysewski[1], Wlodzimierz Maslinski[1]

[1] Department of Pathophysiology and Immunology, National Institute of Geriatrics, Rheumatology and Rehabilitation, Poland

Background

Monocytes are key players in the initiation and maintenance of inflammation through production of proinflammatory cytokines and S100 proteins in rheumatoid arthritis (RA). A number of studies demonstrated that epigenetic drugs affecting DNA methylation are able to modulate the production of proinflammatory mediators. Therefore, the aim of this study was to test specific DNA methylation inhibitor (RG108) or activator (budesonide) in regulation of proinflammatory cytokines and S100 proteins in RA monocytes.

Methods

High-throughput analyses were performed including RNA sequencing (RNA-seq) of healthy control (HC) and RA monocytes and proteomic analysis of HC sera and sera from early RA and advanced RA sera. Cell viability was determined in THP-1 monocytic cell line following RG108 and budesonide treatment. Pro- and anti-inflammatory genes such as the S100 family, TNF, IL-8, MyD88, IL-10RA, TGIF1 were validated by qRT-PCR following DNA methylation-targeted drug treatment.

Results

Based on the RNA-seq analysis, RA monocytes had significantly increased level of S100 family, TNF, IL-8, MyD88 and decreased level of anti-inflammatory IL-10RA and TGIF1. Proteomic analysis also revealed increased level of S100 proteins in sera from advanced RA compared to HC and early RA, suggesting that S100 family might be promising marker of RA progression. In addition, THP-1 monocytic cell line treated with RG108 (DNA methylation activator) had increased level of S100 family (S100A8, -A9, -A11, -A12), IL-8, TNF. In contrast, stimulation of THP-1 cells with budesonide (DNA methylation inhibitor) reduced expression of S100 family, IL-8, TNF genes.

Conclusions

Using multi-omics analysis we have demonstrated that S100 proteins are increased in RA monocytes (transcriptomics) similarly to enhanced S100 production in sera (proteomics) of patients with advanced RA. Interestingly, S100 proteins can be regulated by epigenetic drugs, suggesting their potential use in targeting of RA inflammation.

Keywords

multi-omics, rheumatoid arthritis, biomarkers

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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IO-13

Dysfunction of parkin increases osteoclast activity linking to bone erosion of inflammatory arthritis

Ji-Eun Kim[1,3], Eun-Young Kim[1,3], Bongkun Choi[1,3], Dong Hyun Sohn[4], Yeon-Ho Chung[1], Ji-Eun Park[1,3], Sion Park[1,3], Soyoon Oh[1,3], Ha Rim Shin[1,3], Yongsub Kim[1,3], Dohee Yoon[1,3], Yu Mi Hwang[1,3], So Hye Nam[5], William H. Robinson[6], Yong-Gil Kim[5], Eun-Ju Chang[1,2,3]

[1] Department of Biomedical Sciences, University of Ulsan College of Medicine, Republic of Korea
[2] Department of Biochemistry and Molecular Biology, University of Ulsan College of Medicine, Republic of Korea
[3] Stem Cell Immunomodulation Research Center, University of Ulsan College of Medicine, Republic of Korea
[4] Department of Microbiology and Immunology, Pusan National University School of Medicine, Republic of Korea
[5] Department of Rheumatology, Asan Medical Center, Republic of Korea
[6] Division of Immunology and Rheumatology, Stanford University School of Medicine, USA

Background

Dysfunction of parkin related to the progression of parkinsonism contributes to a progressive systemic skeletal disease characterized by low bone mineral density. However, the role of parkin in bone remodeling has not been elucidated in detail.

Methods

To check the linkage between parkin and inflammatory arthritis, synovial tissues of rheumatoid arthritis (RA) and osteoarthritis (OA) patients were analyzed by using immunofluorescence. The femurs from wild-type (WT) and Parkin-deficient mice were examined by micro-computed tomography. Osteoclast (OC) differentiation was evaluated by tartrate-resistant acid phosphatase staining and bone resorbing activity was determined using dentin. To induce arthritis mouse model, the serum of arthritic K/BxN mice were injected to recipient WT or Parkin-deficient mice and K/BxN serum transfer-induced arthritis mouse model was employed to evaluate inflammatory arthritis.

Results

Parkin expression was significantly downregulated in monocytes of the inflamed synovial tissues of RA patients. Given that monocytes are considered as osteoclast (OC) precursor cells, we thus clarified whether the decrease in parkin in monocytes is linked to the osteoclastic bone resorbing activity. Parkin-deficient mice exhibited an osteoporotic phenotype with a lower bone volume accompanied by increased OC-mediated bone resorbing capacity compared to WT mice. Intriguingly, parkin co-localized with microtubules and parkin depleted-OC precursor cells displayed augmented acetylation of α-tubulin. The Parkin-deficiency mice increased the susceptibility to inflammatory arthritis reflected by higher arthritis score and a marked bone loss after K/BxN serum transfer.

Conclusions

These results reveal parkin as a potential determinant of the maintenance of bone turnover balance by altering microtubule dynamics in OC and assign a homeostatic role to parkin that would limit inflammatory arthritis.

Keywords

Parkin, Inflammatory Arthritis, Osteoclast

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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IO-14

Cell-specific activation of PADI4 promoter in human fibroblast-like synoviocytes from patients with rheumatoid arthritis

Khrystyna Malysheva[1,2,3], Justyna Czarnik-kwaśniak[2,3], Oleksandr Korchynskyi[1,2,3]

[1] Department of Biotechnology and Radiology, S. Gzhytskyi National University of Veterinary Medicine and Biotechnologies, Ukraine
[2] Department of Immunology, Institute of Medical Sciences, College for Medical Sciences, University of Rzeszow, Poland
[3] Centre for Innovative Research in Medical and Natural Sciences, Medical College of Rzeszów University, Poland
[4] Academic Medical Center, University of Amsterdam, Netherlands
[5] Department of Molecular Immunology, Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Ukraine

Background

Citrullination is a normal physiological process which represents conversion of peptidylarginine to peptidylcitrulline catalyzed by peptidylarginine deiminases (PADs). PAD2 and PAD4 are found in hematopoietic cells invading synovial tissue in RA. In Asian population the PADI4 gene that encodes a PAD4 has been associated with susceptibility to RA. To date nothing is known about the regulation of PAD2/4 expression by inflammation. Thus, the study goal was to understand the regulation features of PADI4 gene expression in RA.

Methods

hPADI4 promoter was cloned from HEK293 cells genomic DNA. To perform in vitro analysis of hPADI4 promoter a panel of serial deletion and point mutant constructs was used. Adenoviral constructs were generated to perform assays on undamaged FLS. Luciferase reporter assays were performed to monitor PADI4 promoter activation in NIH-3T3 mouse fibroblasts and hFLS from RA patients upon treatment with proinflammatory cytokines. To study transcription factors that activate PADI4 expression a ChIP assay was performed.

Results

PADI4 mRNA is transiently upregulated in FLS from RA patients upon IL-1β treatment. In silico analysis of PADI4 gene demonstrated that hPADI4 promoter contains NF-κB or c-Rel binding sites that could mediate transcriptional control of PADI4 expression. Thus, hPADI4 gene can be regulated by NF-κB pathway. A serial 5'-deletions gradually increase the activation of the hPADI4 promoter in NIH-3T3 mouse fibroblasts that is in a strong conflict with analysis of PADI4 mRNA expression upon proinflammatory stimulation of primary FLS derived from RA patients. Moreover ChIP assay demonstrated that RA-associated gene C-Rel bound to hPADI4 promoter in human FLS upon their stimulation with proinflammatory cytokines.

Conclusions

Proinflammatory cytokines stimulated activation of PADI4 expression in FLS might be cell-type specific and possibly contributes to RA pathology. Therefore, a detailed investigation of regulation of PADI4 expression in FLS can provide an important insight into understanding of RA pathophysiology.

Figure & Table

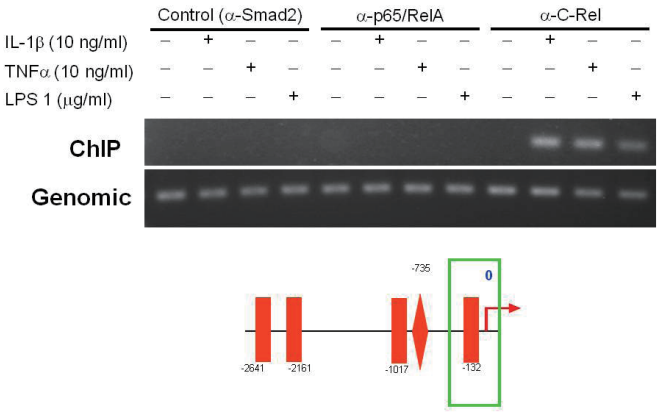

Figure. C-Rel is bound to hPADI4 promoter upon NF-κB activation

Keywords

Rheumatoid Arthritis, Fibroblast-like Synoviocytes, Citrullination

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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IO-15

Effect of disease-modifying anti-rheumatic drugs on lung microenvironment of SKG mice

Sung Hae Chang[1,2], Jeong Seok Lee[3,4], Jeongjun Choe[5], Seon Uk Kim[6,7], Jeong Yeon Kim[4,6], Eun Young Lee[6,7]

[1] Department of Internal Medicine, Division of Rheumatology, Soonchunhyang University College of Medicine, Republic of Korea
[2] Department of Internal Medicine, Division of Rheumatology, Soonchunhyang University College of Medicine, Cheonan Hospital, Republic of Korea
[3] Graduate school of Medical Science and Engineering, Korea Advanced Institute of Science and Technology, KAIST, Republic of Korea
[4] Department of Multiomics, GENOME INSIGHT Techonologies, Republic of Korea
[5] Department of Health Science and Technology, SAIHST, Sungkyunkwan University, Republic of Korea
[6] Laboratory of Autoimmunity, Seoul National University Cancer Research Institute, Republic of Korea
[7] Department of Internal Medicine, Division of Rheumatology, Seoul National University College of Medicine, Republic of Korea

Background

Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is one of the pivotal extrapulmonary conditions. However, the pathophysiology of RA-ILD, including the effect of disease-modifying anti-rheumatoid drugs (DMARDs) is largely unknown. To study the effect of methotrexate and TNFα inhibitor on lung microenvironment of SKG mice using single-nucleus RNA sequencing.

Methods

Male SKG mice of eight to ten weeks received a single intraperitoneal zymosan A (ZyA) injection to induce arthritis and pneumonitis. We gave them twice-weekly intraperitoneal injections of PBS, methotrexate (7.5 mg/kg; MilliporeSigma), or TNFα inhibitor (100 μg/kg; R&D Systems, Inc., Minneapolis, MN, USA). Nuclei were prepared from frozen lung tissue under ribonuclease-free conditions by a method adapted from an existing protocol.

Results

Macroscopically, pneumonitis was most evident in SKG mice with ZyA and methotrexate treatment. A total of 59,860 nuclei were obtained from sixteen mice, four mice from each of the four groups. We classified each cell type using previous reports on the single-nucleus cells of mouse lungs. The most frequently observed cell was the type 2 alveolar (AT2) cell among all four groups. Alveolar epithelial cells were further subclustered into six clusters. Cluster 2 highly expressed type 1 alveolar (AT1) cell marker genes. Interestingly, a distinct cluster 3 was observed after methotrexate treatment. This distinctive alveolar epithelial cell cluster (cluster 3) showed IL-1, TNF, IFNα, and IFNγ perturbation-response signatures using Library of Integrated Network-Based Cellular Signatures (LINCS) 1000 ligand perturbation analysis. In addition, enrichment analysis revealed that cluster 3, as well as cluster 2 (i.e., AT1 cells) significantly enriched genes of BMI1 knockout mice that fail to self-renew their lung cells after damage.

Conclusions

The current study shows that methotrexate exacerbates lung inflammation via attenuation of the regenerative potential of AT2 cells.

Keywords

rheumatoid arthritis-associated interstitial lung disease, single nucleus RNA sequencing, SKG mouse

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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IO-16

Peptoniphilus gorbachii ameliorates collagen-induced arthritis in mice by improving intestinal homeostasis and immune regulation

Young Sun Suh[1], Sung Hak Chun[2], Seong-Tshool Hong[3], Hanna Lee[2], Mingyo Kim[2], Yun-Hong Cheon[2], Hyun-Ok Kim[1], Suhee Kim[2], Sang-Il Lee[2]

[1] Internal Medicine, College of Medicine, Gyeongsang National University and Changwon Hospital, Changwon, Republic of Korea
[2] Internal Medicine, College of Medicine, Gyeongsang National University and Hospital, Jinju, Republic of Korea
[3] Biomedical Sciences and Institute for Medical Science, Chonbuk National University Medical School, Jeonju, Republic of Korea

Background

Although numerous studies demonstrated altered microbiome in rheumatoid arthritis (RA), there is still a lack of information about the RA-specific microbial species. Recent studies reported that specific microbial species and derived molecules in the blood reflect systemic pathological events. Thus, the aim of this study was to identify RA-related microbial species in the serum of RA patients and explore the therapeutic effect and mechanism of candidate microbial species.

Methods

Serum antibody microarray for 384 microbial species was performed from RA patients (n=81) and healthy control (n=50). We verified the therapeutic effect and mechanism of the candidate microbial species by evaluating arthritis severity, immune response, intestinal barrier integrity, and fecal microbiota using collagen-induced arthritis (CIA) mice.

Results

Total 36 microbial species were altered in the serum of RA patients with increased 15 and decreased 21 microbial species compared to controls. Of reduced microbial species, Peptoniphilus gorbachii (PG) was inversely correlated with RA disease activity and produced acetate and butyrate in culture. The administration of PG suppressed arthritis in CIA mice by reducing inflammatory monocytes in mesenteric and inguinal lymph nodes. Moreover, PG supplementation restored intestinal barrier integrity with a decreased level of serum zonulin and increased expression of intestinal tight junction (Zo-1 and Ocln). Fecal microbiota abundant in PG-treated mice was correlated with improved intestinal barrier integrity and decreased inflammatory reaction.

Conclusions

This study provided serum microbial species associated with RA and suggested the therapeutic effect of PG through restoring the intestinal barrier function and suppressing the immune response against RA.

Keywords

Rheumatoid arthritis, Peptoniphilus gorbachii, Serum microbial species

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

IO-17

The immune mechanism of Janus kinase inhibitors on Shingles in rheumatoid arthritis patients

Hong Ki Min[1], Ji-Yeon Lee[2], Se Hee Kim[1], Hae-Rim Kim[2], Sang-Heon Lee[2]

[1] Rheumatology, Konkuk University Medical Center, Republic of Korea
[2] Rheumatology, Research Institute of Medical Science, Konkuk University School of Medicine, Republic of Korea

Background

Incidence of shingles is increased in rheumatoid arthritis (RA) patients than healthy control (HC), and this is especially increased in RA patients with janus kinase inhibitor (JAKi) use. We aimed to investigate immune response of JAKi in aspect of CD4+/CD8+ T cells, cytokines production, and regulation of transcriptional factors in RA patients, then compared these with HC.

Methods

Peripheral blood mononuclear cells (PBMCs) were obtained from RA patients and HCs. Varicella zoster virus lysates (5 μg/ml) was pre-stimulated with PBMCs for 24hrs, then three JAKi (ruxolitinib 10/20 μM [JAK1/2 inhibitor], AG490 20/40 μM [JAK2 inhibitor], WHI-P154 125/250 μM [JAK3 inhibitor]) + methotrexate (10 nM) were administrated in vitro. Population of CD4+IFN-γ+, CD4+CD69+IFN-γ+, CD8+IFN-γ+, CD8+CD69+IFN-γ+, CD4+CD25highFoxp3+ cells were measured by flow cytometry. Cytokines levels of culture media were evaluated by ELISA. Last, the transcriptional factors were measured by RT-qPCR.

Results

Experiments were conducted in a total 14 RA patients and 7 HCs. The decrease CD4+IFN-γ+, CD4+CD69+IFN-γ+, CD8+IFN-γ+, CD8+CD69+IFN-γ cells and increase of CD4+CD25highFoxp3+ cells by three JAKi were observed in both RA patients and HCs, and the amount of changes were similar between RA group and HC group. In ELISA, the expression levels of IFN-γ and granzyme B were decreased by JAKi dose-dependently. The mRNA levels of STAT1 and Tbet decreased, however, STAT5 and Foxp3 increased by JAKi. Addition of methotrexate did not significantly altered population of T cells, levels of IFN-γ and granzyme B, and expression levels of transcriptional factors.

Conclusions

The present study showed immune regulatory effects of JAKi toward decreasing Th1/cytotoxic T cell response, and increasing Treg response. However, these were not only presented in RA patients driven cells, but also in HCs driven cells. These imply that virulent factor or memory T cell function may be more important on explanation of increased Shingle risk in RA patients than HCs.

Keywords

rheumatoid arthritis, Shingles, janus kinase inhibitor

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

IO-18

Identification of the HLA-B*51:01 immunopeptidome in Behçet's disease

Ye-Ji Lee[1], Kyung-Cho Cho[2], So Hyun Kim[2], Byung Kyu Cho[2], Eugene C. Yi[2], Eun Bong Lee[1,2]

[1] Internal Medicine, Seoul National University College of Medicine, Republic of Korea
[2] Molecular Medicine and Biopharmaceutical Sciences, Seoul National University, Republic of Korea

Background

Immunopeptidomes are peptides, bound to human leukocyte antigens (HLA), that play a key role in immune responses. HLA-B*51:01 is an HLA allele associated with Behçet's disease (BD)[1]. However, the characteristics and the role of HLA-B*51:01 immunopeptidome are not revealed in Behçet's disease.

Methods

HLA-bound peptide profiles were established through analysis of plasma samples from HLA-B*51:01–positive BD patients and HCs. HLA-class I molecules were immunoprecipitated, and liquid chromatography-tandem mass spectrometry (LC-MS/MS) was performed. Then, HLA-B*51:01–binding peptides were assessed in terms of binding affinity using NetMHCpan. Finally, the immunological characteristics of selected peptides were analyzed in BD patients and HCs, using ELISpot, flow cytometry, and dextramer staining.

Results

2,306 peptides were present only in BD patients, while 3,145 peptides were detected only in HCs. Immunopeptidome of BD patients preferentially showed hydrophobic amino acids at amino acid position 2 (Figure 1). Ten peptides were selected which were confirmed to be preferentially expressed in BD patients compared with HCs. When bound to HLA-B*51:01 in monocyte-derived dendritic cells (Mo-DCs) or peripheral blood mononuclear cells, these peptides activated T cells and induced surface expression of CD69 and CD107α, as well as the secretion of inflammatory cytokines such as interferon (IFN)-γ and tumor necrosis factor (TNF)-α.

Conclusions

HLA-B*51:01 immunopeptidome can play a critical role in the development of BD by activating T cells and inducing the secretion of inflammatory cytokines.

Figure & Table

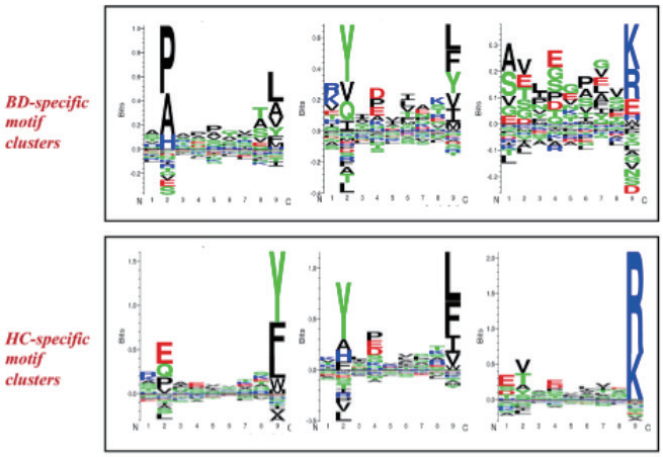

Figure. Venn diagram of the identified 8–13-mer peptides and graphs showing the motif clusters.

Keywords

Immunopeptidome, Behçet's disease, Proinflammatory cytokines

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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May 19(Thu) - 21(Sat), 2022

IO-19

Inhibition of NADPH oxidases prevent the development of osteoarthritis

Jin Han[1], Seungwoo Han[2]

[1] Laboratory for Arthritis and Cartilage Biology, Kyungpook National University, Republic of Korea
[2] Departments of Internal Medicine, School of Medicine, Kyungpook National University, Republic of Korea

Background

Increased oxidative stress in osteoarthritic (OA) cartilage mediates catabolic signal transduction leading to extracellular matrix degradation and chondrocyte apoptosis. This study aimed to explore the contribution of NADPH oxidase (NOX), a major source of cellular reactive oxygen species (ROS), to the catabolic process of chondrocytes and to OA.

Methods

Primary chondrocytes were obtained from E15.5 C57BL/6 mouse long bones. Interleukin (IL)-1β (10 ng/mL) was applied to recapitulate the catabolic stress mimicking OA conditions, and the function of NOX isoforms was inhibited with a pan-NOX inhibitor (APX-115). Surgical OA was induced in 12-week-old male C57BL/6 mice by destabilization of the medial meniscus (DMM), and 60 mg/kg APX-115 was intraperitoneally injected twice a week. NOX-induced changes in chondrocyte metabolism were analyzed using the Seahorse XF Extracellular Flux Analyzer.

Results

The inhibition of NOX isoforms with APX-115 significantly decreased IL-1β-induced ROS production in chondrocytes and most potently suppressed the expression of oxidative stress marker genes and catabolic proteases compared with the inhibition of other ROS sources. Catabolic stimuli by IL-1β-treatment and in post-traumatic OA conditions upregulated the expression of NOX2 and NOX4 in chondrocytes. In the post-traumatic OA model, the pharmacologic inhibition of NOX protected mice against OA by modulating oxidative stress and the expression of MMP-13 and Adamts5 in chondrocytes. Mechanistically, NOX inhibition suppresses p38, JNK, and NF-kB signaling and restores oxidative phosphorylation in IL-1β-treated chondrocytes.

Conclusions

NOX inhibition prevented the development of OA by attenuating catabolic signaling and restoring mitochondrial metabolism, and can thus be a promising class of drug for OA.

Keywords

Osteoarthritis, NADPH oxidase, Oxidative stress

Workshop

Clinical Research Workshop for Rheumatologists: Planning and Conducting Clinical Research

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

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Setting up a prospective cohort

Sang-Cheol Bae
Hanyang Univ., Korea

This talk will briefly summarize the concept of clinical research and the study design for clinical research. And then the practical issues of setting up a prospective cohort study will be discussed with the examples of cohorts of rheumatoid arthritis and systemic lupus erythematosus which I and my colleagues have established: 1) Getting started: Objectives, Planning choosing study subjects and data collection, Sample size and Power calculation, IRB issue, 2) Data collection period with quality control, 3) Data cleaning period, 4) Data analysis period, 5) Dissemination period. For setting up a prospective cohort well, a better coordination among patients, clinicians, clinical researchers is required.

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Conducting a retrospective clinical study using Korea National Health Insurance data

Hyun Jung Kim
Korea Univ., Korea

Medical researches are increasingly conducted using large data sets based on routinely collected administration data and patient's health care institution utilization data. While these data are collected primarily for health insurance reimbursement and healthcare administration, the nature and scale of the data make them potentially exciting resources for research.

In Korea, such large databases that are managed by the National Health Insurance Service (NHIS). The NHIS database of South Korea is a repository of claims data collected in the process of reimbursing healthcare providers. Under the universal coverage system, having fee-for-services covering all citizens in South Korea, the NHIS database contains comprehensive information pertaining to healthcare services such as treatments, pharmaceuticals, procedures, and diagnoses for almost 50 million beneficiaries. The NHIS database includes data on all children, regardless of presence of disability.

The National Health Screening Program NHSP is a screening program which offers all beneficiaries biannual health checkups that include lifestyle habits and metabolic profile, which are recorded in the database. The NHSP questionnaire contains questions on drinking status, other lifestyle characteristics of each study participant, including body mass index (BMI), blood pressure, fasting blood glucose and cholesterol levels.

National Health Screening Program for Infants and Children (NHSIC) database records screening data of the growth and development of all children. The Korean government launched the NHSIC program in November 2007 as a population surveillance system, While the NHSIC screening is not mandatory but optional, children can participate in the NHSIC program up to maximal 7 times, from the age of 4–71 months. Physicians conduct anthropometric measurements as well as history taking, physical examination, screening for visual acuity, and health education. The NHSIC database and the NHIS database are linked using a personal identifier number.

The advantages of these database include large sample size, population coverage and heterogeneity, which allow researchers to reflect the "real world" practice Moreover, data are usually available for quite long periods, allowing trend analysis. Other advantages are the absence of additional costs for gathering data, long observation periods, and the possibility of linking different databases that contain information on the patient.

The disadvantages include the variable quality of collected data, which will be discussed in the following section, and the absence of specific information of interest for clinical research.

In using coded in these data, validation of coding accuracy is key. This is important for both the methodologic evaluation of articles. Other disadvantages are the difficulties in drawing causal conclusions due to the presence of bias or confounding and the misclassification bias.

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How to start IITs from scratch

Howard Lee
Seoul Nat'l Univ., Korea

An IIT, also known as an investigator-initiated study (IIS) or research (IIR), is a clinical trial, where the investigator has to play a dual-role, i.e., as an investigator and sponsor. This is why an investigator in any IIT is frequently referred to as a sponsor-investigator. He/she has to conceive the research idea, to develop the protocol, to conduct the trial, to oversight the research team and to provide it with required resources, and to be responsible for the regulatory mandates. Therefore, the obligations and work amounts of a sponsor-investigator in any IIT are huge, preventing many want-to-be sponsor-investigators from starting an IIT on their own. However, the importance of IITs cannot be underestimated because they are truly narrowing the difference between sponsor-initiated trials and day-to-day, real-world clinical practices. In addition, IITs may demonstrate how efficiently participating investigators, institutions, and organizations collaborate, commit, and manage to attain a set of overarching research objectives.

The presenter has introduced the concept and utilities of the microdosing and microtracing study in new drug development since 2014. As of today, the presenter has completed a total of five microdosing/microtracing studies with 2 more studies under plan, four of which were IITs. In this presentation, the presenter will share his experiences in starting an IIT from scratch as to what obstacles he had to overcome and how.

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e-CRF tools for Investigator Initiated Trial

Soo-Hwan Kim
Dt&CRO, Korea

Clinical trial management that includes specified software systems and processes can help to produce timely and efficient project outcomes. Specially, clinical data management is one of the most critical functions in overall clinical trial management.

Clinical trial data management activities include that CRF design, annotation, tracking / DB design, build, and testing / Data collecting and entry including lab data / Query generation / Medical Coding / DB locking / Data extraction and transmission / Data archiving. Every data management procedure should be limited based on the assigned roles and responsibilities of the users. All study members have different levels of access to the software (or system), as designated in the protocol or delegation. Data management steps also ensure there is an audit trail and the users can only access their respective required functions without the ability to make other changes.

Some of data management processes in IIT will necessarily be from paper forms filled out by the patient or investigators on their behalf. Instead of paper, some activities may use devices or software to fill out this direct-entry data electronically. If investigators use electronic systems, they can easily confirm data and track data changing history. However, it is not easy to use an electronic system because most of investigators do not have enough time to set-up system or their own staffs for data management.

In this session, we will be familiar with what data management is and find an easy way to management clinical data.

Workshop

Editorial Committee Workshop

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Suggestions to be indexed in SCIE and get high impact factor

Hyun Jun Park
Pusan Nat'l Univ., Korea

In order to evaluate the excellence of a medical journal, the most important measure is how high-quality research papers are published. All medical journals want their published papers to be widely exposed to readers and also to be cited as material for new research. This increases the value of journals and improves their reputation. In order for papers to be widely exposed and cited, the journal must be listed in a reputable database. Currently, the world-recognized database is Science Citation Index Expanded (SCIE), a Web of Science core collection managed by Clarivate, and Scopus, operated by ELSEVIER. Among them, SCIE is the more well-known and highly trusted. Being indexed in the SCIE means that the journal has been recognized for its academic value worldwide. Among the many conditions for inclusion in the SCIE, the most important is the impact factor of the journal. In this lecture, I am going to cover the factors necessary to be indexed in the SCIE and how to increase the impact factor.

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Successful submission strategy on SCI journal

Hwichool Kim
Editage, Korea

We would like to learn about successful submission strategies on sci(e) journal. Specifically, we focus on author order, title expression, keywords selection, importance of abstract, method of reviewing, importance of flowchart in research method, result expression, logical process for results and the most common mistakes when writing medical research papers etc.

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Biostatistics for clinical researchers

Hyonggin An
Korea Univ., Korea

In this talk, I would like to review statistical considerations in clinical articles. These include study design, sample size, statistical analysis, presentation of results, and common statistical errors in clinical articles.

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New PubMed: Searching tips & more!

Sung Ae Park
Korea Univ. Medical Library, Korea

This lecture is about the concept of PubMed and offers searching principles, rules, and some helpful tips for using PubMed. Understanding the information about PubMed will help you find out the research papers efficiently.

PubMed is the most famous free searching engine in the field of bioscience and biomedical science, which is made and managed by the National Library of Medicine(NLM) of the National Institutes of Health(NIH). Medline database including Old Medline(1946-1966) contains citations and abstracts of 5,281 journals in 40 different languages. Also, you can use the full text of journals archived in PubMed Central(PMC) and the books kept in NLM for free.

The biggest feature of PubMed is to index research papers using a medical thesaurus named MeSH. PubMed's Automatic Term Mapping (ATM) is also related to this. The lecture will help you understand the search principles of PubMed and learn how search results can vary by different ways of searching on the same topic, including keyword(natural language) search, field tag search, MeSH search, and a combination of MeSH and keyword search. Consequently, you will be able to plan your search strategy by using proper keywords and making searching formula based on the information in the lecture.

Finally, the lecture will offer some useful abilities of PubMed: Filters that can limit search results, Clinical Queries that can look up clinical papers efficiently, and My NCBI, which allows you to receive customized services using your account.

Hope this lecture helps you choose your search methods and find out the valuable papers you want.

KCR 2022

42nd Korean College of Rheumatology Annual Scientific Meeting and the 16th International Symposium

May 19(Thu) - 21(Sat), 2022

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DAY 02

PROGRAM

May 20(Fri)

Breakfast Symposium I
AbbVie

Strategies to Solve the Problem of Rheumatoid Arthritis with AbbVie's Assets

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Management of rheumatoid arthritis considering safety

Ki-Jo Kim
The Catholic Univ. of Korea, Korea

Safety of medication is one of the most important issues in the management of rheumatoid arthritis. 2019 EULAR guideline recommended that treatment decisions are based on not only disease activity but also safety issues and other patient factors, such as comorbidities. And safety issue of tofacitinib was mentioned in ACR guideline updated in 2021.

Recent JAK inhibitor safety issues were started by press release of Pfizer in Jan 2021 about ORAL Surveillance which is the post marketing long-term safety study comparing major adverse cardiovascular events (MACE) and malignancies excluding nonmelanoma skin cancer (NMSC) between tofacitinib and TNF inhibitors; adalimumab and etanercept. The results of ORAL surveillance were published in NEJM Jan 2022. In this article, it was reported that MACE and cancers occurred more often with tofacitinib than with a TNF inhibitor in patients with rheumatoid arthritis who were 50 years of age or older and had at least one additional cardiovascular risk factor. However, the higher hazard ratio of MACE and malignancies excluding NMSC in North Americans and patients aged 65 years or older suggests that there may be limitations in the study design of this study.

TNF inhibitors were used as a control in ORAL Surveillance to demonstrate tofacitinib's non-inferiority in the risk of MACE and malignancies. This might be due to the proven safety profile of TNF inhibitors in MACE and malignancies. Patients with rheumatic and musculoskeletal diseases (RMD) including rheumatoid arthritis (RA) have higher risk of atherosclerosis and malignances versus general population. In contrast to other non-TNF inhibitors, it was already well reported that the use of TNF inhibitor was associated with a decreased risk of MACE in patients with RMDs including RA. And the long-term safety of adalimumab in malignancies was reported to be similar to that of the normal population.

Considering recently published data and selectivity for Janus kinases (JAK), it seems that all JAK inhibitors may not be more dangerous than TNF inhibitors in MACE and malignancies. Upadacitinib is a selective and reversible JAK inhibitor engineered by AbbVie, which showed 40~190 times higher JAK1 selectivity other than JAK2, JAK3 or TYK2. The safety profile of upadacitinib has been established across six clinical trials for RA indication with over 7,000 patient-years of exposure. The risk of MACE, venous thromboembolism (VTE), and malignances excluding NMSC of upadacitinib were similar to that of adalimumab in the integrated safety analysis up to 4.5 years exposure. In SELECT-COMPARE, the safety profile of upadacitinib 15mg was generally comparable to adalimumab for adverse events of special interest, including MACE, VTE, malignancies, and deaths through 3 years. Also, upadacitinib continued to demonstrate consistently better clinical responses compared with adalimumab including remission rates, physical function, and pain severity through 3 years. In conclusion, upadacitinib 15mg can be the one of the reasonable options for inadequate responder to methotrexate based on its favorable benefit-risk profile for RA patients.

Breakfast Symposium II
Celltrion

Real-world Switching Case of CT-P17

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Clinical data and real-world switching case of CT-P17

Hubert Marotte
Centre Hospitalier Universitaire (CHU) de Saint-Étienne, INSERM, 1059, Saint-Étienne, France

Adalimumab is an anti-TNF monoclonal antibody that effectively improves rheumatoid arthritis (RA). Biosimilars are highly similar to their reference products in terms of quality characteristics, biological activity, safety, and efficacy. Since 2016, several adalimumab biosimilars have been licensed by the EMA and the US FDA. European League Against Rheumatism (EULAR) recommendations for the treatment of RA position biosimilar DMARDs (bsDMARDs) equivalently to their reference products in treatment algorithms, and suggest that lower-priced biosimilars are preferred for their potential to reduce healthcare expenditures. CT-P17 is administered at 100 mg/mL, reflecting the high-concentration, low volume formulation of reference adalimumab, and is also citrate and latex free, which could reduce discomfort during injection. In addition, CT-P17 can be stored at ambient temperature (<25°C) up to 30 days which is more convenient for patients in case of vacation for example. In this talk, I am going to briefly introduce the pivotal study (phase III) of CT-P17 and review the features of CT-P17. In addition, I am also going to share several real-world switching cases from reference adalimumab to CT-P17.

Breakfast Symposium III
Pfizer

Real-World Perspectives of Ankylosing Spondylitis Management

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Insights from real-world: Practical approach to anti TNF therapy for AS treatment

Jun Won Park
Seoul Nat'l Univ., Korea

Keynote Lecture

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Current threats to the specialty of rheumatology in the US and internationally: A call to action

Kenneth Saag
The Univ. of Alabama at Birmingham, USA

The Covid pandemic has highlighted many challenges to the field of rheumatology but it has also created some unique opportunities for our collective growth. Covid has created a sense of new-found vulnerability that has shaped the way many rheumatologists see their day to day activities and many have re-evaluated their work-life balance. It has had profound impact on our daily clinical operations, created new telehealth opportunities and promoted "hybrid" work for some in the clinical research community and those doing departmental and organizational administration. Some doctors have begun to feel more "burned out" and there is a heightened recognition in many geographical areas about the need for more health care providers addressing rheumatic and musculoskeletal disorders. In particular, we are seeing shortages in trainees pursuing careers in clinical and fundamental science, which threatens the future of our specialty. Enhanced training opportunities and funding for early stage investigators offer hope to maintain this critical element of our workforce. Our specialty organizations are under special strain as the typical sources of their support are also challenged by pandemic-related issues. Creative new sources of revenue will assure their continued ability to support our profession. The ACR, through its new strategic plan, fully embraces the opportunity to build international collaborations around research, teaching and patient care. Underlying all these concerns is a recognition of greater medical mistrust, fueled by the pandemic and social media. We must do everything we can to exercise our cautious authority as experts in our disease and trusted counselors to our patients with whom we have long-standing relationships.

International Symposium

Recent Advances in Pathogenesis of Systemic Lupus Erythematosus

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New concepts on the pathogenesis of lupus nephritis

George Tsokos
Harvard Medical School, Beth Israel Deaconess Medical Center, USA

Lupus nephritis (LN) is common in people with systemic lupus erythematosus (SLE) and is invariably linked to high morbidity and mortality. We still lack reliable disease biomarkers and the golden diagnostic tool, kidney biopsy, is not easily repeatable and not without risks. Treatment still relies on the use of immunosuppressive and cytotoxic drugs while the newly approved Benslysta and Voclosporin may offer minimal advantage. While trying to understand why T cells from patients with SLE do not produce interleukin (IL)-2 while the produce excessive amounts of IL-17 we discovered that a serine/threonine kinase, calcium/calmodulin kinase 4 (CaMK4) shuts off the IL-2 locus while it opens the IL-17 locus. Subsequently we found that podocytes, mesangial cells and tubular epithelial cells in people and mice with lupus display increased amounts of CaMK4 and that this accounts for the malfunction of these cells. We found that IgG from patients with LN is abnormally glycosylated and after entering podocytes to suppress proteins responsible for the function and structure of podocytes. CaMK4 overexpression in mesangial cells was found to cause increased proliferation. In parallel we discovered that in mice and people with SLE that besides mesangial cells, podocytes and tubular epithelial cells express increased levels of IL-23 receptor. IL-23, which is increased in lupus, causes podocyte malfunction, whereas in tubular epithelial cells suppresses the levels of arginase 1 which leads to abundance of arginine in the surrounding microenvironment and lymphocyte proliferation in the tubulointerstitial space. Genetic deficiency of CaMK4 in podocytes or in tubular epithelial cells suppresses LN and more importantly, cell-targeted delivery of a CamK4 inhibitor to podocytes or tubular epithelial cells suppresses LN thus offering great therapeutic opportunities. In parallel we have developed two novel approaches of liquid kidney biopsy to replace needle kidney biopsy. In the first, we find that CaMK4 expression is increased only in podocytes from people with LN whereas in the second, only IgG from people with active LN can upregulate CaMK4 in cultured podocytes. In summary, our work offers new insights in the interface between the autoimmune response and kidney resident cells through which kidney damage is eventually executed and two novel liquid kidney approaches.

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New insights into the role of antinuclear antibodies in systemic lupus erythematosus

Peter E. Lipsky
AMPEL BioSolutions, USA

Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease characterized by antinuclear antibodies (ANAs) that form immune complexes and mediate disease pathogenesis by tissue deposition or cytokine induction. Some ANAs bind DNA or associated nucleosome proteins, whereas others bind protein components of complexes of RNA and RNA binding proteins (RBPs).

Levels of anti-DNA antibodies can fluctuate widely, unlike those of anti-RBP antibodies, which tend to be stable. Because anti-DNA antibody levels can reflect disease activity, repeat testing is common; by contrast, a single anti-RBP antibody determination is classically thought to suffice for clinical purposes.

Of the mechanisms for the generation of tissue lesions in SLE, the formation and deposition of immune complexes in the kidney has received the most investigative interest. DNA and anti-DNA antibodies can form immune complexes that localize to the kidney, where complement is activated. Immune complexes and their components (such as immunoglobulins and complement) have been demonstrated in the kidney of lupus nephritis by light, electron and immunofluorescence microscopy. Increased anti-DNA antibody levels and decreased amounts of complement component proteins C3 and C4 during active disease also support a pathogenic role for immune complexes. As immune complex formation and deposition can take place over time and precede clinical events, concentrations of immunoreactants might not be raised at the time of patient presentation. Indeed, autoantibody levels might be reduced because of tissue deposition.

In the pathogenesis of nephritis, cytokines released by cells, such as monocytes and macrophages, can promote inflammation. In addition to inducing complement activation in the kidney, immune complexes can induce the production of pro-inflammatory cytokines, most notably type I interferon. Anti-DNA antibodies can bind to DNA and effectively be internalized into innate immune cells, most prominently plasmacytoid dendritic cells. Once inside the cell, DNA can interact with the endosomal Toll-like receptor (TLR), TLR9, as well as with other nucleic acid sensors in the cytoplasm. These sensors can either access DNA following its uptake as part of an immune complex, or they can respond to DNA that is aberrantly present in the cell as a result of infection by intracellular organisms, mitochondrial release of DNA from stressed or damaged mitochondria, or the formation of micronuclei in response to genotoxic agents or chromosomal instability. Thus, nucleic acid sensors represent a type of internal host defence system, for which DNA in immune complexes is just one potential trigger.

Of these sensors, the cyclic GMP-AMP synthase (cGAS)–stimulator of interferon genes (STING) system mediates the production of type I interferon and other cytokines. Once bound by DNA, cGAS catalyzes the formation of cyclic GMP-AMP that binds to STING. The outcome of these interactions is the stimulation of type I interferon production and its downstream effects. This stimulation only occurs with certain anti-DNA antibodies; however, the properties of the antibodies that enable the formation of immune complexes that can stimulate type I interferon production are not known. Furthermore, it is not clear whether the DNA–anti-DNA immune complexes that are deposited in the kidney can induce cytokine production by plasmacytoid dendritic cells.

Although initial studies on cytokine induction by immune complexes implicated anti-DNA antibodies as an important factor, subsequent research has shown that immune complexes with anti-RBP antibodies can stimulate type I interferon production and appear to be the main promoters of this pathway. The differing results of these studies probably reflects the demographics of the patient populations studied, as there is increased expression of anti-RBP antibodies in patients with African ancestry. In this mechanism, immune complexes containing RNA are ingested by phagocytes, after which the cargo interacts with internal RNA sensors in the endosome (such as TLR3 and TLR7) or in the cytoplasm. In addition, cytoplasmic sensors of RNA, including the retinoic acid-inducible gene 1 (RIG-I) and melanoma differentiation-associated protein 5 (MDA5) pathways, can lead to the production of type I interferon when stimulated by RNA that has entered cells in the form of immune complexes with anti-RBP antibodies. Studies suggest that anti-RBP antibodies of all known specificities can form immune complexes that have immunostimulatory activity; however, it is possible that, depending on the immunochemical properties of autoantibodies such as fine specificity or avidity, only certain anti-RBP antibodies can induce these responses.

Notably, although signalling via TLR7 and TLR9 superficially seems similar, the induction of proinflammatory cytokines and pathological outcomes can be quite different. In mouse models of SLE, TLR7 engagement seems to exacerbate disease, whereas TLR9 engagement seems to suppress disease; nevertheless, both TLR7 and TLR9 can bias the production of autoantibodies that recognize RNA and DNA, respectively. The differences in clinical and serological outcomes following TLR7 and TLR9 engagement likely reflect the various effects of TLR stimulation during cellular development and activation.

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ETV5 promotes Tfh cell differentiation and the pathogenesis of systemic lupus erythematosus

Yoontae Lee
POSTECH, Korea

Follicular helper T (Tfh) cells induce germinal center response to produce high affinity antibodies against a specific pathogen. Excessive formation of Tfh cells is closely associated with the onset of antibody-mediated systemic autoimmune diseases, such as systemic lupus erythematosus (SLE). Our previous study has shown that ETV5 promotes murine Tfh cell differentiation. However, its role in human Tfh cell differentiation and the pathogenesis of SLE has not been investigated. In this study, we show that ETV5 is a transcription factor that promotes the pathogenesis of lupus autoimmune disease via enhancing Tfh cell differentiation. ETV5 deficiency in T cells substantially suppresses autoimmunity in lupus mouse models. Tfh cells have higher levels of ETV5 than non-Tfh cells in humans as well as mice. ETV5 overexpression also promotes human Tfh cell differentiation. Furthermore, ETV5 levels are significantly higher in CD4 T cells from SLE patients than in those from healthy control, suggesting that ETV5 may be an SLE-promoting factor. We are currently investigating the molecular mechanism of how ETV5 promotes Tfh cell differentiation.

Free Paper Session

Epidemiology
& Health Services Research

KCR 2022 May 19(Thu) - 21(Sat), 2022
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Vol. 29, Suppl. 1, May, 2022
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O-01

Safety and clinical influences of COVID-19 vaccination in patients with autoimmune rheumatic diseases

Youngjae Park[1], Hanna Park[1], Minae Oh[1], Jung Gon Kim[1], Se Gwang Jang[2], Howook Jeon[3], Jennifer Jooha Lee[1], Su-Jin Moon[3], Seung-Ki Kwok[1]

[1] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's hospital, The Catholic University of Korea, Republic of Korea
[2] The Rheumatism Research Center, Catholic Research Institute of Medical Science, The Catholic University of Korea, Republic of Korea
[3] Division of Rheumatology, Department of Internal Medicine, Uijeongbu St Mary's Hospital, The Catholic University of Korea, Republic of Korea

Background

Since the beginning of COVID-19 pandemic, various types of vaccines against SAR-CoV-2 have been introduced. Although these vaccines demonstrated efficacy in clinical trials involving healthy populations, information on their safety and clinical impacts on disease activities in patients with autoimmune rheumatic diseases (ARDs) is still limited. In this multi-centered observational study, we aimed to evaluate safety profiles and clinical influences of COVID-19 vaccines in patients with various ARDs.

Methods

Between July 2021 and December 2021, 494 ARD patients who completed COVID-19 vaccinations were enrolled from two university-affiliated hospitals for the present study. Data on adverse events related to COVID-19 vaccinations and indices representing disease activities for each ARD were collected. In addition, immunogenicity in ARD patients was measured using a commercialized kit for SARS-CoV-2 neutralizing antibody.

Results

Until February 2022, 278 ARD patients completed evaluations. Targeted patients included 129 rheumatoid arthritis (RA), 55 ankylosing spondylitis (AS), 47 systemic lupus erythematosus (SLE), 38 Sjogren's syndrome, and 9 systemic sclerosis patients. Median ages and disease durations were 52 years and 71 months, respectively. There was no case of severe adverse events requiring medical interventions. Incidence rate of adverse events at the first and the second dose of vaccines were similar. Most frequent local events were pain (18%) and tenderness (4%) at the site of injection while fatigue (11%) and headache (9%) were most frequent among systemic reactions. Seven cases (5%) of disease flares were observed in RA patients after vaccinations while 4 cases (7%) in AS and 1 case (2%) in SLE patients, respectively. About 97% of ARD patients acquired immunogenicity after complete COVID-19 vaccinations. Remaining 3% of patients who failed to acquire immunogenicity included 4 RA, 2 AS, and 2 SLE patients.

Conclusions

The COVID-19 vaccination is safe and effective, and rarely results in disease flares in patients with ARDs.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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May 19(Thu) - 21(Sat), 2022

O-02

Autoantibody profiles in patients with COVID-19 infection

Hyemin Jeong[1], Chan Hong Jeon[1]

[1] Internal Medicine, Soonchunhyang University Hospital, Bucheon, Republic of Korea

Background

Triggering of autoimmunity by severe COVID-19 infection has been proposed. However, there is insufficient data on the profiles of autoantibodies. The aim of this study was to evaluate positivity of autoimmune serologic markers in patients with COVID-19 infection and to analyze the association between autoantibody positivity and the prognosis of COVID-19 infection.

Methods

We retrospectively collected 80 consecutive patients who referred to Soonchunhyang university hospital for COVID-19 infection. All patients were tested for presence of antinuclear antibody (ANA), rheumatoid factor (RF), anti-citrullinated peptide antibody (ACPA), and anti-cytoplasmic neutrophil antibody (ANCA). Laboratory data, comorbidities, and outcomes were collected.

Results

Mean age was 67.4 ± 14.0 years and 35 (43.8%) patients were women. Thirty-one (38.8%) patients tested positive for ANA, 16 (20%) patients were positive for RF, and 2 (2.5%) patients were positive for ACPA. ANCA was negative in all patients. Connective tissue disease was not present nearly all patients except one patient with rheumatoid arthritis. Hypertension was (52.5%) was most common comorbidity, followed by diabetes (38.8%). Forty-four (55.5%) patients were required care in the intensive care unit (ICU) and 34 (42.5%) patients underwent intubation. Fifteen (18.8%) patients were expired due to severe respiratory failure. Patients who were positive for RF showed significantly higher rates of intubation and death than others (32.4 vs 11.6%, p = 0.026 and 40.0 vs. 16.1%. p = 0.041, respectively). In univariable analysis, RF positivity was associated with mechanical ventilation (OR 3.63. 95% CI 1.12-11.79, p = 0.032), but not in multivariable analysis. In multivariable analysis, D-dimer (OR 1.25, 95% CI 1.01-1.53, p = 0.036) and C-reactive protein (OR 1.13, 95% CI 1.02-1.25, p = 0.015) were associated with mechanical ventilation.

Conclusions

Patients who positive for RF showed poor prognosis in COVID-19 infection. Further study will be required to investigate the association of RF and severe pneumonia in COVID-19 infection.

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

O-03

Association between cardiovascular outcome and rheumatoid arthritis: Nationwide population-based cohort study

Seonyoung Kang[1], Kyung-Do Han[3], Yeonghee Eun[2], Seulkee Lee[1], Hoon-Suk Cha[1], Eun-Mi Koh[1], Jaejoon Lee[1], Hyungjin Kim[4]

[1] Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
[2] Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
[3] Department of Statistics and Actuarial Science, Soongsil University, Seoul, Republic of Korea
[4] Department of Medical Humanities, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Background

Large scale studies which examined the association between characteristic of RA patients and cardiovascular disease (CVD) risk, and studies which adjusted for various confounding factors are lacking. This study aimed to investigate the association between CVD risk and RA in large-scale, nationwide cohort of Korean population.

Methods

We enrolled 136,469 patients with RA who participated in national health examinations within 2 years of RA diagnosis between 2010 and 2017 and non-RA controls matched by age and sex (n= 682,345). The cohort was followed until the end of 2019 . The outcome was occurrence of myocardial infarction (MI) or stroke. The Cox proportional hazard model and Kaplan Meier curve were used for the analysis.

Results

The incidence rate of CVD was higher in RA group than control (MI: 3.20 vs 2.08; stroke: 2.84 vs 2.33 per 1,000 person-years). The risk of CVD was higher in RA patients. (MI: adjusted HR 1.54, 95% CI 1.46-1.61; Stroke: adjusted HR 1.22, 95% CI 1.16-1.28). The association between RA and CVD was prominent in female (MI: adjusted HR 1.41 in male, 1.60 in female, p for interaction = 0.0293; Stroke: adjusted HR 1.13 in male, 1.27 in female, p for interaction = 0.03) and younger-age subgroups (MI: adjusted HR 2.9 in <40 years, 1.52 in 40-64 years, 1.51 in ≥65 years, p for interaction<0.0001; Stroke: adjusted HR 2.35 in <40 years, 1.21 in 40-64 years, 1.21 in ≥65 years, p for interaction = 0.0100) after adjusting for confounding variables. The association between RA and risk of MI was significant in those without DM. (adjusted HR 1.30 in DM, 1.61 in non-DM, p for interaction = 0.0005)

Conclusions

RA patients had increased risk of CVD events compared to age- and sex-matched control group, and this association was stronger in female and younger-age subgroups.

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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O-04

Increased risk of malignancy in patients with Takayasu's arteritis: A population-based cohort study in Korea

Seulkee Lee[1], Seonyoung Kang[1], Yeonghee Eun[2], Hyungjin Kim[1], Jaejoon Lee[1], Eun-Mi Koh[1], Hoon-Suk Cha[1]

[1] Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea
[2] Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Republic of Korea

Background

This study aimed to evaluate the relative risk of malignancy in patients with Takayasu's arteritis compared to that in the general population.

Methods

This retrospective nationwide cohort study used data from the Korean Health Insurance Review and Assessment Service database. All newly diagnosed patients with Takayasu's arteritis were identified between January 2009 and December 2019. They were observed until the diagnosis of malignancy, death, or end of the observational period, December 2020. The standardized incidence ratios (SIRs) of the overall and site-specific malignancies were estimated and compared with the incidence of cancer in the general population retrieved from the National Cancer Registry.

Results

We identified 1,449 newly diagnosed patients with Takayasu's arteritis during the observational period (9,196 person-years). A total of 74, 66, and 8 patients had overall, solid, and hematologic malignancies, respectively. The risks of overall (SIR, 1.62; 95% confidence interval [CI], 1.27–2.03), solid (SIR, 2.04; 95% CI, 1.56–2.61), and hematologic (SIR, 4.05; 95% CI, 3.72–7.98) malignancies were increased compared to those in the general population. In solid malignancies, breast (SIR, 2.07; 95% CI, 1.16–3.42), ovarian (SIR, 4.45; 95% CI, 1.21–11.39), and major salivary gland (SIR, 19.04; 95% CI, 2.31–68.76) cancers had an increased risk. In hematologic malignancies, the risk of myelodysplasia increased (SIR, 18.02; 95% CI, 3.72–52.66). Immunosuppressive agent use was not associated with malignancy. There was no specific period when cancer more frequently occurred.

Conclusions

An increased risk of malignancy was observed in patients with Takayasu's arteritis compared to that in the general population in this large-scale nationwide population study of Korean health insurance data.

Keywords

Takayasu, Malignancy, Population study

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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O-05

Increased risk of herpes zoster in patients with rheumatoid arthritis using tofacitinib compared with tumor necrosis factor inhibitor

Yeo-Jin Song[1,2], Soo-Kyung Cho[1,2], Hyoungyoung Kim[1,2], Hye Won Kim[2], Eunwoo Nam[2], Ja-Young Jeon[3], Hyun-Jeong Yoo[3], Chan-Bum Choi[1,2], Tae-Hwan Kim[1,2], Jae-Bum Jun[1,2], Sang-Cheol Bae[1,2], Dae Hyun Yoo[1,2], Yoon-Kyoung Sung[1,2]

[1] Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea
[2] Hanyang University Institute for Rheumatology Research, Seoul, Republic of Korea
[3] Pfizer Pharmaceuticals Korea Ltd., Seoul, Republic of Korea

Background

There have been studies suggesting an increased risk of herpes zoster (HZ) in patients with rheumatoid arthritis (RA) treated with tofacitinib, especially in East Asia. This study aimed to determine the increased risk of HZ in Korean patients using tofacitinib compared with tumor necrosis factor (TNF) inhibitor.

Methods

From two prospective cohorts of RA patients who started tofacitinib or TNF inhibitor in Hanyang University Hospital for Rheumatic Diseases, patients who started tofacitinib between March 2017 and May 2021; and those who started TNF inhibitor between July 2011 and May 2021 were included. Baseline features of tofacitinib users and TNF inhibitor users were balanced through inverse probability of treatment weighting (IPTW) using propensity score. Then, incidence rate (IR) of HZ in each group and incidence rate ratio (IRR) were calculated. The IRR of severe HZ was further analyzed.

Results

A total of 912 patients were included: 200 tofacitinib users and 712 TNF inhibitor users with observation period of 329.4 person-years (PYs) and 1950.7 PYs, respectively. Tofacitinib users were older, and had longer disease duration of RA than TNF inhibitor users. In addition, disease activity including patient-reported outcomes was higher in tofacitinib users. The crude IR of HZ was 6.37 cases per 100 PYs in tofacitinib users and 1.85 cases per 100 PYs in TNF inhibitor users. In IPTW analysis with a balanced sample, IRR was 8.80 (95% confidence interval [CI] 3.24–32.93). When the outcome was severe HZ, however, the IRR was 0.99 (CI 0.12–8.20).

Conclusions

Tofacitinib use increased the risk of HZ compared with TNF inhibitor in Korean patients with RA, but not the severity of HZ.

Keywords

herpes zoster, rheumatoid arthritis, tofacitinib

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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O-06

Clinical course and risk factors for development and progression of interstitial lung disease in primary Sjögren's syndrome: a single centered, retrospective, observational study

Kyung-Ann Lee[1], Bo-Da Nam[2], Jung Hwa Hwang[2], Hyun-Sook Kim[1]

[1] Internal medicine, Soonchunhyang University Seoul Hospital, Republic of Korea
[2] Radiology, Soonchunhyang University Seoul Hospital, Republic of Korea

Background

Interstitial lung disease (ILD) is the most common lung manifestation in patients with primary Sjögren syndrome (pSS) and is associated with poor outcomes. This study aimed to investigate the long term clinical course and prognostic factors in patients with pSS-ILD.

Methods

This single-centered, retrospective study included 120 pSS patients who underwent at least two high-resolution computed tomography (HRCT) and had relatively complete clinical data. Clinical symptoms, laboratory data, high-resolution computed tomography (HRCT), and pulmonary function test (PFT) results were collected. HRCT were scored blindly by two expert thoracic radiologists: extent of ground glass opacities (GGO), fine/coarse reticulations, presence of honeycombing (HC), and coarseness score of fibrosis.

Results

In patients without pSS-ILD at baseline (n=81), any development of ILD was not found during median follow up 2.7 (1.1-4.1) years. Among those with pSS-ILD (n=39) at baseline, 19 (48.7%) had progressive ILD, 4 (10.3%) patients died, and 3 (7.7%) experienced acute exacerbation during median 3.2 (1.4-4.9) years of follow-up. In progressive ILD group, extent of coarse reticulations (p=0.003), coarseness score of fibrosis (p=0.037) and HC involved sections increased significantly, while extent of GGO and fine reticulations did not. Age (Odds ratio [OR]: 1.158, p=0.003), smoking (HR=16.420, p=0.038), lactic dehydrogenase (LDH) (OR=1.015, p=0.007), and anti-Ro52 (OR=1.626, p=0.007) were significantly associated with presence of ILD. UIP pattern was an independent risk factor for ILD progression (OR 8.769, p=0.024). Baseline PFT, extent of ILD, auto-antibody profiles, glandular and extra-glandular manifestations except ILD were not associated with ILD progression.

Conclusions

No development of ILD was observed in pSS patients without ILD at baseline. ILD progressed occurred in 48.7% of the patients with pSS-ILD. pSS patients with older age, smoking, LDH, and high titers of anti-Ro52 were at higher risk of presence of ILD. UIP pattern on HRCT indicated ILD progression.

Keywords

Sjogren syndrome, Interstitial lung disease

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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O-07

Comparison of prescription drug use patterns during pregnancy and postpartum in Korean women with rheumatic conditions: A national population-based study

Jin Su Park[2], Jisoo Lee[1], Chan Hee Lee[2], Min Kyung Chung[1], Hyunsun Lim[2]

[1] Rheumatology/Internal Medicine, Ewha Womans University College of Medicine, Republic of Korea
[2] Rheumatology/Internal Medicine, National Health Insurance Service Ilsan Hospital, Republic of Korea

Background

The aim of this study was to compare the patterns of medication use before, during, and after pregnancy in women with systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), or ankylosing spondylitis (AS) to gain knowledge regarding disease activity and management during pregnancy and postpartum of women with rheumatic diseases.

Methods

We identified pregnancies ending in delivery in women aged 20 - 44 years with SLE (n=1,753), seropositive RA (n=1,652), or AS (n=879) in Korean National Health Insurance Service-National Health Information Database (NHIS-NHID), 2009–2016. We assessed proportions of pregnancies exposed to prescribed antirheumatic drugs including nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids (CSs), and disease-modifying anti-rheumatic drugs (DMARDs) in 8 window periods; 3 months before pregnancy (pre-pregnancy), each trimester of pregnancy (T1, T2, T3) and 3, 6, 9, 12 months postpartum (PP1, PP2, PP3, PP4).

Results

More pregnancies among women with SLE were exposed to antirheumatic drugs (62.4%) than in women with RA (42.9%) or women with AS (14.6%). CSs and hydroxychloroquine (HCQ) were most frequently used agents during pregnancy. Overall, use of antirheumatic drugs during pregnancy and postpartum in rheumatic diseases showed V shaped pattern, i.e. decreased use as pregnancy progressed from T1 to T3 and increased use in postpartum. In SLE, use of CSs did not decrease during pregnancy and postpartum, but rather increased in T2 and PP1 compared with pre-pregnancy. Use of HCQ decreased during SLE pregnancies with 65.9% in pre-pregnancy, 58.6% in T1, 53.9% in T2, and 48.4% in T3.

Conclusions

This population-based study offer real-world data regarding the disease activity and management of the disease during pregnancy and postpartum in women with rheumatic conditions. The decreased use of medications including HCQ during pregnancy suggest a need for strategies to improve medication adherence.

Keywords

rheumatic diseases, medication, pregnancy

JRD Journal of Rheumatic Diseases
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KCR 2022
May 19(Thu) - 21(Sat), 2022

O-08

Multidimensional correlates to chronic pain among patients with musculoskeletal pain in different rheumatic diseases: Based on the Biopsychosocial approach

Hee Jun Kim[1], Hyoun-Ah Kim[2], Ju-Yang Jung[2], Ji-Won Kim[2]

[1] College of Nursing, Ajou Medical Center, Ajou University, Republic of Korea
[2] Department of Rheumatology, Ajou University School of Medicine, Republic of Korea

Background

Chronic pain is a complex and subjective experience influenced by multiple factors, including biological, psychological, and social factors. Chronic pain is a condition known to be difficult to treat and comprehensive and accurate assessment on chronic pain and long-term plans based on evidence of factors influencing pain outcomes are necessary to better serve the patients.

Methods

An exploratory, cross-sectional design was used to explore multi-dimensional factors associated with clinical pain intensity. In total, 220 patients with musculoskeletal chronic pain from various rheumatic diseases were participated. Experimental pain sensitivity was measured using quantitative sensory testing (QST) for pressure pain threshold, mechanical cutaneous pain threshold, and temporal summation of mechanical cutaneous pain . Pain catastrophizing , depressive symptoms, and pain intensity was measured using Brief Pain Inventory. Descriptive analyses and a multivariate linear regression was conducted.

Results

Fifty five percent of the participants were having rheumatoid arthritis, 23.6% were diagnosed with ankylosing spondylitis, and 14.1% were diagnosed with osteoarthritis. First multivariate regression model included biological measures, including age, gender, pain-related disease type, pain duration, and comorbidity. The model was significant, $F(10, 208) = 2.63$, $p = .005$, accounting for 11.2% of the variance in the pain intensity. Adding the QST measures explained an additional 0.6% of variation in pain intensity ($F(14, 204) = 1.97$, $p = .022$). Introducing social factors, including levels of education and perceived economic status, religion, marital status, and types of residency, explained an additional 9.6 % of the variance in the dependent variable ($F(23, 194) = 2.30$, $p = .001$). Depressive symptoms and pain catastrophizing explained the additional 22.2% of the variation in pain intensity ($F(25, 190) = 7.66$, $p < .001$).

Conclusions

Psychological factors, including depressive symptoms and pain catastrophizing influenced pain experience the most significantly, and these factors should be included in pain assessment and pain management.

Free Paper Session

Sjögren's Syndrome, Systemic Sclerosis, and Inflammatory Myositis

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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O-09

IL-17 and CCR9+α4β7– Th17 cells promote salivary gland inflammation, dysfunction, and cell death in Sjögren's syndrome

Jin-Sil Park[1], Sun-Hee Hwang[1], Jin Seok Woo[1], SeungCheon Yang[1], JeongWon Choi[1], Mi-La Cho[1,2], Sung-Hwan Park[1,3]

[1] Rheumatism Research Center, The Catholic University of Korea, Republic of Korea
[2] Department of Medical Lifescience, The Catholic University of Korea, Republic of Korea
[3] Division of Rheumatology, The Catholic University of Korea, Republic of Korea

Background

Previous studies have evaluated the roles of T and B cells in the pathogenesis of Sjögren's syndrome (SS); however, their relationships with age-dependent and metabolic abnormalities remain unclear.

Methods

We examined the impacts of changes associated with aging or metabolic abnormalities on populations of T and B cells and SS disease severity.

Results

We detected increased populations of IL-17-producing T and B cells, which regulate inflammation, in the salivary glands of NOD/ShiLtJ mice. Inflammation-induced human submandibular gland cell death, determined based on p-MLKL and RIPK3 expression levels, was significantly increased by IL-17 treatment. Among IL-17-expressing cells in the salivary gland, peripheral blood, and spleen, the α4β7 (gut-homing integrin)-negative population was significantly increased in aged NOD/ShiLtJ mice. The α4β7-positive population markedly increased in the intestines of aged NOD/ShiLtJ mice following retinoic acid (RA) treatment.

Conclusions

A significant increase in α4β7-negative IL-17-expressing cells in salivary glands may be involved in the onset and progression of SS. These results suggest the potential therapeutic utility of RA in SS treatment.

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Journal of Rheumatic Diseases
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O-10

Correlations between salivary scintigraphic and histopathologic data of salivary glands in patients with Sjögren's syndrome

Ji-Won Kim[1], Young-Sil An[2], Jin Roh[3], Jae ho Han[3], Ju-Yang Jung[1], Chang-Hee Suh[1], Hyoun-Ah Kim[1]

[1] Department of Rheumatology, Ajou University School of Medicine, Republic of Korea
[2] Department of Nuclear Medicine and Molecular Imaging, Ajou University School of Medicine, Republic of Korea
[3] Department of Pathology, Ajou University School of Medicine, Republic of Korea

Background

Our aim was to evaluate the association of salivary scintigraphic and clinical parameters with histological characteristics of salivary glands in patients with Sjogren's syndrome (SS).

Methods

In 41 patients with suspected SS, salivary scintigraphy and salivary gland biopsy were performed. Salivary scintigraphy was interpreted as semi-quantitative methods obtained by calculating peak uptake and washout of each gland using region of interests. All specimens were examined by pathologists for focus scores and positivity for leukocyte common antigen (LCA) explaining the degree of inflammatory infiltration. The correlations between histological data of salivary gland and salivary scintigraphic and clinical parameters were analyzed.

Results

The mean age of SS patients was 46.4 years, 82.9% of them were female, and the mean symptom duration was 2.5 years. The focus score was negatively correlated to the mean peak uptake (r=-0.396, p=0.019) and mean washout (r=-0.391, p=0.02). In addition, the focus score and number of LCA positive cell per mm2 were correlated with the clinical parameters including ESR (r=0.582, p<0.001 and r=0.591, p<0.001, respectively), globulin (r=0.521, p=0.001 and r=0.501, p=0.001), and RF (r=0.533, p<0.001 and r=0.608, p<0.001, respectively), unstimulated (UWS) (r=-0.512, p=0.006 and r=-0.471, p=0.013, respectively) and stimulated whole saliva flow (SWS) (r= -0.491, p=0.009 and r=-0.519, p=0.006) and only number of LCA positive cell per mm2 was negatively correlated to leukocyte (r=-0.37, p =0.019), and hemoglobin (r=-0.367, p=0.02).

Conclusions

Salivary gland biopsy in patients with SS showed a significant correlation with the mean peak uptake and washout of both parotid and submandibular gland in salivary scintigraphy, and clinical features such as cytopenia, high ESR, lower UWS and SWS. Although the diagnostic role of salivary gland biopsy is widely accepted according to the classification criteria of SS, salivary scintigraphy may be an alternative method if non-invasive test is required.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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O-11

Impact of age on the diagnostic performance of unstimulated salivary flow rates and salivary gland ultrasound for primary Sjögren's syndrome

Kyung-Ann Lee[1], Se-Hee Kim[2], Hae-Rim Kim[2], Hyun-Sook Kim[1]

[1] Internal medicine, Soonchunhyang University Seoul Hospital, Republic of Korea
[2] Internal medicine, Konkuk University Medical Center, Republic of Korea

Background

Age-related changes and different patterns of salivary gland abnormalities according to age may affect the diagnostic performance of unstimulated salivary flow rate (USFR) and salivary gland ultrasound (SGUS) for primary Sjögren's syndrome (pSS). To evaluate the threshold and diagnostic performance of USFR and whether incorporating SGUS or replacing USFR with SGUS affects the performance of the ACR/EULAR criteria for pSS according to age.

Methods

This retrospective study included patients with suspected pSS who completed evaluations for pSS. Patients were classified based on age at pSS evaluation: elderly (≥65 years), middle-aged (40–64), and young (<40). The USFR's optimal thresholds were evaluated using the ROC curve. The diagnostic performances of the USFR and modified ACR/EULAR criteria were compared.

Results

In total, 239 pSS patients and 92 controls were included. The cut-off of USFR ≤0.1 mL/min was irrelevant to age, demonstrating the best sensitivity (44.3–53.0%) and specificity (74.1–90.9%). SGUS had a significantly better AUC than USFR in the young (p<0.01) and middle-aged groups (p<0.01). The middle-aged group demonstrated better diagnostic performance of the ACR/EULAR criteria incorporating SGUS (AUC 0.957) (p<0.01) and criteria replacing USFR with SGUS (AUC 0.957) (p<0.001) compared to the original criteria (AUC 0.916). In the young and elderly groups, adding SGUS to the ACR/EULAR criteria or replacing USFR with SGUS did not significantly increase the AUC.

Conclusions

We confirmed the thresholds of USFR ≤0.1 mL/min for all age groups. Using SGUS would improve diagnostic accuracy by supplementing the USFR, especially in middle-aged patients.

Figure & Table

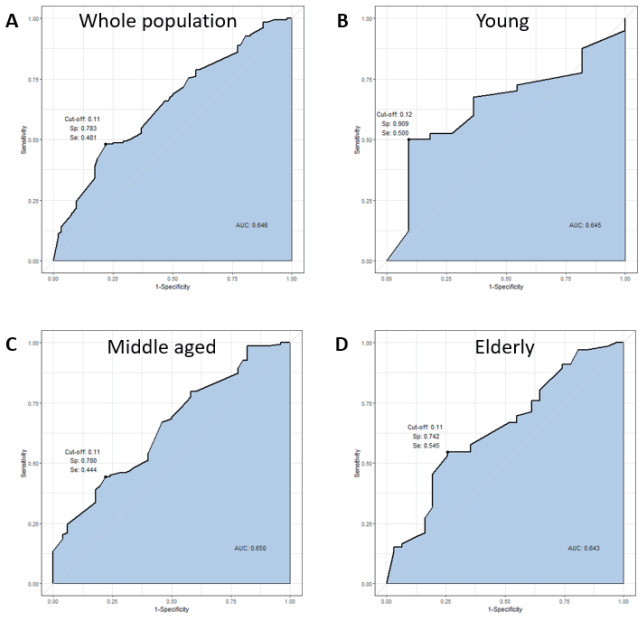

Figure. ROC curves of USFR for diagnosis of pSS according to age groups

Keywords

Sjogren syndrome, Saliva, Diagnosis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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O-12

Reduced Rxr-α signaling increases dry eye disease inducing γδ T17 cells in the conjunctiva

Jehan Alam[1]

[1] Ophthalmology, Baylor College of Medicine, USA

Background

To investigate the mechanism for developing dry eye disease in the Pinkie mouse strain with a loss of function RXRa mutation.

Methods

Measures of dry eye disease were assessed in the cornea and conjunctiva. Expression profiling was performed by single-cell RNA sequencing (scRNA-seq) to compare gene expression in conjunctival immune cells. Conjunctival immune cells were immunophenotyped by flow cytometry and confocal microscopy. The activity of RXRa ligand 9-cis retinoic acid (RA) was evaluated in cultured monocytes and γδ T cells.

Results

Compared to wild type (WT) C57BL/6, Pinkie has increased signs of dry eye disease, including corneal barrier disruption, corneal/conjunctival cornification and goblet cell loss, and corneal vascularization, opacification, and ulceration with aging. ScRNA-seq of conjunctival immune cells identified γδ T cells as the predominant IL-17 expressing population in both strains and there is a 4-fold increased percentage of γδ T cells in Pinkie. Compared to WT, significantly increased expression of IL-17a and IL-17f in conventional T cells and IL-17f in γδ T cells was found in Pinkie. Flow cytometry and immunostaining revealed an increased number of IL-17+ γδ T cells in Pinkie. Tear concentration of the IL-17 inducer IL-23 is significantly higher in Pinkie. 9-cis RA treatment suppresses stimulated IL17 production by γδ T and stimulatory activity of monocyte supernatant on γδ T cell IL-17 production. Compared to WT bone marrow chimeras, Pinkie chimeras have increased IL17+ γδ T cells in the conjunctiva after desiccating stress and anti-IL-17 treatment suppresses dry eye induced corneal MMP-9 production/activity and conjunctival goblet cell loss.

Conclusions

These findings indicate that RXRa suppresses generation of dry eye disease inducing γδ T17 cells in the conjunctiva and identifies RXRa as a potential therapeutic target in dry eye.

Figure & Table

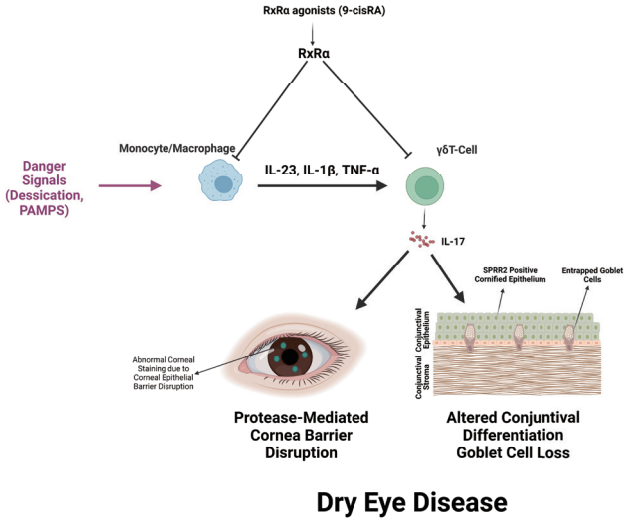

Figure. Summary of RXRa mediated suppression of IL-17 production by γδ T cells and IL-17 mediated dry eye disease.

Keywords

gamma delta T cells, Sjögren's syndrome, Retinoic acid

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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May 19(Thu) - 21(Sat), 2022

O-13

Angiographic characteristics of vasculopathy in patients with idiopathic inflammatory myopathies and systemic sclerosis

Jina Yeo[1,2], Eun-Ah Park[3], Eun Bong Lee[2], Jin Kyun Park[2]

[1] Rheumatology, Gil Medical Center, Gachon University College of Medicine, Republic of Korea
[2] Rheumatology, Seoul National University Hospital and College of Medicine, Republic of Korea
[3] Radiology, Seoul National University Hospital and College of Medicine, Republic of Korea

Background

To describe the peripheral angiographic features of non-thrombotic proliferative vasculopathy in idiopathic inflammatory myositis (IIM) and systemic sclerosis (SSc) in comparison to polyarteritis nodosa (PAN).

Methods

Angiograms of 47 extremities (24 upper and 23 lower) of 11 patients with IIM (n=5) and SSc (n=6), and 12 patients with PAN who presented with critical limb ischemia were retrospectively analyzed with regards to the presence of stenosis, occlusion, aneurysms and delayed distal flow, and degree of neovascularization.

Results

Diffuse narrowing was more frequent (66.1 vs. 38.0%, p=0.001), whereas multifocal stenosis (6.5% vs. 26.8%, p=0.002), abrupt occlusion (11.3% vs. 29.6%, p=0.010) and aneurysm formation (1.6% vs. 11.3%, p=0.037) were less frequent in IIM/SSc than PAN. In distal arteries, tapered occlusion (95.5% vs. 72.0%, p=ns) and delayed flow (77.3% vs. 48.0%, p=0.039) were more common in IIM/SSc than PAN. After 1 year, auto- or surgical amputation tended to be more frequent in IIM/SSc than PAN (36.4% vs. 16.7%, p=ns).

Conclusions

In conclusion diffuse narrowing, tapered occlusion and delayed distal flow on conventional angiograms tend to be more frequent in IIM/SSc than PAN. Moreover, IIM/SSc-vasculopathy might be associated with a worse outcome than PAN. Further studies are needed to verify these findings in a larger prospective cohort.

Figure & Table

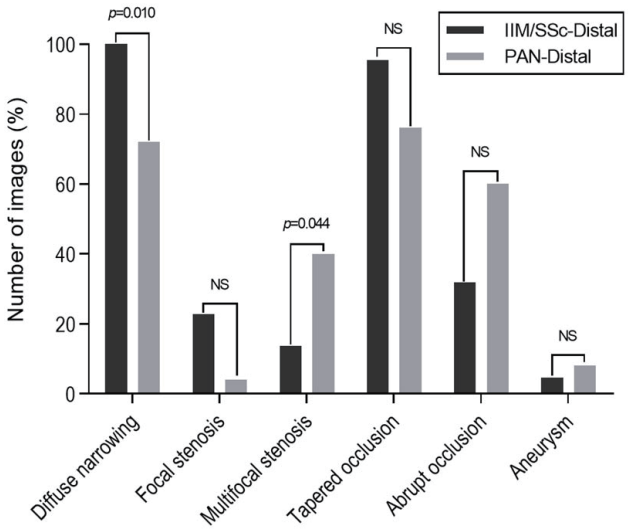

Figure. Angiographic parameters in the extremities of patients with IIM/SSc-vasculopathy and PAN.

Keywords

Vasculopathy, Idiopathic inflammatory myositis, Systemic sclerosis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

O-14

The association of anti-cyclic citrullinated peptide antibody with interstitial lung disease in systemic sclerosis: a retrospective analysis

Jangwoo Ha[1], Yoo Jin Hong[2], Hyun Jin Cha[1,3], Jeonghun Daniel Moon[4], Jung Yoon Pyo[1], Sang-Won Lee[1], Yong-Beom Park[1], Chul Hwan Park[5], Jason Jungsik Song[1,6]

[1] Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea
[2] Department of Radiology and Research Institute of Radiological Science, Severance Hospital, Yonsei University College of Medicine, Republic of Korea
[3] Synapse Center, Yonsei University College of Medicine, Republic of Korea
[4] Division of Rheumatology, University of Washington Medicine, Valley Medical Center, USA
[5] Department of Radiology and Research Institute of Radiological Science, Gangnam Severance Hospital, Yonsei University College of Medicine, Republic of Korea
[6] Institute for Immunology and Immunological Diseases, Yonsei University College of Medicine, Republic of Korea

Background

An anti-cyclic citrullinated peptide (CCP) antibody test is a diagnostic test for rheumatoid arthritis (RA), which is associated with clinical features of interstitial lung disease (ILD). In this study, we aimed to investigate the clinical and radiographic features of ILD in patients with systemic sclerosis (SSc) who tested positive for anti-CCP antibody.

Methods

We performed a retrospective analysis at a tertiary medical center in Seoul, South Korea, between 2005 and 2019. Patients with SSc, systemic lupus erythematosus (SLE), and polymyositis/dermatomyositis (PM/DM) were evaluated for anti-CCP antibody and ILD. Additionally, medical records of SSc patients with ILD were retrospectively reviewed for clinical, laboratory, high resolution computed tomography (HRCT), and pulmonary function test data.

Results

Patients with SSc had the highest anti-CCP antibody positivity rate compared to those with SLE and PM/DM (9.2% [SLE, n=936] vs. 11.5% [PM/DM, n=156] vs. 16.2% [SSc, n=260], p=0.006). The incidence of ILD was higher in SSc patients with anti-CCP antibody than in those without (64.3% vs. 41.3%, p=0.006). The usual interstitial pneumonia incidence was higher in the anti-CCP antibody-positive group than in the anti-CCP antibody-negative group (55.6% vs. 31.1%, p=0.021). The DLCO was lower in the anti-CCP antibody-positive group than in the anti-CCP antibody-negative group (57.5% vs. 67.0%, p=0.023).

Conclusions

Anti-CCP antibody positivity may be associated with a higher incidence and a more severe course of ILD in SSc

Figure & Table

	ILD with anti-CCP antibody (-)	ILD with anti-CCP antibody (+)	P-value
SLE	59/850 (6.9%)	14/86 (16.3%)	**0.002**
PM/DM	59/138 (42.8%)	7/18 (38.9%)	0.755
SSc	90/218 (41.3%)	27/42 (64.3%)	**0.006**

Bold text indicates statistical significance. Values are expressed as n (%).

SLE, systemic lupus erythematous; PM, polymyositis; DM, dermatomyositis; SSc, systemic sclerosis; ILD, interstitial lung disease

Table. Relationship between anti-CCP antibody and interstitial lung disease in connective tissue diseases

Keywords

Anti-cyclic citrullinated peptide antibody, Systemic sclerosis, interstitial lung disease

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Ultrasound may detect subclinical interstitial lung disease in systemic sclerosis

MARWIN Gutierrez[1,2], Luis E. Gomez-quiroz[3], Chiara Bertolazzi[1], Esteban Cruz-arenas[4], Denise Clavijo-cornejo[1], Fausto Salaffi[5]

[1] Division of Musculoskeletal and Reumatic Diseases, Instituto Nacional de Rehabilitacion, Mexico
[2] Rheumatology, Excellence Center of Rheumatoogy, Mexico
[3] Departamento de Ciencias de la Salud, Universidad Autónoma Metropolitana, Mexico
[4] Epidemiology Unit, Instituto Nacional de Rehabilitacion, Mexico
[5] Clinica Reumatologica, Università Politecnica delle Marche, Italy

Background

Interstitial lung disease (ILD) is common in systemic sclerosis (SSc) patients and despite recent advances in the treatment represents still the major cause of death. It may be established within the first 4 years of SSc and frequently is subclinical.

We investigated the validity of US in detecting subclinical ILD in SSc and to determine its potential in the follow-up of these patients

Methods

133 patients without respiratory symptoms and 133 healthy controls were included. Borg scale dyspnea index, Rodnan skin score (RSS), and pulmonary auscultation were performed. X-ray and respiratory function tests (RFT) were performed the same day. An expert rheumatologist blinded to the clinical assessment performed the US. To determine the concurrent validity high-resolution CT (HRCT) scans were performed. HRCT findings were scored according to Warrick score whereas US findings were classified according to the previously proposed scale. Inter-observer reliability was performed. A follow-up including US, RFT, and Borg scale was done every 3 months for 12 months

Results

A total of 54 of 133 SSc patients (40.6%) showed US signs of ILD in contrast to healthy controls (4.8%) (p=0.0001). The clinical and laboratory variables associated with ILD were anti-centromere antibodies (p=0.005) and RSS (p=0.004). A positive correlation was demonstrated between the US and HRCT findings (p=0.001). The sensitivity and specificity of US in detecting ILD was 91.2% and 88.6% respectively. Good inter-observer reliability was also observed (k = 0.72).

In the follow-up, a total of 30 patients (22.6%) that demonstrated US signs of ILD at baseline showed the US worsening. Nine patients (30%) developed symptoms of ILD

Conclusions

US is valid to detect subclinical ILD-SSc. Our results showed a high prevalence of this complication. Despite encouraging data. it seems still controversial its role in monitoring the ILD progression in SSc

Keywords

Systemic Sclerosis, Ultrasound, interstitial lung diseases

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Expressions of CCR2 and CCL2, and association between their expression and NET stimulation in adult-onset Still's disease

Ju-Yang Jung[1], Mi-Hyun Ahn[1], Ji-Won Kim[1], Chang-Hee Suh[1], Hyoun-Ah Kim[1]

[1] Department of Rheumatology, Ajou University School of Medicine, Republic of Korea

Background

Adult-onset Still's disease (AOSD) is a systemic inflammatory disease, which is characterized by the activation of monocyte-derived cells and release of neutrophil extracellular traps (NET). C-C motif ligand 2 (CCL2), known as monocyte chemoattractant protein -1, is a chemoattractant attracting monocytes, and interaction with its ligand, C-C motif chemokine receptor (CCR) 2, mediates monocyte recruitment and activation.

Methods

CCL2 and CCR2 levels in serum were measured by enzyme-linked immunosorbent assay (ELISA) and their expressions in tissue were detected by immunohistochemistry staining. After stimulation of NET formation using neutrophils from patients with AOSD, THP-1 cell lysates were analyzed by western blot and ELISA.

Results

Concentration of CCL2 in serum was higher in AOSD patients (476.4 ± 689.1 pg/mL) compared to rheumatoid arthritis (RA) patients (169.2 ± 118.7 pg/mL, p = 0.007) and healthy controls (HC) (135.1 ± 71.7 pg/mL, p = 0.003). Expressions of CCL2 in skin of AOSD were increased compared with those in HC (p = 0.03), and expressions of CCR2 in lymph node of AOSD were increased compared with those in tuberculosis (p = 0.02) and reactive hyperplasia (p = 0.04). THP-1 cells stimulated with NET induced increased secretion of CCR2 and inflammatory cytokines including IL-1β, IL-6, and IL-18.

Conclusions

CCL2 was expressed highly in serum and skin, and CCR2 was expressed highly in the lymph node in patients with AOSD. In addition, CCR2 expression was associated with NET formation in AOSD.

Keywords

Adult-onset Still's disease, CCL2, neutrophil extracellular traps

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Increased expression of receptor for advanced glycation end-products in sarcopenic patient skeletal muscle

Ji Sup Hwang[1], Hyun Sik Gong[1]

[1] Department of Orthopedic Surgery, Seoul National University Bundang Hospital, Republic of Korea

Background

Animal studies suggest that advanced glycation end-products (AGEs) and their interaction with receptor for AGEs (RAGE) are involved in sarcopenia, but their relationship in human skeletal muscles has yet to be elucidated. We aimed to determine whether RAGE expression in human skeletal muscle is associated with serum AGE levels and sarcopenia-related changes.

Methods

We reviewed 33 consecutive women (mean age, 65 years) with distal radius fracture who had consented to donate a sample of forearm muscle for research purposes, which was taken during surgical fracture repair. The muscle RAGE expression was measured with immunohistochemistry staining and serum AGE levels using ELISA method. We compared RAGE expression and AGE levels in patients with and without sarcopenia. We also correlated RAGE expression with such clinical parameters as demographic factors, as well as sarcopenia-related changes, including grip strength, appendicular skeletal muscle mass, and muscle cross-sectional area (CSA) ratios.

Results

Twelve patients (36%) were diagnosed with sarcopenia. They had a significantly higher RAGE expression ($p = 0.044$) and AGE level ($p < 0.001$) than those without sarcopenia. The RAGE expression correlated significantly with a high AGE level ($r = 0.510$, $p = 0.011$) and correlated inversely with a muscle CSA ratio ($r = -0.696$, $p < 0.001$).

Conclusions

This study shows that RAGE expression increases in sarcopenic patient skeletal muscles. This expression also correlates positively with serum AGE levels and inversely with muscle CSA ratios. Further studies are necessary to determine whether targeting RAGEs can be a therapeutic option for sarcopenia.

Figure & Table

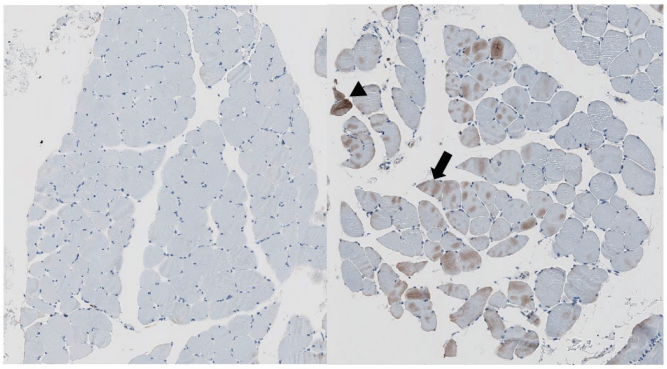

Figure. Disparity in RAGE expression in skeletal muscle tissues obtained from two different patients

Keywords

Sarcopenia, Advanced glycation end-product, Skeletal muscle

Luncheon Symposium IV
Lilly

The Role of Baricitinib in the Treatment of RA

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

Baricitinib in the real-world data

Yun-Hong Cheon
Gyeongsang Nat'l Univ., Korea

Current guidelines for the management of rheumatoid arthritis (RA) recommend early treatment and a treat-to-target goal of remission or low disease activity. Long-term treatments that are safe and efficacious are needed to reduce disease symptoms, to prevent irreversible joint damage, and to reduce the burden of disease from comorbidities.

Janus Kinases (JAK) mediate the intracellular signaling of pivotal cytokines implicated in the pathogenesis of rheumatoid arthritis (RA). Targeting the JAK pathway represents a novel approach to inhibiting the effects of multiple cytokines. Baricitinib, an oral, selective and reversible Janus kinase (JAK) 1 and 2 inhibitor approved for the treatment of adult patients with moderately to severely active RA, was the first JAK inhibitor to demonstrate superiority to MTX and adalimumab.

Baricitinib has now been evaluated in four phase III clinical trials,the data to date suggest that this drug with its once daily dosing, rapid onset of action and efficacy as monotherapy represents an important addition to the RA therapeutic armamentarium. In RA BEAM Baricitinib provided significantly greater improvement in most PROs compared with placebo and adalimumab, including physical function MJS, pain, fatigue and quality of life. Improvement was maintained to the end of the study.

Emerging real-world data helps to provide further insights in the use of Baricitinib in routine clinical practice, including treatment patterns (bio-naïve vs bio-experienced, monotherapy, discontinuations, drug retention). High remission and low disease activity rates were observed from 6 months to 12 months, regardless of the activity index used. Baricitinib demonstrated a significantly higher overall drug maintenance than TNFi, and similar drug maintenance to OMA, both in a bDMARD-naïve population and in the overall population. Baricitinib retention rates are consistent across different Real World Data sources, with retention rates at 6 months ranging between 75% and 82%.

Baricitinib is well tolerated with treatment experience out to 9.3 years; incidence rates for safety topics of interest in DMARD therapy, including serious infections, major adverse cardiovascular event (MACE), venous thromboembolism (VTE), and malignancy are in-line with incidences observed in the overall RA population and have not increased over time.

Baricitinib demonstrated consistent efficacy and acceptable safety outcomes over the long-term and it is supported by global real-world data. Since its launch, Baricitinib has been prescribed to ~3,000 rheumatoid arthritis patients in Korea.

Luncheon Symposium V
BMS

Real World Evidences in Long-term RA Treatment with Biologics

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

Real world evidences and considerations for long-term persistence of biologics in RA

Sang-Hyon Kim
Keimyung Univ., Korea

As treatment of rheumatoid arthritis evolves with various treatment options of biologics, treatment choice based on patient conditions is getting more important.

Especially as long-term management of biologics treatment becomes more important recently, it is crucial to consider factors that are related to drug persistence.

Drug persistence, drug maintenance or drug retention are defined as 'the duration of time from initiation to discontinuation therapy'. It is thought to reflect both the effectiveness and the tolerance of a given drug, representing an outcome close to clinical decision-making, although numerous other factors may influence drug persistence and make it hard to interpret. Although treatment persistence is thought to reflect mainly a drug's tolerance and its effectiveness, other reasons may lead to discontinuation of a treatment, such as pregnancies or remission. Ideally, the broad reasons for discontinuation should be analysed separately, when analysing drug persistence.

In this lecture we will explore real world data to understand considerations for long-term persistence of biologics in RA. This includes studies on drug retention by serostatus, by disease duration, by co-morbidities and by age from many different regions around the world including US, EU and Japan.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Real world evidences of RA treatment with biologics in Korea

Jennifer Jooha Lee
The Catholic Univ. of Korea, Korea

Rheumatoid arthritis (RA) is a chronic, autoimmune inflammatory disease characterized by progressive synovitis resulting in, if untreated, bone erosion and joint destruction.

The disease-modifying antirheumatic drugs (DMARDs) is known to change the natural course of the disease. At the time of the diagnosis, DMARDs should be initiated as early as possible. First, conventional synthetic DMARDs (cSDMARDs) including methotrexate are prescribed. According to aim of treat-to-target, patients with inadequate response to csDMARDs are then treated with biological DMARDs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs). Since the introduction of first bDMARDs targeting Tumor necrosis factor (TNF), several different classes of bDMARDs have been developed. More recently, small molecule inhibitors –tsDMARDs- are developed and added as therapeutic options.

Data from clinical trials suggest that the efficacies of these targeted therapies (bDMARDs and tsDMARDs) are comparable between the drugs in general, and the recommendations for RA treatment recommend with no priority of one drug upon another one. Therefore, the choice of a certain drug is rather dependent on other conditions such as ages, infection risks, or comorbidities as recently suggested in the 2021 ACR recommendations for RA treatment. Furthermore, recent studies suggest auto antibody status may affect the effectiveness of the certain DMARDs.

In general, real world evidences (RWEs) have many limitations to interpret the results of analyses because we can't control possible biases. However, on the other hands, they reflect the real data of the daily practices and provide physicians with practical data which can be applied in the clinics.

Here we show the RWEs of RA treatment with biologics in Korea focusing on the good performance of abatacept compared to other biologics used in Korean RA patients. The first population-level study to compare the persistence of TNF inhibitors and non-TNF inhibitors in South Korean RA patients showed that non-TNF inhibitors presented relatively higher treatment persistence than those on TNF inhibitors in both bDMARD initiators and switchers. Further, abatacept was effective and had better tolerability in patients without adequate response to methotrexate or TNF inhibitors, and also significantly higher persistence in patients with inadequate response to previous bDMARDs. Abatacept showed highest persistence rate in bio-naïve patients as well.

Luncheon Symposium VI
Yuhan Corporation

The New Adalimumab Option in Rheumatic Diseases Treatment

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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ADALLOCE®(SB5) adalimumab in rheumatic diseases: Data from clinical trials and the real world

Carlo Selmi
Humanitas Univ., Italy

This lecture is intended to review the available data fromn clinical trials and real-world evidence regarding the use of SB5 biosimilar adalimumab in rheumatic diseases and its comparison with the originator. Critical issues and advantages in terms of safety and efficacy will be discussed.

International Symposium

2022 Clinical Research Update of Sjögren's Syndrome

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Big data Sjögren project consortium

Manuel Ramos-Casals
Univ. of Barcelona, Spain

The Big Data Sjögren Project Consortium is an international, multicentre registry that was designed in 2014 to take a "high-definition" picture of the main features of primary Sjögren syndrome (SjS) using worldwide data-sharing cooperative merging of pre-existing clinical SjS databases from leading centres in clinical research in SjS from the five continents. The centres share a harmonized data infrastructure and conduct cooperative online efforts in order to refine already-collected data in each centre. The codebook containing instructions on the variables and data codification was firstly discussed and approved by the Steering Committee members, and was further shared with the consortium partners. Data bases from each centre were harmonized into a single data base by applying specific pre-processing techniques such as the detection and treatment of outliers, influential observations, errors and missing data. By January 2022, the participant centres had included more than 15000 valid patients from 70 research centers of 24 countries. The Big Data Sjögren Project has provided the first evidence for a strong influence of geolocation and ethnicity on the phenotype of primary SjS at diagnosis. It also confirmed a strong influence of immunological markers on the phenotype of primary SjS at diagnosis in the largest multi-ethnic international cohort ever analysed, with a greater influence for cryoglobulinaemic-related markers in comparison with Ro/La autoantibodies and ANA. The Sjögren Big Data Project has achieved to multiply by 7 the largest number of patients ever included in an international registry, and by 15 the largest number of patients included in Nationwide multicentric cohorts. The individual contribution of every participating centre, even those that included a modest number of cases, continues to increase progressively year by year, which reflects that participation in the project serves as an enhancer of the clinical experience and acknowledgement that each centre acquires at a regional/national level. And the almost 5 years of close collaboration has created a solid nucleus of clinical research, led by internists and rheumatologists but with active participation of many other medical specialties, with more than 100 people currently involved. And with the active participation in each centre of young researchers, who will be the future experts in Sjögren. could also be successfully addressed through the use of Big Data Sharing.

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Journal of Rheumatic Diseases
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ESSPRI, a single term with multiple meanings: A consideration based on Korean studies

Yun Jong Lee
Seoul Nat'l Univ., Korea

Although Sjögren's syndrome (SS) has originally been described as a disease affecting the lacrimal and salivary glands, many studies continue to add valuable and additional insights as a systematic disease. But our understanding on this Janus-faced disease remains incomplete yet. Consequently, there is a large perception gap between physicians as well as between physicians and patients.

The assessment of SS disease activity has been a challenge because SS is a clinically heterogeneous and has a lower incidence of flares. EULAR task force on SS developed two validated measurements, EULAR SS Patient Reported Index (ESSPRI) and EULAR SS disease activity index (ESSDAI), in 2011 and 2015 respectively. ESSPRI is a patient's reported, subjective symptom index and consists of three questions on the cardinal symptoms such as dryness, fatigue, and joint or muscle pain. The patient acceptable symptom state (PASS) has been defined as ESSPRI score <5. Additionally, its minimal clinical improvement has been defined as a decrease of 1 point or more or decrease by 15% from baseline score. On the other hand, ESSDAI is an established outcome measure for objective systemic disease activity. ESSDAI classifies disease activity in 3 to 4 levels according and consists of 12 organ-specific domains. Because ESSPRI and ESSDAI reflect two different facets, benign sicca symptoms and severe systemic manifestations, their correlation level is quite smaller.

This lecture will discuss the clinical implications of ESSPRI beyond its definition, based on observational studies in Korean SS patients. First, ESSPRI is clearly related with health-related quality of life (HR-QOL) in Korean SS. A high ESSPRI level can be translated into poor HR-QOL state of SS patients. Second, high ESSPRI levels are linked with poor sleep quality in Korean SS. It may indicate that improved sleep can improve patients' HR-QOL or ESSPRI. Third, in total SS patients, longitudinal ESSPRI and clinical ESSDAI levels are not significantly changed. But, although the response rates varied according to different criteria, 17% to 51% showed a treatment response to currently available standards of care in Korean SS patients. Low ESSPRI is a predictor for a better treatment response or subsequent PASS state. Especially, low ESSPRI and high ESSDAI may lead to favorable outcome even with conventional care. Fourth, ESSPRI or ESSDAI alone may not be an adequate endpoint in clinical trials because Korean studies suggest no small effect of background medications. Additionally, several randomized controlled clinical trials with ESSDAI as primary endpoint had failed and showed large response rates in placebo group. Therefore, we make the effort to develop new composite measurements in SS. Fifth, SS is a relatively stable disease because ESSPRI, clinical ESSDAI, or symptom-based phenotypes remain constant over 3 to 5 years in Korean SS. It means that there is a high level of unmet therapeutic need in SS. Also, it can be said that early diagnosis of SS is important, especially when SS patients have residual exocrine function. Furthermore, the stable course of SS, unlike SLE and RA, informs us that we must be careful about overtreatment with immunosuppressive drugs.

Conclusively, ESSPRI is easy to calculate and is something more than the simple sum of symptom triads. It should be considered that ESSPRI is incorporated in routine clinical practice.

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Current and future treatment of primary Sjögren's syndrome

Xavier Mariette
Hôpitaux Universitaires Paris-Sud Bicêtre, France

Primary Sjögren syndrome (pSS) is a systemic autoimmune disease that is characterized by a triad of symptoms that affect all patients (dryness, pain and fatigue). In addition, systemic involvement can affect between one-third and one-half of patients. The management of patients with pSS has been negatively affected by a lack of effective treatments; however, knowledge of the epidemiology of pSS has increased, and advances in developing classification criteria, systemic disease activity scoring and patient-reported outcomes have been made during the past decade. Progress has also been made in understanding the mechanisms that underlie the pathogenesis of pSS, which has enabled a more targeted therapeutic approach to be taken. At present, therapeutic decisions rely on the evaluation of symptoms and systemic manifestations and are mostly formed on the basis of experience, rather than evidence, and on similarities with other autoimmune diseases, although the 2019 management recommendations from EULAR are now being used to inform clinical management of pSS. This Review summarizes the available evidence for systemic treatments for pSS and includes discussions of advances in outcome assessment, the current evidence for DMARD use and an overview of promising future therapeutics.

Symposium

KCR-KAI Joint Symposium

KCR 2022 May 19(Thu) - 21(Sat), 2022
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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

Role of bystander T cells in autoimmune diseases

Je-Min Choi
Hanyang Univ., Korea

Autoimmune disease is known to be caused by unregulated self-antigen specific T cells, causing tissue damage. Although antigen specificity is an important mechanism of the adaptive immune system, antigen non-related T cells have been found in the inflamed tissues in various conditions. Bystander T cell activation refers to the activation of T cells without specific antigen recognition. During an immune response to a pathogen, bystander activation of self-reactive T cells via inflammatory mediators such as cytokines can trigger autoimmune diseases. Other antigen-specific T cells can also be bystander-activated to induce innate immune response resulting in autoimmune disease pathogenesis along with self-antigen-specific T cells. In this presentation, we discuss the role of innate-like T cell response in autoimmune diseases. In our studies, memory phenotype CD4 T cells ($CD62L^{high}/CD44^{low}$) can be activated by inflammatory cytokines without TcR stimulation, and their effector functions contributed MOG antigen specific T cell response in experimental autoimmune encephalomyelitis model. $CCR6^{high}$ memory phenotype cells are bystander activated by IL-1β and IL-23 and infiltrate the spinal cord with producing IL-17A, interferon (IFN)-γ, and GM-CSF. These bystander-activated T cells contributed to the susceptibility of the recipients to encephalomyelitis in an IL-1 receptor, Bhlhe40, and GM-CSF dependent manner. Therefore, we propose the innate-like pathogenic function of antigen non-related memory CD4 T cells are important contributor for development, progression, or relapse of autoimmune diseases. A better understanding of bystander-activated T cells versus antigen-stimulated T cells would provide a novel insight to control autoimmune disease pathogenesis.

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Exploration of the key driving molecules in systemic sclerosis-associated interstitial lung disease by the advanced bioinformatic analysis

Ki-Jo Kim
The Catholic Univ. of Korea, Korea

Interstitial lung disease (ILD) is a significant comorbidity and the leading cause of mortality in patients with systemic sclerosis (SSc). Transcriptomic data of SSc-associated ILD (SSc-ILD) were analyzed to evaluate the salient molecular and cellular signatures in comparison with those in related pulmonary diseases, and to identify the key driver genes and target molecules in the disease module. A transcriptomic dataset of lung tissues from patients with SSc-ILD (n=52), idiopathic pulmonary fibrosis (IPF) (n=549), non-specific interstitial pneumonia (n=49), and pulmonary arterial hypertension (n=81), and normal healthy controls (n=331) was subjected to filtration of differentially expressed genes, functional enrichment analysis, network-based key driver analysis, and kernel-based diffusion scoring. The association of enriched pathways with clinical parameters was evaluated in patients with SSc-ILD. SSc-ILD shared key pathogenic pathways with other fibrosing pulmonary diseases but was distinguishable in some pathological processes. SSc-ILD showed general similarity with IPF in molecular and cellular signatures but stronger signals for myofibroblasts, which in SSc-ILD were in a senescent and apoptosis-resistant state. The p53 signaling pathway was the most enriched signature in lung tissues and lung fibroblasts of SSc-ILD and significantly correlated with carbon monoxide diffusing capacity of lung, cellular senescence, and apoptosis. EEF2, EFF2K, PHKG2, VCAM1, PRKACB, ITGA4, CDK1, CDK2, FN1, and HDAC1 were key regulators with high diffusion scores in the disease module. Integrative transcriptomic analysis of lung tissues revealed key signatures of fibrosis in SSc-ILD. A network-based Bayesian approach provides deep insights into key regulatory genes and molecular targets applicable to treating SSc-ILD.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

ZIP8 exacerbates collagen-induced arthritis by increasing pathogenic T cell responses

Sung-Gyoo Park
Seoul Nat'l Univ., Korea

Rheumatoid arthritis (RA) is a type of autoimmune disease, which is characterized by chronic inflammation and T cell activation. Thus, the disease condition is affected by T cell activation induced by autoantigen-specific T cell receptor (TCR). During the T cell activation, antigen recognition by TCR induces intracellular signaling cascade, which processes are essential for T cell proliferation and function. The TCR-induced signaling cascades activates transcription factors including NF-κB, NF-AT, AP-1, etc. These transcription factor activations turn on many T cell function-related genes for expression of cytokines, adhesion molecules, receptors, etc. The TCR-induced signaling is mainly mediated by molecule-molecules interactions and kinase cascades. In addition, some of the molecule-molecule interactions and the kinase cascades are regulated by intracellular ion concentrations such as zinc. Thus, during the T cell activation, intracellular ion flux control affects the TCR-mediated T cell activation. In here, we identified that zinc transporter ZIP8 regulates zinc flux during the collagen-induced arthritis. Even though some reports have suggested that the zinc supplement is beneficial for immune regulation, our data suggest the specific zinc flux possible exacerbates inflammatory disease such as RA. Thus, specific targeting of zinc transporter such as inhibition of ZIP8 may beneficial outcome for RA treatment.

Free Paper Session

Osteoarthritis and Orthopedics

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

O-18

Sodium chloride affects cartilage associated marker expression during in vitro chondrogenesis from induced pluripotent stem cell

Kijun Lee[1], Son Byeonggwan[1], Ji Hyeon Ju[1,2]

[1] CiSTEM Laboratory, Catholic iPSC Research Center, College of Medicine, The Catholic university, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, The Catholic University, Republic of Korea

Background

Induced pluripotent stem cells (iPSC) have the ability to differentiate into various lineages and are one of the sources of stem cells that have been studied in recent years. Upregulation of osmotic pressure has been found to have a positive effect in the differentiation process of chondrocytes and is known to affect inflammation and hypertrophy, but the results of studies on cartilage differentiation in 3D cell culture have not been accurately performed. Sodium chloride (NaCl) has been reported in several studies in terms of inflammation and cartilage formation in osteoarthritis and various cartilage-related diseases. We aimed to investigate whether sodium chloride could help cartilage formation in the 3D cartilage differentiation process of iPSCs.

Methods

In order to create high osmotic pressure environments, a chondrogenic differentiation medium with a high osmolarity of up to 420 mOsm was prepared using NaCl as well as mannitol, one of the sugar alcohols. Embryoid body-outgrowth cells (EBOGCs) derived from iPSCs were differentiated in a chondrogenic differentiation medium supplemented with different concentrations of NaCl or mannitol for 4 weeks, and pro-inflammatory mediators, cartilage-related markers, and hypertrophy-related markers were evaluated.

Results

Here we demonstrate that NaCl affects cartilage-associated marker expression during in vitro chondrogenesis from iPSC. Depending on which osmotic agent is used under the same osmotic pressure, various effects on inflammatory markers including hypertrophy, bone, and cartilage-related markers can be obtained. Appropriate concentration and use of NaCl during chondrogenesis may play an important role in cartilage regeneration or the inflammatory milieu of joints.

Conclusions

Our findings suggest that it is important to properly use Hyperosmotic conditions for high cartilage formation, which is potentially applicable for cell therapy in patients with cartilage lesions.

Keywords

iPSC-derived chondrocyte, anti-inflammation, NaCl

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O-19

Immunomodulation by mesenchymal stromal cell exosomes in osteoarthritis

Kristeen Ye Wen Teo[1], Shipin Zhang[1], Sai Kiang Lim[2,3], Wei Seong Toh[1,4,5]

[1] Faculty of Dentistry, National University of Singapore, Singapore
[2] Institute of Molecular and Cell Biology, Agency for Science, Technology and Research (A*STAR), Singapore
[3] Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[4] Department of Orthopaedic Surgery, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[5] Tissue Engineering Program, Life Sciences Institute, National University of Singapore, Singapore

Background

Mesenchymal stromal cell (MSC) exosomes were reported to be efficacious in alleviating joint pain and degeneration in temporomandibular joint osteoarthritis (TMJ-OA). However, the immunomodulatory effects of MSC exosomes in TMJ-OA remain to be elucidated.

Methods

Forty-seven rats were randomly assigned to OA+Exo, OA+PBS, sham, and naïve groups. Two weeks after OA induction by monoiodoacetate injection, OA+Exo rats received 3 weekly intra-articular injections of exosomes (1.3×10^{1} particles), whereas OA+PBS rats received equivalent phosphate-buffered saline (PBS) injections. Sham rats received needle pricks while naïve rats were age-matched unoperated control. Weekly nociceptive response was analysed by head withdrawal threshold (HWT) measurement. At 1 week, TMJ condylar cartilage and synovium tissues were harvested for transcriptomic analysis. At 1 and 8 weeks, TMJs were harvested for micro-computed tomography and histology, and blood samples for immunophenotyping and multiplex cytokine assay.

Results

At 1 week, OA+Exo rats showed preferential infiltration of anti-inflammatory CD206 M2 over pro-inflammatory CD86 M1 macrophages in the synovium, and increased M2 over M1-related genes in both cartilage and synovium, that culminated in an improved synovium inflammation score of 0.7±0.5 over 1.8±1.0 in OA+PBS rats (P=0.032). Relative to OA+PBS rats, OA+Exo rats also showed early suppression of systemic inflammation, with significantly reduced circulating SSCHiCD43HiRP1Hi neutrophils and CD43LoHis48Hi classical monocytes, and suppressed levels of pro-inflammatory cytokines including IL6, IL12, IL17A, IFNγ and TNFα. By 8 weeks, OA+Exo rats showed pain recovery with increased HWT, enhanced cartilage and subchondral bone restoration with improved Mankin score (1.9±0.9 vs 5.9±2.6, P=0.043) and augmented bone structural parameters that were significantly better than OA+PBS rats, and were comparable to that of sham and naïve rats (P>0.05).

Conclusions

MSC exosomes alleviate local inflammation by enhancing M2 over M1 macrophage infiltration, and suppress systemic inflammation with reduction of circulating neutrophils, classical monocytes and associated pro-inflammatory cytokines, to collectively promote joint repair and pain recovery.

Keywords

osteoarthritis, exosomes, immunomodulation

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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Mitochondrial transplantation ameliorates the development and progression of osteoarthritis

A Ram Lee[1,2], Seon-Yeong Lee[1], Jin Seok Woo[1], Chae Rim Lee[1,2], Keun-Hyung Cho[1,2], Seok Jung Kim[4], Sung-Hwan Park[5], Mi-La Cho[1,2,3]

[1] The Rheumatism Research Center, The Catholic University of Korea, Republic of Korea
[2] Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea, Republic of Korea
[3] Department of Medical Lifescience, College of Medicine, The Catholic University of Korea, Republic of Korea
[4] Department of Orthopedic Surgery, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Republic of Korea
[5] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Republic of Korea

Background

Osteoarthritis (OA) is a common degenerative joint disease characterized by breakdown of joint cartilage. Mitochondrial dysfunction of the chondrocyte is a risk factor for OA progression. We examined the therapeutic potential of mitochondrial transplantation for OA.

Methods

Mitochondria were injected into the knee joint of monosodium iodoacetateinduced OA rats. Chondrocytes from OA rats or patients with OA were cultured to examine mitochondrial function in cellular pathophysiology.

Results

Pain, cartilage destruction, and bone loss were improved in mitochondrial transplanted-OA rats. The transcript levels of IL-1β, TNF-α, matrix metallopeptidase 13, and MCP-1 in cartilage were markedly decreased by mitochondrial transplantation. Mitochondrial function, as indicated by membrane potential and oxygen consumption rate, in chondrocytes from OA rats was improved by mitochondrial transplantation. Likewise, the mitochondrial function of chondrocytes from OA patients was improved by coculture with mitochondria. Furthermore, inflammatory cell death was significantly decreased by coculture with mitochondria.

Conclusions

Mitochondrial transplantation ameliorated OA progression, which is caused by mitochondrial dysfunction. These results suggest the therapeutic potential of mitochondrial transplantation for OA.

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O-21

Soluble CCR2 gene therapy controls joint inflammation, cartilage damage, and the progression of osteoarthritis by targeting MCP-1 in a monosodium iodoacetate (MIA)-induced OA rat model

Hyun Sik Na[1,2], Seon-Yeong Lee[1], Keun -Hyung Cho[1,2], A Ram Lee[1,2], Chae Rim Lee[1,2], Seok Jung Kim[5], Sung-Hwan Park[4], Mi-La Cho[1,2,3]

[1] The Rheumatism Research Center, The Catholic University of Korea, Republic of Korea
[2] Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea, Republic of Korea
[3] Department of Medical Lifescience, College of Medicine, The Catholic University of Korea, Republic of Korea
[4] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Republic of Korea
[5] Department of Orthopedic Surgery, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Republic of Korea

Background

Osteoarthritis (OA) is the most common type of degenerative arthritis and affects the entire joint, causing pain, joint inflammation, and cartilage damage. Various risk factors are implicated in causing OA, and in recent years, a lot of research and interest have been directed toward chronic low-grade inflammation in OA. Monocyte chemoattractant protein-1 (MCP-1; also called CCL2) acts through C-C chemokine receptor type 2 (CCR2) in monocytes and is a chemotactic factor of monocytes that plays an important role in the initiation of inflammation. The targeting of CCL2–CCR2 is being studied as part of various topics including the treatment of OA.

Methods

In this study, we evaluated the potential therapeutic effects the sCCR2 E3 gene may exert on OA. The effects of sCCR2 E3 were investigated in animal experiments consisting of intra-articular injection of sCCR2 E3 in a monosodium iodoacetate (MIA)-induced OA rat model. The effects after intra-articular injection of sCCR2 E3 (fusion protein encoding 20 amino acids of the E3 domain of the CCL2 receptor) in a monosodium iodoacetate-induced OA rat model were compared to those in rats treated with empty vector (mock treatment) and full-length sCCR2.

Results

Pain improved with expression of the sCCR2 gene. Improved bone resorption upon sCCR2 E3 gene activation was confirmed via bone analyses using micro-computed tomography. Histologic analyses showed that the sCCR2 E3 gene exerted protective effects against cartilage damage and anti-inflammatory effects on joints and the intestine.

Conclusions

These results show that sCCR2 E3 therapy is effective in reducing pain severity, inhibiting cartilage destruction, and suppressing intestinal damage and inflammation. Thus, sCCR2 E3 may be a potential therapy for OA.

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Journal of Rheumatic Diseases
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O-22

The potential role of SIRT1 in osteoarthritis pain treatment by blocking the nerve growth factors

Sang Yeob Lee[1], So Youn Park[1], Sung Won Lee[1], Won Tae Chung[1], Jun Young Park[1]

[1] Division of Rheumatology, Internal medicine, Dong-A university hospital, Republic of Korea

Background

Background: Current treatment of osteoarthritis (OA) is variable, including compounds targeting nerve growth factor (NGF). In this study, we showed the blocking of NGF, BDKRB2 and TAC1, by SIRT1 in OA synoviocytes in vivo and vitro and we showed the potential role of SIRT1 in OA pain treatment.

Methods

GEO DataSets were analyzed for OA pain gene. OA synoviocytes were isolated from synovium of OA knee patients. NGF, BDKRB2 and TAC1 expression was analyzed using immunohistochemistry, immunofluorescence, and immunoblot. IL-1β, IL-2, IL-15 expression was measured by ELISA assay. Experiments were also conducted in SIRT1-tg mice model.

Results

NGF, BDKRB2 and TAC1 was expressed in human OA synoviocytes and IL-1β, IL-2 and IL-15 had a synergic effect on the expression of NGF, BDKRB2 and TAC1 in human OA synoviocytes. But, SIRT1 had inhibitory role in expression of NGF, BDKRB2 and TAC1. Furthermore, SIRT1 inhibitory mechanism was associated with the expression of IL-1β, IL-2 and IL-15 in OA human synoviocytes. We also reproduced the SIRT1 inhibitory mechanisms on SIRT1-tg mice model.

Conclusions

SIRT1 had suppressed in pain signaling transmitters and had potential role in OA pain management.

Figure & Table

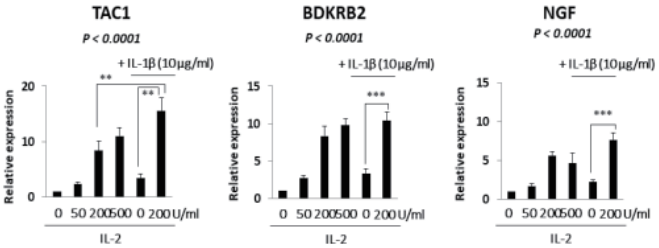

Figure. TAC1, BDKRB2 and nerve growth factor were expressed in synoviocyte from osteoarthritis patients, after administration of IL-2 and IL-1β.

Keywords

osteoarthritis

JRD Journal of Rheumatic Diseases
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O-23

Coenzyme Q10 encapsulated in micelles ameliorates osteoarthritis by inhibiting inflammatory cell death

Hyun Sik Na[1,2,3], Jin Seok Woo[1,3], Jeong Su Lee[1,2,3], In Gyu Um[1,2,3], Mi-La Cho[1,2,3], Sung-Hwan Park[4]

[1] The Rheumatism Research Center, Rheumatism Research Center, Catholic Research Institute of Medical Science, College of Medicine, The, Republic of Korea
[2] The Catholic University of Korea, Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea,, Republic of Korea
[3] Lab of Translational ImmunoMedicine, Lab of Translational ImmunoMedicine, Catholic Research Institute of Medical Science, College of Med, Republic of Korea
[4] Devision of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Med, Seoul St. Mary's Hospital, Republic of Korea

Background

Osteoarthritis (OA) is the most common degenerative joint disease and is characterized by breakdown of joint cartilage. Coenzyme Q10 (CoQ10) exerts diverse biological effects on bone and cartilage; observational studies have suggested that CoQ10 may slow OA progression and inflammation. However, any effect of CoQ10 on OA remains unclear. Here, we investigated the therapeutic utility of CoQ10-micelles.

Methods

Six-week-old male Wistar rats were injected with monosodium iodoacetate (MIA) to induce OA. CoQ10-micelles were administered orally to MIA-induced OA rats; celecoxib served as the positive control. Pain, tissue destruction, and inflammation were measured. The expression levels of catabolic and inflammatory cell death markers were assayed in CoQ10-micelle-treated chondrocytes.

Results

Oral supplementation with CoQ10-micelles attenuated OA symptoms remarkably, including pain, tissue destruction, and inflammation. The expression levels of the inflammatory cytokines IL-1β, IL-6, and MMP-13, and of the inflammatory cell death markers RIP1, RIP3, and pMLKL in synovial tissues were significantly reduced by CoQ10-micelle supplementation, suggesting that CoQ10-micelles might attenuate the synovitis of OA. CoQ10-micelle addition to cultured OA chondrocytes reduced the expression levels of catabolic and inflammatory cell death markers.

Conclusions

CoQ10-micelles might usefully treat OA.

Keywords

Osteoarthritis, Inflammatory cell death, Coenzyme Q10 (CoQ10)

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Journal of Rheumatic Diseases
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O-24

Associations between body composition measurements of obesity and the radiographic progression of hand osteoarthritis: Data from the Dong-gu Study

Sung-Eun Choi[1], Dong-Jin Park[1], Ji-Hyoun Kang[1], Min-Ho Shin[2], Shin-Seok Lee[1]

[1] Division of Rheumatology, Department of Internal Medicine, Chonnam National University Medical School and Hospital, Republic of Korea
[2] Department of Preventive Medicine, Chonnam National University Medical School, Republic of Korea

Background

Previous studies have found that obesity is a risk factor for hand osteoarthritis (OA), but most have been cross-sectional studies and thus causality is uncertain. Longitudinal studies are instead needed to explore the association between obesity-related characteristics, including fat deposition/distribution and hand OA. The present study examined the association between changes in body composition measurements and the radiographic progression of hand OA in a longitudinal cohort.

Methods

In the Dong-gu Study population, 1,277 patients had hand radiographs at baseline and at the 4-year follow-up. X-rays of the hand joints were scored using a semi-quantitative grading method. Body composition was simultaneously measured in a bioelectrical impedance analysis using an InBody 520 analyzer. The relationship between changes in body composition measurements and the radiographic progression of hand OA was assessed in a multiple linear regression analysis.

Results

Total hand joint scores increased from 16.3 ± 5.74 at baseline to 18.8 ± 8.11 at year 4 ($P < 0.001$). Changes of body mass index, hip circumference (HC), waist-to-hip circumference (WHC), and fat mass were significantly associated with changes in the total hand joint scores ($P = 0.012$, $P < 0.001$, $P = 0.017$, $P = 0.008$, respectively). HC and WHC were significantly associated with radiographic progression of the hand joints, after adjusting for age, sex, physical activity, education status, smoking, alcohol consumption, hypertension, diabetes mellitus, dyslipidemia, chronic pulmonary disease, chronic liver disease, cardiovascular disease, cerebrovascular disease, and malignancy ($P < 0.001$, $P = 0.001$, respectively).

Conclusions

Changes in fat distribution were significantly associated with the radiographic progression of hand OA over 4 years, suggesting a role for the systemic effect of adipose tissue.

Keywords

hand osteoarthritis, obesity, radiographic progression

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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O-25

Association of serum uric acid level with bone mineral density in peri-menopausal and postmenopausal Korean women: A single-center study of 3566 cases

Seongmin Kang[1] Seung Won Choi[1], Su Jin Choi[1], Doo-Ho Lim[1]

[1] Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Ulsan University Hospital, Republic of Korea

Background

Uric acid (UA) may be related to bone health through its role as either an anti-oxidant or pro-oxidant properties, or through its effect on vitamin D-parathyroid hormone axis. Although the association of serum UA level with bone mineral density (BMD) has been investigated in previous studies, the results are conflicting. This study investigated the influence of serum UA on BMD among peri-menopausal and postmenopausal Korean women.

Methods

We evaluated 3566 women without renal disease (estimated glomerular filtration rate>60mL/min/1.73m2), aged 50-80 years, who voluntarily underwent laboratory tests and BMD measurement by dual-energy X-ray absorptiometry as a part of general health examination from May 2014 to September 2019. The participants were stratified into quartiles according to their serum UA levels. Between-group comparisons were performed using Pearson's chi-square test for categorical variables, and the one-way analysis of variance for numerical variables, as appropriate. Univariable and multivariable analyses were performed using a linear regression model to analyze the association between Serum UA and BMD.

Results

The mean age of individuals was 56.9 ± 5.8 years. The BMD at all sites was significantly higher in the group of women with high serum UA and increased continuously across quartiles of serum UA (Table). In simple linear regression analysis, significant R-square (R2) values were obtained at all skeletal sites (lumbar spine, femur neck and total hip) (p<0.001). Furthermore, serum UA level showed independent positive associations with BMD at all site [lumbar spine BMD (unstandardized coefficients (B)=0.010, p<0.001), femoral neck BMD (B=0.004, p=0.016) and total hip BMD (B=0.007, p<0.001)], after adjustment for confounding factors including age, body mass index, smoking, drinking, diabetes and alkaline phosphatase.

Conclusions

Our results suggest that raised serum UA levels are associated with higher BMD in peri-menopausal and postmenopausal Korean women, suggesting its protective role in bone metabolism.

Figure & Table

variables	Total	Uric acid				
		quartile 1	quartile 2	quartile 3	quartile 4	
	n = 3566	< 3.80 mg/dl (n = 867)	3.91 ~ 4.30 mg/dl (n = 929)	4.31 ~ 5.10 mg/dl (n = 945)	> 5.10 mg/dl (n = 825)	p-value
BMD (g/cm^2)						
L1 spine	0.823 ± 0.129	0.814 ± 0.129	0.818 ± 0.131	0.827 ± 0.128	0.833 ± 0.126	< 0.001
L2 spine	0.879 ± 0.141	0.867 ± 0.140	0.873 ± 0.143	0.884 ± 0.140	0.894 ± 0.140	< 0.001
L3 spine	0.932 ± 0.151	0.914 ± 0.147	0.924 ± 0.153	0.941 ± 0.151	0.950 ± 0.149	< 0.001
L4 spine	0.959 ± 0.161	0.941 ± 0.157	0.947 ± 0.160	0.965 ± 0.159	0.985 ± 0.164	< 0.001
L spine, total	0.903 ± 0.140	0.888 ± 0.138	0.895 ± 0.141	0.909 ± 0.139	0.921 ± 0.139	< 0.001
Hip neck	0.689 ± 0.104	0.682 ± 0.106	0.685 ± 0.103	0.692 ± 0.103	0.700 ± 0.101	0.002
Hip trochanter	0.611 ± 0.092	0.600 ± 0.093	0.607 ± 0.089	0.615 ± 0.092	0.624 ± 0.092	< 0.001
Hip inter-trochanter	1.016 ± 0.139	0.999 ± 0.140	1.009 ± 0.138	1.020 ± 0.141	1.036 ± 0.136	< 0.001
Hip, total	0.836 ± 0.113	0.822 ± 0.114	0.832 ± 0.111	0.840 ± 0.114	0.852 ± 0.110	< 0.001

Values are mean ± Standard deviation.

Table. Bone mineral density according to the quartiles of serum uric acid levels.

Keywords

Uric acid, Bone mineral density, Osteoporosis

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The relationship between the osteoporosis and cortial index of the mandibular bone in rheumatoid arthritis

Gürkan Iden[1]

[1] orthopedics and traumatology, R. Yaşar Eryılmaz Doğubeyazıt Devlet Hastanesi, Turkey

Background

Osteoporosis is a common finding in rheumatic diseases. The aim of this study is to determine the detectability of systemic osteoporosis in rheumatoid arthritis using mandibular radiography and indices.

Methods

In our study, 93 patients with rheumatoid arthritis whose radiographs were taken were evaluated. Data consists of DXA, mandibular radiography and rheumatologic status, body mass index (BMI) and demographic values. The morphology of the mandibular inferior cortex (MCI) was determined by two observers and classified according to the Klemetti scale (1) (G1-G2-G3). Student's t test, ANOVA and Kappa statistics were applied. In addition, sensitivity, specificity and positive and negative predictive values of MCI were determined in the detection of systemic bone loss.

Results

93 rheumatoid arthritis patients were included in the study. There was no significant difference between the groups in terms of age and gender. Considering the lumbar spine values, 26% of the patients were found to have osteoporosis (G3), 43% to have osteopenia (G2) and 31% to be healthy (G1). Considering the femoral head values, 17% of the patients were found to have osteoporosis (G3), 28% to have osteopenia (G2) and 55% to be healthy (G1). A strong agreement (kappa=0.677) was found between the 2 observers in the evaluation of MCI on mandibular radiography. The mean sensitivity, specificity, and positive and negative predictive values were 68.9, 83.8, 63.9, and 82.1 for the lumbar spine, and 47.2, 83.1, 79.2,

Conclusions

As a result of this study, it has been seen that mandibular radiography and MCI can be used as an auxiliary diagnostic tool in osteoporosis developing in rheumatoid arthritis.

Keywords

Rheumatoid arthritis, Osteoporosis, Cortial index

International Symposium

Vasculitis Session

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Seoul Dragon City, Seoul, Korea

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Somatic mutations in rheumatologic diseases: VEXAS syndrome and beyond

Peter C. Grayson
Nat'l Institutes of Health, USA

Discovery of the VEXAS syndrome demonstrates that somatic mutations in blood can cause adult-onset, complex inflammatory diseases. Unlike germline mutations, somatic mutations occur throughout the lifespan, are restricted to specific tissue types, and may play a causal role in non-heritable rheumatologic diseases, especially conditions that start in later life. Improvements in sequencing technology has enabled researchers and clinicians to detect somatic mutations in various tissue types, especially blood. Alterations in the genome are dynamic events that can occur throughout life. Understanding the relationships between cell-specific acquired mutations and inflammation is likely to yield key insights into causal factors that underlie many rheumatologic diseases. The objective of this lecture is to detail how somatic mutations are likely to be relevant to clinicians who care for patients with rheumatologic diseases, including patients with the VEXAS syndrome. After the talk, participants should be able to identify the important clinical features of VEXAS syndrome, understand the pathogenetic mechanism of VEXAS, and recognize that somatic mutations play a role in an expanding list of non-malignant diseases.

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Recent basic studies in ANCA-associated vasculitis

Akihiro Ishizu
Hokkaido Univ., Japan

ANCA-associated vasculitis (AAV) is a vasculitis that affects systemic small vessels especially in the kidneys and lungs, accompanied by the presence of ANCA in the serum. Similar to other autoimmune diseases, AAV develops in patients with a predisposing genetic background who have been exposed to causative environmental factors. Several genes such as HLA have been listed as susceptible or resistant genes, and it has been shown that environmental factors, including infectious agents and drugs, are involved in the development of this disease. The pathogenic mechanisms includes 1) priming of neutrophils, 2) ANCA binding to the primed neutrophils and an excessive activation of neutrophils with neutrophil extracellular trap (NET) release , 3) vascular endothelial cell injury due to NETs, and 4) disordered NET regulation and ANCA production. Recent studies have suggested the contribution of pro-inflammatory cytokines and the complements to the priming of neutrophils. Although NETs are essential elements in the innate immunity, decrease in serum activity of DNase I (physiological NET degradation factor), disorder of the semaphorin 4D and plexin B2 system (physiological NET regulation system), and acquired resistance to DNase I have been demonstrated in AAV patients. Therefore, a vicious cycle of NET formation and ANCA production is considered to be involved in the pathogenesis of AAV. In addition to this role of NETs in AAV, some other important discoveries have been made in the last few years. Incorporating these new insights into our understanding of the pathogenesis of AAV is needed to fully understand and ultimately overcome this disease.

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Vol. 29, Suppl. 1, May, 2022
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Systemic vasculitis in Korea

Chan-Bum Choi
Hanyang Univ., Korea

Systemic vasculitis is a group of chronic systemic autoimmune diseases mainly affecting blood vessels. It can present with diverse manifestation from constitutional symptoms to specific symptoms according to organ involvements. There have been significant advances in classification and management of systemic vasculitis. Clinical studies in Korea have also shown significant growth in recent years.

First report of systemic vasculitis was a case report of granulomatosis with polyangiitis by an ophthalmologist in 1959 in Journal of Korean Ophthalmologist Society. Observational study of 18 patients with microscopic polyangiitis was published in Journal of Korean Medical Science in 2009. Since then, number of publications in peer-reviewed journal is in steady increase and 137 studies were listed in National Library of Medicine in 2021.

Many studies involved discovery and validation of biomarkers for disease activity assessment and prognosis prediction from a single center cohort of Antineutrophil cytoplasmic autoantibodies (ANCA)-associated vasculitis (AAV), mainly form the Severance Hospital ANCA-associated VasculitidEs (SHAVE) cohort. As AAV is a rare disease, studies using national claims database can have significant value and several studies have been conducted.

Korean Vasculitis Society of Korean College of Rheumatology have established a cohort of systemic vasculitis, mainly AAV, and have organized collection of clinical characteristics, management, and outcomes of Korean systemic vasculitis patients with blood samples with support from the Korean Disease Control and Prevention Agency. It will contribute to advancement of systemic vasculitis research in Korea.

Free Paper Session

Rheumatoid Arthritis Clinical Research

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Journal of Rheumatic Diseases
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O-27

Comparative effectiveness of janus kinase inhibitors and biologic disease-modifying antirheumatic drugs in Korean patients with rheumatoid arthritis; an interim analysis of the real-world study

Soo-Kyung Cho[1,2], Hyoungyoung Kim[1,2], Yeo-Jin Song[1,2], Hye Won Kim[2], Eunwoo Nam[2], Shin-Seok Lee[3], Jae Hoon Kim[4], Seung-Ki Kwok[5], Yeon Ah Lee[6], Sung Hae Chang[7], Hyun-Sook Kim[8], Bo Young Yoon[9], Min-Chan Park[10], Yong-Gil Kim[11], Hae-Rim Kim[12], Hye soon Lee[13], Jisoo Lee[14], Hyoun-Ah Kim[15], Sung-Hoon Park[16], Jeongim Choi[17], Wan-sik Uhm[18], Yoon-Kyoung Sung[1,2]

[1] Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea
[2] Hanyang University Institute for Rheumatology Research, Seoul, Republic of Korea
3 Department of rheumatology, Chonnam National University Medical School and Hospital, Gwangju, Republic of Korea
[4] Department of rheumatology, Korea University College of Medicine, Republic of Korea
[5] Department of rheumatology, Seoul Saint Mary's Hospital, College of Medicine, The Catholic University of Korea, Republic of Korea
[6] Department of rheumatology, School of Medicine, Kyung Hee University, Seoul, Republic of Korea
[7] Department of rheumatology, Soonchunhyang University College of Medicine, Cheonan, Republic of Korea
[8] Department of rheumatology, Soonchunhyang University Seoul Hospital, Seoul, Republic of Korea
[9] Department of rheumatology, Inje University Ilsan Paik Hospital, Goyang, Republic of Korea
[10] Department of rheumatology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea
[11] Department of rheumatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea
[12] Department of rheumatology, Konkuk University School of Medicine, Seoul, Republic of Korea
[13] Department of rheumatology, Hanyang University Guri Hospital, Guri, Republic of Korea
[14] Department of rheumatology, Ewha Womans University College of Medicine, Seoul, Republic of Korea
[15] Department of rheumatology, Ajou University School of Medicine, Suwon, Republic of Korea
[16] Department of rheumatology, Catholic University of Daegu School of Medicine, Daegu, Republic of Korea
[17] Department of rheumatology, Busan Saint Mary's Hospital, Busan, Republic of Korea
[18] Department of rheumatology, Uhm's Rheumatism Clinic, Seoul, Republic of Korea

Background

To evaluate the effectiveness and safety of Janus kinase inhibitors (JAKi) compared to biologic disease modifying anti-rheumatic drugs (bDMARDs) in Korean patients with rheumatoid arthritis (RA) who had an inadequate response to conventional synthetic DMARDs in a real-world setting.

Methods

This study is a prospective, real-world, observational, multicenter, phase 4 study, enrolled RA patients when initiating JAKi or bDMARDs. Treatment decisions were made by a shared decision-making process between RA patients and rheumatologists. An interim analysis was conducted. The primary endpoint was the proportion of achieving low disease activity (LDA) based on disease activity score (DAS) 28- erythroid sedimentation rate (ESR) at 24 weeks (<3.2) and other clinical outcomes and safety during 24 weeks were secondary outcomes. To adjust confounders for effectiveness outcomes, multivariable analyses were performed.

Results

Among the total of 407 patients enrolled from 17 institutions between Apr. 2020 and Feb. 2022, 223 patients (133 JAKi and 90 bDMARDs) were included in this analysis. After 24 weeks of treatment, 45.9% of JAKi users and 48.9% of bDMARDs users achieved LDA, respectively. Remission rates by DAS28-ESR were also comparable between JAKi users and bDMARDs users (26.3% and 30.0%, respectively). In the multivariable analyses, the rate of achieving LDA [odds ratio (OR) 0.75; 95% confidence interval (CI) 0.42 to 1.34] or remission [OR 0.69; 95% CI, 0.36 to 1.35] of JAKi users were comparable with those who used bDMARDs. There were clinically meaningful improvements for quality of life by EQ-5D or HAQ-DI in both groups.

Conclusions

Our interim finding of this ongoing real-world, pragmatic, multicenter, study revealed that JAKi has similar effectiveness compared to bDMARDs.

Keywords

Janus kinase inhibitor, effectiveness, rheumatoid arthritis

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O-28

Comparative effectiveness and safety profiles of baricitinib and tofacitinib in rheumatoid arthritis: A real-world, single center study

Bong-Woo Lee[1], Youngjae Park[2], Seung-Ki Kwok[2], Ji Hyeon Ju[2], Wan-Uk Kim[2], Sung-Hwan Park[2], Jennifer Lee[2]

[1] Division of Rheumatology, Department of Internal Medicine, Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Background

In the midst of recent controversy over adverse events of janus kinase inhibitor (JAKi), we investigated the occurrence of adverse events in RA patients who were prescribed tofacitinib and baricitinib at Seoul St. Mary's Hospital, a single center, and additionally tried to compare effectiveness and retention rate at 12 months after starting the drug.

Methods

This retrospective study was conducted with patients with seropositive RA who started tofacitinib or baricitinib treatment between 2015 and 2020 at Seoul St. Mary's Hospital. Total 240 patients with RA, who were treated with tofacitinib (n = 136) or baricitinib (n = 104), were enrolled. We evaluated and compared the efficacy and safety between tofacitinib and baricitinib.

Results

The tofacitinib-treated patients showed a significantly improved DAS28-ESR from 5.19 (0.61) at baseline to 2.73 (0.95) at 6 months, 2.47 (0.78) at 12 months. The baricitinib-treated patients also showed a significantly improved DAS28-ESR from 5.09 (0.69) at baseline to 2.58 (0.94) at 6 months, 2.38 (0.75) at 12 months. The retention rate of tofacitinib was 88.2% at 12 months and that of baricitinib at 12 months was 83.7%. (log rank test: p value = 0.294) On adverse events, MACE occurrence was not observed in both groups, and VTE/PTE was observed in 2 cases only in the tofacitinib group. There was no significant difference in the incidence of herpes zoster, serious infection and malignancy between the two drugs. But, in the case of dyslipidemia, the incidence was higher in baricitinib. [IRR: 2.79 (1.81–4.32); p <0.001]

Conclusions

Our data shows that tofacitinib and baricitinib are being used in real world as effective RA therapeutic agents, considering high proportion of LDA or remission achievement and retention rate at 12 months. On adverse events, the incidence of dyslipidemia was higher in baricitinib. The occurrence of MACE was not observed in both groups.

Figure & Table

	Baricitinib (N=104)			Tofacitinib (N=136)			
	Event (%)	IR (95% CI) 100 patient -years	IRR (95%CI)	Event (%)	IR (95% CI) 100 patient -years	IRR (95%CI)	p-value
Herpes zoster	9 (8.7%)	5.51 (2.69-10.1)	1.23 (0.56-2.69)	20 (14.7%)	4.49 (2.82-6.81)	1 (ref)	0.611
Dyslipidemia	41 (39.4%)	25.08 (18.24-33.7)	2.79 (1.81-4.32)	40 (29.4%)	8.98 (6.50-12.11)	1 (ref)	<0.001
Malignancy	1 (1%)	0.61 (0.03-3.02)	0.68 (0.08-6.09)	4 (2.9%)	0.90(0.29-2.17)	1 (ref)	0.7297
Serious infection	1 (1%)	0.61 (0.03-3.02)	0.34 (0.04-2.72)	8 (5.9%)	1.80 (0.83-3.41)	1 (ref)	0.2867

Table. Incidence Rates and Incidence Rate Ratios of Adverse Events by drugs (baricitinib and tofacitinib)

Keywords

Rheumatoid arthritis, Janus kinase inhibitor

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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O-29

Comparative efficacy and safety of IL-6/JAK/STAT pathway inhibitors in rheumatoid arthritis: systematic review and network meta-analysis

Rudra Goswami[1], Pallavi Vij[2], Arindam Banerjee[3]

[1] Rheumatology, AIIMS, New Delhi, Assistant Professor, India
[2] Rheumatology, AIIMS, New Delhi, Senior Resident, India
[3] Mathematics, IIT, Kharagpur, Assistant Professor, India

Background

Rheumatoid arthritis (RA) is one of the most common chronic inflammatory diseases. Treatment for RA has diversified in recent years with introduction of multiple small molecule inhibitor of the interleukin-6 (IL-6)/JAK/STAT pathway. No systematic reviews are available on these drugs. We conducted this systematic review and network-meta-analysis to assess the comparative efficacy and safety of IL-6/JAK/STAT pathway inhibitors (tocilizumb, tofacitinib, baricitinib, filgotinib and upadacitinib) in RA.

Methods

PubMed Database was searched to identify randomised controlled trials on RA and any of the above drugs confined to a predefined inclusion and exclusion criteria. A systematic review and network-meta-analysis was performed on the included studies on efficacy (ACR20 response) and safety signals (infections, major cardiac adverse events (MACE) and malignancy).

Results

Overall, 43 trials were included (five in naïve patients (n=2342), 23 in disease modifying drug inadequate-responders (DMARD-IR, n=8734) and seven in biologics inadequate-responders (BIR, n=1878).

Among naïve patients, tocilizumab, tofacitinib, baricitinib and upadacitinib monotherapy data were available, and all were superior to methotrexate. Data on all the drugs were available for DMARD-IR patients in combination with methotrexate, all of which were superior to methotrexate but regarding monotherapy tocilizumab (Odd's Rratio (OR): 2.52, 95% confidence interval (CI): 0.83-7.62) were similar to methotrexate. Data on BIR were available for tocilizumab, tofacitinib, baricitinib and upadacitinib, all of which were superior to control.

Serious infections were higher in tocilizumab group (OR: 1.73, 95% CI: 1.01-2.94); herpes zoster infections were higher with baricitinib (OR: 3.58, 95% CI: 1.2-10.7) and tofacitinib (OR: 3.05, 95% CI: 2.28-4.09). MACES were similar among all. Rates of malignancy were higher with tofacitinib (OR: 2.94, 95% CI: 1.56-5.53).

Conclusions

In DMARD-IR population, combination with methotrexate showed higher effect sizes. No increased risk of MACE was observed for any of the drugs. An increased risk of malignancy was seen with tofacitinib.

Keywords

Rheumatoid arthritis, IL-6/JAK/STAT pathway, Network meta analysis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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O-30

Impact of early age at menopause on disease outcomes in postmenopausal women with rheumatoid arthritis: Results from a large observational cohort of Korean patients with rheumatoid arthritis

Eun Hye Park[1], Sang Tae Choi[1], Jung Soo Song[1], Eun Ha Kang[2], Yun Jong Lee[2], You-Jung Ha[2]

[1] Division of Rheumatology, Department of Internal Medicine, Chung-Ang University College of Medicine, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Republic of Korea

Background

To assess the differences in clinical outcomes between RA patients with early menopause (EM) (age at menopause <45 years) and usual menopause (UM) (age at menopause ≥45 years), and identify potential impact of EM on longitudinal changes in RA activity and patient-reported outcomes (PROs) during follow-up.

Methods

A total of 2878 postmenopausal women with RA were included from the Korean Observational Study Network for Arthritis. Each patient was examined at baseline and for five consecutive years using the simplified disease activity index (SDAI), health assessment questionnaire-disability index (HAQ-DI), and other PROs. Among patients with a baseline SDAI >11, generalized estimating equation (GEE) analyses were performed to evaluate the impact of EM on longitudinal changes in RA activity and PROs during follow-up.

Results

The EM group (N=437) was younger than the UM group (N=2,441) [58.0±9.5 vs. 60.8±8.0 years, p<0.001], but RA duration was similar between the two groups. The EM group had higher education level and was more likely to be seronegative at enrollment. Moreover, the EM group demonstrated higher disease activity [SDAI 15.4±11.7 vs. 13.9±10.0, p=0.011] and patient-reported visual analogue scale (VAS) scores for global assessment, fatigue, and sleep disturbance (all p<0.05), and worse EQ-5D-VAS [59.9±22.2 vs. 63.0±19.5, p=0.006] at baseline. The rate of previous fracture and neoplastic disease, especially uterine/cervical neoplasm, was higher while that of hypertension was lower among the EM group. The GEE model revealed that EM significantly influenced the rate of SDAI change (β=1.265, p=0.004), after adjusting for age, RA duration, biologic use, and SDAI at baseline. The EM group was also significantly associated with increase in HAQ-DI (β=0.088, p=0.003), and decrease in EQ-5D utility value (β=-0.031, p=0.016) during 5-year follow-up period.

Conclusions

RA patients with EM demonstrate higher disease activity and poorer health-related quality of life. EM significantly affects longitudinal changes in disease activity and PROs in RA.

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Journal of Rheumatic Diseases
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The implication of persistent pain in patients with rheumatoid arthritis albeit in DAS28-remission: Data from the KOBIO registry

Hyoun-Ah Kim[1], So Young Park[2], Kichul Shin[2]

[1] Department of Rheumatology, Ajou University School of Medicine, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, SMG-SNU Boramae Medical Center, Republic of Korea

Background

Patient-reported symptoms such as pain and fatigue may persist despite remission in rheumatoid arthritis (RA). We thereby assessed the prevalence of pain in patients after achieving remission according to the Disease Activity Score of 28 joints (DAS28)-erythrocyte sedimentation rate (ESR), and analyzed the demographic and clinical characteristics of these patients.

Methods

Data from 1891 patients with RA registered in the KOBIO (from Dec 2012 to Sep 2020) were obtained. DAS28-remission was defined as DAS28-ESR < 2.6. Pain Visual Analogue Scale (VAS) was evaluated. The intensity of pain was classified as severe (VAS ≥ 7 out of 10), moderate (VAS ≥ 4), and mild (VAS < 4). The association between baseline clinical characteristics and pain VAS after 1-year treatment with biologics or Jak inhibitors (JAKis) were assessed using a multivariate logistic regression model.

Results

Our analysis showed that 52.6% of the patients complained of severe pain at the time of starting biologics or Janus kinase inhibitors (JAKis). Despite 36.0% (n = 680) of these patients achieving remission after the use of biologics or JAKis at their 1-year follow-up, 21.5% (n = 146) had moderate to severe pain, lower frequency of married status, higher frequency of feet erosions, and comorbidities such as endocrine, renal, and neurological disorders than patients with a milder degree of pain. In the multiple regression analysis, higher values in patient global assessment or routine assessment of patient index data 3, and higher ESR were independently associated with moderate to severe pain in patients with RA despite achieving remission. In contrast, patients having renal disorders or using abatacept had a lesser likelihood to eliciting moderate to severe pain.

Conclusions

Displeasing pain is yet a lingering problem in a good deal of patients in clinical remission. New treatment guidelines need to incorporate strategies to better alleviate pain in patients with RA.

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Journal of Rheumatic Diseases
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Increased risk of dementia in patients with rheumatoid arthritis: A nationwide population-based cohort study

Yeonghee Eun[1], Kyungdo Han[2], Seonyoung Kang[3], Seulkee Lee[3], Hoon-Suk Cha[3], Eun-Mi Koh[3], Jaejoon Lee[3], Hyungjin Kim[3,4]

[1] Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Republic of Korea
[2] Department of Statistics and Actuarial Science, Soongsil University, Republic of Korea
[3] Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea
[4] Department of Medical Humanities, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea

Methods

Among patients diagnosed with RA between 2010 and 2017, patients who had undergone a national health examination within two years prior to RA diagnosis were included in the study (n = 138,592). Control group included age- and sex-matched non-RA controls who received a health check-up at the same time as RA patients (n = 692,960). The primary outcome of the study was incident dementia, which was defined by an ICD-10 code and the use of dementia medications. Kaplan-Meier curves and Cox proportional hazards regression analysis were used for the analysis.

Results

Mean follow-up duration of the study was 4.7 ± 2.2 years. RA patients had a 1.2 times higher risk of dementia than controls (adjusted hazard ratio [aHR] 1.19, 95% CI 1.16–1.23). In patients with RA, the aHR for Alzheimer's disease (AD) was 1.21 (95% CI 1.67-1.25) and the aHR for vascular dementia (VD) was 1.10 (95% CI 0.99-1.21). In a stratified analysis according to age, gender, lifestyle factors and co-morbidities, the association between RA and dementia was consistently found.

Conclusions

In a large nationwide population-based cohort, RA was associated with an increased risk of incident dementia. Appropriate evaluation of dementia is required when cognitive impairment occurs in RA patients. Further studies are warranted to identify mechanisms of increased risk of dementia in RA patients.

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Journal of Rheumatic Diseases
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Retention rate and safety of biologics or targeted synthetic disease modifying anti-rheumatic drugs in patients with rheumatoid arthritis associated with interstitial lung disease: Results from the KOBIO registry

Sun-Kyung Lee[1], Kichul Shin[2], Hyoun-ah Kim[3]

[1] Department of Mathematics, College of Natural Sciences, Hanyang University, Republic of Korea
[2] Division of Rheumatology, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Republic of Korea
[3] Department of Rheumatology, Ajou University School of Medicine, Republic of Korea

Background

The aim was to evaluate long-term drug retention and safety of biologics or targeted synthetic disease modifying anti-rheumatic drugs (tsDMARDs) and to identify predictors of adverse events (AE) to biologics or tsDMARDs in patients with rheumatoid arthritis (RA) associated with interstitial lung disease (ILD) enrolled in the Korean College of Rheumatology Biologics (KOBIO) registry.

Methods

Patients included adults with RA (n=2266) who received biologics or tsDMARDs between December 2012 and December 2021. Of 2266 patients, 169 had ILD. A propensity score-matching (PSM) analysis was conducted on data from patients with RA who had ILD or not. We compared the retention rate of biologics or tsDMARDs therapy between the two groups, and evaluated AE and its predictors in RA with ILD.

Results

PSM was effective in matching 159 RA with ILD and 477 RA without ILD. Five-year retention rates were 44.0 % for RA with ILD and 52.4% for RA without ILD (p=0.04). Overall, 31.5% (with ILD) and 24.3% (without ILD) of patients discontinued biologic or tsDMARDs therapy, and 24.5% (with ILD) and 23.3% (without ILD) changed biologics or tsDMARDs therapy. The cause of drug withdrawal was AE (45.2% in RA with ILD and 30.3% in RA without ILD, p<0.001), and inefficacy (35.5% in RA with ILD and 41.1% in RA without ILD, p=0.498). Among AE, infections were more common in RA with ILD than those in RA without ILD (p<0.001). Age and current smoking were associated with AE in RA with ILD treated with biologics or tsDMARDs.

Conclusions

RA patients with ILD more likely discontinued biologics or tsDMARDs than those without ILD. Occurrence of AE during biologic or tsDMARD treatment was associated with age and current smoking of patients with ILD.

Keywords

Rheumatoid arthritis, interstitial lung disease, biologic agents

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O-34

Tumor Necrosis Factor (TNF) inhibitors does not accelerate the progression of RA-ILD: Results from the KORAIL cohort

Yeon-Ah Lee[1], Sang Wan Chung[1], Sujin Jeong[1], Ji Sung Lee[2], Jeong Seok Lee[3], Chan Ho Park[4], Min Uk Kim[5], You-Jung Ha[6], Eun Ha Kang[6], Sung Hae Chang[7], Yongbeom Park[8], Ji Won Kim[9], Jung-Yoon Choe[9], Eun Young Lee[10]

[1] Division of Rheumatology, Department of Internal Medicine, Kyung Hee University Hospital, Republic of Korea
[2] Clinical Research Center, Asan Institute for Life Sciences, Asan Medical Center, Department of Medicine, Republic of Korea
[3] GENOME INSIGHT Inc., GENOME INSIGHT Inc., Republic of Korea
[4] Radiology, Soonchunhyang University College of Medicine, Republic of Korea
[5] Radiology, SMG-SNU Boramae Medical Center, Republic of Korea
[6] Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Republic of Korea
[7] Division of Rheumatology, Department of Internal Medicine, Soonchunhyang University College of Medicine, Republic of Korea
[8] Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea
[9] Division of Rheumatology, Department of Internal Medicine, Catholic University of Daegu College of Medicine, Republic of Korea
[10] Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Republic of Korea

Background

There has been much controversy over the role of TNF-inhibitors and non-TNF biologics (abatacept, tocilizumab, and rituximab) on RA-ILD. The aim of this study was to compare the influence of TNF-inhibitors and non-TNF biologics on the progression of pre-existing ILD in patients with RA.

Methods

The Korean Rheumatoid Arthritis ILD (KORAIL) is the multi-center prospective cohort and aims to investigate the effect and safety of therapeutic options for RA-ILD. RA-ILD was diagnosed based on either 1987 or 2020 ACR criteria and by HRCT. We performed PFT, 6 minutes walking test, semi-quantitative scoring of HRCT and DAS28 at baseline and annually up to 36 months. For the inclusion in the present study, RA-ILD patients had to be initiated with a specific type of biologics within the 4 weeks of baseline chest HRCT and maintained at least 24 weeks.

Results

Patients who received TNF inhibitors (n=20), non-TNF biologics (n=45) and csDMARD only (n=146) were identified. Most of the patients had UIP pattern and early stage of ILD with CT extent less than 10% (103 patients). Generally, there were no significant differences in annual change of lung physiology and CT scoring between RA patients receiving TNF inhibitors and those receiving non-TNF biologics or csDMARD only. However, the change of DLCO (%) over the 3 years was relatively preserved in TNF inhibitor group (0.43 ± 1.67) as compared with non-TNF biologics group (-1.96 ± 2.72, p=0.53) or with csDMARDs group (-1.15 ± 2.34, p=0.04). The change of total CT score for 3 years was less progressed in TNF inhibitor group when compared with csDMARD group (- 0.25 vs 1.64, p=0.04).

Conclusions

The progression of RA-ILD does not seem to be increased following treatment with TNF inhibitors compared with non-TNF biologics and csDMARDs. TNF inhibition may provide a relatively safe option for early RA-ILD.

Keywords

RA-ILD, TNF-inhibitors, non-TNF biologics

Symposium

Medical Humanities: Work Ethics and Labor Relation in the COVID-19 Era

KCR 2022 May 19(Thu) - 21(Sat), 2022
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Vol. 29, Suppl. 1, May, 2022
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The ethics of hospital human resource development during the pandemic: Ethical principles

Ilhak Lee
Yonsei Univ., Korea

Ethical HRM is essential to maintain HCW's vitality and professionalism[2] throughout the crisis such as COVID-19 pandemics. To strengthen the institutional and professional identity and improve the quality of care, it is essential to increase the satistaction of healthcare workers(HCW) and to maintain their loyalty.

The continuing COVID-19 pandemic necessiates the re-thinking every aspects of healthcare management. As for healthcare worker management, following tasks were given; (1)educating HCW to prepare for caring of the COVID-19 patients while protecting themselves from being infected, (2)allocating new work burdens and risks among the HCWs, (3)preparing fair rewards for the extra-works and risks, (4)maintaining the trust of the HCWs to the leadership, and (5)engaging the HCW in the practice of social responsibilities of healthcare instititutes. To respond these tasks, it is necessary to affirm the role and priciples of leadership of HCW management.

The presentation will start with the review of the HCW's experiences of COVID-19 pandemic with the purpose of grasping the issues of human resource management (HRM) during the pandemics. The Korean HCW's experiences of COVID-19 can be summarised in a positive and negative way. The literatures show that the negative experiences such as fear, anxiety, depression, physical and mental exhaustion, loss of resilience, and losses of connection from the loved ones are common experiences while the positive experiences such as re-affirmation of professionalism and social responsibilities are also reported. These negative experiences may be explained by insufficient infra-structure of Korean health care delivery system., rapid progress of the pandemics, limited knowledge resources, and fear of the new infectious disease. These experiences are found among the medical trainees such as residents and fellows as well as nursing professionals. The experiences of abandonment by the institutes called institutional betrayal[1] can lead to the moral distress and injury of HCWs.

The second part of the presentation will sketch the ethical issues of HRM during COVID-19 pandemics: exhaustion and recovery, protecting HCWs by providing PPE and rewarding, dealing the conflics while allocating the burden of care, requirement of vaccinations and other counter measures on HCWs.

The final part of the presentation will explore the role of ethical reasoning and related ethical principles that will help HRM leaders during COVID-19 pandemics. The ethical principle of autonomy, beneficence, and fairness are standards of ethical reasoning of protecting HCW's personal rights and allocating works.

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Labor issues in the COVID-19 situation: Cases and alternatives

Dong Wook Yun
Law Firm Seo-Hee, Korea

COVID-19 caused new labor law problems in untact technology and the 4th industrial revolution.

Corporate personnel and labor managers were worried about whether they could cut the salaries of workers infected with COVID-19 and whether they could give them a week of paid leave.

Changes in the way of working and personnel and labor management before and after the outbreak of COVID-19 are inevitable.

Based on the current laws and the Ministry of Employment and Labor's guidelines for responding to workplaces, labor issues in the COVID-19 situation will be examined focusing on cases and alternatives.

In particular, hospitals and clinics should consider the method of disciplining expected legal issues such as calculating working hours, managing absenteeism, evaluating performance, protecting worker privacy, and working accidents while working from home.

In addition, it is also a question to consider whether it is necessary to change the direction of labor management that guarantees workers a work and life balance that pursues a balanced life.

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DAY 03

PROGRAM

May 21(Sat)

Breakfast Symposium IV
Yuhan

Valuable Options
for Treatment Rheumatic Disease

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Vol. 29, Suppl. 1, May, 2022
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Biosimilar: Past, present and future

Seung-Jae Hong
Kyung Hee Univ., Korea

In the 2000s, biologics began to be used in the treatment of rheumatic diseases.

From the beginning of the use of biological agents, problems such as an increase in the economic burden of patient treatment, a decrease in access to treatment, and the high cost and complexity of product development began to arise.

After 2010, as the patent for biologics was terminated, conditions were created for the release of biosimilars, and biosimilars began to be used in the treatment of many patients with drivers such as Technological Innovation and Regulatory Initiatives.

Currently, several biosimilars are approved and released in many countrys such as Korea, Europe, and the United States.

We have data that meet the strict acceptance criteria required by the regulatory agency through technological innovation of biosimilars.

In addition, biosimilars are playing a role in increasing accessibility to patient treatment through the advantage of cost-effectiveness.

Through these advantages, the clinical treatment through biosimilars is increasing, and the real world evidence is proving the equivalence with reference biologics.

In the future, patents for products in many therapeutic areas are expected to terminate, and biosimilars are expected to be released accordingly. Therefore, it is expected that more rheumatoid disease patients will have more opportunities to be treated with better quality products.

Breakfast Symposium V
Lilly

Ixekizumab:
Recent Updates on the Treatment of Spondyloarthritis

KCR 2022 May 19(Thu) - 21(Sat), 2022
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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

IL-17 inhibition in spondyloarthritis: The efficacy of Ixekizumab and clinical relevance

Yeon-Ah Lee
Kyung Hee Univ., Korea

The spondyloarthritides (SpA) comprise related but phenotypically distinct inflammatory diseases including axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA). AxSpA including ankylosing spondylitis (AS) usually starts with sacroiliac joint inflammation and progresses to irreversible spinal ankylosis. PsA is characterized by nail and skin changes, peripheral arthritis, enthesitis, dactylitis, and axial disease, which can be present alone or in combination with each other. Both diseases are progressive with joint damage accumulating over time with multifaceted symptoms that seriously degrade the quality of life.

Although the pathogenic mechanisms underlying axSpA and PsA are not fully understood, evidences suggest that immune responses mediated by interleukin 17A (IL-17A) play a pivotal role in both diseases. Following the TNF inhibitors that have been prescribed primarily as a treatment for axSpA in Korea, a new IL-17A inhibitor, ixekizumab, has been approved for the reimbursement from October 1st, 2020 in Korea. And ixekizumab has been expanded the 1st line reimbursement for the biologics-naive paitents with PsA from Aug 1st, 2021.

This talk addresses long-term efficacy and safety of ixekizumab in phase III study (SPIRIT P1) for biologics-naive paitents with active PsA and in COAST-Y, 2 years extension of the COAST-V, -W trials for axSpA, recently published. In the 3 years extension of the SPIRIT P1, ixekizumab showed significantly greater treatment responses vs placebo as early as week 4 for ACR50, persisted through week 156 and also significantly less progression of structural damage assessed by mTSS change at week 24, sustained up to 3 years in PsA. ASAS 40 response rates of ixekizumab 80 mg every 4 weeks at weeks 52 and 116 were 52.2% and 56.7%. Most patients treated with ixekizumab for 2 years did not show radiographic progression. There were no unexpected safety signals reported in 3 years extension of SPIRIT P1 study and in COAST-V, -W and COAST-Y trials.

Ixekizumab, one of the IL-17 inhibitors show efficacy in treating multiple facets of SpA, including psoriasis, enthesitis, synovitis, bone erosion, new bone formation and pain, which indicates the importance of IL-17A in disease pathophysiology.

Breakfast Symposium VI
Janssen

Redefine Persistence in AS Management

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

Long-lasting Golimumab in AS: Learnings from real-world evidence

Bon San Koo
Inje Univ., Korea

Ankylosing spondylitis (AS) is a chronic inflammatory arthritis that predominantly affects the sacroiliac joint and spine and is characterized by chronic back pain and stiffness. The primary goals of treating ankylosing spondylitis (AS) patients are to maximize long-term health-related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, and preservation of function. Knowledge of the pathogenesis of AS has led to number of improvements in its treatment, and in particular the development of biologic agents has been of great benefit. Tumor necrosis factor-a inhibitors (TNFis) are the main therapeutic agents used to treat patients with AS for whom non-steroidal anti-inflammatory drugs are ineffective or are contraindicated. And as far as drug survival of these treatment options, it is an important proxy measure for effectiveness of treatments for AS.

A study aimed to investigate drug retention rates for various TNF inhibitors (TNFis) commonly prescribed to Korean patients with ankylosing spondylitis (AS) in the Korean College of Rheumatology Biologics registry (KOBIO; December 2012–June 2016). And registry data provides a unique way to study the real-world use of medication. A fundamental limitation of clinical trials is that the included patients differ from patients seen in daily practice. Discontinuation was defined as switching or stopping the biologic agent. The drug retention rate for golimumab (82.2%) was highest, followed by adalimumab, infliximab biosimilar, etanercept, and infliximab originator. The rate of adverse events decreased to 9.7%, and the rate of significant clinical improvement also dropped to 6.5% for golimumab compared to another TNFi, although the inefficacy rate was similar among the TNFis from etanercept to golimumab ranging from 27.8 to 45.2%.

Thus, this real-life study showed that around 82% of patients with AS maintained golimumab at about 4-year follow-up. And it can be concluded that golimumab has demonstrated proven persistence in AS.

Keynote Lecture

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

The future of rheumatology

Antony Rosen
The Johns Hopkins Univ. School of Medicine, USA

The autoimmune rheumatic diseases are a highly complex group of disorders, with complexity residing in numerous dimensions, including genetics, environment, phenotype, trajectory, outcomes, responses to therapy, and specificity of the immune response. In spite of this multi-dimensional complexity, the future is bright in terms of understanding disease mechanism, and more effective, patient-focused care. This optimism stems from two major opportunities: (i) the accumulated clinical wisdom that has recognized homogeneous disease subgroups within the larger inhomogeneous disease category; these subgroups are based on subtle but distinct phenotypic features and trajectories over time; and (ii) the exceptional tools that the current technology revolutions (measurement, computation and connectivity) are bringing forward for human discovery and clinical use. This presentation focuses on the power of the immune system, coupled with distinct clinical trajectories over time, and the co-occurrence of cancer and autoimmune disease presentations in deconvoluting mechanisms in the rheumatic diseases. It then focuses on the role of the target tissue in shaping and driving immune-mediated injury in the rheumatic diseases. Lastly, the talk will define the requirements and opportunities that will ensure that the revolutions in measurement and connectivity will drive real improvements in patient care in the rheumatic diseases to usher in a new era of patient-centered, more precise and more predictive diagnosis and therapy in the rheumatic diseases.

International Symposium

Treatment of Osteoarthritis: To be Used and Abused?

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

Hype and truth - treatment paradigm of osteoarthritis

David Hunter
Univ. of Sydney, Australia

Osteoarthritis is a prevalent and disabling disease that affects millions of people worldwide. Characteristic management of this disease is unfortunately low value and inappropriate. This lecture will focus on areas of care that are full of myths, misconceptions and hype. This will extend from our understanding of the pathophysiology of disease, the sources of pain, methods of diagnosing the disease, communicating with our patients about this and disease prognosis. Particular focus will be given to controversial therapeutic areas, including paracetamol, opioids, viscosupplements, arthroscopy. To ensure the audience gains value, each hype, myth, and misconception will be distilled, and clear messages about optimal management will be conveyed.

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Addicted to prescription, medical abuse of osteoarthritis

Yuqing Zhang
Massachusetts General Hosp., USA

Osteoarthritis (OA) is the most common joint disease. The World Health Organization estimated that 18% of women and 9.6% of men ages >60 years have symptomatic OA; of them, 80% have some limitation in mobility and 25% are unable to perform their major daily activities. Pain from OA is a major clinical manifestation and a key factor leading people to seek medical care. To date, there is no known cure. The main goals of contemporary management of OA continue to be control of pain and improvement in both function and health-related quality of life, with avoidance of therapeutic toxicity.

Most commonly used pain relief medication for OA consists of non-steroidal anti-inflammatory drugs (NSAIDs) and opioids. Numerous studies have shown that these medications, if used inappropriately, are associated with an increased risk of intestinal bleeding or ulcer, renal injury, cardiovascular disease and even deaths. Several guidelines have emphasized that the cornerstone of OA management should focus on patient education, weight loss, exercise, and self-efficacy and self-management. Topical NSAID is strongly recommended for knee OA. Oral NSAIDs and intraarticular steroid injections can be considered, if needed. The use of opioid analgesics should be avoided.

There is paucity of data on whether the physicians and OA patients follow the professional guidelines on OA management. Results from the United Kingdom indicated that topical NSAID prescription almost tripled from early 2000's to middle of 2010's. The initial prescription of oral Cox-2 inhibitors decreased. Oral opioid prescription increased from 2000 to early 2010's, and there was no indication that such a trend has changed recently. Results from epidemiological studies that describe the practice pattern of OA management, especially inappropriate medication use, secular trend of pain-relief medication use, and factors associated with inappropriate pain-relief medication use, will guide appropriate actions to take to improve OA management.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Use or abuse? APM for degenerative meniscus in osteoarthritis

Hyun Ah Kim
Hallym Univ., Korea

With the advent of sophisticated imaging, such as magnetic resonance imaging (MRI), noninvasive examination of pathologic changes in the joint and periarticular structures of the knee, which sometimes correlate with symptoms, is possible. Although MRI shows high sensitivity and specificity for the detection of abnormalities in the articular soft tissues, clinical significance of such lesions detected by MRI is in many cases unclear, and even consensus on when to perform MRI in knee OA subjects is not reached.

In previous studies of middle-aged and elderly men and women representative of the general population, incidental meniscal findings on MRI of the knee were common, and the majority of meniscal damage was found in persons without knee symptoms. In addition, meniscal damage was not significantly associated with the presence of knee pain or its severity among subjects with radiographic knee OA. These data suggest that the therapeutic efficacy of arthroscopic surgery for degenerative meniscal tears may not be high. Although arthroscopic partial meniscectomy (APM) is one of the most common type of knee surgery, evidence of its efficacy lags behind since a long time.

Rigorous outcome studies conducted after the 2000s began to shed light on the clinical value of arthroscopic surgery. Randomized controlled trials of arthroscopic management of degenerative meniscal tears showed that surgery was no better than physical therapy (PT) or even a sham surgery in improving pain or functional status.

In this lecture, the relationship between OA anatomical abnormality revealed by imaging and pain and knee function is examined. In addition, the evidence of clinical efficacy of arthroscopic meniscectomy for OA and degenerative meniscal tear is reviewed.

Free Paper Session

Spondyloarthritis

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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O-35

Physical trauma exacerbates arthritis and enthesitis in curdlan-administered SKG mice model

Seung Hoon Lee[1], Chanhyeok Jeon[1,2], Sungsin Jo[1], Tae-Hwan Kim[1,3]

[1] Rheumatology Research, Hanyang University Institute for Rheumatology Research,, Republic of Korea
[2] Translational Medicine, Graduate School of Biomedical Science and Engineering, Hanyang University, Republic of Korea
[3] Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea

Background

Ankylosing spondylitis (AS) is a chronic inflammatory disease accompanied by spinal and peripheral joint inflammation. Intriguingly, some of AS patients have experienced physical trauma before disease onset, but the contribution of trauma to the pathophysiology of AS is still debated. The aim of this study was to determine whether physical trauma affected curdlan-induced arthritis and/or enthesitis in SKG mice.

Methods

For physical reaction to trauma, the right hindlimb of 7 weeks male SKG mice were immobilized using a surgical sticking plaster and pipette tip for a week. After immobilization, the fixing tip was removed from the ankle and the mouse was intraperitoneally injected with 3mg curdlan. We monitored clinical arthritis for 5 weeks and scored every week. The physical changes in ankles were evaluated by H&E, Safranin O, and Toluidine blue staining. Various bone indicators for traumatic experienced right and non-traumatic experienced left (inflamed bone volume, structure separation, structure linear density, and structure thickness) ankles were measured by microCT.

Results

During arthritis induction, the arthritis scores of the traumatic experienced right hindlimb were obviously increased in curdlan-administered SKG mice compared to left hindlimb. Histological analysis showed that destruction of joint cartilage, frequency of enthesitis, and severity of arthritis at the ankle were significantly augmented in the traumatic experienced right hindlimb. Also, microCT analysis revealed that inflamed bone volumes significantly increased in traumatic experienced right hindlimb compared with non-traumatic experienced left hindlimb.

Conclusions

We conclude that physical right hindlimb with trauma is experienced to exacerbate the destruction of joint cartilage, frequency of enthesitis, and severity of arthritis in the curdlan-administered SKG mice model. Therefore, physical trauma might be a significant initiator or mediator of the ankylosing spondylitis.

Keywords

Physical Trauma, Curdlan-administered SKG mice, ankylosing spondylitis

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KCR 2022
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PPM1A promotes matrix mineralization of osteoblasts differentiation via FOXO1A-RUNX2 pathway in ankylosing spondylitis

Subin Weon[1], Sungsin Jo[1], Ye-Soo Park[2], Yong-Gil Kim[3], Tae-Hwan Kim[1,4]

[1] Rheumatology Research, Hanyang University Institute for Rheumatology Research, Republic of Korea
[2] Orthopedic Surgery, Guri Hospital, Hanyang University College of Medicine, Republic of Korea
[3] Rheumatology, Asan Medical Center, University of Ulsan College of Medicine, Republic of Korea
[4] Rheumatology, Hanyang University Hostpital for Rheumatic Diseases, Republic of Korea

Background

Ankylosing spondylitis (AS) patients exhibited elevated protein phosphatase magnesium-dependent 1A (PPM1A) levels in sera, strongly associated with spinal radiographic progression. RUNX2 is also highly expressed in AS bone tissues, playing an essential role in osteoblast differentiation and bone formation. However, the precise molecular mechanism underlying the relationship between PPM1A and RUNX2 is not well understood. Here we investigate the potential mechanism of PPM1A and RUNX2 of the excessive bone formation in AS.

Methods

Primary osteoprogenitor cells of the interspinous process were obtained from 5 AS patients and 6 disease controls. The isolated progenitor cells were differentiated into mature osteoblasts and assessed by the bone formation in vitro assay. To investigate the effect of PPM1A on AS, we treated various doses of exogenous PPM1A in AS-osteoprogenitor cells and analyzed using RT-PCR and immunoblotting. Furthermore, we examined the alteration in FOXO1A-RUNX2 regulatory mechanism by exogenous treatment of PPM1A using various biochemistry and molecular methods.

Results

Expression levels of PPM1A and RUNX2 were increased in destructive bone tissues of AS and its osteoprogenitor cells compared to disease control. During osteoblast differentiation, exogenous treatment of PPM1A accelerated the matrix mineralization in AS-osteoprogenitor cells but not in disease control. Intriguingly, RUNX2 and PPM1A protein expressions were significantly upregulated at the matrix mineralization stage. Mechanically, exogenous treatment of PPM1A dephosphorylates FOXO1A and translocates FOXO1A protein into the nucleus to induce RUNX2 transcript level. Moreover, exogenous treatment of PPM1A promoted matrix mineralization of overexpressed FOXO1A in control during osteoblasts differentiation.

Conclusions

These results indicate that treatment with PPM1A induces RUNX2 transcript levels through dephosphorylation of FOXO1A in AS-osteoprogenitor cells, thereby accelerating the bone mineralization of osteoblast differentiation. Our results provide a regulatory mechanism whereby a high PPM1A level contributes to excessive bone mineralization of AS.

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A pilot study on deep learning-based grading of the corner of vertebral body for the assessment of radiographic progression in patients with ankylosing spondylitis

Bon San Koo[1], Jae Joon Lee[2], Jae-Woo Jung[2], Chang Ho Kang[3], Kyung Bin Joo[4], Tae-Hwan Kim[4], Seunghun Lee[5]

[1] Internal medicine, Inje University Seoul Paik Hospital, Inje University College of Medicine, Republic of Korea
[2] CRESCOM Co., Ltd., CRESCOM Co., Ltd., Republic of Korea
[3] Department of Radiology, Korea University Anam Hospital, Republic of Korea
[4] Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea
[5] Department of Radiology, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea

Background

This pilot study aimed to develop a deep learning model for grading the corners of the cervical and lumbar vertebral bodies for computer-aided detection of modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) in patients with ankylosing spondylitis (AS).

Methods

Using a key-point detection deep learning model, disc points were detected between the bodies in the cervical and lumbar spinal radiographs. After cropping vertebral regions around the disc point, the lower and upper corners of the vertebral bodies were classified as grade 3 (total bony bridges) or grades 0, 1, or 2 (non-bridges). We trained a convolutional neural network model to predict the grades in the lower and upper corners of the vertebral bodies. The performance of the model was evaluated in a validation set, which was separate from the training set.

Results

Among 1,280 patients with AS for whom mSASSS data were available, 5,083 cervical and 5,245 lumbar lateral radiographs were reviewed. The total number of corners where mSASSS was measured in the cervical and lumbar vertebrae, including the upper and lower corners, was 119,414. Among them, the number of corners in the training and validation sets was 110,088 and 9,326, respectively. The mean accuracy, sensitivity, and specificity for mSASSS scoring in one corner of the vertebral body were 0.91604, 0.80288, and 0.94244, respectively (Table 1).

Conclusions

A high-performance deep learning model for grading the corners of the vertebral bodies was developed for the first time. This model must be improved and further validated to develop a computer-aided tool for assessing mSASSS in the future.

Figure & Table

Grade	True positive	True negative	False positive	False negative	Sensitivity	Specificity	Positive predictive value	F1score	Accuracy
0	2250	6085	623	368	0.85943	0.90713	0.78315	0.81952	0.89374
1	2169	6034	500	623	0.77686	0.92348	0.81266	0.79436	0.87958
2	700	8005	225	396	0.63869	0.97266	0.75676	0.69273	0.93341
3	2641	6288	218	179	0.93652	0.96649	0.92375	0.93009	0.95743

Table. Performance for each scoring in the test set.

Keywords

Ankylosing spondylitis, mSASSS, Deep learing

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Journal of Rheumatic Diseases
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Analysis of radiographic progression in patients with ankylosing spondylitis: Using group-based trajectory modeling and decision trees

Juyeon Kang[1], Tae-Han Lee[2], Bon San Koo[3], Seo Young Park[4], Seunghun Lee[5], Tae-Hwan Kim[6]

[1] Division of Rheumatology, Internal Medicine, Inje University Busan Paik Hospital, Republic of Korea
[2] Division of Rheumatology, Internal Medicine, Keimyung University Dongsan Medical Center, Republic of Korea
[3] Division of Rheumatology, Internal Medicine, Inje University Seoul Paik Hospital, Republic of Korea
[4] Department of Statistics and Data Science, Korea National Open University, Republic of Korea
[5] Department of Radiology, Hanyang University College of Medicine, Republic of Korea
[6] Division of Rheumatology, Internal Medicine, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea

Background

Ankylosing spondylitis (AS) is characterized by long-term disease progression. During progression, various radiographic changes occur in the spine, which eventually lead to disability in the patient's lifetime. Although the duration of the disease, aging, and passage of time are predicted to be highly associated with spinal progression of AS, it is difficult to accurately predict its progression in the spine of patients. Thus, we aimed to find ways to predict spinal progression over time in patients with AS and analyze its associated clinical factors.

Methods

Data from the medical records from Hanyang university hospital for rheumatic diseases were extracted between 2001 and 2018. We analyzed the data on patients who fulfilled the modified New York Criteria for AS and had two or more sets of radiographs taken during the observation period. The modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) was estimated by two independent radiologists. Group-based trajectory modeling (GBTM) was used to classify patients into distinct subgroups of longitudinal mSASSS. And when these trajectories and statistically associated factors acted on a patient, which group the patient was most likely to belong to was predicted using a decision tree analysis.

Results

The trajectories were evaluated by dividing them into three groups based on duration of the disease. We identified that sex, age at diagnosis, ocular involvement and peripheral joint involvement were associated with the classified spinal progression trajectories, and predictions through decision trees were similarly identified. AS onset in older age and ocular involvement were associated with worse radiographic progression, while female sex and peripheral joint involvement were associated with radiographic progression.

Conclusions

We identified three patterns of radiographic progression according to duration of the disease. The progression trend of patients with AS identified in this study is expected to be helpful in the treatment and management of patients in actual clinical settings.

Figure & Table

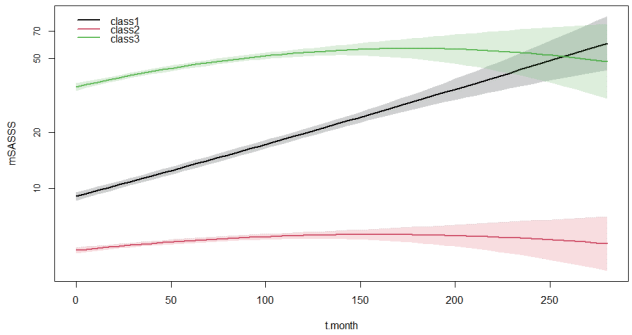

Figure. Longitudinal mSASSS trajectory groups for disease duration

Time in month is shown along the x-axis, and logarithmic transformed total mSASSS is shown along the y-axis. The solid line represents the estimated mean in the same-colored area representing the 95% confidence interval.

mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score

Keywords

Ankylosing spondylitis, Radiographic progression, Trajectory analysis

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Vol. 29, Suppl. 1, May, 2022
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The spinal radiographic change correlates with past alkaline phosphatase levels in patients with ankylosing spondylitis

Bon San Koo[1], Seo Young Park[2], Ji Hui Shin[3], Seunghun Lee[4], Kyung Bin Joo[3], Tae-Hwan Kim[3]

[1] Internal medicine, Inje University Seoul Paik Hospital, Inje University College of Medicine, Republic of Korea
[2] Department of Statistics and Data Science, Korea National Open University, Republic of Korea
[3] Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea
[4] Department of Radiology, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea

Background

ALP is generally produced in the liver, bone, and kidneys. In serum, bone and liver specific isoform of ALP form more than 90% of total serum ALP with 1:1 ratio. The aim of this study is to determine the relationship between alkaline phosphatase (ALP) levels and the radiographic change over time in patients with ankylosing spondylitis (AS).

Methods

Longitudinal electronic medical records of patients diagnosed with AS from January 2001 to December 2018 were analysed. To determine the relationship between the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) and ALP levels over time, linear mixed models with mSASSS and ALP levels with different lag times (3 month intervals) were used. Using the lag time of ALP levels with the highest beta coefficients, linear mixed models including clinical variables were further investigated.

Results

A total of 37,852 intervals were obtained from 1122 patients. Among different lag times, the ALP level in the previous 5 years and 3 months and mSASSS showed significant beta coefficients. In the linear mixed model that included clinical variables, the ALP level in the previous 5 years 3 months was significantly associated with mSASSS (β=0.021, 95% CI: 0.017–0.025, p<0.001) (Table 1).

Conclusions

The ALP level previous 5 years and 3 months were significantly correlated with the present spinal radiographic change. Therefore, ALP levels may be helpful in predicting long-term radiographic progression than CRP levels.

Figure & Table

	Model 1				Model 2			
	Beta estimate	95% CI		p-value	Beta estimate	95% CI		p-value
		LB	UB			LB	UB	
(Intercept)	-2.917	-3.711	-2.123	<0.001	-3.759	-7.519	0.000	0.050
mSASSS.base	1.096	1.064	1.127	<0.001	1.066	1.030	1.102	<0.001
time (3month intervals)	0.211	0.206	0.217	<0.001	0.218	0.212	0.223	<0.001
ALP at previous 5 years 3 months	0.020	0.017	0.024	<0.001	0.021	0.017	0.025	<0.001
log CRP at previous 18 months	-0.140	-0.262	-0.018	0.025	-0.117	-0.247	0.014	0.079
TNF inhibitor	-0.833	-0.992	-0.673	<0.001	-0.850	-1.020	-0.680	<0.001
AST at previous 5 years 3 months					0.001	-0.007	0.010	0.794
ALT at previous 5 years 3 months					0.000	-0.006	0.005	0.907
Female					-1.065	-3.096	0.966	0.304
Eye involvement					2.973	1.761	4.185	<0.001
Peripheral involvement1					-2.078	-3.288	-0.867	0.001
HLA-B27					-0.558	-4.139	3.023	0.760
Smoking(ref: nonsmoker)								<0.001
ex_smoker					3.139	1.603	4.675	<0.001
smoker					2.159	0.673	3.646	0.004

mSASSS: the modified Stoke Ankylosing Spondylitis Spinal Score; ALP: alkaline phosphatase; CRP: C-reactive protein; TNF: tumor necrosis factor; AST: aspartate aminotransferase; ALT: alanine aminotransferase; HLA: human leukocyte antigen.

Table. Linear mixed models including clinical variables

Keywords

Ankylosing spondylitis, Alkaline phosphatase, Radiogrpahic progression

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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CCL20 inhibition for treating inflammation in ankylosing spondylitis

Hui-Ju Kim[1], Hae-in Lee[1], So-Hee Jin[1], Ah-Ra Choi[1], Soon Mi Choi[1], Moon-ju Kim[2], Yu Jeong Lee[2], Kyeong Hwan Byeon[2], Seong Hoon Kim[2], Eun Jeong Won[2], Tae-Jong Kim[1]

[1] Department of Rheumatology, Chonnam National University Medical School and Hospital, Republic of Korea
[2] Department of Parasitology and Tropical Medicine, Chonnam National University Medical School and Hospital, Republic of Korea

Background

Ankylosing spondylitis (AS) is a rheumatic disease characterized by chronic inflammation. Several lines of evidence implicate interleukin (IL)-17A-secreting T helper (Th)17 cells in AS pathogenesis. One of the receptors of Th17, C-C motif chemokine ligand 20 (CCL20) is known to attract C-C chemokine receptor 6 (CCR6) expressing cells to the site of inflammation. However, the role and mechanism of CCL20 in AS are not well understood. Therefore, this study was to evaluate whether CCL20 inhibition could treat chronic inflammation in AS.

Methods

Peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) were obtained from AS patients. Inflammatory cytokine-producing cells were analyzed using flow cytometry and enzyme-linked immunosorbent assay (ELISA). To determine the direct effect of AS serum and synovial fluid on CCL20 positive cell migration, a Transwell migration assay was performed. Female SKG mice were treated with CCL20 blocking antibody or vehicle. Inflammation was evaluated using immunohistochemistry, and positron emission tomography image.

Results

Percentages of CCL20 positive cells were significantly higher in synovial fluid than those in peripheral blood.

IL-17A and GM-CSF level were highly increased in CCL20 positive cells, compared to CCL20 negative cells.

The migration of CCL20 cells was significantly increased in the presence of AS synovial fluid compared with AS serum. In animal study, the development of arthritis was significantly delayed in CCL20 Inhibitor-treated mice, compared to vehicle-treated mice. The mean values of maximum standardized uptake values of ankle joint from CCL20 Inhibitor were also significantly lower than those from vehicle-treated mice in PET image.

Conclusions

This study demonstrates CCL20 blockade ameliorated inflammation in AS. Thus, CCL20-target therapy could be a promising treatment for AS.

Keywords

Ankylosing Spondylitis, CCL20, Inflammation

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Metagonimus yokogawai-derived protein attenuates inflammation in ankylosing spondylitis

Moon-Ju Kim[2], Yu Jeong Lee[2], Kyeong Hwan Byeon[2], Seong Hoon Kim[2], Hae-in Lee[1], Hui-Ju Kim[1], So-Hee Jin[1], Ah-Ra Choi[1], Soon Mi Choi[1], Sungsin Jo[3], Tae-Hwan Kim[3], Eun Jeong Won[2], Tae-Jong Kim[1]

[1] Department of Rheumatology, Chonnam National University Medical School and Hospital, Republic of Korea
[2] Department of Parasitology and Tropical Medicine, Chonnam National University Medical School and Hospital, Republic of Korea
[3] Department of Rheumatology, Hanyang University Institute for Rheumatology Research, Republic of Korea

Background

Helminth infections and their components have been shown to have a potential of immune modulation and could attenuate immune response. This study aimed to evaluate potential protective effect of Metagonimus yokogawai –derived protein (MYp) on ankylosing spondylitis (AS).

Methods

We assessed cytotoxicity of MYp treatment at different doses before performing experiments. The anti-inflammatory properties of MYp on cytokines (IFN-γ, IL-17A) were assessed using peripheral blood mononuclear cells (PBMCs) obtained from AS patients. Inflammatory cytokine-producing cells were analyzed using flow cytometry. In SKG mouse model, inflammation was evaluated using immunohistochemistry and positron emission tomography.

Results

The frequencies of IFN-γ and IL-17A producing cells were significantly reduced after MYp treatment in PBMCs from AS patients. In vivo mouse model, a remarkable regression of AS symptom score and reduced frequencies of IFN-γ, IL-17A, and TNF-α producing cells among splenic cells were found in the MYp–treated mice. 18F-FDG uptake was significantly lower in MYp treated mice than in vehicle treated mice.

Conclusions

We provide the first evidence demonstrating the ameliorative effect of MY proteins on the clinical signs and cytokine derangements in AS.

Keywords

Ankylosing Spondylitis, Metagonimus yokogawai, Immune response

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Long-term treatment with ixekizumab in patients with axial spondyloarthritis: Two-year results from COAST-Y

Jürgen Braun[1], Uta Kiltz[1], Atul Deodhar[2], Tetsuya Tomita[3], Maxime Dougados[4], Rebecca Bolce[5], David Sandoval[5], David Adams[5], Chen-Yen Lin[5], Jessica Walsh[6], Young In Eom[7]

[1] Rheumatology, Ruhr-Universität Bochum, Germany
[2] Rheumatology, Oregon Health & Science University, USA
[3] Rheumatology, Osaka University Graduate School of Medicine, Japan
[4] Rheumatology, Hôpital Cochin, France
[5] Rheumatology, Eli Lilly and Company, USA
[6] Rheumatology, University of Utah, USA
[7] Rheumatology, Lilly Korea Ltd, Republic of Korea

Background

To study the efficacy and safety of the interleukin-17 inhibitor ixekizumab (IXE) in the treatment of patients with radiographic (r-) and non-radiographic axial spondyloarthritis (nr-axSpA) for up to 116weeks.

Methods

COAST-Y (NCT03129100) is the 2-year extension of the COAST-V, -W, and -X trials. Patients continued with the dose received at the end of the originating trial at Week52, either with 80mg IXE Q4W or Q2W. Patients who had been assigned to adalimumab or placebo were re-randomized to IXE Q4W or Q2W at Week16 in COAST-V and -W. Patients who had received placebo for 52weeks in COAST-X were switched to IXE Q4W in COAST-Y. Patients who switched from placebo or adalimumab treatment to IXE (COAST-V, -W, or -X) or from IXE Q4W to open-label IXE Q2W (COAST-X) during the originating studies were analyzed separately from patients continuously treated with IXE. Standardized efficacy measures were used (Table).

Results

Of the 773 patients enrolled in COAST-Y, 86.0% completed Week116 of treatment (52weeks of one of the originating trials and 64weeks of COAST-Y). Among the patients continuously treated with IXE for 116weeks (IXE Q4W: N=157; IXE Q2W: N=195), 46.9% achieved low disease activity (ASDAS <2.1), and 19.9% achieved ASAS partial remission at 116weeks (Table). In comparison to baseline, 56.0% achieved ASAS40 (Table). The mean change from baseline at Week116 was −1.70 for ASDAS, −2.98 for BASFI, and 9.22 for SF-36 Physical Component Summary (Table). Similar observed responses were achieved between the patients continuously treated with IXE and patients initially treated with placebo or adalimumab. For the 932 patients in the safety population, no new safety signals were identified.

Conclusions

IXE treatment led to consistent and sustained long-term improvements in disease activity and quality of life in patients with r- and nr-axSpA, with no new safety signals after up to 2 years of treatment.

Figure & Table

	IXE Q4W N=157		IXE Q2W N=195	
Demographics				
Age	42.7 (13.0)		41.8 (11.2)	
Male (n, [%])	124 (79.0)		132 (67.7)	
Baseline ASDAS	3.92 (0.80)		3.95 (0.76)	
Baseline BASDAI	7.07 (1.26)		7.18 (1.35)	
Baseline BASFI	6.57 (1.76)		6.74 (1.86)	
Baseline BASMI	4.08 (1.46)		3.97 (1.52)	
Baseline SF-36 PCS	33.90 (7.27)		33.26 (6.88)	
Outcome measure				
Response (n, [%])	Week 52	Week 116	Week 52	Week 116
ASDAS <2.1	75 (47.8)	69 (43.9)	88 (45.1)	96 (49.2)
ASAS partial remission	34 (21.7)	31 (19.7)	35 (17.9)	39 (20.0)
ASAS40	82 (52.2)	89 (56.7)	99 (50.8)	108 (55.4)
BASDAI50	78 (49.7)	75 (47.8)	83 (42.6)	99 (50.8)
Change from baseline				
ASDAS	-1.64 (1.05)	-1.60 (1.15)	-1.63 (1.03)	-1.78 (1.04)
BASFI	-2.88 (2.31)	-2.76 (2.39)	-2.83 (2.38)	-3.15 (2.34)
BASMI	-0.57 (0.95)	-0.57 (0.93)	-0.53 (0.92)	-0.60 (1.00)
SF-36 PCS	9.03 (8.62)	8.43 (8.70)	8.87 (7.57)	9.86 (8.45)

Data are mean (SD) unless otherwise noted. Non-responder imputation was used for categorical variables, and modified baseline observation carried forward for continuous variables.

Table. Demographic and efficacy results for patients continuously treated with IXE for 116 weeks

Keywords

Ixekizumab, Radiographic, Axial spondyloarthritis

Free Paper Session

Systemic Lupus Erythematosus

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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B cell-specific deletion of Crif1 drives lupus-like autoimmunity by activation of IL-17, IL-6, and pathogenic Tfh cells

Jin-Sil Park[1], SeungCheon Yang[1], Sun-Hee Hwang[1], JeongWon Choi[1], Seung-Ki Kwok[1,2]
Young-Yun Kong[3], Jeehee Youn[4], Mi-La Cho[1,5,6], Sung-Hwan Park[1,2]

[1] Rheumatism Research Center, Catholic University of Korea, Republic of Korea
[2] Divison of Rheumatology, Catholic University of Korea, Republic of Korea
[3] School of Biological Sciences, Seoul National University, Republic of Korea
[4] Laboratory of Autoimmunology, Hanyang University, Republic of Korea
[5] Department of Medical Lifescience, Catholic University of Korea, Republic of Korea
[6] Department of Biomedicine & Health Sciences, Catholic University of Korea, Republic of Korea

Background

CR6-interacting factor 1 (Crif1) is a nuclear transcriptional regulator and a mitochondrial inner membrane protein; however, its functions in B lymphocytes have been poorly defined. In this study, we investigated the effects of Crif1 on B-cell metabolic regulation, cell function, and autoimmune diseases.

Methods

Using mice with B cell-specific deletion of Crif1 (Crif1ΔCD19), we assessed the relevance of Crif1 function for lupus disease parameters including anti-double-stranded DNA, cytokines, and kidney pathology. RNA sequencing was performed on B cells from Crif1ΔCD19 mice. The phenotypic and metabolic changes in immune cells were evaluated in Crif1ΔCD19 mice. Roquinsan/+ mice crossed with Crif1ΔCD19 mice were monitored to assess the functionality of Crif1-deficient B cells in lupus development.

Results

Crif1ΔCD19 mice showed an autoimmune lupus-like phenotype, including high levels of autoantibodies to double-stranded DNA and severe lupus nephritis with increased mesangial hypercellularity. While loss of Crif1 in B cells showed impaired mitochondrial oxidative function, Crif1-deficient B cells promoted the production of IL-17 and IL-6 and was more potent in helping T cells develop into T follicular helper cells. In an autoimmune lupus mouse model, depletion of Crif1 in B cells exacerbated lupus severity and Crif1 overexpression prevented lupus development in Roquinsan/san mice.

Conclusions

These results showed that Crif1 was negatively correlated with disease severity, and overexpression of Crif1 ameliorated disease development. Our findings suggest that Crif1 is essential for preventing lupus development by maintaining B cell self-tolerance.

Keywords

Systemic lupus erythematosus, CR6-interacting factor 1, B cells

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Biological insights into systemic lupus erythematosus through an immune cell-specific transcriptome-wide association study

Xianyong Yin[1,2,3], Kwangwoo Kim[4], Hiroyuki Suetsugu[5,6,7], Chikashi Terao[6,8,9], Yong Cui[3], Sang-Cheol Bae[10,11]

[1] Biostatistics, University of Michigan, Ann Arbor, USA
[2] Department of Dermatology, Anhui Medical University, China
[3] Department of Dermatology, China-Japan Friendship Hospital, China
[4] Department of Biology, Kyung Hee University, Republic of Korea
[5] Laboratory for Bone and Joint Diseases, RIKEN Center for Medical Sciences, Japan
[6] Laboratory for Statistical and Translational Genetics Analysis, RIKEN Center for Integrative Medical Sciences, Japan
[7] Department of Orthopaedic Surgery, Kyushu University, Japan
[8] Clinical Research Center, Shizuoka General Hospital, Japan
[9] Department of Applied Genetics, University of Shizuoka, Japan
[10] Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea
[11] Hanyang University Institute for Rheumatology Research, Hanyang University Institute for Rheumatology Research, Republic of Korea

Background

Genome-wide association studies (GWAS) have identified >100 risk loci for systemic lupus erythematosus (SLE), but the effector genes at most loci remain unclear, hampering translation of these genetic discoveries. We aimed to prioritize genes underlying the 110 SLE loci identified in the latest East Asian GWAS meta-analysis.

Methods

We built gene expression predictive models from blood B-cells, CD4+ and CD8+ T-cells, monocytes, natural killer cells, and peripheral blood cells from 105 Japanese individuals. We performed a transcriptome-wide association study (TWAS) using data from the latest genome-wide association meta-analysis of 208,752 East Asians and searched for effector genes using TWAS and three data-driven computational approaches.

Results

The TWAS identified 171 genes for SLE (P<1.0x10-5); 114 (66.7%) showed significance only in a single cell type; 127 (74.3%) were in SLE GWAS loci. TWAS identified a strong association between CD83 and SLE (P<7.7×10-8). We subsequently found a novel single-variant association at rs72836542 (OR=1.11, P=4.5×10-9) around CD83 after adding 1,498 cases and 3,330 controls. For the 110 SLE loci, we identified 276 effector gene candidates, including 104 genes at recently-identified SLE novel loci. We demonstrated in vitro that the causal variant rs61759532 in ACAP1 exhibited an allele-specific regulatory effect on this gene, and that presence of the SLE risk allele decreased ACAP1 expression.

Conclusions

Cell-level TWAS in six types of immune cells complemented SLE gene discovery and guided the identification of novel genetic associations. The gene findings shed biological insights into SLE genetic associations.

Keywords

systemic lupus erythematosus, transcriptome-wide association study, effector genes

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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The association between CD40 rs4810485 polymorphism and susceptibility of systemic lupus erythematosus: Systematic review and meta analysis

Rizki Febriawan[1], Nurul Fajri Widyasari[2]

[1] Medicine, Utama Hospital Belitung, Indonesia
[2] Medicine, PKU Muhammadiyah Sampangan Hospital Surakarta, Indonesia

Background

Some studies reported that CD40 rs 4810485 (T/G) gene polymorphism may related to Systemic Lupus Erythematosus (SLE) susceptibility, but there are great differences among study conclusion. The aim of this study was determined CD40 rs 4810485 Polymorphism and risk of SLE

Methods

Literature search was conducted using PubMed and scopus databese until January 2022 to find case-control studies on association between CD40 (rs4810485) Polymorphism and SLE risk. The Quality of study was determine using the New castle ottawa (NOS) Scale. Effect meassured with Odds ratio (OR) and 95%CI. We Performed data analysis using Revman 5.4.

Results

A total of seven studies involved 2377 SLE case and 4076 control participants in this meta analysis. Pooled analysis show that there is no significant association between CD40 rs4810485 polymorphism and SLE Risk in dominant model GG+GT vs TT (P=0.34), recessive model GG vs GT+TT (P=0.63) and Allelic model G vs T (P=0.92). In the Stratified analysis by region, dominant model of CD40 rs4810485 polymorphism contribute increased risk of SLE in Europe (OR 3.0, 95%CI: 2.0 - 4.49; P<0.001) and Turkish (OR 5.39, 95%CI: 2.3 - 12.67; P<0.001). Recessive model of CD40 rs4810485 polymorphism increased risk of SLE (Europe OR 1.28, 95%CI: 1.05 - 1.57; P=0.02), and decreased risk of SLE (Asia OR 0.79, 95%CI: 0.68 - 0.91; P=0.001; America OR 0.66, 95%CI: 0.47 - 0.92; P=0.01) significantly. Allelic model of CD40 rs4810485 polymorphism increased risk of SLE (Europe OR 1.4, 95%CI: 1.2 - 1.63; P<0.001; Turkish OR: 1.74, 95%CI: 1.26-2.42, P<0.001) and decreased risk of SLE (Asia OR 0.86, 95%CI: 0.78 - 0.95; P=0.004; America OR 0.69, 95%CI: 0.52 - 0.92; P=0.01) significantly.

Conclusions

CD40 rs4810485 Polymorphism was associated with SLE susceptibility. TT genotype and T Alelle decreased risk of SLE in Europe and Turkish, but increased risk of SLE in Asia and America.

Figure & Table

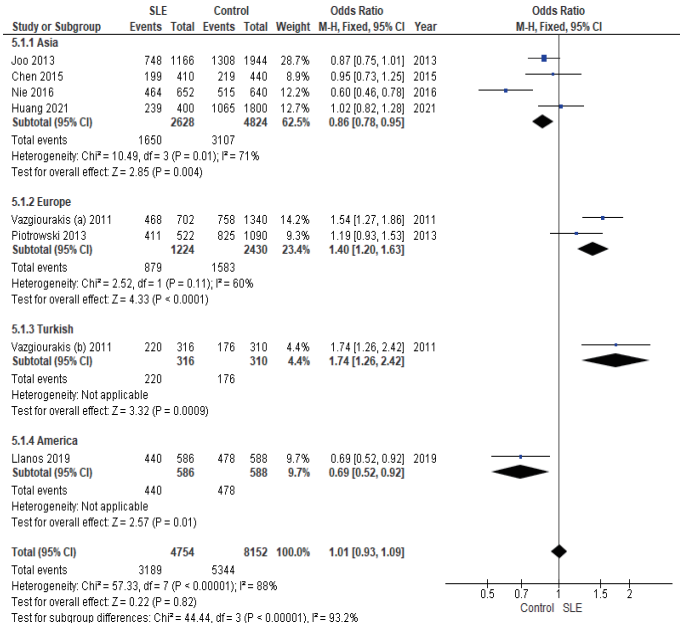

Figure. Forrest Plot Gene G vs T (Allelic Model)

Keywords

CD40 rs4810485, Systemic Lupus Erythematosus, Polymorphism

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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The role of sphingolipids in patients with systemic lupus erythematosus

Ji-Won Kim[1], Ju-Yang Jung[1], Hyoun-Ah Kim[1], Chang-Hee Suh[1]

[1] Department of Rheumatology, Ajou University School of Medicine, Republic of Korea

Background

Sphingolipids, an essential signaling molecules for the biological and structural functions of cells, are increasingly recognized as playing an important signaling role in the pathophysiology of chronic inflammatory diseases. We hypothesized that the pathogenesis of systemic lupus erythematosus (SLE), a chronic autoimmune disease, is related to altered composition and dysregulation of sphingolipids.

Methods

We performed liquid chromatography tandem mass spectrometry to evaluate the levels of sphingolipids in plasma from 38 women with SLE, including 11 lupus nephritis, and 30 controls. The receiver operating characteristic curve (ROC) was analyzed to calculate the area under the curves (AUC) to determine whether sphingolipids can be efficiently used to diagnose SLE. Further, Pearson's correlation coefficient was used to analyze the correlation between sphingolipids and the disease activity markers.

Results

The mean age of SLE patients was 44.5 years and the mean disease duration was 110.7 months. The levels of serum ceramide (Cer) and Cer to sphingosine-1-phosphate (S1P) ratio subspecies were increased in patients with SLE, while the levels of sphingomyelins were decreased compared to the controls. The ratio of Cer16:0 to S1P showed especially strong increments in patients with lupus nephritis, and the AUC value for discriminating lupus nephritis from controls was 0.739 (95% confidence interval, 0.581□0.898). In addition, their levels were associated with disease duration, anti-double stranded DNA antibody, SLE disease activity index 2000, and Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

Conclusions

Serum sphingolipids can be a good candidate for SLE diagnostic markers, and in particular, Cer16/S1P has the best ability to distinguish against lupus nephritis.

Figure & Table

Sphingolipids (ng/mL)	SLE (n = 27)	LN (n = 11)	HC (n = 30)	p-value[1]	p-value[2]
S1P	707.44 ± 93.09	644.89 ± 114.86	710.55 ± 119.28	0.208	0.380
Sphingosine	3.92 ± 2.35	2.7 ± 1.02	3.25 ± 1.56	0.155	0.680
Cer14:0	7.04 ± 2.31	7.86 ± 1.91	7.07 ± 1.95	0.512	0.671
Cer16:0	184.05 ± 47.86	198.17 ± 33.24	177.86 ± 35.79	0.372	0.140
Cer18:0	98.96 ± 35.17	106.09 ± 27.83	94.02 ± 34.67	0.591	0.081
Cer18:1	18.05 ± 6.33	20.83 ± 5.81	18.9 ± 6.55	0.479	0.649
Cer20:0	116.7 ± 34.43	125 ± 30.49	120.31 ± 29.12	0.754	0.319
Cer24:0	2,197.34 ± 706.74	1,977.69 ± 545.01	2,314.07 ± 569.7	0.313	0.145
Cer24:1	770.97 ± 217.36	795.61 ± 149.6	720.48 ± 155.08	0.406	0.387
SM(d18:0/16:0)	25,902.07 ± 6,263.2	26,625.82 ± 4,281.66	27,659.76 ± 4,922.28	0.474	0.583
SM(d18:0/18:0)	5,894.02 ± 1,498.08	6,290.09 ± 1,070.86	6,554.73 ± 1,498.31	0.231	0.140
SM(d18:0/18:1)	58,766.05 ± 12,976.89	62,823.39 ± 11,531.87	63,925.33 ± 11,869.54	0.277	0.546
SM(d18:0/24:0)	17,126.86 ± 4,263.68	16,441.45 ± 5,358.13	19,453.68 ± 4,611.38	0.081	0.053
SM(d18:0/24:1)	34,201.36 ± 9,038.26	34,652.83 ± 6,113.78	34,414.91 ± 7,179	0.986	0.934
Cer14/S1P	0.010 ± 0	0.012 ± 0	0.010 ± 0	0.110	**0.031**
Cer16/S1P	0.27 ± 0.09	0.32 ± 0.09	0.26 ± 0.06	**0.027**	**0.019**
Cer18/S1P	0.14 ± 0.06	0.17 ± 0.07	0.13 ± 0.05	0.189	0.107
Cer18:1/S1P	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.209	0.519
Cer20/S1P	0.17 ± 0.05	0.2 ± 0.07	0.17 ± 0.05	0.215	0.283
Cer24/S1P	3.12 ± 1	3.15 ± 1.14	3.35 ± 1.06	0.691	0.198
Cer24:1/S1P	1.11 ± 0.34	1.28 ± 0.37	1.04 ± 0.27	0.111	**0.031**

LN; lupus nephritis, HC; healthy control, Cer; ceramide, SM; sphingomyelin, S1P; sphingosine-1-phosphate

[1]SLE+LN vs. HC, [2]LN vs. HC. Bold values indicate significant P value.

Table. Sphingolipid profiles in patients with systemic lupus erythematosus and controls

Keywords

SLE, sphingolipid, Cer16/Sphingosine-1-Phosphate

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Combined model of renal histopathology and clinical parameters better predict one year renal outcomes in lupus nephritis: Analysis of 334 kidney biopsies

Aishwarya Gopal[1], Chengappa Kavadichanda[1], Devender Bairwa[1], Sanket Shah[1], BH Srinivas[2], Molly Thabah[1], Vir Negi[1]

[1] Department of Clinical Immunology, Jawaharlal Institute of Postgraduate Medical Education and Research(JIPMER), India
[2] Department of Pathology, Jawaharlal Institute of Postgraduate Medical Education and Research(JIPMER), India

Background

Diagnosis of Lupus Nephritis (LN) is currently based on laboratory tests and renal histopathology. Role of histopathological features in determine long term outcomes is unclear.

Objectives:

To assess if clinical and biochemical parameters at baseline could identify renal histopathological class.

To assess the clinico-histopathological predictors of renal response.

Methods

This is a single centre retrospective study comprising 334 LN renal biopsies. Clinical and biochemical parameters at the time of biopsy were noted and their association with histopathological class, activity and chronicity scores (AS/CS) (ISN/RPS -2016 criteria) were evaluated. Complete, partial or no response(CR, PR, NR) for renal outcome (EULAR/EDTA) at 1 year were calculated for 293 patients. Binary logistic regression was done to look for the predictors of NR.

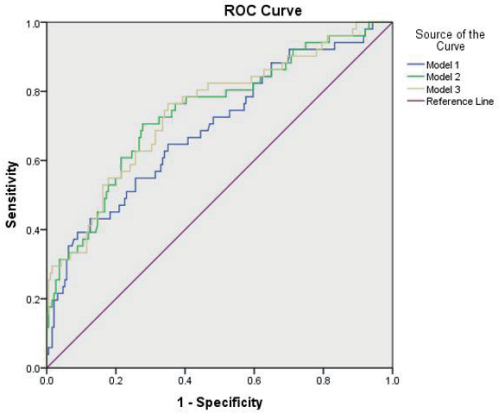
Results

Class III/IV LN was seen in 240(71.8%). Hypertension was seen in (52.1%) of class III/IV and <25% each with class II, V and combined class(p<0.001). Class III/IV had lower eGFR [87.6(62.75-118.8)] (p<0.001) than the other classes. Nephrotic range proteinuria was seen in 32% of class V and 21% in class III/IV (p=0.004). Among class-III/IV AS had weak correlation with baseline UPCR (r=0.31) and eGFR (r=-0.172) (p<0.01). CS had weak negative correlation with eGFR (r=-0.212,p<0.01). NR at 1 year was higher in males (OR-4.6,95%CI-1.9-10.8,p<0.001), those with abnormal serum creatinine (OR-3.3,95%:CI1.6-7.02, p-0.001), higher renal SLEDAI (p<0.05), higher AS, CS (p<0.001), interstitial inflammation and tubular atrophy(p<0.005). On binary logistic regression a combined clinico-histopathological model comprising of serum creatinine, UPCR, male sex and CS performed best in predicting NR (figure 1).

Conclusions

Clinical and biochemical parameters can predict the renal histological class to a fair extent but has limited value in predicting the activity and chronicity parameters. Since a combination of clinical and histopathology parameters are better in predicting renal outcomes, performing renal biopsies should be encouraged in LN.

Figure & Table



Model 1: Baseline serum creatinine, urine PCR, male sex; AUC – 0.694(0.609-0.779), p <0.001
Model 2: Baseline serum creatinine, urine PCR, male sex, chronicity score; AUC – 0.740(0.660-0.820), p<0.001
Model 3: Baseline serum creatinine, urine PCR, male sex, chronicity score, crescents, interstitial inflammation; AUC – 0.744(0.664-0.824), p<0.001

Figure. ROC curve and AUC for the three different models

Keywords

Lupus nephritis, Renal biopsy, Predictors

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Coexisting tubulointerstitial inflammation and damage is a risk factor for chronic kidney disease in patients with lupus nephritis: Results from the KORNET registry

Dong-Jin Park[1], Sung-Eun Choi[1], Ji-Hyoun Kang[1], Shin-Seok Lee[1]

[1] Division of Rheumatology, Department of Internal Medicine, Chonnam National University Medical School and Hospital, Republic of Korea

Background

An increasing body of evidence suggests a prognostic role of tubulointerstitial lesions in patients with lupus nephritis (LN). Although persistent tubulointerstitial inflammation (TII) usually precedes tubulointerstitial damage (TID) in LN, the two conditions can be simultaneously present to varying degrees. Thus, we examined whether coexisting TII/TID predicts progression to chronic kidney disease (CKD) in LN patients.

Methods

The 175 LN patients enrolled in the study had clinical data obtained at the time of renal biopsy and stored in the KORNET registry. These patients were divided into two groups: those with and without coexisting TII/TID. The two groups were compared with respect to their demographic, clinical, histological, laboratory findings, and long-term prognosis. Uni- and multivariable Cox proportional hazard regression models were used to identify independent risk factors for CKD in LN patients.

Results

Of the 175 LN patients, 110 (62.9%) had coexisting TII/TID and 65 (37.1%) did not. Patients with coexisting TII/TID were older, had higher ESR and 24 h proteinuria, and lower eGFR and hemoglobin levels than those without coexisting TII/TID. Anti-Ro and ribosomal-P antibodies were detected less frequently in patients with coexisting TII/TID. Patients with coexisting TII/TID more often had LN of the proliferative type and a larger proportion had a chronicity score > 4. During a mean follow-up of 89.9 months, CKD and ESRD developed more frequently in patients with than without coexisting TII/TID. Finally, the coexisting TII/TID was associated with a higher risk for CKD progression: adjusted HR = 2.677, p = 0.006 for all LN patients; HR = 3.265, for those with class III, IV and V LN; HR = 3.045, for those with class III, IV, V LN, and eGFR ≥ 30 mL/min/1.73 m2.

Conclusions

LN patients with coexisting TII/TID are at greater risk for deterioration of kidney function at LN onset and for developing CKD over time.

Keywords

tubulointerstitial inflammation, chronic kidney disease, lupus nephritis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Subtherapeutic hydroxychloroquine concentration is associated with increased disease activity and greater organ damage during 5-year follow-up in patients with systemic lupus erythematosus

Ji-Hyoun Kang[1], Sung-Eun Choi[1], Dong-Jin Park[1], Shin-Seok Lee[1]

[1] Division of Rheumatology, Department of Internal Medicine, Chonnam National University Medical School and Hospital, Republic of Korea

Background

Hydroxychloroquine (HCQ) is a cornerstone drug in patients with systemic lupus erythematosus (SLE), as it decreases the risk of flares and comorbidities and improves survival. This study investigated the effects of the serum HCQ concentration on clinical manifestations, disease activity, and organ damage in SLE patients.

Methods

The 338 SLE patients from the Korean Lupus Network registry were assessed with respect to their demographic, clinical and laboratory findings, PGA, and adjusted mean SLEDAI-2000 (AMS) and SLICC damage index scores annually for 5 consecutive years. Patients were divided into two groups according to their serum HCQ concentration at baseline: patients with a subtherapeutic level (< 500 ng/mL) and those with a therapeutic level (≥ 500 ng/mL). The impact of the HCQ concentration on the clinical outcomes was evaluated in a longitudinal analysis using a generalized estimating equation (GEE) and a logistic regression analysis.

Results

Of the 338 patients, 287 (84.9%) were in the subtherapeutic group at baseline. This group had a higher incidence of newly developed lupus nephritis (P = 0.036) and had been prescribed higher mean and cumulative doses of prednisolone (P = 0.003 and P = 0.013) than the therapeutic group. In multivariable analyses by GEE, an association of the subtherapeutic group with both a higher PGA score (β coefficient = 0.328, P < 0.001) and a higher SLICC damage index score (β = 0.366, P = 0.019) was determined across all 5 years. In the multivariate logistic regression analysis, subtherapeutic HCQ was significantly associated with the AMS (OR = 1.142, P = 0.019), mean PGA (OR = 3.697, P < 0.001), and an annual increase in the SLICC damage index score (OR = 1.529, P = 0.047).

Conclusions

HCQ concentration may affect the development of new-onset LN, and had the significant association with higher disease activity and cumulative organ damage.

Keywords

hydroxychloroquine, concentration, lupus nephritis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Effect of smoking on thrombotic events in antiphospholipid syndrome: A large prospective cohort study

Hui Jiang[1], Jiuliang Zhao[1,2,3], Mentao Li[1,2,3], Yan Zhao[1,2,3]

[1] Department of Rheumatology and Clinical Immunology, Chinese Academy of Medical Sciences & Peking Union Medical College, China
[2] National Clinical Research Center for Dermatologic and Immunologic Diseases, Ministry of Science & Technology, China
[3] State Key Laboratory of Complex Severe and Rare Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical Co, China

Background

Cigarette smoking is an established risk factor for several autoimmune diseases and thrombosis. Previous investigations observed an increased smoking rate in antiphospholipid antibody (aPL) carriers. While no clearer role of smoking in antiphospholipid syndrome (APS) was determined. This study was designed to investigate effects of cigarette smoking on clinical manifestations and prognosis in APS.

Methods

This is a prospective single-clinical case-control study from 2013 to 2022, 388 patients fulfilled 2006 Sydney criteria of APS were included. Current smokers and former smokers with one-year consecutive smoking were both included. Investigation was carried between smokers (n=85) and non-smokers (n=303), 60 cases and controls were matched by gender and age.

Results

Main results focused on thrombotic events since most of the smokers were male. Patients with smoking habit were more frequent to have cardiovascular complications (P=0.017), especially coronary heart disease (13.33% vs. 3.33%, P=0.048). Smokers presented much more arterial thromboses in different territories before diagnosed (66.67% vs. 38.33%, P=0.002), including stroke (P=0.035), myocardial infarction (P=0.015), visceral (P=0.023) and retinal arterial thromboses (P=0.022). Venous thromboses were less frequent in smokers (55.00% vs. 81.67%, P=0.002), especially deep vein thromboses (P=0.044) and cranial venous sinus thromboses (P=0.048). During follow up of all patients treated, matched smokers presented increased arterial thrombosis recurrence, matched non-smokers presented increased venous thrombosis recurrence, though statistic analysis was not significant. Survival analysis of all-caused death also indicated poor outcome in smokers (4/60 vs. 0/60, P=0.047). While relation between smoking and antibody-positivity and inflammatory index were not found in this study.

Conclusions

Smoking is related to coronary heart disease, increased arterial events and all-caused death in APS. Patients with APS should be encouraged to avoid smoking.

Figure & Table

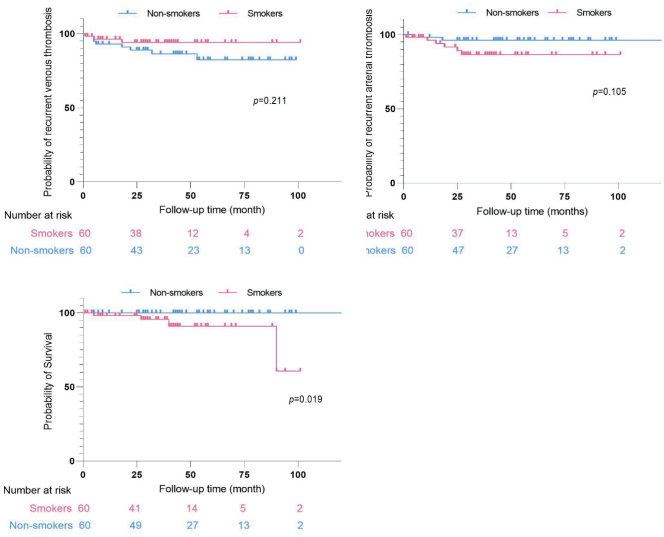

Figure. Baseline and outcomes of smokers and non-smokers in APS

Keywords

antiphospholipid syndrome, smoking

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Efficacy of rivoraxaban in patients with antiphospholipid syndrome

Zumrad Ubaydullaeva[1], Anis Alyavi[1], Jamol Uzokov[1], Bekzod Karimov[1]

[1] Internal Medicine, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Uzbekistan

Background

Anticoagulants are cornerstone for the treatment of patients with antiphospholipid syndrome. Aim of the study was to evaluate comparative efficacy of rivaroxaban vs. warfarin in patients with antiphospholipid syndrome.

Methods

Eighty-two patients with previous thrombotic antiphospholipid syndrome were enrolled in this prospective study (Mean age 39.12±12.4 years, male=28%). Patients were divided into two groups by forty-one taking either rivaroxaban (Group I) or warfarin (Group II). Mean follow-up was 24±4.8 months. Primary endpoint was recurrent thrombosis and secondary endpoint consisted of fatal and non-fatal arterial and venous thrombosis, time to thrombosis. Overall safety outcome included major bleeding.

Results

Thrombotic events was observed in 12.2 % patients in Group I whilst thrombotic risk was in 15% patients in Group II during the mean follow-up period ($P<0.05$). In 7.0 % of patients were observed stroke in rivaroxaban group whereas in 12 % of patients were observed stroke in warfarin group ($P<0.05$). When we analyzed gender differences, there was not significant changes between men and women. There was similar rate of major bleeding in both groups (29% vs. 31%, $P>0.05$). Even though intracranial bleeding risk was lower in Group I than Group II, there was not any statistically significant changes between groups ($P>0.05$).

Conclusions

Rivaroxaban is superior to warfarin to prevent thrombotic complications in patients with antiphospholipid syndrome. Further studies are needed with large amount of participants to clarify.

Keywords

antiphospholipid syndrome, rivaroxaban, warfarin

Luncheon Symposium VII
Novartis

Understanding IL-17 Inhibition in SpA

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The role of IL-17A in Ankylosing spondylitis and axial PsA

Matthew Brown
King's College London, UK

The axial spondyloarthropathies are a heterogenous group of diseases, with differences in pathogenesis best demonstrated to date through genetic studies, in pattern of clinical disease, and in response to treatment. Axial spondyloarthritis can co-occur with psoriasis and inflammatory bowel disease. In these patients, HLA-B27 carriage is lower, prevalence of acute anterior uveitis is lower, peripheral arthritis is higher, and disease onset is later. Whether other differences observed in clinical features are real or relate to differences in ascertainment is unclear. Patients with axial spondyloarthritis with and without psoriasis both appear to respond well to interleukin-17 inhibition such as with secukinumab, which has been demonstrated in clinical trials and in clinical practice to be very effective for these diseases, and which also benefits additional features of psoriatic disease, including skin and nail disease, peripheral arthritis and dactylitis. These aspects will be discussed.

Luncheon Symposium VIII
Amgen

Move Forward
with the Long-term Protection
of Prolia

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Journal of Rheumatic Diseases
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Denosumab key clinical questions

Sung-Soo Kim
Univ. of Ulsan, Korea

Denosumab is an effective and safe osteoporosis treatment option, with current data up to 10 years of continued use showing continued improvement in BMD with fracture risk reduction. Safety profiles overall are similar to placebo, with no new safety concerns in extension trials, though a theoretical increased risk of infection exists with RANKL inhibition. Denosumab has been available in Korea as a treatment for osteoporosis for 5 years. Clinical trial data for denosumab are limited to 10 years but these show important differences to oral or intravenous bisphosphonates.

RA is a chronic inflammatory condition affecting a significant number of patients and osteoporosis is a common manifestation of the disease. In RA, the activity of infiltrating macrophages and CD4+ T cells results in an increased expression of proinflammatory cytokines (TNF, IL-1, IL-6 and IL-17) which drive osteoclast formation via induction of RANKL in the synovium. Generalized bone loss in RA leading to osteoporosis and fragility fractures further increases the burden of the disease of RA patients. It is also well known that Use of glucocorticoids has been a well-known factor that affects bone and increases the risk of fracture. Denosumab has proven superior efficacy to BPs for BMD increasement in GC-C and GC-I.

FREEDOM and FREEDOM extension studies also show an increase in vertebral fractures and multiple vertebral fractures following denosumab treatment discontinuation. After switching to oral alendronate following only one year of denosumab, spine and hip BMD were generally maintained and did not fall below pretreatment baseline in most trial participants. A recent observational study showed therapy with either oral alendronate or a single intravenous zoledronic acid infusion is partially effective in reducing the increased vertebral fracture risk after denosumab withdrawal. In conclusion, to maintain its anti-fracture efficacy, denosumab treatment needs to be continued in the long-term; this has been demonstrated for up to 10 years in trials. Adverse events associated with long-term denosumab therapy such as atypical femur fractures or medication-related osteonecrosis of the jaw are very rare and treatment benefits far outweigh the risk of these events.

Luncheon Symposium IX
Astellas

Tacrolimus

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Tacrolimus in rhematoid arthritis

Chan-Bum Choi
Hanyang Univ., Korea

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease mainly affecting synovium. It is usually presented with chronic polyarthritis of small joints. Management of RA have significantly improved over the years, especially with introduction of biologic disease modifying antirheumatic drugs (DMARDs) and more recently with target synthetic DMARDs. However, methotrexate still holds its throne as the anchor drug that is most important in management of RA.

Recommendations from various association around the world agree on recommending methotrexate as the first drug after diagnosis of RA, unless contraindicated. But there are subtle differences in guidelines owing to drug approval status, physician's preferences, and patients' preference difference among countries.

Prograf is approved for management of rheumatoid arthritis in Korea and Japan. It has demonstrated safety and efficacy in patients with RA in five randomized placebo-controlled studies in North America including United States of America and in Japan. Its' safety and efficacy were consistently demonstrated in real-world studies in Korea and Japan, including large long-term pharmacovigilance study in Japan. Effectiveness as an add-on therapy in biologic DMARD inadequate responders was demonstrated and its effectiveness in maintenance of remission after tumor necrosis factor inhibitor was demonstrated in a prospective open-label trial. Head-to-head trial with leflunomide showed non-inferiority.

Prograf is a valuable conventional DMARDs in management of RA with its safety and efficacy in various clinical situations.

International Symposium

Synovial Macrophage and Fibroblast in RA

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Synovial macrophages as gatekeepers of inflammation

Gerhard Krönke
Univ. of Erlangen, Germany

Macrophages are considered to contribute to chronic inflammatory diseases such as rheumatoid arthritis[1]. However, both the exact origin and the role of macrophages in inflammatory joint disease remain unclear. We used fate-mapping approaches in conjunction with three-dimensional light-sheet fluorescence microscopy and single-cell RNA sequencing to perform a comprehensive spatiotemporal analysis of the composition, origin and differentiation of subsets of macrophages within healthy and inflamed joints, and study the roles of these macrophages during arthritis. We observed that dynamic membrane-like structures, consisting of a distinct population of CX_3CR1^+ tissue-resident macrophages, form an internal immunological barrier at the synovial lining and physically seclude the joint. These barrier-forming macrophages display features that are otherwise typical of epithelial cells, and maintain their numbers through a pool of locally proliferating CX_3CR1^- mononuclear cells that are embedded into the synovial tissue. Unlike recruited monocyte-derived macrophages, which actively contribute to joint inflammation, these epithelial-like CX_3CR1^+ lining macrophages restrict the inflammatory reaction by providing a tight-junction-mediated shield for intra-articular structures. Additional data suggest that T cells interact with the layer of CX_3CR1^+ lining macrophages prior to onset of arthritis, where they promote a barrier dysfunction and onset of autoantibody inflammation.

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Cellular deconstruction of inflamed synovium defines diverse inflammatory phenotypes in rheumatoid arthritis

Soumya Raychaudhuri
Soumya Raychaudhuri on behalf of the AMP RA Consortium

Rheumatoid arthritis (RA) is a prototypical autoimmune disease that causes destructive tissue inflammation in joints and elsewhere. Clinical challenges in RA include the empirical selection of drugs to treat patients, inadequate responders with incomplete disease remission, and lack of a cure. We profiled the full spectrum of cells in inflamed synovium from patients with RA with the goal of deconstructing the cell states and pathways characterizing pathogenic heterogeneity in RA. Our multicenter consortium effort used multi-modal CITE-seq, RNA-seq, and histology of synovial tissue from 79 donors to build a >314,000 single-cell RA synovial cell atlas with 77 cell states from T, B/plasma, natural killer, myeloid, stromal, and endothelial cells. We stratified tissue samples into six distinct cell type abundance phenotypes (CTAPs) individually enriched for specific cell states. These CTAPs demonstrate the striking diversity of RA synovial inflammation, ranging from marked enrichment of T and B cells (CTAP-TB) to a congregation of specific myeloid, fibroblast, and endothelial cells largely lacking lymphocytes (CTAP-EFM). Disease-relevant cytokines, histology, and serology metrics are associated with certain CTAPs. This comprehensive RA synovial atlas and molecular, tissue-based CTAP stratification reveal new insights into RA pathology and heterogeneity, which could lead to novel targeted-treatment approaches in RA.

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Roles of stromal cells and potential significance for future therapy in RA

Sang-il Lee
Gyeongsang Nat'l Univ., Korea

In addition to various immune cells, it appears that several stromal cells such as fibroblast-like synoviocytes (FLS), lymph node fibro-reticular cells (LN-FRC), and mesenchymal stem/stromal cells (MSC), have been implicated in the pathophysiology of Rheumatoid arthritis (RA). Even though their protective character cannot be denied, in autoimmune pathogenesis, these stromal cells exhibit dysfunctional or aggressive properties influencing the activity of infiltrating immune and other tissue resident cells. Recently we have reported three important perturbations of stromal cells contributing to the immuno-pathogenesis and may providing directions for improving future therapy for RA. First, decreased Raf kinase inhibitory protein (RKIP) or Phospholipase C-eta2 (PLCH2), which are negative regulators in upstream cellular signaling pathway, mediate the aggressiveness of RA-FLS and promote arthritic inflammation and the joint destruction. Second, T cell zone FRCs of LNs (LN-TRCs) express CD25, and CD25-deficient LN-TRCs promote T helper 17 (Th17) cell differentiation and Th17 response-related gene expression in Th17-dependent autoimmune diseases. Third, cellular senescence, due to a long-term exposure to the chronic inflammatory milieu, attenuated immunomodulatory properties of synovial fluid derived-MSC in a long-term RA. Thus, in this lecture, we will summarize recent progress on the molecular signature and the roles of stromal cells contributing pathological progression or presenting promising therapeutic tools for RA and extra-articular complications.

Symposium

KCR-KSBMR Joint Symposium

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Anabolic therapy for osteoporosis

Ha Young Kim
Univ. of Ulsan, Korea

Osteoporosis is identified as a systemic skeletal disorder characterized by low BMD and qualitative changes in microarchitecture of bone tissue. There are two major categories of osteoporosis drugs, antiresorptive agents and bone forming agents. Antiresorptive agents increase bone mineral density and prevent the progression of structural damage but may not restore bone structure. However, bone-forming agents can reverse microarchitectural deterioration of bone tissue because they are associated with a larger increase in bone mass than antiresorptive agents.

In recent clinical guidelines, it is recommended to use bone forming agents as the primary treatment in patients with a very high risk of fracture. Currently, three drugs are available: teriparatide, abaloparatide, and romosozumab, and only teriparatide and romosozumab are available in Korea. Teriparatide, an N-terminal (1–34) fragment of human parathyroid hormone, is the first bone forming drug approved by Food and drug administration in 2003. Avaloparatide is a parathyroid hormone-related protein (PTHrP)-like drug and has a mechanism similar to that of teriparatide. Romosozumab is a new bone-forming agent that inhibits sclerostin with a dual effect on bone, increasing bone formation and decreasing bone resorption. In this session, I will review the characteristics and effects of each drug so that it can be helpful in clinical practice.

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Ideal sequential therapy in osteoporosis management

Kyoung Min Kim
Yonsei Univ., Korea

The majority of osteoporosis medications are antiresorptive agents, which target osteoclasts and inhibits bone resorption. Bisphosphonates, Denosumab, and Selective Estrogen Receptor Modulator (SER) are this group. On the other hand, Teriparatide (PTH 1-34), daily or weekly regimen, and Romosozumab are currently available anabolic therapies for osteoporosis in Korea. Teriparatide acts by direct stimulation of osteoblast activity and recruitment of those cells and, then promotes bone formation, whereas Romosozumab inhibits sclerostin, a key regulator that has the dual properties of promoting bone formation and inhibiting bone resorption. Both anabolic and antiresorptive agents improve bone mineral density (BMD) and reduce risk of fracture. Osteoporosis is chronic disease and not easy to achieve treatment target, indicating osteopenic BMD T-score or absolute low risk of fractures. Therefore, osteoporosis may require treatment for many years to finally achieve the target goal. Moreover, to maintain or improve BMD further, changing the therapeutic regimen should be also considered. However, because osteoporosis drugs affect each other's mechanism of action, their effects differ depending on the order in which they are used. Therefore, in the sequential treatment of osteoporosis, the order of drug selection is very important and thus should be carefully considered.

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Prevention and treatment of fracture in RA

Jun-Ki Min
The Catholic Univ. of Korea, Korea

Patients with rheumatoid arthritis (RA) are at an increased risk of sustaining osteoporotic fractures. In patients with RA, significant amounts of generalized skeletal bone are lost early in the disease which is associated with disease activity. Adults with RA are placed at high risk of falls and fall-related injuries such as fractures. RA-related risk factors including inflammation, presence of anti-citrullinated protein antibodies (ACPA), reduced mobility, sarcopenia, and glucocorticoid (GC) therapy contribute to the increased fracture occurrence in patients with RA. While vertebral fractures can occur without a fall and are often asymptomatic, they are clinically important due to their significant association with greater functional impairment, and an increased risk for future vertebral and non-vertebral fractures in patients with RA.

There is a study showing that the overall mortality rates of hip fractures at 1, 3, 6, and 12 months were 5.0%, 10.6%, 14.8%, 19.8% respectively. Use of opioids, SSRIs and GCs were associated with an increased risk of sustaining any type of fracture (vertebral and non-vertebral) in patients with RA. Bone loss and fracture risk are implicated in inflammatory autoimmune diseases such as rheumatoid arthritis, ankylosing spondylitis, inflammatory bowel disease, and systemic lupus erythematosus. The network of inflammatory cytokines produced during chronic inflammation induces an uncoupling of bone formation and resorption, thereby resulting in significant bone loss in patients with inflammatory autoimmune diseases. Structural bone damage starts before the clinical onset of arthritis in subjects with ACPA. TNFi are associated with decreased vertebral fractures.

All patients taking more than 2.5 mg/day prednisolone or equivalent for more than 3 months are recommended to take adequate calcium and vitamin D. Patients at moderate to high fracture risk should be treated with additional osteoporosis medication. In every RA patient, clinicians should aim to prevent bone loss and reduce fracture risk at the lowest possible disease activity. Strategies must also be considered to reduce and prevent falls and fall-related fractures in patients with RA.

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Free Paper Session

Vasculitis and Metabolic Bone Disease

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Update on comparative cardiovascular safety of febuxostat versus allopurinol among patients with gout

Anna Shin[1], Se Rim Choi[1], Minji Han[2], You-Jung Ha[1,3], Yun Jong Lee[1,3], Eun Bong Lee[3,4], Eun Ha Kang[1,3]

[1] Division of Rheumatology Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea
[2] Department of Health Science and Technology, Graduate School of Convergence Science and Technology, Seoul National University
[3] Division of Rheumatology Department of Internal Medicine, Seoul National University College of Medicine, Seongnam, Korea
[4] Division of Rheumatology Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea

Background

To update comparative cardiovascular (CV) safety of febuxostat versus allopurinol among patients with gout.

Methods

Using the 2011-2019 Korea National Health Insurance database, we conducted a cohort study comparing gout patients initiating febuxostat versus allopurinol, with study participants matched on a propensity score (PS) for >60 covariates at a 1:1 ratio. The primary outcome was composite CV outcome of myocardial infarction, coronary revascularization, and stroke. Secondary outcomes were CV and all-cause mortalities in addition to individual components of the primary outcome. Cox proportional hazards models estimated hazard ratios (HRs) and 95% confidence intervals (CIs), comparing febuxostat versus allopurinol initiators.

Results

We included 160,930 febuxostat users PS-matched on 160,930 allopurinol users (mean age 59.3 years, 79.6% male). During a mean follow-up of 250 days, the incidence rate of the primary outcome was 2.27 and 2.06 per 100 person-years for allopurinol and febuxostat users respectively, with the PS-matched HR [95% CI] of 1.03 [0.95-1.12]. Analysis on secondary outcomes also showed a similar result except for all-cause mortality with a significantly reduced risk among febuxostat users with a PS-matched HR [95% CI] of 0.84 [0.78-0.91] (Table 1).

Conclusions

This large population-based cohort study showed a similar CV safety profile between febuxostat and allopurinol users but found a 16% reduced all-cause mortality among febuxostat users compared to allopurinol, primarily derived from non-CV death reduction.

Figure & Table

	Febuxostat N = 160,930			Allopurinol (Ref) N= 160,930			HR (95% CI)
	Events	PY	[a]IR [95% CI]	Events	PY	[a]IR(95% CI]	
Composite CV endpoint	2635	128,193	2.06 [1.98-2.13]	2,099	92,512	2.27 [2.17-2.37]	1.03 [0.95-1.12]
MI	468	129,873	0.36 [0.33-0.39]	341	93,808	0.36 [0.33-0.40]	1.13 [0.91-1.39]
Coronary revascularization	1085	129,233	0.84 [0.79-0.89]	856	93,293	0.92 [0.86-0.98]	1.10 [0.96-1.26]
Stroke or TIA	1490	129,163	1.15 [1.10-1.21]	1,187	93,252	1.27 [1.20-1.35]	0.99 [0.90-1.10]
Death	2558	130,176	1.97 [1.89-2.04]	2,201	94,007	2.34 [2.24-2.44]	0.84 [0.78-0.91]

[a]IR is per 100 person-years. IR=incidence rate, HR=hazard ratio, CI=confidence interval, MI=myocardial infarction, PY=person-years, TIA=transient ischemic attack

Table. Comparative cardiovascular safety between febuxostat and allopurinol

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The utility of dual-energy computed tomography in predicting gout flares in gout patients after discontinuing colchicine prophylaxis

Min Jung Kim[1], Mi Hyeon Kim[2], Se Rim Choi[2], Youjin Jung[2], Jiin Jung[2], Ju Yeon Kim[2], Sang Hee Kim[1], Jee Won Chai[3], Kichul Shin[1]

[1] Division of Rheumatology, Seoul Metropolitan Government–Seoul National University Hospital Boramae Medical Center, Republic of Korea
[2] Division of Rheumatology, Seoul National University Hospital, Republic of Korea
[3] Department of Radiology, Seoul Metropolitan Government–Seoul National University Hospital Boramae Medical Center, Republic of Korea

Background

To investigate whether monosodium urate (MSU) deposition measured by dual-energy computed tomography (DECT) could help predict acute flares after discontinuing colchicine prophylaxis in gout patients.

Methods

This pilot, prospective observational study included patients with gout meeting the 2015 gout classification criteria who received urate lowering therapy (ULT) plus a prophylactic dose of colchicine for 6 months. DECT (Revolution CT ES, GE healthcare) was performed at the time point when colchicine was discontinued. Images of unilateral foot and ankle joints were analyzed for MSU deposits (set to moderate or high specificity) by a radiology specialist. Total amount of MSU deposits was calculated by the sum of MSU volume detected. Patients were followed up after 2 months. The odds ratio (OR) for developing an acute flare after colchicine discontinuation were determined using a logistic regression model.

Results

Twenty-two patients were enrolled and 19 of the 22 patients were evaluated for MSU volumes. The tophi area on physical exam well correlated with total MSU volume set to moderate specificity in DECT (rho 0.68, p=0.01). Presence of tophi on physical exam was significantly associated with acute flare after discontinuing colchicine prophylaxis (OR 13.33, 95% confidence interval (CI) 1.07-166.37, p=0.04, Table). Total volume of MSU in the foot and ankle joints was associated with an increased risk for acute flare, but it did not reach a statistical significance (OR 1.11, p=0.40 for moderate, OR 43.39, p=0.65 for high specificity). The volume of MSU in the foot set to high specificity yielded an AUC of 0.69 (95% CI 0.33-1.00).

Conclusions

Presence of tophi itself is a major urate burden in gout patients and requires a longer period of colchicine prophylaxis. DECT is useful in terms of identifying invisible, intraarticular tophi during ULT, yet its clinical application in measuring the overall urate burden needs further investigation.

Figure & Table

Variables	Odds ratio (95% CI)	P-value
Age	1.129 (0.998-1.276)	0.053
Duration of gout	1.261 (0.909-1.750)	0.165
Baseline uric acid level	0.865 (0.361-2.073)	0.745
Presence of tophi	13.333 (1.069-166.374)	**0.044**
Tophi size, mm^2	1.098 (0.898-1.343)	0.364
MSU volume assessed with DECT moderate specificity		
Total MSU volume	1.108 (0.875-1.402)	0.396
Total MSU volume > 1.2115[a]	1.333 (0.191-9.311)	0.772
Foot MSU volume >0.4020[b]	2.083 (0.298-14.549)	0.459
MSU volume assessed with DECT high specificity		
Total MSU volume	43.390 (0.000-593442396.6)	0.653
Total MSU volume >0.0265[c]	2.083 (0.298-14.549)	0.459
Foot MSU volume >0.0005[d]	2.400 (0.303-19.041)	0.407

[a]Cut-off value for total MSU volume assessed with DECT moderate specificity in ROC curve analysis
[b]Cut-off value for foot MSU volume assessed with DECT moderate specificity in ROC curve analysis
[c]Cut-off value for total MSU volume assessed with DECT high specificity in ROC curve analysis
[d]Cut-off value for foot MSU volume assessed with DECT high specificity in ROC curve analysis

Table. Logistic regression analysis predicting acute gout flares after discontinuing colchicine prophylaxis

Keywords

Gout, Dual-energy computed tomography, Monosodium urate

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Effects of long-term febuxostat or allopurinol on the progression of chronic kidney disease

Byeongzu Ghang[1], Jinseok Kim[1]

[1] Rheumatology, Jeju National University School of Medicine, Jeju National University Hospital, Republic of Korea

Background

Elevated serum uric acid (sUA) levels are significantly associated with development and progression of chronic kidney disease (CKD). There is controversy over the role of urate-lowering therapy (ULT) in the progression of CKD. We investigated whether ULT has a beneficial effect on slowing the progression of CKD in gout patients.

Methods

We used the data of patients who took study medication for more than 1 year identified from the Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout (CARES) trial, which is a large, multicenter, randomized controlled trial. We analyzed the estimated glomerular filtration rate (eGFR) slope (mL/min/1.73 m2 per year) using the CKD-EPI equation estimates. Using logistic regression, we investigated risk factors for CKD progression, defined as eGFR slope of lower than 0 mL/min/1.73 m2 per year.

Results

During the study period [median (interquartile range, IQR) 3.1 (2.0-4.8) year], 4,144 patients performed median (IQR) 12 (9~15) creatinine tests, the GFR slope was analyzed as median (IQR) 0.5 (-0.8-1.6). The median (IQR) values of the GFR slope were -1.2 (-2.3--0.5) in the CKD progression group (n=1,590) and 1.3 (0.7-2.2) in the CKD progression delayed group (n=2,554). After adjusting well known factors associated with CKD progression, average level of sUA ≥ 6 mg/dL during study period was significantly associated with CKD progression (adjusted odds ratio 1.73; 95% confidence interval 1.49-2.01, p < 0.0001).

Conclusions

This study showed that eGFR did not decrease in more than half of gout patients after long term febuxostat or allopurinol administration. ULT may have a beneficial effect on slowing the progression of CKD in gout patients.

Figure & Table

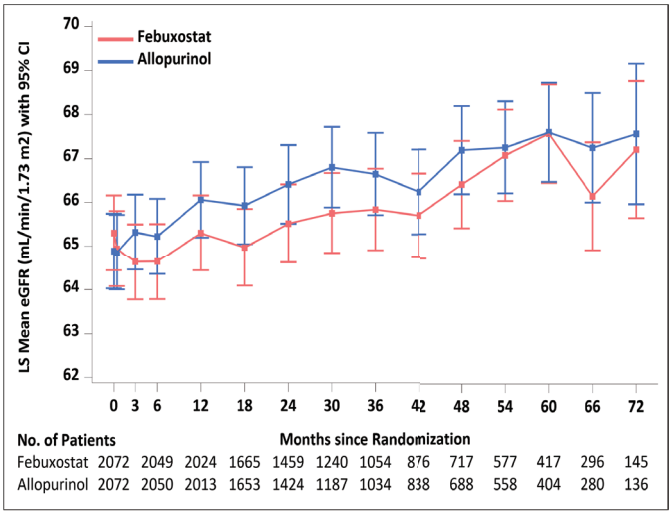

Figure. Changes of estimated glomerular filtration rate during febuxostat or allupurinol administration.

Keywords

Febuxostat, Allopurinol, Chronic renal insufficiency

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A cross-sectional internet survey of gout management and outcomes during established COVID-19 pandemic in 2020-2021

Jasvinder Singh[1], N Lawrence Edwards[1]

[1] Medicine/Rheumatology, UNIVERSITY OF ALABAMA AT BIRMINGHAM, USA

Background

Limited data are available for gout management during the COVID-19 pandemic. Our objective was to assess the management of gout in established COVID-19 pandemic.

Methods

We assessed medication use, healthcare utilization, gout-specific health-related quality of life (HRQOL), psychological distress using patient health questionnaire-4 (PHQ-4), resilience, illness perception, and health literacy in people with physician-diagnosed self-reported gout in established COVID-19 pandemic in a cross-sectional Internet survey.

Results

Among the 130 survey respondents with gout, the mean age was 62.8 years, 65% were male, 83% were White, 59% were prescribed urate-lowering therapy (ULT), and health literacy was adequate in 80%. A third of survey respondents reported more difficulty with their gout management since September 2020. Gout-specific HRQOL deficits were evident. Moderate-severe psychological distress was seen in 22% and resilience score was 6.5 (SD, 1.9; range 0-8). Adjusted for age, and sex, compared to no/mild psychological distress, moderate-severe psychological distress was associated with significantly higher odds ratio (OR; 95% confidence interval) of more difficulty with: (1) getting healthcare for gout in clinic, 3.7 (1.0, 13.2), emergency room/urgent care, 8.1 (1.4, 45.0), and in the hospital, 9.8 (1.6, 59.6) ; (2) getting gout flares treated, 6.6 (1.6, 26.8) , (3) avoiding gout complications, 4.5 (1.2, 16.7) ; and (4) daily activities at home, 4.2 (1.3, 14.1) and performing work, 4.1 (1.2, 13.6).

Conclusions

Respondents with gout reported healthcare gaps, low rates of ULT prescription, high psychological distress, and HRQOL deficits during established COVID-19 pandemic. Moderate-severe psychological distress was associated with difficulties in healthcare access and gout management. Interventions to address these challenges in gout management are needed.

Keywords

gout, COVID-19, management

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The effect of Behçet's disease on carotid intima media thickness and its relationship with disease activity

Merve Polat[1], Gökhan Polat[2], Elshad İsmailov[2]

[1] HEALTH PHYSICS, Karadeniz Technical University, Turkey
[2] Department of Radiology, Ataturk University, Turkey

Background

It is known that atherosclerosis increases in patients with Behçet Disease(BD). In our study, we aimed to examine the effect on carotid intima-media thickness in patients followed up with the diagnosis of BD.

Methods

86 cases (mean age: 34.2) and 36 control cases (mean age: 39.12) followed up with the diagnosis of Behçet were included in the study. The clinical and demographic characteristics of the patients were recorded. Activity classification was made based on the Behçet's Disease Instant Activity Form (BHAAF) score: no activity (BHAAF=0), mild activity (BHAAF 1–2), moderate activity (BHAAF 3–5), high activity (BHAAF 6–12). Carotid ultrasonography was performed in all cases to evaluate subclinical atherosclerosis and intima-media thickness (IMT) was evaluated.

Results

There was no significant difference between the groups in terms of age and gender.The mean duration of disease was 29.6 months, the use of cyclophosphamide was 25.6%, the use of steroids 96.2%, and the use of Interferon alfa-2b was 29.9%. The carotid IMT of Behçet's patients (mean 0.812mm) was significantly higher than the control (mean 0.632mm) (p=0.031). There were 31 patients with BHAAF =0, 16 patients with BHAAF 1–2, 16 patients with BHAAF 3–5, and 22 patients with BHAAF 6–12.A moderate correlation was found between carotid IMT and disease activity (r=0.734, p=0.006).

Conclusions

An increase in carotid intima media thickness is observed in cases with Behçet's disease, and there is a correlation between disease activity and carotid intima media thickness.

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Reclassification of patients with previously diagnosed GPA according to both the 2012 CHCC definitions and the 2007 EMA algorithm using the 2022 ACR/EULAR criteria

Jung Yoon Pyo[1], Sung Soo Ahn[1], Jason Jungsik Song[1], Yong-Beom Park[1], Sang-Won Lee[1]

[1] Internal Medicine, Yonsei University College of Medicine, Republic of Korea

Background

This study applied the 2022 criteria for granulomatosis with polyangiitis (GPA) proposed by the American College of Rheumatology (ACR) and European Alliance of Associations for Rheumatology (EULAR) (the 2022 ACR/EULAR criteria) to Korean patients with previously diagnosed GPA to investigate the number of patients who could be reclassified as having GPA.

Methods

Sixty-five patients with GPA, who met the 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides and the 2007 European Medicines Agency algorithm for GPA, were included in this study. They were reclassified based on the 2022 ACR/EULAR criteria.

Results

Of the 65 patients, 48 patients (73.8%) were reclassified as having GPA. A patient could not be reclassified as having GPA if the patient did not have a total score of 5 despite granulomas on biopsy or clear GPA surrogate markers. Among the 17 patients unclassified as having GPA, 16 patients were reclassified as having MPA and one as having unclassifiable vasculitis, and furthermore, 94.1% of them harboured myeloperoxidase (MPO)-antineutrophil cytoplasmic antibody (ANCA) (or perinuclear (P)-ANCA).

Conclusions

The concordance rate between the 2022 ACR/EULAR criteria for GPA and the previous criteria in patients with previously diagnosed GPA was 73.8%. We carefully suggest three points when the 2022 ACR/EULAR criteria are applied to patients with previously diagnosed GPA: First, escalating the score assigned to granuloma on biopsy and cartilage involvement; second, strongly recommending performing a biopsy in cases of highly suspicious GPA; and third, reconsidering the highest weightage assigned to MPO-ANCA (or P-ANCA) positivity.

Figure & Table

(N=65)

Variables		Values
At the time of diagnosis		
Items for the 2022 ACR/EULAR criteria for GPA and assigned scores to each item (N (%))		
Clinical criteria		
Nasal involvement (discharge, ulcers, crusting, congestion, septal defect/perforation)	**+3**	33 (50.8)
Cartilaginous involvement	**+2**	13 (20.0)
Conductive or sensorineural hearing loss	**+1**	20 (30.8)
Laboratory, imaging and biopsy criteria		
PR3-ANCA (or C-ANCA) positivity	**+5**	36 (55.4)
Pulmonary nodules, mass or cavitation	**+2**	41 (63.1)
Granuloma, granulomatous inflammation, or giant cells on biopsy	**+2**	30 (46.2)
Nasal/paranasal sinusitis or mastoiditis on imaging	**+1**	41 (63.1)
Pauci-immune glomerulonephritis on biopsy	**+1**	18 (27.7)
MPO-ANCA (or P-ANCA) positivity	**-1**	28 (43.1)
Serum eosinophil count ≥ 1000/μL	**-4**	2 (3.1)
Total score for 10 items above		7.0 (7.0)
Patients with total score ≥ 5 (N (%))		48 (73.8)

Values are expressed as median (interquartile range) or number (percentage).

ACR: American College of Rheumatology; EULAR: European Alliance of Associations for Rheumatology; GPA: granulomatosis with polyangiitis; PR3: proteinase 3; C: cytoplasmic; MPO: myeloperoxidase; P: perinuclear.

Table. Application of the 2022 ACR/EULAR criteria for GPA to patietns with previously diagnosed GPA

Keywords

granulomatosis with polyangiitis, 2022 ACR/EULAR classification criteria

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Patterns of coronary involvement of antineutrophil cytoplasmic antibody (ANCA) - associated vasculitis in Korean patients

Jinseok Kim[1], Sang-won Lee[1]

[1] Internal medicine, Yonsei University College of Medicine, Republic of Korea

Background

This study investigated the frequency and clinical features of acute coronary syndrome (ACS) in patients with antineutrophil cytoplasmic antibody (ANCA) -associated vasculitis (AAV).

Methods

Medical records of 262 patients with AAV were retrospectively reviewed (140 with microscopic polyangiitis [MPA], 69 with granulomatosis with polyangiitis [GPA], and 53 with eosinophil GPA [EGPA]). This study defined ACS as only myocardial infarction and unstable angina occurring at and after AAV diagnosis. The vessels affected and the period between diagnosis and ACS were also assessed.

Results

The median age at diagnosis and follow-up period were 59.0 years (92 men) and 37.0 months, respectively. ACS was found in 7 patients with AAV (2.7%; 5 with MPA and 2 with EGPA). Three patients (2 with MPA and 1 with EGPA) had ACS at AAV diagnosis and furthermore, all EGPA patients had ACS before 40 years of age. In particular, two patients who exhibited the refractory course of AAV after ACS experienced ACS recurrence.

Conclusions

EGPA may be associated with ACS occurring in not-elderly patients, and the refractory AAV may be related to ACS recurrence.

Figure & Table

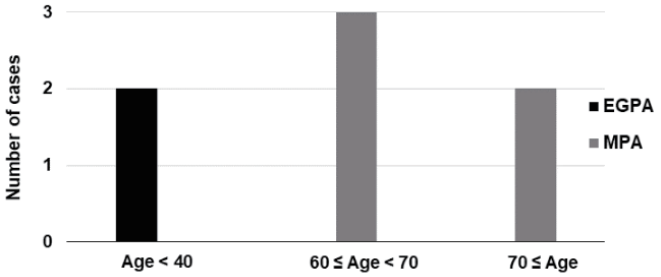

Figure. Age at ACS in patients with AAV, B. Time form AAV diagnosis to ACS

Keywords

ANCA-associated vasculitis, acute coronary syndrome

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Comparison of ultrasound-guided trigger-point needling and blinded needling for myofascial pain syndrome

Recep Sade[1], Meltem Alkan melikoglu[2]

[1] Radiology, Ataturk University, Turkey
[2] Rheumatology, Ataturk University, Turkey

Background

Most myofascial pain syndromes in clinical practice are caused by the myofascial trigger point (MTrP) formation. Recent clinical studies show that MTrP dry needling is most effective to release myofascial pain after local twitch response (LTR) is elicited. The aim of this study was to compare trigger point dry needling (TrP-DN) under ultrasound (US) guidance with TrP-DN without US guidance for myofascial pain management.

Methods

This study consisted of intervention and control groups. The intervention group received dry needling with US guidance and the control group received dry needling without US guidance. This study included 60 patients who had myofascial pain diagnosed after assessment by clinical examination and necessary diagnostic tests. The intervention group consisted of 36 patients: 11 males and 25 females. After US scanning identified the MTrP, dry needling, steel acupuncture needles (28 gauge) were used to elicit the LTR. The needling was performed during 2–4 sessions to inactivate all available trigger points.

Results

TPain, as measured on a visual analogue scale (VAS; 0–10) showed a significant reduction ($P < 0.001$) from 8.1 to 1.3 at 24 hours after dry needling with US in the intervention group (pain level decreased in 88% of the subjects), compared to improvement from 8.4 to 2.5 at 24 hours after dry needling without US guidance (pain level decreased in 72.5% of the subjects) in the control group ($P < 0.001$). There were significant correlations between the level of eliciting LTR during needling and the pain-relief effect (VAS decreased more than average percentage in group; $r = 0.812$).

Conclusions

US guidance significantly increased the pain relief effect, increases the level of eliciting LTR, and significantly decreased the average number of needled trigger points and the average number of treatment sessions. This approach can be utilized further to address musculoskeletal pain and neuromuscular diseases.

Figure & Table

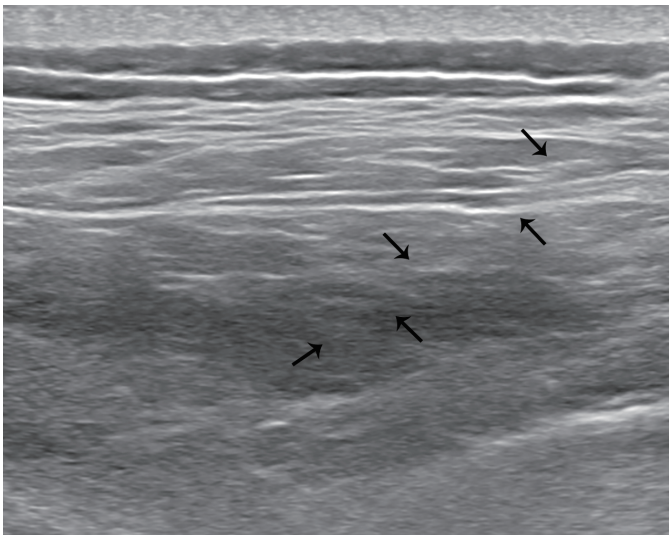

Figure. Ultrasound image of 52-year old females shows neddle (arrows) in the trigger point

Keywords

Myofascial Trigger Points, Ultrasound, Dry Needling

International Symposium

New Horizon of Systemic Sclerosis

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Seoul Dragon City, Seoul, Korea

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Journal of Rheumatic Diseases
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Update in the pathogenesis of systemic sclerosis

Christopher Denton
Royal Free Hosp., UK

Systemic sclerosis (SSc) is an uncommon disease autoimmune connective tissue disease with high medical impact and mortality. There is increasing understanding of aetiopathogenesis that is likely to reflect interplay between host and environmental factors. Host factors include age, gender, and ethnicity together with genetic susceptibility. Genetic aspects have been studies in large multicentric cohorts and have defined important immunogenetic factors as well as establishing genomic risk scores including different genetic traits. In addition, there are robust associations with major histocompatibility haplotypes that particularly link to hallmark antinuclear antibodies. As well as determining susceptibility to SSc, genetic factors that modify severity and organ involvement such as lung complications or renal crisis are being discovered. These may be important in determining clinical diversity in SSc.

Environmental triggers have been described including solvents, chemotherapeutic agents, and vaccination. These triggers have led to clusters of cases and provided additional insights into pathogenic mechanisms. The clinical diversity of SSc reflects shared and subtype specific mechanisms underlying subset classification and organ-based complications. It is likely that triggering events occur linked to the organ involved and this has been defined in preclinical models where lung epithelial injury may lead to fibrosis, or vascular endothelial injury may trigger pulmonary hypertension.

Tissue repair and wound healing provides the most relevant biological correlate of key pathogenic events in SSc, and growing understanding of the regulation and control of tissue repair is providing more insight into likely drivers of SSc fibrosis or vasculopathy. Defining the normal resolution and regression pathways that may operate in skin wound healing is likely to be important in understanding the spontaneous improvement of scleroderma skin fibrosis in SSc that can confound clinical trials testing of new therapies for skin.

Finally, recent studies have applied high dimensional analysis of gene or protein expression in skin or blood and started to map the keep cellular processes and interactions that are perturbed in SSc. Together with comparative studies of different stages or subsets of disease and different ANA subtypes this is giving insight into SSc diversity that will help improve clinical trial design and future treatment.

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Update in interstitial lung disease in SSc

Oliver Distler
Univ. Hosp. Zurich, Switzerland

Systemic

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Update in pulmonary arterial hypertension in SSc

Eun Bong Lee
Seoul Nat'l Univ., Korea

Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis of skin and internal organs. Pulmonary arterial hypertension (PAH) is one of the leading causes of death in patients with SSc. Unlike idiopathic PAH, the pathophysiology of SSc-related PAH is complex. Hypertrophy of pulmonary artery, interstitial lung disease and heart failure all can also contribute to development of PAH. Recently, the cut-off value for the diagnosis of PAH, which is measured by mean pulmonary arterial pressure through right heart catheterization, was changed from 25 mmHg to 20 mmHg. Since there are several effective medications, early diagnosis of PAH is essential. Three major classes of medications are used to treat PAH, which include prostaglandin analogues, endothelin receptor antagonists and phosphodiesterase V inhibitors. The effectiveness of early aggressive combination therapy is being more advocated now.

Free Paper Session

Rheumatoid Arthritis Basic Research

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Seoul Dragon City, Seoul, Korea

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O-60

Orosomucoid acid-2, an acute phase reactant, promotes rheumatoid inflammation

Kimyo Kim[1], Bong-Ki Hong[1], Seung-Ah Yoo[1], Wan Uk Kim[1]

[1] Center for Intergrative Rheumatoid Transcriptomics and Dynamics, The Catholic University of Korea, Republic of Korea

Background

Acute phase proteins, including serum amyloid A and C-reactive proteins, potentially contribute to chronic inflammation, it remains unclear whether orosomucoid-2 (ORM2), one of acute phase proteins mainly produced from liver, directly promotes rheumatoid inflammation. In this study, we investigated the pathogenic mechanism of ORM2 in autoimmune inflammatory arthritis.

Methods

ORM2 expression was determined by ELISA and immunostaining. Fibroblast-like synoviocytes (FLSs) and macrophages were cultured in the presence of ORM2. NF-κB and p38 MAPK expression was assessed by Western blot analysis. Knockdown experiments were carried out using siRNAs for NF-κB p65, p38, and glycophorin C (GYPC). Proximity ligation assay was performed to test whether ORM2 interacts with GYPC as its receptor. Recombinant ORM2 was injected in the affected joints of mice with IL-1-induced arthritis.

Results

ORM2 expression was elevated in the sera, synovial fluids, and synovia of patients with rheumatoid arthritis (RA), and markedly increased by IL-1β and TNF-α stimulation. Major cell type producing ORM2 was synovial macrophages and fibroblasts. Recombinant ORM2 directly upregulated IL-6, TNF-α, IL-8, and CCL2 by macrophages and/or FLSs of RA patients via NF-κB and p38 MAPK pathways. GYPC was the receptor of ORM2. Such increase by ORM2 was reproduced in mouse macrophages and FLSs. Intra-articular injection of ORM2 promoted severity of IL-1-induced arthritis in mice, accelerating infiltration of macrophages in the affected joints. Moreover, in RA patients, circulating ORM2 levels correlated with disease activity, as assessed by DAS28, and represented well radiographic progression in 2 years.

Conclusions

Acute phase protein ORM2, mainly produced by synovial macrophages, directly increases production of pro-inflammatory cytokines/chemokines by macrophages and FLSs, and promotes chronic arthritis in mice, suggesting that it could be a diagnostic and therapeutic target of RA.

Figure & Table

Model of the ORM2 reciprocal activation between macrophages and FLSs in RA joints environments.

Keywords

orsomucoid-2, glycophorin C, rheumatoid arthritis

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LKB1 regulates the migration of fibroblast-like synoviocytes via oxidative stress-induced inflammatory cytokines in patients with rheumatoid arthritis

Ha-Reum Lee[1,2], Jinhyun Kim[2], Su-Jin Yoo[1,2], Ji Ah Park[2], Seong Wook Kang[1,2]

[1] Research Institute for Medical Sciences, Chungnam National University School of Medicine, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Chungnam National University Hospital, Republic of Korea

Background

Liver kinase B1 (LKB1) is known as a tumor suppressor gene and also inhibits reactive oxygen species (ROS) production. It is not clear about the role of LKB1 in rheumatoid arthritis (RA) until now.

Methods

Synovial tissues were obtained from RA patients who were undergoing synovectomy or joint replacement. Fibroblast-like synoviocytes (FLS) were used for experiments after four to six passages. Cells were transfected with siRNA duplex targeting constructs of LKB1 or NOX4 (nicotinamide adenine dinucleotide phosphate (NADPH) oxidase 4) using lipofectamine transfection reagent. After incubation for 24 h, downregulation of target expression was evaluated by real-time PCR and western blot analysis. The levels of inflammatory cytokines were analyzed by RT-qPCR and ELISA. ROS levels were stained using MitoSOX dye using flow cytometry. Cell migratory ability was analyzed using transwell migration assay.

Results

The mRNA expression of LKB1 was decreased by 91 % after transfection with LKB1 siRNA compared to scramble siRNA. LKB1 knock-down caused the increased expressions of NOX4, IL-6, tumor necrosis factor alpha (TNF-α), and VEGF in RA FLS (n=5). Following LKB1 deficiency, ROS levels and cell migration were increased in RA FLS. Because NOX4 catalyze intracellular ROS, NOX4 inhibitor (GLX351322; 2.5 or 5 μM) decreased intracellular ROS expression compared to no treatment in scramble siRNA. Unexpectedly, LKB1 knock-down FLS showed increased ROS rather than declining. To investigate the susceptibility to ROS, RA FLS were stimulated with hydrogen peroxide (1 mM) for 3 hr. Hydrogen peroxide increased ROS expression by 2.78 fold compared to no treatment in scramble siRNA transfected cells. Interestingly, LKB1 deficient FLS showed that hydrogen peroxide increased ROS production by 5.57 fold and elevated IL-1β expression by 6.90 fold compared to control.

Conclusions

LKB1 knockdown induced ROS-mediated pro-inflammatory cytokine productions and increased the susceptibility to oxidative stress than control in RA FLS.

Keywords

rheumatoid arthritis, reactive oxygen species, inflammation

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Postranslational modification in mammals protects citrullinated MCP1/CCL2 chemokine from partial degradation

Nataliia Korchynska[1,2], Ken Yoshida[3], Paul Peter Tak[4], Ger J.M. Pruijn[5], Takeo Isozaki[3], Jeffrey H. Ruth[3], Phillip L. Campbell[3], M.Asif Amin[3], Alisa E. Koch[3,6], Olexandr Korchynskyi[1,4,7]

[1] Medicine, Rzeszow University, Rzeszow, Poland
[2] Ecology, National Forestry University, Lviv, Ukraine, Ukraine
[3] Division of Rheumatology, University of Michigan Medical School,, USA
[4] Clinical immunology and Rheumatology, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands, Netherlands
[5] Department of Biomolecular Chemistry,, Institute for Molecules and Materials, Radboud University, Nijmegen, Netherlands
[6] Department of Veterans Affairs, Medical Center, Ann Arbor, Michigan,, USA
[7] Molecular Immunology, Institute of Biochemistry, National Academy of Sciences of Ukraine, Kyiv,, Ukraine

Background

Citrullination is a postranslational modification of specific proteins. Nowadays citrullination is a hallmark of rheutamoid arthritis and other autoimmune diseases. In our recent study we demonstrated citrullinated ENA78/CXCL5 as an efficient macrophage chemoattractant in a contrast with non-citrullinated chemokine. In our current work we found that citrullinated in vitro bacterially produced MCP1/CCL2 chemokine undergoes partial degradation and cannot be efficiently used in biological assays designed to detect citrullinated chemokines and their activities.

Goal: In our work we aimed generate a procedure for preparation of stable citrullinated MCP1/CCL2 chemokine suitable for research applications and to validate a hypothesis that posttranslational modifications occurring in mammalian cells can stabilize and protect citrullinated chemokines from quick degradation.

Methods

MCP-1/CCL2 was cloned from total RNA isolated from synovial fibroblasts obtained from RA patient. Both bacterially-produced and mammalian cells-produced recombinant human chemokine were citrullinated by commercial rabbit peptidylarginine deiminase (PAD)2, or by HEK293 cells produced human recombinant PAD2, PAD3 or PAD4. Citrullination was confirmed with Western blotting, modified sandwich ELISA assays and mass-spectrometry.

Results

Both commercially available and self-made bacterially produced MCP1/CCL2, undergo quick partial degradation upon their in vitro citrullination by rabbit muscle PAD2, or overexpressed human recombinant PAD2 or PAD4 and cannot be detected with either Western blotting or mass-spectrometry. At the same time mammalian cells-produced properly glycosylated MCP1/CCL2, can be efficiently citrullinated, detected and successfully used as the standards in modified ELISA assays as well as in bioassays. At the same time, a site-directed inactivation of a single potential glycosylation site at asparagine 14 (N14) does not change the stability of mammalian cells produced MCP1/CCL2.

Conclusions

Glycosylation that is lucking in bacterially-produced proteins but occurs in mammalian cells stabilizes citrullinated chemokines thus protecting them from quickly ongoing partial degradation.

Keywords

Monocyte chemotactic protein 1, rheumatoid arthritis, citrullination, peptidylarginine deiminase, glycosylation

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Journal of Rheumatic Diseases
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Assessment of disease activity in patients with rheumatoid arthritis utilizing plasma tumor M2-pyruvate kinase test

Sung Soo Ahn[1], Younhee Park[2]

[1] Internal Medicine, Division of Rheumatology, Yongin Severance Hospital, Yonsei University College of Medicine, Republic of Korea
[2] Laboratory Medicine, Severance Hospital, Yonsei University College of Medicine, Republic of Korea

Background

Pyruvate kinase M2 (PKM2) is an enzyme regulating the final process of glycolysis, which exists in tetrameric and dimeric form. The dimeric form of PKM2 – also known as tumor M2-PK – increases when aerobic glycolysis is augmented, which is a feature observed in rheumatoid arthritis (RA). We evaluated whether plasma tumor M2-PK is elevated in RA patients and correlated to disease activity.

Methods

Plasma obtained from RA (n=151) and osteoarthritis (OA) (n=37) patients, as well as controls (n=37) were utilized to measure tumor M2-PK level. Associations of plasma tumor M2-PK with continuous variables was evaluated by Pearson's analysis, and logistic regression analysis was carried out to determine the relationship between plasma tumor M2-PK with disease activity status.

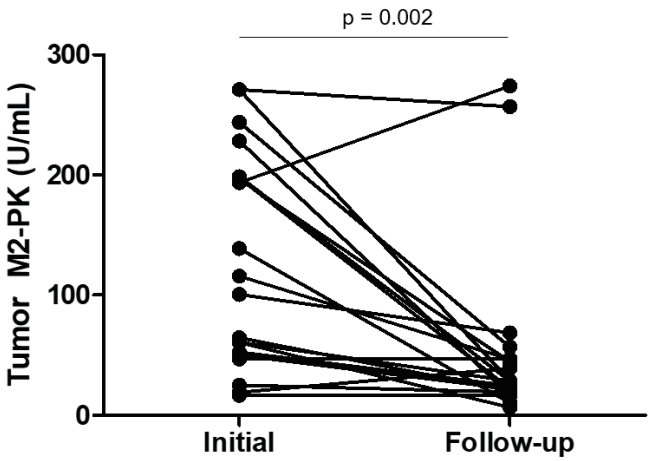
Results

Tumor M2-PK level significantly correlated with disease activity score (DAS)28-erythrocyte sedimentation rate (ESR) (r=0.546, p<0.001) and DAS28-C-reactive protein (CRP) (r=0.589, p<0.001). Serial tumor M2-PK level testing in 20 patients exhibited a significant decline of tumor M2-PK level after reduction of inflammation (p<0.001). Area under the receiver operator curve analysis demonstrated that incorporation of tumor M2-PK, ESR, and CRP had an area under the curve 0.962 in discriminating between moderate/high and remission/low disease activity. Furthermore, adjusted logistic regression analysis revealed that tumor M2-PK > 43.9 U/mL (OR 3.672, p=0.042) independently predicted moderate/high disease activity status. Finally, tumor M2-PK level in RA patients was significantly higher than OA patients and controls (all p<0.001).

Conclusions

Plasma tumor M2-PK level might be a clinically useful indicator for evaluating disease activity and diagnosis of RA.

Figure & Table



Keywords

Tumor M2-pyruvate kinase, rheumatoid arthritis, disease activity

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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Association analysis of a MUC5B promoter variant rs35705950 with rheumatoid arthritis-interstitial lung disease in Korea

Young Bin Joo[1], So-Young Bang[1,2], Soo-Kyung Cho[2,3], Chan-Bum Choi[2,3], Yoon-Kyoung Sung[2,3], Tae-Hwan Kim[2,3], Jae-Bum Jun[2,3], Dae Hyun Yoo[2,3], Sang-Cheol Bae[2,3], Hye-Soon Lee[1,2]

[1] Division of rheumatology, Department of internal medicine, Hanyang University Guri Hospital, Guri, Republic of Korea
[2] Hanyang University Institute for Rheumatology Research, Seoul, Republic of Korea
[3] Department of rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea

Background

It has been suggested that idiopathic pulmonary fibrosis and rheumatoid arthritis-interstitial lung disease (RA-ILD) share genetic background, among which a MUC5B promoter variant rs35705950 has been reported to be the most significant risk variant for RA-ILD in Caucasian populations. However, this MUC5B variant has shown different genetic traits according to ethnicity. Until recently. little is known about the significant association of MUC5B with RA-ILD in Asian populations. This study aimed to identify the association of MUC5B variant rs35705950 with Korean RA-ILD patients.

Methods

Patients were recruited from Hanyang university hospital for rheumatic diseases (n=1,846). RA-ILD was defined based on chest CT or chest x-ray. The MUC5B variant rs35705950 was genotyped by TaqMan genotyping assays. The chi-square test was used to test for differences in MUC5B variant between RA-ILD and RA without ILD group (RA-noILD).

Results

The minor allele frequency of MUC5B variant was 0.0046. The number of wild-type (GG), heterozygous (GT) and mutant genotype (TT) were 1,829, 17, and 0, respectively. There was no difference of heterozygous between two groups (n=2/75, 2.7% for RA-ILD, n=15/1770, 0.8% for RA-noILD, P=0.150). Among the 350 RA patients who had chest CT, the prevalence of RA-ILD was 16.3% (n=57/350). UIP pattern (45.6%) was the most frequent, followed by nonspecific interstitial pneumonia (22.8%), indeterminate (15.8%) and organizing pneumonia (14.0%). No association was observed in chest CT-confirmed RA-ILD with MUC5B variant (heterozygous number=2/57, 3.5% for RA-ILD, n=8/293, 2.7% for RA-noILD, P=0.669)

Conclusions

Although MUC5B variant is common and strongly associated with RA-ILD in Western population, it is rare in Korean RA patients and appears to be insignificant as a genetic risk factor for Korean RA-ILD patients. These results support the concept that the genetic background of RA-ILD differs according to ethnicity, raising the need to search for novel genetic risk factors for RA-ILD in Korean.

Keywords

rheumatoid arthritis-interstitial lung disease, MUC5B, genetic risk factor

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Therapeutic effect of folic acid in collagen-induced arthritis mouse model

Kijun Lee[1], Young Woo Ryu[1], Ji Hyeon Ju[1,2]

[1] Catholic iPSC Research Center, The Catholic University of Korea, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, Institute of Medical Science, College of Medicine, The Catholic University of Korea, Republic of Korea

Background

Folic acid (FA) supplements are commonly prescribed to rheumatoid arthritis (RA) patients suffering side effects of methotrexate (MTX). But patients are still suffering from the side effects of MTX. We undertook this study with the expectation that FA can be a substitute for MTX with its anti-inflammatory effect. This study investigated the anti-inflammatory effects of FA and demonstrated the possibility of FA as an anti-inflammatory drug.

Methods

In vivo and ex vivo experiments were set up to figure out whether the administration of FA induces an anti-inflammatory response. DBA/1J mice were induced into the collagen-induced arthritis model (CIA model) and randomly assigned to six groups. Five groups were each assigned to one of five treatments, and the other group was assigned as the control group. FA, MTX, vehicle was administered through the peritoneum (intraperitoneal injection, i.p.). Histological examination and CIA Scoring were done to examine the severity of RA. In vitro experiments were done with LPS-stimulated mouse splenocytes to observe the anti-inflammatory effects of immune cells. The effect of treatments with different dosages of FA and MTX were analyzed by qRT-PCR, FACS, human phospho-kinase array, and western blot assay.

Results

Histological examination of tarsal joints in the hind paws of mice showed that FA and MTX treatment alleviates synovial inflammation. While normal control showed clear identified joint spaces, the CIA model presented severe inflammatory infiltration resulting in tarsal bone and cartilage destruction. Treatment of FA and MTX alleviated inflammatory lesions of the CIA model. Moreover, a higher dose(500ug/mouse) of FA shows more alleviated inflammatory lesions and cleaner cartilage zone.

Conclusions

According to the results, FA has anti-inflammatory effects on RA. But there's a lack of evidence for whether FA can be a complete substitute for MTX to human RA patients. Practical applications and ideas for further research are suggested.

Figure & Table

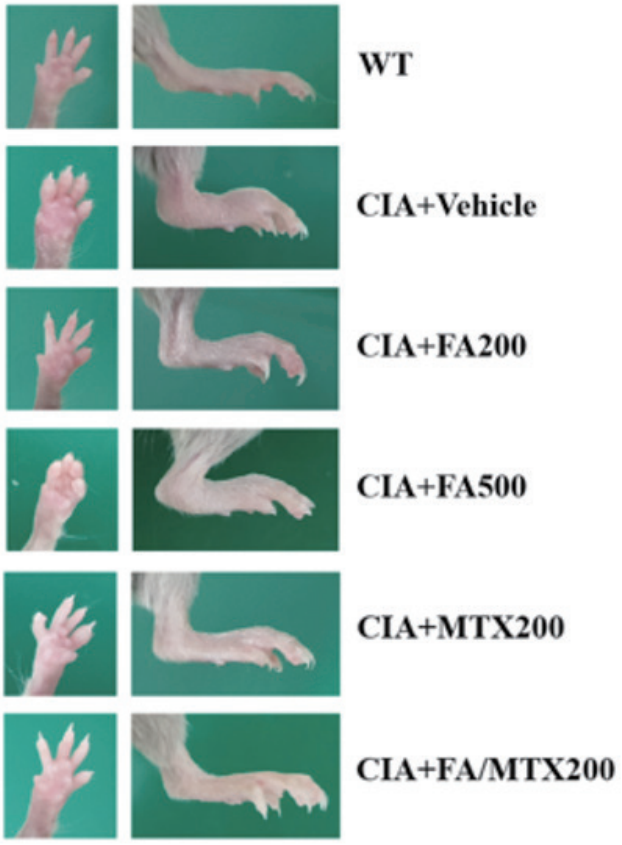

Figure. Effects of folic acid on the severity of CIA demonstrated by clinical arthritis score, incidence rate, visual examination

Keywords

Rheumatoid arthritis, Folic acid, Collagen-induced arthritis model

Symposium

Coding and Insurance Guideline in Rheumatic Disease

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Vol. 29, Suppl. 1, May, 2022
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May 19(Thu) - 21(Sat), 2022

Rheumatic diseases and KCD 8th revision

Sukil Kim
The Catholic Univ. of Korea, Korea

Most of rheumatic diseases are rare and subject to be the target of benefit extension policy by the government. From the patient's point of view, the policy is a favorable to the patients because it relieves the patients from the economic burden caused by the diseases.

On the other hand, to be classified as a rare disease, the incidence should be calculated through coding with proper classification. KCD-8 (Korean Classification of Diseases version 8), which is based on ICD-10 (International Classification of Diseases version 10), has long been used in Korea for the purpose. Some of new diseases have been found by recent medical knowledge and there have been new infectious diseases, such as COVID-19. Any diseases should be listed on the ICD to be utilized for disease epidemiology and health care system. However, the structure of ICD-10 reached a technical limitation and was not able to include new diseases. It is one of the main reasons for the revision of ICD-11.

The World Health Assembly adopted ICD-11 in May 2019. Most countries using ICD-10 are conducting various research or planning for the full-scale introduction of ICD-11, which has a large impact on the health care system of their own. The latest Korean version of ICD-10, KCD-8, was announced in 2020 by Statistics Korea. But none of ICD-11 contents was included in it.

During the national audit for the Health Insurance Review and Assessment Service (HIRA) in the National Assembly in October of last year, Rep. Hye-young Choi addressed inadequate use of the KCD-8 for calculation of rare and incurable diseases. pointed out the problem, and the director of the HIRA said that the ICD-11 would be introduced as an alternative.

The Ministry of Health and Welfare and the HIRA have the governance of ICD-11 required to operate the Korean healthcare system and are planning to introduce ICD-11. They also want to work together with the medical community. The medical community is expected to participate in the management ICD-11 organized by either the Ministry of Health and Welfare in local level or WHO in global level. It will be of great help to the development of related fields.

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Principles and future prospects of insurance benefits in rheumatoid diseases

Gihyeon Seo
Health Insurance Review and Assessment Service, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Insurance Guideline and Tips for Treatment of Rheumatic Disease

Seung-Jae Hong
Kyung Hee Univ., Korea

In this lecture, the causes for the most frequent denial of insurance coverage are presented along with the real-world cases. Some causes are reasonable such as extractable nuclear antigen (ENA) panel/anti-dsDNA test, some genetic maker studies, and radiographic findings, while many other causes are irrational, such as a few days gap in csDMARDs coverage before bDMARD/tsDMARDs prescription. Along with efforts to improve insurance coverage criteria, keen efforts on behalf of clinicians are required to reduce the losses and harm incurred by such denial.

KCR 2022

42nd Korean College of Rheumatology Annual Scientific Meeting and the 16th International Symposium

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E-POSTER PRESENTATION

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E-poster Presentation

RA-pathogenesis and animal model & Cytokines and mediators

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P-001

Anti-arthritic activities of the eleutherococcus senticosus, achyranthes japonica, and atractylodes japonica mixed extract fermented with nuruk in a type II collagen-induced arthritis mouse model

Chong Hyuk Chung[1], Ju-Young Kim[2], Yoon-Hee Cheon[2], So-Young Eun[2], Chang-hoon Lee[1], Myeung-Su Lee[1]

[1] Rheumatology Department, School of Medicine, Wonkwang University, Republic of Korea
2 Musculoskeletal and Immune Disease Research Institute, School of Medicine, Wonkwang University, Republic of Korea

Background

Rheumatoid arthritis (RA) is an autoimmune disease that is accompanied by chronic synovitis, progressive cartilage, and bone destruction and is affected by inflammatory-associated factors. Vigeo is a mixture of fermented extracts of Eleutherococcus senticosus Maxim (ESM), Achyranthes japonica (Miq.) Nakai (AJN), and Atractylodes japonica Koidzumi (AJK) manufactured using the traditional Korean nuruk fermentation method. Although the bioactive effects of ESM, AJN, and AJK have already been reported, the pharmacological effects of Vigeo have not been proven. Therefore, in this study, we investigated whether Vigeo had inhibitory effects on RA and its intracellular mechanisms using a type II collagen-induced arthritis (CIA) mouse model.

Methods

CIA was induced in DBA/1 mice by immunization with bovine type II collagen. The mice were administered orally with Vigeo (200 and 500 mg/kg/day, i.g.) from days 21 to 42 after immunization. The clinical scores, hind paw swelling, and histopathological finding were evaluated in the paw of CIA mice. The levels of tumor necrosis factor α (TNF-α), interleukin (IL)-6, and IL-1β in the serum were measured by enzyme-linked immunosorbent assay.

Results

The results showed that Vigeo 500 mg/kg treatment significantly alleviated the severity of the disease, based on the reduced hind paw swelling and clinical scores, compared with untreated CIA mice. Comparing with untreated CIA mice, Vigeo 500 mg/kg treatment inhibited the levels of TNF-α, IL-6, and IL-1β in the serum.

Conclusions

In conclusion, our results suggest that anti-inflammatory effects of Vigeo against collagen-induced arthritis in mice may be due to its ability to inhibit pro-inflammatory mediators. Vigeo may be a promising potential therapeutic reagent for arthritis treatment.

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P-002

A green-lipped mussel prevents rheumatoid arthritis via regulation of inflammatory response and osteoclastogenesis

Seungcheon Yang[1], Hong Ki Min[2], Jin-Sil Park[1], Hyun Sik Na[1,3], Jooyeon Jhun[1], Mi-La Cho[1,5], Sung-Hwan Park[1,4]

[1] The Rheumatism Research Center, Catholic Research Institute of Medical Science, The Catholic University of Korea, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Konkuk University Medical Center, Republic of Korea
[3] Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea, Republic of Korea
[4] Division of Rheumatology, Department of Internal Medicine, College of Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea, Republic of Korea
[5] Department of Medical Lifescience, College of Medicine, The Catholic University of Korea, Republic of Korea

Background

Rheumatoid arthritis (RA) is a chronic inflammatory disorders characterized by progressive joint destruction. The green-lipped mussels (GLM) are known to have chondro-modulator and anti-inflammatory properties, but studies on the effects and action mechanism of GLM on RA are still insufficient.

Methods

Collagen-induced arthritis (CIA) mice was used, and treated with vehicle, methotrexate, and GLM. The incidence of arthritis, arthritis score, histological score were assessed. Immunohistochemical stains for tumor necrosis factor-α (TNF-α), interleukin (IL)-1β, IL-6, IL-17, and TRAP on ankle joint were evaluated. Splenocytes were used to measure IL-17+ CD4+ cells, and confocal stain for CD4+ IL-17+ in spleen was evaluated. Bone marrow-derived monocyte/macrophage of mice and peripheral blood monocytes of human were used to evaluate osteoclastogenesis.

Results

Application of GLM attenuated the arthritic severity and histologic score in CIA mice than vehicle group. Expression of pro-inflammatory cytokines (TNF-α, IL-1β, and IL-17) were decreased in the ankle joints from GLM-treated CIA mice. Frequencies of IL-17+ CD4+ cells decreased in ex vivo splenocytes from GLM-treated CIA mice, and decrease of IL-17+ CD4+ cells were also observed in confocal stain of GLM-treated CIA mice spleen. Moreover, GLM inhibited osteoclastogenesis of mice BMMs and human monocytes in vitro.

Conclusions

These results suggest that GLM has potential as a therapeutic agent for RA by controlling pathologic immune cells and osteoclastogenesis.

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Journal of Rheumatic Diseases
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P-003

HLA-DRB1 non-SE fine specificity associations with anti-RA33 autoantibody positivity in rheumatoid arthritis patients stratified by different serological phenotypes

Nurul Aain Ahmad fauzi[1], Shereen Ch'ng suyin[2], Hazlyna Baharuddin[2,3], Mollyza Mohd zain[2], Ing Soo Lau[2], Habibah Yusoof[2], Azlin Ahmad[2], Azmillah Rosman[2], Siti Aisyah Abdul ahmad[1], Wahinuddin Sulaiman[4], Heselynn Hussein[5], Nor Shuhaila Shahril[5], Suk Chyn Gun6, Eashwary Mageswaran[5], Mohd Shahrir Mohamed said[7], Ainon Mohd mokhtar[8], Muhaini Othman[4], Shahnaz Murad[1], Leonid Padyukov[10], Lars Alfredsson[11], Lars Klareskog[10], Johan Rönnelid[12], Chun Lai Too[1,10]

[1] Immunogenetic Unit, Allergy and Immunology Research Centre, Institute for Medical Research, National Institutes of Health Complex, Ministry of Health Malaysia, Malaysia
[2] Department of Internal Medicine, Selayang Hospital, Ministry of Health Malaysia, Malaysia
[3] Faculty of Medicine, Universiti Teknologi MARA, Malaysia
[4] Department of Internal Medicine, Raja Permaisuri Bainun Hospital, Ministry of Health Malaysia, Perak, Malaysia
[5] Department of Internal Medicine, Putrajaya Hospital, Ministry of Health Malaysia, Putrajaya, Malaysia
[6] Department of Internal Medicine, Tuanku Ja'afar Seremban Hospital, Ministry of Health Malaysia, Negeri Sembilan, Malaysia
[7] Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia
[8] Department of Internal Medicine, Tengku Ampuan Afzan Hospital, Ministry of Health Malaysia, Kuantan, Pahang, Malaysia
[9] Department of Internal Medicine, Raja Permaisuri Bainun Hospital, Ministry of Health Malaysia, Ipoh, Perak, Malaysia
[10] Division of Rheumatology, Department of Medicine, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden
[11] Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, Malaysia
[12] Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden

Background

Development of seropositive RA is well-associated with presence of HLA-DRB1 SE alleles (i.e., DRB1*01, *04 and *10). We investigated the role of HLA-DRB1 non-SE alleles as risk for anti-RA33 autoantibody positivity in diverse RA serological subsets, as defined by anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) status.

Methods

A total of 550 RA cases comprising seronegative (negative for anti-CCP2, IgG and IgM, n=250), singular anti-CCP2 positive (n=100), double RF positive RA (n=50), seropositive (triple-autoantibody positive, n=150) and triple-autoantibody negative normal controls (n=300) were included from the Malaysian Epidemiological Investigations of RA (MyEIRA) case-control study. All subjects were assayed for anti-RA33 autoantibody and genotyped for four-digit HLA-DRB1 alleles using the PCR-SSO method.

Results

Our data demonstrated that anti-RA33 positivity was 20.9% in all RA cases (i.e., 34% in RF only positive RA; 25% in seropositive RA; 18% in seronegative RA and 18% in anti-CCP2 only positive RA). Carriage of HLA-DRB1 non-shared epitope alleles were 64.5% among RA cases and 81.6% among normal controls. In both the seropositive and RF-only positive subgroups, a trend of association was observed between DRB1*03 and anti-RA33 positivity (odds ratio, OR>1.5; p>0.05). Meanwhile, DRB1*15 was significantly associated with anti-RA33 autoantibody positivity regardless of RF and ACPA status (p<0.05). In the seronegative RA subgroup, carriage of DRB1*08 was significantly associated with risk of anti-RA33 positivity (OR 2.80, 95% CI 1.06 – 7.43, p<0.05) whereas DRB1*07 was found to be negatively associated with anti-RA33 autoantibody (OR 0.12, 95% CI 0.02 – 0.90, p<0.05).

Conclusions

Our findings suggest that different HLA-DRB1 fine specificity alleles are associated with different subsets of RA in the context of anti-RA33 positivity, independent of the well-established risk of DRB1 SE alleles.

Keywords

HLA-DRB1 alleles, Anti-RA33 autoantibody, Rheumatoid arthritis

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P-004

Precision nanomedicine in rheumatoid arthritis: Customized multifunctional polymeric nanocarriers for alleviation of inflammation severity in rheumatoid arthritic rats

ANAS Ahmad[1]

[1] 1 Department of Microbiology, Immunology and Infectious Diseases, Cumming School of Medicine, University of Calgary, Alberta T2N 4N1, Canada., Canada

Background

Rheumatoid arthritis (RA) is among some of the most prevailing autoimmune disorder which affects around 1% of global population. In spite of significant advancements in RA treatments, limitations like higher drug biotransformation and their rapid elimination form the body causes poor drug bioavailabilities. Current research studies have stressed the formulation and development of suitable, biocompatible and biodegradable nanocarriers for drug encapsulation and delivery such that the existing limitations of drugs could be surpassed and their ultimate pharmacological efficacy could be enhanced. For this purpose, customized polymeric core shell nanocarriers were formulated and optimised for delivering two drugs simultaneously in the arthritic rat model.

Methods

Nanocarriers were formulated with two highly biocompatible and biodegradable polymers by the method of nanoprecipitation and solvent evaporation. These were assessed optimized for their particle size, shape, and surface morphology by DLS, TEM, SEM, and AFM, for their drug loading capacity and encapsulation efficiency, biocompatibility, and normal fibroblast cell lines and their anti-inflammatory therapeutic efficacy in arthritic rats, in terms of macroscopic disease index, clinical severity, histopathology, immunohistochemistry and ELISA assays for inflammatory biomarkers.

Results

The nanocarriers were 125-150 nm in diameter, spherical in shape with smooth surfaces, exhibited higher biocompatibility, and considerably brought down the severity of inflammation on Wistar rats. All the macroscopic, histological, immunohistochemical observations demonstrated the amelioration of inflammation in RA. These nanocarriers reduced swellings of joints, and erythema significantly ameliorated bone-erosion noted in radiological observations, inhibited destruction of collagen, reinstated normalcy of synovial tissues, bones, and cartilage histology with suppressed inflammatory cellular infiltrations. Nanocarriers further suppressed several inflammation biomarkers viz. iNOS, COX-2, IL-1β and TNF-α

Conclusions

Outcomes of the present study indicate that these nanocarriers exercised better therapeutic efficacies in RA in comparison to naïve compounds which can be assigned to sustained and controlled release of drugs, and nanocarriers' capability to suppress inflammatory markers.

Keywords

Nanocarriers, Rheumatoid Arthritis, Drug Delivery

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P-005

APE1 inhibits the inflammation of fibroblast-like synoviocytes via oxidative stress regulation in patients with rheumatoid arthritis

Ha-Reum Lee[1,2], Jinhyun Kim[2], Su-Jin Yoo[1,2], Ji Ah Park[2], Hee Kyoung Joo[1,3], Yu Ran Lee[1,3], Sungmin Kim[1,3], Byeong Hwa Jeon[1,3], Seong Wook Kang[1,2]

[1] Research Institute for Medical Sciences, Chungnam National University School of Medicine, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Chungnam National University Hospital, Republic of Korea
[3] Department of Physiology, College of Medicine, Chungnam National University, Republic of Korea

Background

Although apurinic/apyrimidinic endonuclease 1 (APE1) is highly expressed in synovial fluids from patients with rheumatoid arthritis (RA), the effect of APE1 in RA pathogenesis remains unclear. This study aimed to examine the role of APE1 in fibroblast-like synoviocytes (FLS) from patients with RA.

Methods

Synovial tissues were obtained from RA patients (n=5) who were undergoing synovectomy or joint replacement. After removing fat and fibrous tissues, the synovium was cut into small pieces and incubated with 0.1% collagenase in Dulbecco's modified Eagle's medium (DMEM) at 37°C for 2 h. Cells were used for experiments after three to six passages. FLS were stimulated with or without recombinant interleukin 17 (IL-17; 10 ng/ml), tumor necrosis factor alpha (TNF-α; 10 ng/ml), and long-lasting recombinant human APE1 (MR201; 1, 10, 100 ng/ml) for 24 h. The mRNA and protein levels of inflammatory cytokines were analyzed by RT-qPCR and ELISA, respectively. Reactive oxygen species (ROS) levels were stained using MitoSOX dye using flow cytometry. Cell migratory ability was examined using wound migration assay and transwell migration assay.

Results

RA FLS treated with APE1 showed slightly decreased level of inflammatory cytokines and mitochondrial specific ROS. When RA FLS were stimulated with IL-17/TNF-α, recombinant APE1 significantly decreased the expression of inflammatory cytokines, including IL-1β, IL-6, and IL-8. IL-17/TNF-α-induced mitochondrial specific ROS production was also downregulated by cotreatment with recombinant APE1. When FLS cultures were approximately 90% confluent, FLS monolayers were wounded with pipette tips and treated with IL-17/TNF-α and APE1 for 24 hr. IL-17/TNF-α-enhanced cell migration was inhibited by cotreatment with recombinant APE1.

Conclusions

Recombinant APE1 significantly inhibited mitochondrial specific ROS production and IL-17/TNF-α-induced cell migration in RA FLS. These data suggested that APE1 is a key mediator to cytokine-enhanced migration via ROS modulation in RA FLS.

Keywords

rheumatoid arthritis, reactive oxygen species, inflammation

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P-006

A novel cytokine consisting of p40 and EBI3 subunits suppresses experimental autoimmune arthritis via reciprocal regulation of Th17 and Treg cells

Seon-Yeong Lee[1], Young-Mee Moon[1], Su-Jin Moon[2], A Ram Lee[1,4], Chae Rim Lee[1,4], Seung-Ki Kwok[2], Sung-Hwan Park[2], Mi-La Cho[1,3,4]

[1] The Rheumatism Research Center, The Catholic University of Korea, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Republic of Korea
[3] Department of Medical Lifescience, College of Medicine, The Catholic University of Korea, Republic of Korea
[4] Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea, Republic of Korea

Background

The interleukin (IL)-12 cytokine family is closely related to the development of T helper cells, which are responsible for autoimmune disease enhancement or suppression. IL-12 family members are generally heterodimers that share three α-subunits (p35, p19, p28) and two β-subunits (p40, EBI3). However, a β-sheet p40 homodimer has been shown to exist and antagonize IL-12 and IL-23 signaling 1. Therefore, we assumed the existence of a p40-EBI3 heterodimer in nature, and sought to investigate its role in immune regulation.

Methods

The presence of p40-EBI3 heterodimer was confirmed by ELISA, immunoprecipitation, and western blotting. A p40-EBI3 vector and p40-EBI3-Fc protein were synthesized to confirm the immunological role of the protein in mice with collagen-induced arthritis (CIA). The anti-inflammatory effects of p40-EBI3 were analyzed with regard to clinical, histological, and immune cell regulatory aspects in mice with CIA.

Results

Clinical arthritis scores and expression levels of proinflammatory cytokines (e.g., IL-17, IL-1β, IL-6, and TNF-α) were significantly attenuated in p40-EBI3-overexpressing and p40-EBI3-Fc-treated mice with CIA, in comparison to vehicle-treated mice with CIA. Structural joint damage and vessel formation-related genes were also reduced by p40-EBI3 heterodimer treatment. In vitro, p40-EBI3-Fc protein significantly suppressed the differentiation of Th17 cells; it reciprocally induced CD4+CD25+Foxp3+ (regulatory T) cells. p40-EBI3 also inhibited osteoclast formation in a concentration-dependent manner.

Conclusions

In this study, p40-EBI3 antagonized proinflammatory conditions both in vivo and in vitro. We propose that p40-EBI3 is a novel anti-inflammatory cytokine involved in suppressing the immune response through the expansion of Treg cells and suppression of Th17 cells and osteoclastogenesis.

E-poster Presentation

RA-clinical aspects

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Seoul Dragon City, Seoul, Korea

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KCR 2022
May 19(Thu) - 21(Sat), 2022

P-007

Seasonal analysis of relative search volume of rheumatoid arthritis in Korea

Eunsung Kim[1]

[1] Internal Medicine, Bumin hospital, Republic of Korea

Background

This study aims to investigate the searching interest of seasonal variation in rheumatoid arthritis (RA) by evaluating search term trends.

Methods

We included relative search term trends for RA(searched in Korean) from January 2018 to December 2021 in Naver DataLab. For seasonal analysis, we fitted a cosinor model for monthly relative RA searching terms. In addition monthly mean rate ratio and 95% confidence interval were studied using December as a reference month.

Results

The cosinor analysis showed a significant seasonality that amplitude was 7.0 (absolute scale) and phase was 5.8 months (adjusted p-value 0.025). Relative RA search volume was highest in June and was lowest in December.

Conclusions

The seasonal analysis results show that searching interests show significant seasonal variation. Based on the result of this study, the seasonal analysis model is helpful to estimate the interests of the people about RA in Korea.

Figure & Table

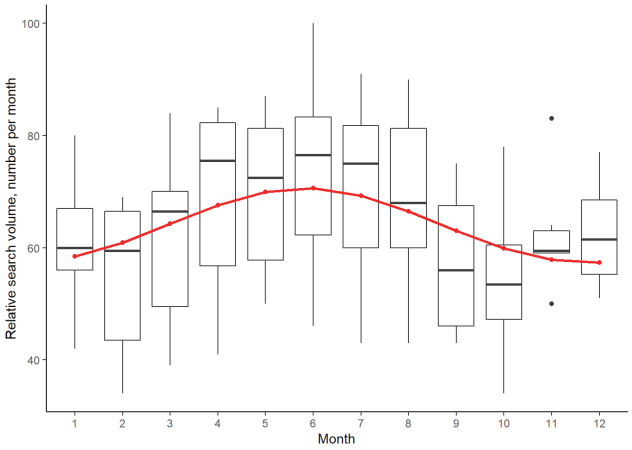

Figure. Relative search volume of 'rheumatoid arthritis'. Boxplots show concentration of relative search volume, number per

Keywords

relative search volume, seasonal analysis, cosinor analysis

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P-008

Cardiac hydatid cyst in a patient with rheumatoid arthritis

Giorgi Apkhazava[1], Grigol Nemsadze[2], Megi Kurtanidze[1]

[1] Radiology Department, Tbilisi City Medical, Georgia
[2] Radiology Department, TSSU First University, Georgia

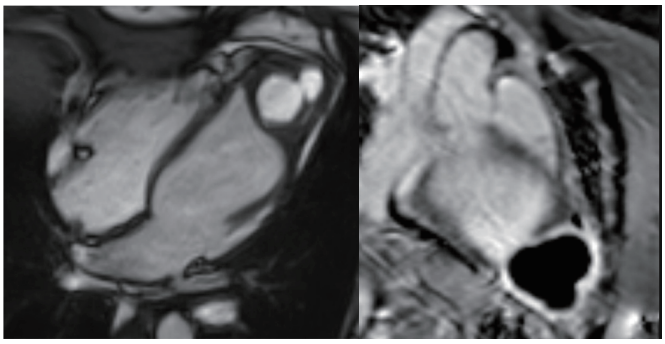
Description

A 33-year-old male presented to the cardiology clinic with complaints of intermittent atypical chest pain, resembling acute myocardial infarction. The patient had been followed up and treated for rheumatoid arthritis for 5 years. An electrocardiography revealed non-specific T wave changes, whereas physical examination was unremarkable. Transthoracic echocardiography showed the cystic lesion with compressing the left cardiac ventricle. Cardiac magnetic resonance imaging(MRI) was performed. MRI revealed left ventricular myocardial cyst that was hyperintense T2-weighted (T2W) images, and it was peripheral enhanced after contrast administration (Fig.1). The blood level of Echinococcus IgG by ELISA was 158 RU/mL, which was considered as a positive serologic test for Echinococcus infection. According to radiological and laboratory findings, the lesions were evaluated hydatid cyst infection involvement of the ventricular. Therefore, albendazole therapy was introduced. The patient underwent surgical treatment. The lesion was identified as a hydatid cyst infection via pathological examination.

Conclusions

Hydatid cyst infections is a parasitic epidemiological infection caused by larvae of Echinococcus granulosus, although less frequently Echinococcus multilocularis . Hydatid cyst infections can be located in various tissues, although they are most common in the liver and the lung . As a conclusion, cardiac hydatid cyst is extremely uncommon. Therefore, cardiac localization, which is an atypical location for clinicians in non-endemic countries, should be kept in mind as it may cause lethal complications.

Figure & Table



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P-009

Course of COVID-19 in patients with rheumatoid arthritis (own data)

Eugenia Aronova[1], Galina Gridneva[1], Boris Belov[1]

[1] department of comorbid infections, V.A. Nasonova Research Institute of Rheumatology, Russian Federation

Background

The aim of study was to characterize the features of the course of COVID-19 in patients with rheumatoid arthritis (RA).

Methods

We studied the material of questionnaires filled out by patients who underwent COVID-19, verified by RT-PCR to SARS-CoV-2 RNA, for the period from 05/15/2020 to 12/01/2021.

Results

The study included 42 adult (over 18 years old) patients (38 women, 90.5%) with a reliable diagnosis of RA. The average age of patients was 51.17±15.78 years. At the time of development of COVID-19, the severity of RA symptoms, assessed by VAS, was 4.68±2.94. As an antirheumatic therapy, 11 (26.2%) patients took glucocorticoids at an average dose of 5.7±3.4 mg/day (prednisolone equivalent), 31 (73.8%) - DMARDs. 22 patients received biologics, incl. 15 - rituximab (66.6%, of which received the last infusion within 6 months or less before the onset of the first symptoms of COVID-19).

Among the clinical manifestations of COVID-19, the most common were weakness, fatigue - in 38 (90.5%), fever - in 30 (71.4%), anosmia - in 28 (66.7%), dysgeusia - in 24 (57.1%), increased arthralgia - in 24 (57.4%). There was a significant positive correlation between increased arthralgia during COVID-19 and RA activity. On average (median), each patient reported 13 [9.25;13.75] symptoms associated with COVID-19. 14 patients (33.3%) were hospitalized, of which 10 required oxygen support. Patients treated with rituximab were hospitalized more frequently (RR 2.7, 95% CI 1.192–6.117). Complications were registered in 5 cases (11.9%): venous thrombosis in 2 patients, acute respiratory failure in another 2 patients, and cerebrovascular accident in 1 patient.

Conclusions

33.3% of COVID-19 patients in the study group required inpatient treatment. In 11.9% - COVID-19 proceeded with complications. The number of symptoms associated with COVID-19 did not correlate with RA activity. However, patients with higher RA activity more often noted increased arthralgia.

Keywords

COVID-19, rheumatoid arthritis, Rituximab

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-010

Study of the features of post-covid syndrome in patients with rheumatoid arthritis

Eugenia Aronova[1], Galina Gridneva[1], Boris Belov[1]

[1] department of comorbid infections, V.A. Nasonova Research Institute of Rheumatology, Russian Federation

Background

We conduct a comparative assessment of clinical and demographic indicators in groups of patients with rheumatoid arthritis who underwent COVID-19, with and without PCS.

Methods

The material of the questionnaires filled in by patients of the V.A. Nasonova Research Institute of Rheumatology, who underwent COVID-19, verified by RT-PCR for SARS-CoV-2 RNA.

Results

The study included 42 adult (over 18 years old) patients with a reliable diagnosis of rheumatoid arthritis (ACR/EULAR). Of these, 22 (52.4%) patients noted the development of PCS (Group 1), and 20 patients underwent COVID-19 without consequences (Group 2). Both groups were represented predominantly by women (90.9% and 90%, respectively). The average age in both groups did not differ significantly and amounted to 55.04±13.92 years in group 1, and 46.90±16.64 years in group 2. The median number of comorbid diseases was 2 [1;2.75] in group 1 and 1 [0;2] in group 2. PCS was represented by the following symptoms: memory impairment - in 13 patients; weakness, problems with attention - in 12; increased pain in the joints - in 12. The number of COVID-19 symptoms in the infectious phase in group 1 was higher than in group 2 ($P<0.05$): 18 [13;21.75] and 10.5 [7;13], respectively. At the time of development of COVID-19, the severity of RA symptoms, assessed by VAS, was 5.0±3.02 in group 1 and 4.35±2.88 in group 2.

Conclusions

Even though when assessing the socio-demographic characteristics, no statistically significant differences were found between the study groups, the average age, the number of comorbid diseases, and the severity of RA symptoms at the time of COVID-19 were higher in the group of patients with RA and PCS. Patients with PCS reported higher rates of hospitalizations and more severe COVID-19. There were also repeated cases of COVID-19 in this group. It is necessary to continue the study on a larger cohort.

Keywords

post-covid syndrome, rheumatoid arhritis, COVID-19

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-011

Ultrasound as a potential tool to detect interstitial lung disease in daily clinical setting of patients with rheumatoid arthritis

MARWIN Gutierrez[1], Santiago Ruta[2], Denise Clavijo-cornejo[1], Gabriela Fuentes-moreno[1], Samuel Reyes-long[3], Chiara Bertolazzi[1]

[1] Division of Musculoskeletal and Reumatic Diseases, Instituto Nacional de Rehabilitacion, Mexico
[2] Rheumatology Unit, Hospital Italiano, La Plata, Argentina
[3] División de Neurociencias, Instituto Nacional de Rehabilitacion, Mexico

Background

In the last years, the pulmonary ultrasound (US) has been proposed to assess ILD in rheumatic diseases. The aim of this study is to investigate the potential role of the US in the detection of ILD in a real-life cohort of patients with rheumatoid arthritis RA.

Methods

Patients with a diagnosis of RA were consecutively enrolled. All patients underwent pulmonary examination, laboratory data, DLCO measure, chest HRCT and radiographs, and US examination. A healthy group was included as a control group.

US was performed according the 14-intercostal space scanning protocol using the following semiquantitative scale [0= normal (≤5 B-lines); 1=slight (≥6 and ≤15 B-lines); 2=moderate, (≤16 and ≥30 B-lines); 3=severe (≥30 B-lines)]

Results

74 RA patients and 74 healthy controls were included. Thirty of 74 patients (40.5%) showed US signs of ILD with respect to the healthy (4.1%) (p=0.0001); whereas HRCT showed ILD in 27 (36.4%) of 74 patients.

Among the 30 patients with US findings of ILD, 17 (56.6%) were asymptomatic. The sensitivity and specificity of US were 92% and 89% respectively.

A positive correlation between US and HRCT findings was found (p= < 0.0001) whereas no correlation was found with chest radiographs and DLCO findings (p = 0.2971 and 0.7856 respectively). Positive association between US and DAS28, RF and anti-CCP (p=0.0076, 0.0044, 0.0074) was found.

Conclusions

Our results support the potential of the US in detecting accurately ILD in a real-life cohort of patients with RA and provide a rationale to consider it as a friendly screening tool to be implemented in the early phases of the disease.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-012

Rheumatoid factor (RF) and anti-cyclic citrullinated protein autoantibodies (ACPA) seroconversion and seroreversion in rheumatoid arthritis patients between 2005 and 2021

Chun Lai Too[1,2], Nurul Aain Ahmad-fauzi[1], Haziqah Itqan Alias[1], Nur Aida Sabrina Mohd-rashid[1], Siti Aisyah Abdul-ahmad[1], Mollyza Mohd-zain[3], Ing Soo Lau[3], Hazlyna Baharuddin[3], Diana Lee Min Ang[4], Lisa Mohamed-nor[4], Rashidah Bahari[4], Amnahliza Abdul-rahman[4], Ping Seung Ong[5], Noraini Mat-husin[5], Wahinnudin Sulaiman[5], Suk Chyn Gun[6], Nadiah Mohd-nor[6], Heselynn Hussein[4], Eashwary Mageswaran[4], Mohd Shahrir Mohamed-said[7], Ainon Mohd-mokhtar[8], Azmillah Rosman[3], Muhaini Othman[5], Mohd Zainuldin Taib[9], Shahnaz Murad[1], Leonid Padyukov[2], Lars Alfredsson[10], Lars Klareskog[2], Johan Ronnelid[11], Nor Shuhaila Shahril[4]

[1] Ministry of Health Malaysia, Immunogenetic Unit. Allergy and Immunology Research Center. Institute for Medical Research. MOH, Malaysia
[2] Department of Medicine, Division of Rheumatology. Karolinska Institutet and Karolinska University Hospital. Stockholm., Sweden
[3] Department of Medicine, Selayang Hospital. Ministry of Health Malaysia. Selangor., Malaysia
[4] Department of Medicine, Putrajaya Hospital. Ministry of Health Malaysia. Putrajaya., Malaysia
[5] Department of Medicine, Raja Permaisuri Bainun Hospital. Ipoh. Perak, Malaysia
[6] Department of Medicine, Tuanku Ja'afar Seremban Hospital. Ministry of Health Malaysia, Malaysia
[7] Medical Deparment, Universiti Kebangsaan Malaysia Medical Centre. Cheras. Kuala Lumpur., Malaysia
[8] Department of Medicine, Tengku Ampuan Afzan Hospital. Ministry of Health Malaysia., Malaysia
[9] Medical Resource Research Centre, Institute for Medical Research. Ministry of Health Malaysia. Selangor., Malaysia
[10] Institute of Environmental Medicine, Karolinska Institute. Stockholm., Sweden
[11] Department of Immunology. Genetics and Pathology., Uppsala University. Uppsala., Sweden

Background

Previous studies demonstrated that RF and ACPA seroconversion/seroreversion is possible, but rarely occurs. We determined the proportions of RA patients who underwent autoantibodies conversion or reversion at two time-points and described the clinical characteristics of these subgroups.

Methods

A total of 240 RA patients enrolled during the Malaysian Epidemiological Investigation of RA study (MyEIRA, 2005-2009) were followed up in the RA progression study (RAPID, 2018-2021). ACPA and RF isotypes (i.e., IgG, IgM, and IgA) were measured using the commercial ELISA kits, similar to the kits used for baseline measurement. RA patients with one or more autoantibodies converted between baseline (MyEIRA) and follow-up (RAPID) time point were defined as seroconverters. RA patients with one or more autoantibodies disappeared during study period were defined as seroreverters. Paired samples test, univariate and multivariate analysis were performed. The clinical characteristics of seroconverters and seroreverters were assessed.

Results

The proportion of overall RA patients who experienced seroconversion (n=91, 37.9%) ranged from 3.7% (ACPA) to 22.8% (IgA RF), while seroreversion (n=52, 21.7%) ranged from 3.7% (IgM RF) to 14.1 %(IgG RF). When data from RAPID were compared to MyEIRA, the seroconverters demonstrated significant differences for IgG RF (p=0.01), IgM RF (p<0.0001) and IgA RF (p<0.0001). We observed significant differences for ACPA (p=0.004), IgG RF (p<0.0001) and IgA RF (p=0.02) for the seroreverters. Clinical characteristics revealed that hand and feet deformities were common among the seroconverters. Ocular and pulmonary associated extra articular manifestations were more prevalent in seroconverters. Comorbidities profile was comparable between the seroconverters and seroreverters.

Conclusions

Our data suggest that one fifth of the overall RA patients experienced antibody conversion for IgA RF (22.8%), while IgG RF (14.1%) is commonly disappeared (i.e., reverted) for 10 years follow up. Interestingly, ACPA is the most stable RA autoantibody with only approximately 5% conversion or reversion.

Keywords

seroconversion, seroreversion, RF isotypes and ACPA

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-013

Autoantibodies sustainability in rheumatoid arthritis (RA) patients and their clinical characteristics: Malaysian real-world data between 2005 and 2021

Chun Lai Too[1,2], Nurul Aain Ahmad-fauzi[1], Haziqah Itqan Alias[1], Nur Aida Sabrina Mohd-rashid[1], Siti Aisyah Abdul-ahmad[1], Mollyza Mohd-zain[3], Ing Soo Lau[3], Hazlyna Baharuddin[3], Diana Lee Min Ang[4], Lisa Mohamed-nor[4], Rashidah Bahari[4], Amnahliza Abdul-rahman[4], Ping Seung Ong[5], Noraini Mat-husin[5], Wahinuddin Sulaiman[5], Suk Chyn Gun[6], Nadiah Mohd-noor[6], Heselynn Hussein[4], Eashwary Mageswaran[4], Mohd-shahrir Mohamed-said[7], Ainon Mohd-mokhtar[8], Azimillah Rosman[3], Muhaini Othman[5], Mohd Zainuddin Taib[9], Shahnaz Murad[1], Leonid Padyukov[2], Lars Alfredsson[10], Lars Klareskog[2], Johan Ronnelid[11], Nor Shuhaila Shahril[4]

[1] Ministry of Health Malaysia, Immunogenetic Unit. Allergy and Immunology Research Center. Institute for Medical Research. MOH, Malaysia
[2] Department of Medicine, Division of Rheumatology. Karolinska Institutet and Karolinska University Hospital. Stockholm, Sweden
[3] Department of Medicine, Selayang Hospital. Ministry of Health Malaysia. Selangor, Malaysia
[4] Department of Medicine, Putrajaya Hospital. Ministry of Health Malaysia. Putrajaya, Malaysia
[5] Department of Medicine, Raja Permaisuri Bainun. Ministry of Health Malaysia. Ipoh. Perak, Malaysia
[6] Department of Medicine, Tuanku Ja'afar Seremban Hospital. Ministry of Health Malaysia. Putrajaya, Malaysia
[7] Medical Department, Universti Kebangsaan Malaysia Medical Centre. Cheras. Kuala Lumpur., Malaysia
[8] Department of Medicine, Tengku Ampuan Afzan Hospital. Ministry of Health Malaysia. Kuantan. Pahang., Malaysia
[9] Medical Resource Research Centre., Institute for Medical Research. Ministry of Health Malaysia., Malaysia
[10] Institute of Environmental Medicine, Karolinska Institutet. Stockholm., Sweden
[11] Department of Immunology, Genetics and Pathology, Uppsala University. Uppsala., Sweden

Background

We aimed to examine the autoantibody sustainability (i.e., positivity versus negativity) over more than 10 years period in rheumatoid arthritis (RA) patients and their clinical characteristics in each studied groups.

Methods

Serum measurement and analysis for rheumatoid factor isotypes (i.e., IgG, IgM and IgA) and anti-citrullinated protein antibody (ACPA) was performed on 240 blood samples taken at baseline (2005-2009) and follow-up (2018-2021), using similar commercial ELISA kits. RA patient positive for one or more autoantibodies during baseline and remained positive upon follow-up were defined as antibody positive sustainer (APS). RA patient negative for one or more autoantibodies during baseline and remained negative upon follow-up were defined as antibody negative sustainer (ANS). The disease characteristics for APS and ANS groups were assessed.

Results

Seventy-one percent RA cases sustained one or more autoantibodies, while 46% remained negative between the two study time points. Clinical assessment revealed that the prevalence of various hand and feet deformities were higher among the APS group. Similarly, a trend of increased tender joint counts was found among APS, with higher zero counts observed among ANS group. Functional status assessment showed that the patient and physician reported outcomes were comparable between APS and ANS groups. Notably, overall functional status scores were comparatively lower when assessed by physicians than RA patients. We observed higher proportion of HLA-DRB1 shared epitope alleles (SE) among APS as compared to ANS (p=0.0009). Paired samples analysis in APS group revealed significant differences between baseline and follow-up data, with tendency of increased titers of anti-CCP2 (p<0.0001), RF IgM (p<0.0001) and IgA (p=0.001), and only RF IgM in ANS group (p=0.004).

Conclusions

The disease characteristics (i.e., disease activity, deformity and functional status) are differed between APS and ANS groups. In addition, the autoantibodies titers profile are significantly different for baseline and follow-up period.

Keywords

Autoantibody sustainability, rheumatoid arthritis, RF and anti-CCP

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-014

Use of disease-modifying anti-rheumatic drugs after cancer diagnosis in rheumatoid arthritis patients

Kyung-Su Park[1], Young-Bin Joo[2], Seung Min Jeong[1], Yune-Jung Park[1], Ki-Jo Kim[1]

[1] Rheumatology, Catholic University St. Vincent's Hospital, Republic of Korea
[2] Rheumatology, Hanyang University Guri Hospital, Republic of Korea

Background

There is no recommendation for the use of disease-modifying anti-rheumatic drugs (DMARDs) in patients with rheumatoid arthritis (RA) who developed cancer. We examined changes in the prescription patterns of DMARDs associated with cancer diagnosis in RA patients.

Methods

We reviewed the medical records of 2,161 RA patients who visited rheumatology clinics between January 2008 and February 2017 and found 40 patients who developed cancer during RA treatment. In these patients, we examined DMARDs prescription before and right after cancer diagnosis and at recent outpatient clinic visits.

Results

Before cancer diagnosis, methotrexate (MTX)-combined conventional synthetic DMARDs (csDMARDs) were most commonly prescribed (22, 55.0%) and biological DMARDs (biologics) in nine patients (22.5%). For cancer treatment, 19 patients received chemotherapy (including adjuvant chemotherapy) and 21 patients had surgery only. Right after cancer diagnosis, DMARDs prescription patterns were similar in discontinuation (13, 32.5%), switching (14, 35.0%), and maintenance (13, 32.5%). DMARDs were discontinued more frequently in the chemotherapy group (9/19, 47.4%) than the surgery only group (4/2, 19.0%) ($p = 0.015$). Among the 13 patients who discontinued DMARDs, nine (69.2%) resumed DMARDs after a median of 5.5 months (interquartile range <IQR> 2.9, 18.3) due to arthritis flare. At a median of 4.6 years (IQR 3.3, 6.7) after cancer diagnosis, 25 patients were evaluated at recent outpatient clinic visits. Four patients received no DMARD, three MTX monotherapies, 11 combined csDMARDs, and seven biologics.

Conclusions

A significant number of RA patients who developed cancer during RA treatment were still receiving DMARDs after cancer treatment.

Keywords

cancer, Disease-modifying anti-rheumatic drugs, Rheumatoid arthritis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-015

The relationship between Anti-CCP, C-reactive protein in serum and rheumatoid factor in synovial fluid in patients with rheumatoid arthritis in the Kyrgyz Republic

Nazgul Omurzakova[1], Akpay Sarybaev[1]

[1] Rheumatology and High Mountain Diseases, National Center of Cardiology and Internal Medicine, Kyrgyzstan

Background

Study of the clinical-functional peculiarity of clinical course in patients with rheumatoid arthritis with determining of relationship between Anti-CCP, C-reactive protein (CRP) in serum and rheumatoid factor (RF) in synovial fluid in rheumatoid arthritis (RA).

Methods

We have conducted a 8-year study (5,2 ± 2,5 years) and monitoring of 390 (average age 41,2 ± 25,2 years) patients with early RA, diagnosed according to criteria ACR (American College of Rheumatology, 1987). 281 of them are women and 109 are men. They measured the concentration of Anti-CCP, RF and titers of CRP in serum and synovial fluid of different degree of disease activity (DAS 28).

Results

The close relationship between the level of Anti-CCP, RF, CRP in the serum and the titer of RF in synovial fluid has been determined. According to studies, the specificity of RF in the synovial fluid in the diagnosis of RA in the early stages is 81%, the combination of RF in synovial fluid + Erythrocyte Sedimentation Rate (ESR) - 88%. RF and CRP titers in the serum and RF in synovial fluid - 91%; Anti-CCP +RF in the blood serum + synovial fluid titers CRP + ESR - 94%; Anti-CCP in serum + RF in synovial fluid + polyarticular pain - 94%; Anti-CCP + RF in synovial fluid + morning stiffness - 97%. With a high degree of activity of the process increases the level of Anti-CCP, RF and CRP in the blood (1:192 mg / L and above) and increases the titer of RF (96 IU/ml and above) in the synovial fluid.

Conclusions

Anti-CCP in serum can be very useful in early diagnosis of RA, when manifest only a few clinical symptoms. In addition, noted a high risk of atherosclerotic complications in patients with elevated CRP levels, which persisted for a long time during the treatment.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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May 19(Thu) - 21(Sat), 2022

P-016

Impact of comorbidity on disease activity and functional status in patients with rheumatoid arthritis receiving biologic DMARDs, a longitudinal analysis of the KOBIO-RA

Ju Yeon Kim[1], Kichul Shin[2], Eun Bong Lee[1], Jun Won Park[1]

[1] Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Seoul Metropolitan Government-Seoul National Boramae Medical Center, Seoul, Republic of Korea

Background

This study aims to evaluate the impact of comorbidities on disease activity and functional disability in patients with RA treated with biological disease-modifying anti-rheumatic drugs (bDMARDs).

Methods

We analyzed longitudinal data of 2127 patients in a nationwide cohort of RA receiving bDMARD in South Korea (KOBIO-RA). Patients were enrolled at the time of starting bDMARD and followed up yearly thereafter. In this study, follow-up was censored when initial bDMARD was discontinued or at seventh visit, whichever came first. Functional status was assessed using Routine Assessment of Patient Index Data 3 (RAPID3). In each follow-up visit, we assessed whether the patient attained the minimal clinically important difference (MCID, defined as a 3.6-point decrease from baseline) in RAPID3 and low disease activity (LDA) based on Clinical Disease Activity Index (CDAI). Effect of comorbidities on these responses was analyzed using generalized estimating equations (GEE).

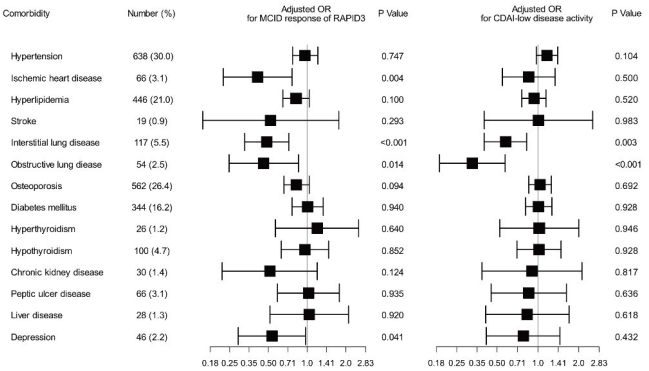
Results

At baseline, the mean (SD) disease activity was 15.25 (5.67) for RAPID3 and 26.85 (11.15) for CDAI. During the follow-up encompassing 5244 1-year intervals, 3489 (66.5%) and 3788 (74.0%) intervals achieved the MCID-RAPID3 and CDAI-LDA, respectively. Ischemic heart disease (adjusted OR 0.41 [0.22-0.76]), interstitial lung disease (adjusted OR 0.49 [0.33-0.72]), obstructive lung disease (adjusted OR 0.46 [0.25-0.85]), and depression (adjusted OR 0.56 [0.29-0.97]) were associated with poor RAPID3 response (Figure). Other comorbidities did not significantly influence the functional status. Presence of comorbidities was not associated with disease activity of RA except for pulmonary disease. Patients with interstitial lung disease or obstructive lung disease showed a significantly less likelihood of achieving CDAI-LDA (adjusted OR 0.58 [0.40-0.83] and 0.33 [0.19-0.57], respectively).

Conclusions

Pulmonary diseases were associated with higher patient reported functional index and disease activity in RA, while ischemic heart disease and depression were associated function index independent of the disease activity.

Figure & Table



Keywords

Rheumatoid arthritis, comorbidity

E-poster Presentation

RA-treatment

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-017

Is a cumulative dose of methotrexate important for rapid remission in rheumatoid arthritis?

Galina Gridneva[1], Eugenia Aronova[1], Natalia Baymeeva[2], Svetlana Glukhova[1], Yury Muraviev[1]

[1] Comorbid Infections and Safety of Drug Therapy, V.A.Nasonova Rheumatology Research Institute, Russian Federation
[2] Drug Monitoring, Mental Health Centre, Russian Federation

Background

To determine the correlations between the cumulative dose of methotrexate (MTX), the concentration of MTX metabolites in cells and the achievement of remission in patients with RA.

Methods

A prospective follow-up study included 79 patients, 65(82%) women and 14(18%) men, aged 53±11 years, naiive to MTX. All patients were prescribed MTX at the rate of 10-15 mg/m2 of body surface. After 4, 12 and 24 weeks of therapy, RA activity was assessed by DAS28, the total dose of methotrexate was calculated, MTX monoglutamate, polyglutamates with 2, 3 and 4 glutamate residues (MTXPGs 2-4), 7-hydroxymethotrexate (7-OH-MTX) were determined in erythrocytes (ER) and mononuclear cells (MO) by tandem chromatomass spectrometry. Statistical data was performed using Statistica 10 for Windows (StatSoft Inc., USA).

Results

The total dose of MTX after 4 weeks of treatment was 58±15 mg and directly correlated with the concentration of MTXPG4 in the ER(CC=0.29) and MO(CC=0.31) and MTXPG3 in the ER(CC=0.27), $p<0.05$ in all cases. The total dose of MTX in week 12 was 202±54 mg and directly correlated with the concentration of MTXPG4 in the MO(CC=0.3), $p<0.05$. The total dose of MTX after 24 weeks was 398±100 mg, no correlations were found between its value and the concentration of various metabolites. The correlation analysis with the achievement of remission in week 24 directly correlates the level of 7-OH-MTX in the ER in week 12 (CC=0.27), the level of 7-OH-MTX in the MO in week 24 (CC=0.355) and cumulative dose of MTX in week 12.

Conclusions

Conclusion: high values of 7-OH-MTX and the cumulative dose of MTX at week 12 of therapy may be a predictor of remission after 24 weeks of treatment.

Keywords

methotrexate, therapeutic drug monitoring, poliglutamate

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-018

Clinical predictors of inadequate response to conventional synthetic and biologic DMARDs in Chinese patients with rheumatoid arthritis

Hui Zhong[1], Yanhong Wang[2], Jiuliang Zhao[1], Nan Jiang[1], Qian Wang[1], Xinping Tian[1], Dong Xu[1], Mengtao Li[1], Xiaofeng Zeng[1]

[1] Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, China
[2] Department of Epidemiology and Biostatistics, Institute of Basic Medical Sciences Chinese Academy of Medical Sciences, China

Background

To describe the characteristics of patients with csDMARDs inadequate response (IR) and patients with bDMARDs-IR, and identify risk factors for csDMARDs-IR and bDMARDs-IR in Chinese patients with rheumatoid arthritis (RA).

Methods

This study was conducted based on the online registry established by Chinese Rheumatism Data Center. Patients with active RA(DAS28-CRP>3.2) were included. IR was defined as either of the following: Patients used ≥1 csDMARDs or bDMARDs for 6 to 12 months but failing to reach DAS28≤3.2; patients used ≥1 csDMARDs or bDMARDs for 3 to 6 months but failing to reach DAS28≤3.2 or at least 50% improvement. Patients with prior use of bDMARDs were excluded in analysis of csDMARDs-IR. Baseline clinical characteristics and multivariable logistic regression were analyzed in csDMARDs-IR and bDMARDs-IR groups respectively.

Results

A total of 8326 out of 72737 RA patients in the database were eligible for inclusion, and 3705(55.50%) out of 6676 patients treated by csDMARDs were csDMARDs-IR and 819(49.64%) out of 1650 patients treated by bDMARDs were bDMARDs-IR. Compared with adequate responders, patients in both IR groups were older at RA diagnosis, with longer disease duration and higher baseline DAS28-CRP and DAS-ESR; while adequate responders to csDMARDs had more structural joint damage. Age at diagnosis ≥ 65 years (OR 1.24, 95%CI 1.07-1.43), disease duration ≥ 1 year(OR 1.49, 95%CI 1.35-1.65), and higher baseline DAS28-CRP(OR 1.40, 95%CI 1.35-1.47) were risk factors for csDMARDs-IR; while the existence of structural joint damage (OR 0.556, 95%CI 0.465-0.664) was a protective factor. Similarly, disease duration ≥ 1 year (OR 1.39, 95%CI 1.41-1.69), and higher baseline DAS28-CRP (OR 1.25 95%CI 1.15-1.35) were risk factors for bDMARDs-IR.

Conclusions

Based the large RA registry in China, we identified longer disease duration and higher baseline DAS28-CRP were independent risk factors for IR, which may be helpful for clinicians to make therapeutic decisions.

Keywords

rheumatoid arthritis, treatment, inadequate response

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-019

"Stereotypical" adverse reactions to non-biologic Disease Modifying Anti-Rheumatic Drugs in patients with rheumatoid arthritis requiring biological therapy

Elena Matianova[1], Galina Gridneva[1], Eugenia Aronova1

[1] Comorbid Infections and Safety of Drug Therapy, V.A.Nasonova Rheumatology Research Institute, Russian Federation

Background

To study the frequency of the same (so-named "stereotypical") adverse drug reactions (SADRs), to different non-biologic DMARDs, in patients with rheumatoid arthritis (RA) who need therapy with a genetically engineered biological agents (GEBA) or targeted synthetic DMARDs (tsDMARDs).

Methods

We analyzed medical history of 522 RA patients, 9%men, 91%women, aged 54±11 years, duration of RA was 9[4;24] years, RF-positive were 87%(n=47), ACCP-positive were 79.6%(n=43), extra-articular symptoms had 53.7%(n=29). They were hospitalized from Jan,2021 to Jan,2022 due to an exacerbation of the disease, and required therapy with GEBAs/tsDMARDs. Group 1 were 54(10.3%) patients with a history of SARDs, that occur when taking different DMARDs(not in co-administration). Group 2 were patients without a history of SARDs.

Results

The most common SARD was nausea - in 14(2.7%) patients. Of these, 12 were treated with methotrexate (MTX), 7 with leflunomide(LEF), 7 with sulfasalazine(SSZ) and 3 with hydroxychloroquine(HQ). A stereotypic increase of liver enzymes was noted in 13(2.5%) patients while taking MTX, in 2 when switch on LEF, in 2 when switch on SSZ, in 1 when switch on HQ. In 4 of them (38.8%), chronic hepatitis was detected (in 3 viral, in 1 non-viral). Skin rash as SARD (n=12(2.3%)) was:in 9 patients with MTX, in 9 with SS, in 6 with LEF, in 2 with HQ. In 5 (0.96%) patients, leukopenia was observed as SARDs: on MTX (in 5), on SSZ(in 4), on LEF(in 2), on HQ (in 1). SARDs such as diarrhea, stomatitis and infections were observed each in 3 cases; shortness of breath - in 2 cases. Increased blood pressure, intestinal bleeding and dizziness were presented in single cases.

Conclusions

The frequency of "stereotypical" ADRs on DMARDs in history of RA patients who need GEBAs/tsDMARDs was 10.3%. The most common SARDs were nausea (n=14(2.7%)), increased liver enzymes (n=13(2.5%)), skin rash (n=12(2.3%)), leukopenia (n=5(0.96%)).

Keywords

adverse reactions, medical history, safety

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-020

The efficacy and safety of biologic DMARDs on progression of RA-ILD

Sang Wan Chung[1], Sujin Jeong[1], Ji Sung Lee[2], Jeong Seok Lee[3], Chan Ho Park[4], Min Uk Kim[5], You-Jung Ha[6], Eun Ha Kang[6], Sung Hae Chang[7], Yongbeom Park[8], Jung-Yoon Choe[9], Eun Young Lee[10], Yeon Ah Lee[1]

[1] Rheumatology, Kyung Hee University Medical Center, Republic of Korea
[2] Clinical Research Center, Asan Institute for Life Sciences, Asan Medical Center, Department of Medical Stastics, Republic of Korea
[3] GENOME INSIGHT Inc.,, GENOME INSIGHT Inc.,, Republic of Korea
[4] Department of Radiology,, Soonchunhyang University College of Medicine,, Republic of Korea
[5] Department of Radiology, SMG-SNU Boramae Medical Center, Republic of Korea
[6] Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Republic of Korea
[7] Division of Rheumatology, Department of Internal Medicine, Soonchunhyang University College of Medicine, Republic of Korea
[8] Division of Rheumatology, Department of Internal Medicine,, Yonsei University College of Medicine, Republic of Korea
[9] Division of,Rheumatology, Department of Internal Medicine, Catholic University of Daegu College of Medicine, Republic of Korea
[10] Division of Rheumatology, Department of Internal Medicine,, Seoul National University College of Medicine, Republic of Korea

Background

RA-ILD is associated with significant increase in mortality and worse quality of life compared to patients who do not have ILD. However, nowadays there are no therapeutic recommendations for the treatment of RA-ILD. The aim of this study was to evaluate the efficacy and safety of biologic DMARDs on progression of RA-ILD

Methods

The Korean Rheumatoid Arthritis ILD (KORAIL) cohort is the prospective observational cohort and aims to investigate the natural course of RA-ILD. Based on either 1987 or 2020 ACR criteria, patients diagnosed with RA and ILD based on CT scan were recruited from six tertiary medical hospitals in Korea since January 2015. Pulmonary function tests (PFT) and CT scan were conducted annually. 47 Patients who started bDMARDs within one month before and after baseline CT and maintained treatment with one type of bDMARDs for more than 24 weeks were enrolled.

Results

We analyzed 139 patients at baseline, 122 at 1-year, 112 at 2-year, and 101 at 3-year follow-up. At baseline, there were no significant differences in demographic features between two groups, only the disease duration of RA was longer in bDMARDs group than that of non-bDMARDs group. UIP is the most common CT pattern and 46 patients (33%) had CT extent greater than 10%. There was no significant difference between the two groups in PFT at baseline, however, the change in DLCO and FVC, predicted at 3 years was -1.45 and 0.06 in the biologics group, whereas it was -3.09 and -0.39 in the non-biologics group (p=0.68, p=0.74, respectively) indicating that the decrease in DLCO and FVC was small in the biologics group. The change of total CT score at 3 years was 1.11 in the biologics group, wheareas it was 2.02 in the non-biologics group (p=0.09).

Conclusions

Biologics may contribute to slowing the progression of RA-ILD

Keywords

RA-ILD, Biologics, PFT

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-021

Management of rheumatoid arthritis in China: a study of the implementation of 2021 ACR guideline

Shangyi Jin[1], Nan Jiang[1], Qian Wang[1], Mengtao Li[1], Xinping Tian[1]

[1] Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, China

Background

Implementation of evidence-based guidelines for the management of rheumatoid arthritis (RA) in clinical practice has lagged behind expectations. This study aimed to examine the concordance between management of RA in China and the 2021 ACR guideline.

Methods

Newly diagnosed and DMARD-naïve RA patients were screened from the Chinese Registry of rhEumatoiD arthrITis (CREDIT). Initial treatment for patients with moderate to high or low disease activity at baseline was analyzed separately. Comparison between different initial therapies was made to identify potential factors associated with therapeutic decisions. A follow-up study was conducted to evaluate whether timely treatment escalation occurred if treatment targets were not achieved.

Results

A total of 15220 patients were included. Among 12723 patients with moderate to high disease activity at baseline, 3633 (28.6%) received csDMARD monotherapy, and 1737 were methotrexate monotherapy users. Combination csDMARDs were initiated in 6474 patients (50.9%), and 1721 (13.5%) initiated biologics or JAK inhibitors (291 as monotherapy and 1421 in combination with csDMARDs). Initiating monotherapy as recommended by ACR was associated with younger age, shorter disease duration, lower disease activity and more experienced providers. In 2497 patients with low disease activity at baseline, 778 (31.1%) undertook csDMARD monotherapy as the first strategy. Hydroxychloroquine was given to only 132 patients, though it was recommended over other csDMARDs in the ACR guideline. In the follow-ups of MTX monotherapy users, 8.7% patients had treatment escalated after the failure of the first strategy. Among patients initiating biologics or JAK inhibitors, when the treatment targets were not achieved within 3 or 6 months, none of them received timely treatment adjustment.

Conclusions

Management of RA in China showed insufficient concordance with the 2021 ACR guideline for RA. Future collaborative efforts of patients and physicians are required to improve the implementation of international guidelines in China.

Figure & Table

	Total
N (%)	15220 (100)
Demographic features	
Female (%)	11694 (76.8)
Age (y)	51.9 ± 13.5
Clinical characteristics	
RF/CCP+ (%)	13528 (88.9)
RA duration (m)	0 (0-2)
DAS28-CRP	4.6 ± 1.6
DAS28-ESR	5.2 ± 1.7
CDAI	23.4 (13.7-37.0)
SDAI	25.8 (15.1-40.7)
HAQ-DI	0.63 (0.13-1.13)
Joint replacement (%)	101 (0.66)
CAD (%)	280 (1.8)
Stroke (%)	159 (1.0)
Fragility fracture (%)	203 (1.3)
Malignancy (%)	137 (0.9)
GC combination (%)	4533 (29.8)

Table. Baseline Characteristics of study population

Keywords

rheumatoid arthritis, ACR guideline, implementation study

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Journal of Rheumatic Diseases
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KCR 2022
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P-022

Study of methotrexate metabolism in patients taking statins

Galina Gridneva[1], Eugenia Aronova[1], Elena Samarkina[1], Natalia Baymeeva[2]

[1] Comorbid Infections and Safety of Drug Therapy, V.A.Nasonova Rheumatology Research Institute, Russian Federation
[2] Drug Monitoring Department, Mental Health Research Center, Russian Federation

Background

To describe the clinical and pharmacokinetic characteristics of a group of patients with rheumatoid arthritis (RA) treated with statins and methotrexate (MTX).

Methods

The study included 79 MTX-naiive RA patients, 65(82%) women and 14(18%) men, aged 53±11 years. All patients were prescribed MTX at the rate of 10-15 mg/m2 of body surface. After 12, 24 and 36 weeks of therapy, RA activity was assessed by DAS28, a blood test was performed to determine MTX monoglutamate (MGMTX), polyglutamates with 2, 3 and 4 glutamate residues (MTXPGs2-4) , 7-hydroxymethotrexate (7-OH-MTX) in erythrocytes (ER) and mononuclear cells (MO) by tandem chromatography-mass spectrometry.

Results

Statins were taken by 8 patients (group 1), 3 men, 5 women. Comparison group(2), n=71, were not prescribed statins. The groups did not differ in gender, body mass index, disease activity, cumulative dose of MTX. Group 1 patients were older (63±7 years versus 52±11 years in the comparison group, p=0.03). Only 2 (25%) patients from group 1 achieved the targets of therapy (remission or low disease activity) by week 24, while in group 2 this figure was 42% (p<0.05). At the same time, the levels of MTXMG(ER), MTXPGs(MO) and 7-OH-MTX(MO) on week 12, as well as MTXPG4(ER) on week 36, were higher than in group 2. The frequency of achieving therapy targets by week 36 did not differ between the groups.

Conclusions

Our finding was the detection of higher levels of MTX metabolites in the cells of patients with RA treated with statins, however, the groups differed significantly in number, and patients in group 1 were older. Statins has a positive effect on the accumulation of MTX metabolites, however, despite this, the treatment response by 24 weeks in these patients may be worse due to other clinical characteristics, such as age.

Keywords

methotrexate, statins, poliglutamates

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-023

Digital Aging and Mental Health Deteriorations: How Can We Mitigate the Risk Among the Elderly with Rheumatoid Arthritis Disease in Indonesia?

Rosinta Hotmaida Pebrianti Purba[1]

[1] Poverty Alleviation and Community Empoerment, Bappenas, Indonesia

Background

Indonesia is entering an aging society, with an older population of 26.82 million people (9.92 percent), and 18.95 percent of them are predicted to have rheumatoid arthritis. This proportion is nearly three times higher than the national average of 7.3 percent (MoH, 2018). Due to comorbidities and inadequate digital literacy, the older person is the covid-19 most at risk. This problem contributes to Indonesia's aging market, yet insufficient digital literacy has a negative impact on QoL.

Methods

The purpose of this study is to examine mental health issues and mobile phone ownership in older persons (60+) with Rheumatoid Arthritis illness using data from the 2014 Indonesia Family Life Survey (IFLS) wave 4th.

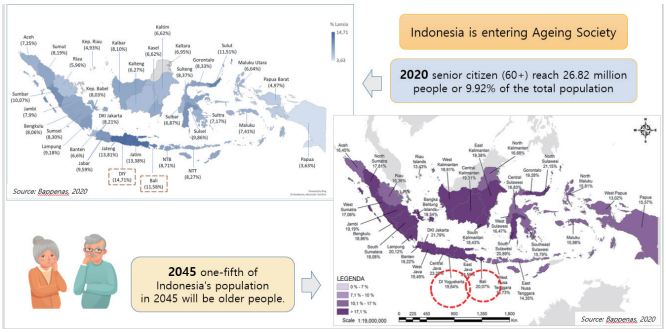
Results

According to the results, the proportion of older adults with RA is 22.7%, with women contributing for 44%. Furthermore, 26.47 percent of them had mental health problems, with men having a higher proportion. However, using a cellphone reduces the percentage of seniors with RA disease reporting mental health difficulties by 6,78%. In Indonesia, the senior SES is distributed fairly diverse throughout provinces. 55,8 percent of them continue to work. Elementary school, which accounts for 46.05 percent of older people's educational attainment, accounts for nearly half of their educational achievement. They report feeling not trying enough, sleeping restless, bothered by things, hopeless, unable to concentrate, and feeling unhappy. The least disturbance felt by them was feeling afraid. In general, the elderly who are more digitally literate prefer to seek care from a formal health facility rather than traditional practitioners such as shamans. They prefer to receive outpatient care at a community health center or Puskesmas (44,11%), a specialist (29,41%), or a private hospital (11,76 %).

Conclusions

Increased digital aging promotes older health literacy while minimizing mental health issues. Integrating the digital aging issue can assist the elderly get the knowledge

Figure & Table



Keywords

Mental health, Rheumatoid arthritis, Elderly with RA Disease

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-024

Comparison of drug persistence between tumor necrosis factor-α inhibitors and tocilizumab in patients as first-line treatment with rheumatoid arthritis using the Korean Health Insurance Review and Assessment Service database

Byung Wook Song[1], Dong-Hyuk Moon[1], Aran Kim[1], Seung-Geun Lee[1]

[1] Division of Rheumatology, Department of Internal Medicine, Pusan National University Hospital, Republic of Korea

Background

Drug persistence represents long-term therapeutic performance in real clinical setting. We aimed to compare persistence rate between tumor necrosis factor-alpha (TNF-α) inhibitors and tocilizumab in patients with rheumatoid arthritis (RA) using the Korean Health Insurance Review and Assessment Service (HIRA) database.

Methods

In this retrospective cohort study, patients with RA who started TNF-α inhibitors such as adalimumab, etanercept, infliximab and golimumab or tocilizumab as first-line biologic therapy between Jan 2014 and Dec 2017 on HIRA database were analyzed and were followed up to Dec 2019. Drug persistence was defined as the duration from the initiation to the first discontinuation including stopping and switching to other biologic therapy.

Results

A total of 5,449 RA patients were analyzed in this study. Mean age was 53.4 years and 4,423 (81.2%) patients were female. TNF-α inhibitors and tocilizumab were prescribed for 4,202 (adalimumab, 1,413; etanercept, 1,100; infliximab, 769; golimumab 920) and 1,247 RA patients, respectively. RA patients treated with tocilizumab was significantly older and had a significantly higher frequency of female compared with those treated with TNF-α inhibitors. During the study period, 2,090 (49.7%) and 477 (38.3%) RA patients discontinued TNF-α inhibitors and tocilizumab, respectively. Drug persistence was significantly lower in TNF-α inhibitors group than tocilizumab group (log-rank test, p<0.001). In multivariable Cox regression model, TNF-α inhibitors was significantly associated with a higher risk of discontinuation compared with tocilizumab (HR=1.63, 95% CI=1.47-1.81, p<0.001). In subgroup analyses, adalimumab (HR=1.73, 95% CI=1.54-1.95, p<0.001), etanercept (HR=1.87, 95% CI=1.66-2.11, p<0.001) and golimumab (HR=1.57, 95% CI=1.37-1.79, p<0.001) but not infliximab (HR=1.23, 95% CI=1.06-1.42, p=0.054) showed a significantly higher risk of discontinuation compared with tocilizumab after adjusting confounding factors.

Conclusions

Our findings indicate that tocilizumab had a better long-term persistence than TNF-α inhibitors in patients in RA in real clinical setting.

Keywords

Rheumatoid Arthritis, Tumor necrosis factor-alpha inhibitors, Tocilizumab

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-025

Impact of Korean red ginseng on fatigue in patients with rheumatic disease: A randomized, double-blind study

Soo-Kyung Cho[1], Hyoungyoung Kim[1,2], Yeo-Jin Song[1,2], Hye Won Kim[2], Eunwoo Nam[2], Yoon-Kyoung Sung[1,2]

[1] Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea
[2] Hanyang University Institute for Rheumatology Research, Seoul, Republic of Korea

Background

In this randomized clinical trial, we evaluated impact of Korean Red Ginseng (KRG) on fatigue in patients with rheumatic diseases.

Methods

A total 120 patients [Sjogren syndrome (n=53), rheumatoid arthritis (n= 43), and both diseases (n=24)] were randomly assigned to either KRG (2g/day, n=60) or placebo (n=60) groups for 12 weeks of blind phase. Primary outcomes were improvement rate for fatigue using fatigue visual analogue scale (VAS) and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue at 12 weeks. Multiple imputations by chained equations generated 20 complete datasets based on variables such as; age, sex, type of rheumatic diseases, rheumatoid factor positivity, erythrocyte sedimentation rate, drug compliance, medications, two fatigue scales for intention to treatment analysis. Adverse events (AEs) were presented in each treatment group for 24 weeks.

Results

Total 120 patients were aged 50.9 ±11.6 years with 117 female (97.5%), and baseline characteristics were similar between two groups. After treatment, fatigue was significantly improved in both groups (P <0.001 in each group). The primary endpoints analysis of improvements rates in fatigue VAS and FACIT-Fatigue after 12 weeks showed that there were not different between two groups [50.0% vs 43.3%; odds ratio (OR) with 95% confidence interval (CI), 1.31 (0.64, 2.68), P=0.583 for fatigue VAS; 38.3% vs placebo 26.7%; OR with CI, 1.71 (0.79, 3.71), P=0.242 for FACIT-Fatigue, respectively). However, numerical improvements favoring KRG were observed, in which both response rates were higher in KRG than placebo group. Nine and seven patients reported AEs during whole study period in each KRG and placebo group, respectively.

Conclusions

Fatigue was significantly improved in both the KRG and placebo groups, and there was no significant difference between the two groups. Considering the positive perceptions of KRG in Korea, a long-term study with a large sample is needed to elucidate the effectiveness of KRG.

Keywords

Korean Red Ginseng, Rheumatic diseases, fatigue

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-026

The preoperative patient's expectations and it's clinical outcomes after rheumatoid forefoot deformity surgery

Dong Hong Kim[1], Il-Hoon Sung[1]

[1] Department of Orthopaedic surgery, Hanyang University Hospital, Republic of Korea

Background

Rheumatoid forefoot deformity (RFD) is common and several surgical techniques include joint sacrificing and saving procedures. Currently, there are only few studies about patient's expectation for RFD. We evaluated patient's expectation and its fulfillment following RFD surgery.

Methods

We retrospectively analyzed 40 feet which underwent RFD surgery of joint sacrificing-modified Dwyer's operation. Overall satisfaction was measured in 5-digit scale (5; very high, 4; high, 3; average, 2; low, 1; very low). Questionnaire of the expectation of surgery and its fulfillment for greater toe and lesser toes were given to all patients, and the answers were based on a 5-digit scale in 5 different categories, prevention of deformity progression(D), reduction in pain(P), improvement in shoe wearing(S), improvement in foot function(F) and improvement in appearance(A). Multiple regression analysis was done for correlation with postoperative satisfaction.

Results

Female; male was 39;1, Age was 55.1±8.2. VAS was reduced from 7.2±2.1 to 2.2±1.8. Overall satisfaction was 4.0±0.82. Preoperative hallux valgus angle (HVA), intermetatarsal angle (IMA) was 47.5±9.9, 16.7±4.3 in average which improved postoperatively to 14.0±4.2, 9.9±3.5, respectively. For the greater toe, expectation (D, P, S, F, A) was 4.2, 4.1, 2.9, 2.8, 2.6 in average and its fulfilment was 4.1, 4.0, 3.4, 3.5, 3.2, respectively. For the lesser toes, expectation (D, P, S, F, A) was 3.9, 4.1, 3.3, 3.0, 2.8 and its fulfilment was 3.3, 4.0, 3.4, 3.6, 2.8, respectively. D and P were the highest expectation. Multiple regression analysis showed P for the greater toe (p=0.009) and F for the lesser toes (p=0.009) showed a significant positive correlation with postoperative satisfaction.

Conclusions

Rheumatoid forefoot surgery is a salvage procedure and so, it is important to discuss expectation of patients and its fulfilment before surgery which will have an effect on clinical outcome.

Figure & Table

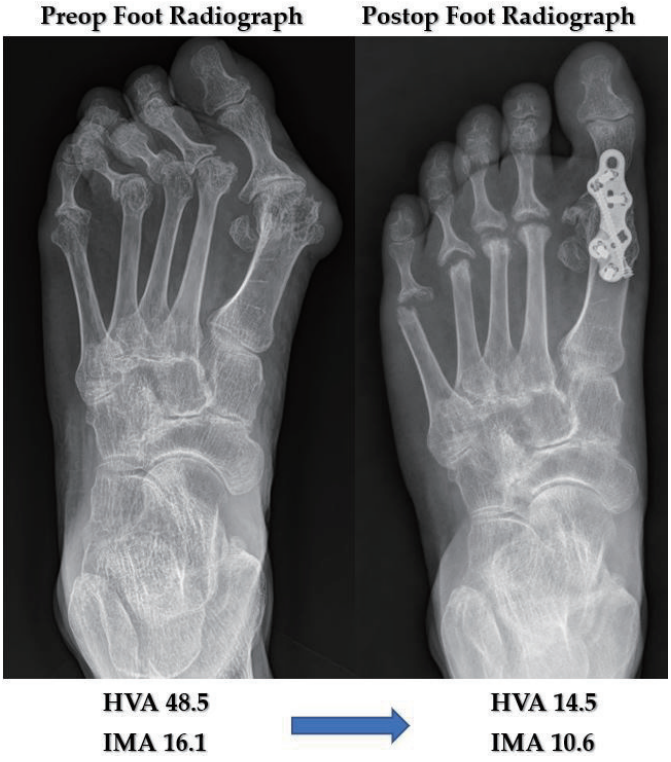

Figure. Preop and Postop Foot Radiograph

Keywords

Rheumatoid forefoot deformity, Expectation, Patient satisfaction

E-poster Presentation

SLE-clinical aspects, APS

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Seoul Dragon City, Seoul, Korea

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P-027

Effect of systemic lupus erythematosus on carotid intima media thickness and its relationship with disease activity

Gökhan Polat[1], Elshad Ismailov[1], Merve Polat[2]

[1] Radiology, Atatürk University, Turkey
[2] Health Physics, Karadeniz Technical University, Turkey

Background

It is known that atherosclerosis increases in patients with systemic lupus erythematosus (SLE). In our study, we aimed to examine the effect on carotid intima-media thickness in patients followed up with the diagnosis of SLE.

Methods

183 cases (mean age: 36.2) and 104 control subjects (mean age: 38.1) followed up with the diagnosis of SLE were included in the study. The clinical and demographic characteristics of the patients were recorded. Activity classification was made based on the SLEDAI score: no activity (SLEDAI=0), mild activity (SLEDAI 1–5), moderate activity (SLEDAI 6–10), high activity (SLEDAI 11–19), very high activity (SLEDAI) ≥20). Carotid ultrasonography was performed in all cases to evaluate subclinical atherosclerosis and intima-media thickness (IMT) was evaluated. Presence of IMT>1 mm was evaluated as subclinical atherosclerosis.

Results

There was no significant difference between the groups in terms of age and gender.The mean disease duration was 49.6 months, cyclophosphamide use was 35.6%, steroid 97.8%, and azathioprine use was 29.9%. Hematological involvement was 72%, serositis was 14.8%, renal involvement was 48.9%, arthritis was 73.4%, and neurological involvement was 22.7%. Carotid IMT of SLE patients (mean 0.724mm) was significantly higher than the control (mean 0.618mm) (p=0.0414). While the rate of IMK>1mm was 13.2% in the SLE group, it was 3.1% in the control group (p=0.135). There were 84 patients with SLEDAI=0, 36 patients with SLEDAI 1-5, 28 patients with SLEDAI 6-10, 24 patients with SLEDAI 11-19, and 11 patients with SLEADI ≥20.A moderate correlation was found between carotid IMT and disease activity (r=0.639, p=0.009.

Conclusions

An increase in carotid intima-media thickness is observed in patients with SLE, and there is a correlation between disease activity and carotid intima-media thickness.

Keywords

Systemic lupus erythematosus, Carotis Intima media thickness, Carotid ultrasonography

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-028

Wernicke encephalopathy secondary to systemic lupus erythematosis enteropathy

Arzu Shahveranova[1]

[1] Department of Radiology, Adana Çukurova Üniversity, Turkey

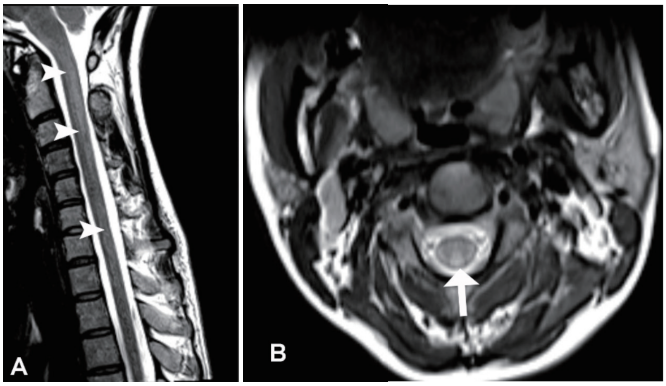
Description

A 24-year-old female patient was followed for 1 year with the diagnosis of Systemıc Lupus Erythematosıs(SLE). The patient was receiving oral prednisone and oral azathioprine for the diagnosis of SLE. The patient applied to our clinic with complaints of vomiting, diarrhea, and weight loss. In laboratory tests, hemolytic anemia, positive antinuclear antibodies, positive anti-Smith antibodies, and hypoalbuminemia were observed. physical examination revealed drowsiness and truncal and limb ataxia. A spinal MRI was performed. In MRI, there was an increase in signal in the posterior column in fluid-sensitive sequences. The signal increase was observed in the cervical and thoracic regions(Figure 1). Radiological involvement suggested Wernicke's encephalopathy due to SLE enteropathy. The patient was started on IV methylprednisolone and thiamine treatment. Improvement was observed in the patient's neurological symptoms.

Conclusions

Vitamin B1 absorption may be impaired as a result of severe vomiting and diarrhea, causing SLE enteropathy. Thiamine deficiency should be kept in mind in neurological symptoms following SLE enteropathy.

Figure & Table



Journal of Rheumatic Diseases
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P-029

Prognostic factors for the development of systemic lupus erythematosus in patients with immune thrombocytopenia

Soo Min Ahn[1], Eun-Ji Choi[2], Ji Seon Oh[1], Yong Gil Kim[1], Chang-Keun Lee[1], Bin Yoo[1], Seokchan Hong[1]

[1] Department of Rheumatology, Asan Medical Center, Republic of Korea
[2] Department of Hematology, Asan Medical Center, Republic of Korea

Background

Patients with immune thrombocytopenia (ITP) have a risk of developing systemic lupus erythematosus (SLE). We sought to examine the clinical characteristics of patients with primary ITP who later developed SLE, and identified the risk factors for the development of SLE.

Methods

We retrospectively examined patients who were diagnosed with primary ITP at a tertiary hospital between August 2001 and November 2019. We compared the clinical characteristics according to the development of SLE. Logistic regression analysis was performed to identify the factors associated with the development of SLE.

Results

Of 130 patients with primary ITP, 10 (7.7%) were later diagnosed with SLE during follow-up (median, 30 months [IQR, 15.5–105]). The presence of skin bleeding, organ bleeding, lymphocytopenia, anemia, and positive antinuclear antibody (ANA) titer (> 1:160) were more common among patients who later developed SLE than did those who did not develop SLE. Multivariate analysis showed that young age (< 40 years; odds ratio [OR], 8.359 [95% confidence interval (CI), 1.230–56.793]; p = 0.033), organ bleeding (OR, 18.349 [95% CI, 2.771–121.517]; p = 0.003), and ANA positivity (>1:160; OR, 7.692 [95% CI, 1.482–39.910]; p = 0.015) were significantly associated with the development of SLE.

Conclusions

Young age (< 40 years), organ bleeding, and ANA positivity (> 1:160) were risk factors for the development of SLE in patients with primary ITP. Close follow-up is needed to detect the development of SLE in patients with ITP and the abovementioned risk factors.

Figure & Table

	Univariate			Multivariate		
	OR	95% CI	P value	OR	95% CI	P value
Young age[a]	5.444	1.332–22.250	0.018	8.359	1.230–56.793	0.033
Female	4.333	0.530–35.422	0.17			
BMI	0.873	0.717–1.070	0.20			
Skin bleeding	8.419	1.034–68.533	0.046			
Mucosa bleeding	1.250	0.247–6.330	0.79			
Organ bleeding	14.864	3.633–60.815	< 0.001	18.349	2.771–121.517	0.003
Platelet counts, × 10^9/L	0.911	0.828–1.002	0.055			
ANA positivity (>1:160)	16.500	3.984–68.341	< 0.001	7.692	1.482–39.910	0.015
Leukopenia[b]	2.786	0.653–11.892	0.17			
Neutropenia[c]	2.111	0.229–19.499	0.51			
Lymphocytopenia[d]	4.846	1.189–19.759	0.028			
Anemia[e]	10.118	2.044–50.091	0.005			

SLE: systemic lupus erythematosus, ITP: immune thrombocytopenia, BMI: body mass index, ANA: antinuclear antibody, OR: odds ratio, CI: confidence interval.

[a]Young age = age < 40 years
[b]Leukopenia = white blood cell count < 4000 /μL
[c]Neutropenia = Absolute neutrophil count < 1500 /μL
[d]Lymphocytopenia = Absolute lymphocyte count < 1500 /μL
[e]Anemia = Hemoglobin < 12 g/dL

Table. Factors associated with the development of SLE in patients with primary ITP

Keywords

Thrombocytopenia, Systemic lupus erythematosus, Antinuclear antibody

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-030

A case of portal and hepatic vein occlusion in systemic lupus erythematosis

Mehmet Selim Kan[1], Muhammed Eyyüp Çelik[1], Elshad İsmailov[2]

[1] medical faculty, Atatürk University, Turkey
[2] Department of Radiology, Ataturk University, Turkey

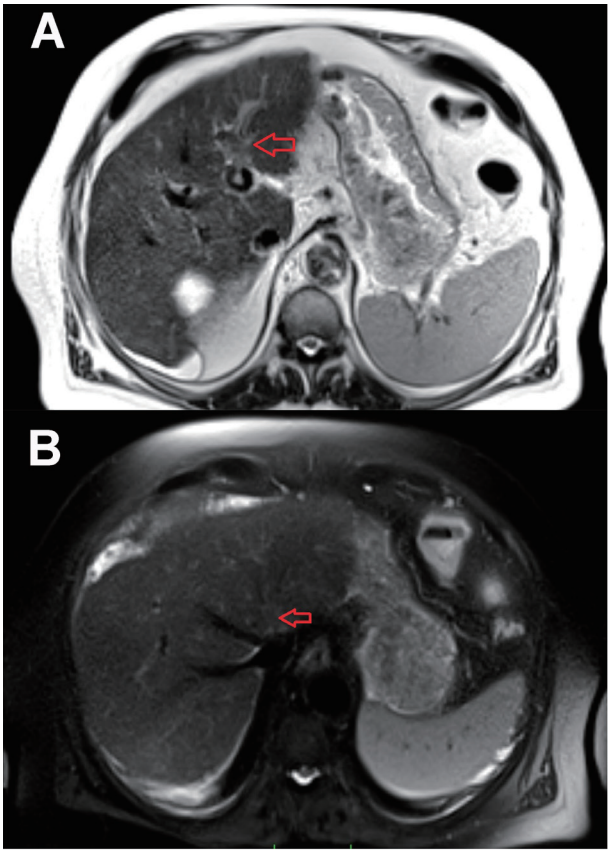
Description

A 47-year-old woman was diagnosed with SLE based on malar rash, positive ANA, high anti-dsDNA titer (160 IU/mL, normal <10). The patient was admitted to the hospital because of his right upper quadrants. Laboratory data revealed the following results: WBC 6,800/mm3 (normal 4,500– 11,000); hemoglobin, 14.3 g/dL (normal 12-16); platelets, 198,000/mm3 (normal 150,000–400,000); BUN, 26 mg/dL (normal 7–20); creatinine, 0.6 mg/dL (normal 0.5-1); alanine aminotransferase, 61 U/L (normal <31); aspartate transaminase, 64 U/L (normal <31); albumin, 1.4 g/dL (normal 3.4–4.8); d-dimer, 4016 ng/mL (normal < 500); fibrinogen, 848 mg/dL (normal 200–400). in examinations. No filling was observed in the left branch of the portal vein and in the left hepatic vein in the upper abdomen magnetic resonance imaging of the patient(Figure 1). Therefore, thrombus was considered. The patient's thrombus was confirmed by Doppler ultrasonography. The patient was initially given anticoagulants (low molecular weight heparin) and intravenous methylprednisolone 250 mg daily for three days.

Conclusions

Antiphospholipid syndrome(APS) is an autoimmune disorder characterized by venous or arterial thrombosis, thrombocytopenia, and recurrent spontaneous abortions. There are few seronegative APS in the literature. A significant proportion of APS cases are associated with SLE. Other conditions associated with secondary APS include lupus-like syndrome, rheumatoid arthritis, primary Sjögren's syndrome, systemic vasculitis, systemic sclerosis, and dermatomyositis. Most cases of APS show peripheral or pulmonary thrombosis and neurologic manifestations, but intra-abdominal involvement is much rarer. It should be kept in mind in cases where liver functions are affected in SLE patients.

Figure & Table



JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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May 19(Thu) - 21(Sat), 2022

P-031

Disease flare of systemic lupus erythematosus in patients with end-stage renal disease on dialysis

Young-Eun Kim[1], Su Jin Choi[2], Doo-Ho Lim[2], Soo Min Ahn[1], Ji Seon Oh[3], Yong-Gil Kim[1], Chang-Keun Lee[1], Bin Yoo[1], Seokchan Hong[1]

[1] Department of Rheumatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, Republic of Korea
[2] Department of Rheumatology, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Republic of Korea, Republic of Korea
[3] Information Medicine, Big Data Research Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, Republic of Korea

Background

The systemic lupus erythematosus (SLE) disease activity in patients with lupus nephritis (LN) generally declines after the initiation of renal replacement therapy (RRT); this is known as the "burn out" phenomenon that possibly occurs due to the suppression of cellular and humoral immunity in the end-stage renal disease (ESRD) state and elimination of disease pathogenic factor by dialysis. However, several studies showed that SLE flares could occur even during RRT. Nevertheless, the details of disease flares of SLE in patients under dialysis have not been studied yet. We aimed to investigate the clinical features, risk factors, and treatment details of SLE patients experiencing disease flare under RRT.

Methods

The medical records of SLE patients who received dialysis at two tertiary referral hospitals in Seoul and Ulsan, South Korea were reviewed. All patients in this study were either clinically or histologically diagnosed with LN.

Results

Of a total of 121 patients with SLE on dialysis, 96 (79.3%) were on hemodialysis (HD) and 25 (20.6%) were on peritoneal dialysis (PD). During a median follow-up of 45 months (IQR, 23–120) after the initiation of dialysis, 32 (26.4%) patients experienced SLE flare (HD, n = 25; PD, n = 7). The most common features of SLE flare were hematologic (40.6%) and constitutional manifestations (40.6%). Treatments for disease flares were based on corticosteroids, and 11 (34.3%) patients required additional immunosuppressants including cyclophosphamide and mycophenolate mofetil. There was no case of severe adverse events related to medication. non-renal SLE Disease Activity Index (SLEDAI) score before dialysis initiation (HR 1.235; 95% CI, 1.122–1.359; P = 0.001) was a significant risk factor for disease flare during dialysis.

Conclusions

More than one-quarter of SLE patients experienced disease flare during dialysis, which most commonly had hematologic manifestations. Continued follow-up and appropriate treatments including immunosuppressants should be considered for patients with SLE under dialysis.

Figure & Table

	Hazard ratio	95% CI	*P*-value
Non-renal SLEDAI at the initiation of dialysis	1.235	1.122–1.359	0.001
Hematologic manifestation prior to dialysis	1.256	0.690–2.826	0.150
Cumulative amount of steroid during 1 year prior to the initiation of dialysis	1.040	0.995–1.087	0.086
Dialysis modality: hemodialysis	0.766	0.262–2.243	0.630

Table. Multivariable analysis of factors associated with SLE flare under dialysis

Keywords

Lupus nephritis, Renal replacement therapy, SLE

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-032

Clinical relevance according to staining patterns and titers of antinuclear antibody

Mi Ryoung Seo[1], Jina Yeo[1], Hyo-Jin Choi[1], Han Baek[1]

[1] Division of Rheumatology, Department of IM, Gil Medical Center, Gachon University College of Medicine, Republic of Korea

Background

Immunofluorescent antinuclear antibody (ANA) test using HEp-2 cells still plays an important role in the diagnosis of autoimmune diseases. The aim of this study was to investigate the clinical relevance of ANA according to titers and patterns.

Methods

We identified patients who were newly positive in the ANA test between December 2010 to November 2016, and collected data such as, diagnosis, ANA titer and pattern, and specific autoantibody test results.

Results

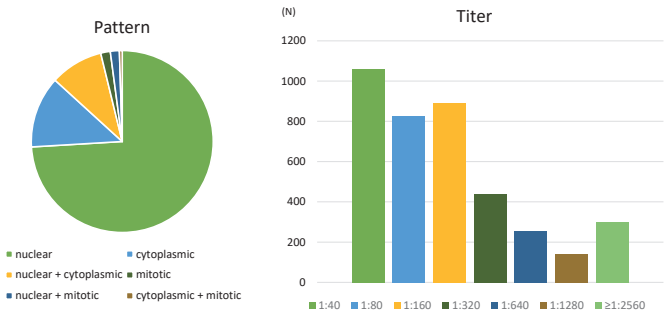
In total, 7591 patients were included in this study. The average age was 51 (IQR 35-63) years, and 69.4% were women. Figure 1 showed the patient distribution according to ANA patterns and titers. The diseases with a difference in prevalence according to ANA titer were systemic lupus erythematosus (SLE), Sjögren syndrome (SjS), polymyositis/dermatomyositis (PM/DM), systemic sclerosis (SSc), autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), liver cirrhosis, hemolytic anemia, immune thrombocytopenic purpura, interstitial lung disease (ILD), chronic obstructive pulmonary disease/bronchiectasis (COPD/BE), cerebrovascular accident, and crystal induced arthropathy (CIA). In multivariable analysis, diseases with increased prevalence with increasing ANA titer were SLE, SjS, PM/DM, SSc, AIH, PBC, and ILD, and the opposite result showed in COPD/BE and CIA.

SLE was the most prevalent in patients with mixed pattern of nuclear and cytoplasmic (6.4% in ≥1:40, 40% in ≥1:2560) (Figure3). SjS and SSc showed the similar results. The prevalence of PM/DM, AIH, PBC and ILD was highest in mixed pattern of nuclear and cytoplasmic in all patients, but it was highest in cytoplasmic pattern from 1:160 or more of ANA titer.

Conclusions

SLE, SjS, PM/DM, SSc, AIH, PBC and ILD were the diseases in which ANA titer independently affected disease prevalence. Patients with mixed pattern of nuclear and cytoplasmic had a higher prevalence of SLE, SjS and SSc than purely nuclear pattern.

Figure & Table



Keywords

antinuclear antibody, systemic rheumatic disease

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-033

Long-term renal outcomes of patients with non-proliferative lupus nephritis

Eunsong Kang[1], Seokchan Hong[1], Yong Gil Kim[1], Ji Seon Oh[2], Soomin Ahn[1], Chang Keun Lee[1], Bin Yoo[1]

[1] Rheumatology, Asan medical center, Republic of Korea
[2] Department of Information Medicine, Asan medical center, Republic of Korea

Background

Although proliferative (class III or IV) lupus nephritis (LN) is the most common finding in the classification of LN, non-proliferative LN can occur as a form of pure membranous (class V) or mesangial (class I or II) LN. Even though non-proliferative LN has been considered as a less severe LN with good outcomes, data on long-term renal prognosis are limited. Thus, we investigated the long-term outcomes and prognostic factors in non-proliferative LN.

Methods

We retrospectively reviewed the medical records of patients with systemic lupus erythematosus who were diagnosed with LN class I, II, V or II+IV by kidney biopsy between 1997 and 2021 at a tertiary referral center. Poor renal outcome was defined as an estimated glomerular filtration rate (eGFR) of < 60 mL/min/1.73m2. Univariate and multivariate analyses were performed with the Cox proportional hazard model to identify the factors associated with poor renal outcomes.

Results

We included 71 patients with non-proliferative LN (4:class I; 17:class II; 48:class V; 2:class II+V). Median follow-up duration was 103 months (interquartile range 27–185) and the overall rate of poor renal outcomes was 29% (21/71), including end-stage renal disease (n=2). Univariate analysis indicated that older age (HR 1.05; 95% CI: 1.00–1.09), low eGFR (HR 0.97; 95% CI: 0.95–0.99), failure to reach complete remission at 6 months (HR 0.33; 95% CI: 0.12–0.92) and LN chronicity score >4 (HR 3.81; 95% CI: 1.19–12.14) or activity score >6 (HR 20.51; 95%CI: 2.13-197.37) were significantly associated with poor renal outcomes. Multivariate analysis revealed that low eGFR at 6 months (HR 0.97; 95%CI: 0.95–0.99, p=0.035) was significantly associated with poor renal outcomes.

Conclusions

Poor renal outcomes occurred in approximately 30% of patients with non-proliferative LN after long-term follow-up. Our findings suggest that more active management may be needed for non-proliferative LN.

Figure & Table

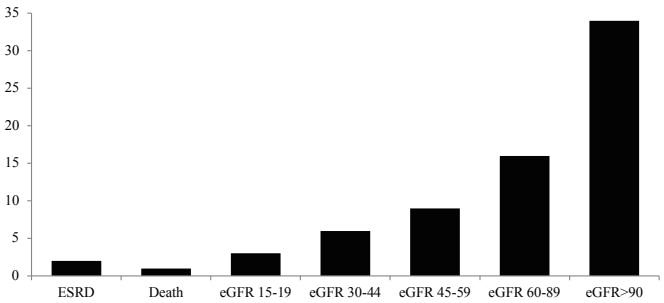


Figure. Long-term outcomes of total patients according to the renal function
eGFR, estimated glomerular filtration rate (ml/min/1.73m^2)

Keywords

Lupus nephritis, Renal function

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-034

Computer aided detection of the white matter lesions associated with systemic lupus erythematosus in cranial magnetic resonance imaging

Ahmet Yalcin[1], Fatih Alper[1]

[1] Radiology, Ataturk University, Faculty of Medicine, Turkey

Background

Specific vasculitis-related white matter lesions detected in cranial magnetic resonance imaging (MRI) are crucial as those lesions might also be encountered in various other pathologies such as multiple sclerosis (MS) and small vessel disease (SVD) (1). In this study, we aim to differentiate brain involvement of SLE from other white matter diseases by using a computer-assisted white matter lesion detection algorithm.

Methods

MRI of 11 patients with SLE, 13 patients with MS, and 18 patients with SVD were analyzed retrospectively. T1 weighted and FLAIR images were extracted from the patients' DICOM image folders and uploaded to the online volBrain segmentation application (https://www.volbrain.upv.es/) (2). Total intracranial volume (cm3), total white matter volume (cm3), gray matter volume (cm3), total lesion count, lesion location, absolute lesion volume (cm3), and lesion burden (total lesion volume/white matter volume) were automatically calculated for each patient. Statistical analyses were conducted depending on these parameters in three groups.

Results

The difference of mean age and gender distribution were insignificant in all groups (p for ANOVA= 0.526 and p for chi-square = 0.148 respectively). Total intracranial volume and gray matter volume were similar in all groups (p for Kruskal-Wallis= 0.369 and 0.426 respectively). White matter volume was significantly lower in SVD with no difference between MS and SLE (p for Kruskal-Wallis= 0.039). Total lesion count and absolute lesion volumes were insignificant in all groups (p for ANOVA= 0.896 and 0.692 respectively). Juxtacortical lesion burden was more prominent in SLE-related white matter disease compared to MS and SVD (p for Kruskal-Wallis=0.023) whereas periventricular lesion burden was significantly higher in SVD (p for Kruskal-Wallis < 0.001).

Conclusions

A computer-aided lesion detection algorithm can detect and classify the lesion burden in white matter lesions. SLE-related white matter lesions were associated with increased juxta cortical lesion burden with no significant white matter volume loss.

Keywords

systemic lupus erythematosus, magnetic resonance imaging, white matter lesion

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-035

Internuclear ophthalmoplegia in lupus cerebritis: double jeopardy

Paul Shiu[1], Navneet Kaur[2], Anil Harrison[3], Howard Feinberg[2]

[1] Department of Internal Medicine, St Joseph's Medical Center - Graduate Medical Education, USA
[2] Department of Rheumatology, Touro University Medical Group, USA
[3] Department of Internal Medicine, Touro University Medical Group, USA

Description

We report this case of a 42-year-old woman with a history of systemic lupus erythematosus (SLE) who presented in June 2021 with profound encephalopathy and a left internuclear ophthalmoplegia (INO) in the setting of lupus cerebritis. This patient was initially diagnosed with lupus in 2016 when she developed a photosensitive rash and further evaluation revealed immune thrombocytopenia as well as a positive antinuclear antibody (ANA), chromatin, and sm-RNP. She had been non-compliant with immunosuppressive regimens since 2016. Neurological examination was remarkable for somnolence and a left-sided INO without evidence of any additional focal cortical dysfunction. She was also noted to have oral ulcers. Initial blood work showed multiple electrolyte abnormalities, anemia and thrombocytopenia. Blood cultures and toxicology screens were negative. Cerebrospinal fluid analysis was unremarkable (WBC 1/mm3, RBC 5/mm3, glucose 56 mg/dL, protein 38 mg/dL). A CT and MRI of the brain revealed no acute intracranial abnormalities including for masses, midline shifts, hemorrhagic or ischemic changes. Because her altered sensorium did not improve after correction of underlying electrolyte and metabolic derangements, a consideration of lupus cerebritis was suspected. Erythrocyte sedimentation rate (ESR) was 102 mm/hour. C3 and C4 levels were within normal limits. Following the initiation of intravenous steroids, this patient had a dramatic recovery within 24 hours achieving a normal sensorium and was discharged on oral steroids and cyclophosphamide. During her two week follow up, she was noted to have a near complete resolution of her INO.

Conclusions

The development of internuclear ophthalmoplegia as a consequence of lupus cerebritis is rare. Herein, we report a woman with neurological manifestations of SLE with encephalopathy and internuclear ophthalmoplegia with prompt resolution of the aforementioned following early diagnosis and treatment.

Keywords

internuclear ophthalmoplegia, systemic lupus erythematosus, encephalopathy

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-036

Working memory and processing speed in systemic lupus erythematosus: correlation with disease activity

Rudrani Chatterjee[1], Rudra Goswami[2], Parasar Ghosh[3]

[1] Clinical Psychology, IOP (COE), Clinical Psychologist, India
[2] Rheumatology, Assistant Professor, AIIMS, New Delhi, India
[3] Rheumatology, Professor and Head, IPGMER, Kolkata, India

Background

Systemic lupus erythematosus (SLE) is a chronic, autoimmune multisystem inflammatory disorder. Cognitive impairment is difficult to monitor in SLE and relationship with disease activity is dubious. Attention, working memory (WM) and processing speed (PS) are closely related cognitive domains that are commonly disrupted in SLE.

Our goal was to determine whether WM and PS dysfunction in SLE patients are related to disease activity.

Methods

Adult female patients with SLE were without known neurologic or psychiatric co-morbidity, medications, co-morbid clinically manifest antiphospholipid syndrome (APS) or SLE damage index (SDI) >0 were enrolled. Patients were grouped as “active lupus” (BILAG A or B) or “persistent remission” (SLEDAI=0 on ≤7.5mg/day prednisolone). Age matched female control subjects were recruited. Cognitive assessments were done including tests for working memory (WM): verbal and visual n – back tests (1 and 2 back); and digit symbol substitution test (DSST) for processing speed (PS).

Results

We recruited 71 female patients with lupus (mean age 27.5±7.6 years, mean disease duration 30.4 ± 28.6 months, 39 with active disease) and 31 female control subjects (mean age 29.4 ± 7.5 years). Antiphospholipd antibody (aPL) were positive in 17 patients.

In univariate analysis patients both lupus groups performed worse on all cognitive domains compared to controls (Table 1). Patients with active lupus had worse PS compared to patients in remission. In multivariate Poisson regression visual 1-back (Odd’s ratio (OR): 0.54, 95% confidence interval (CI): 0.32-0.91, p=0.022) was associated with lupus activity. In gamma regression PS was associated with disease activity (OR: 0.988, 95% CI: .982-0.994, p<0.001) and positive aPL (OR: 1.006, 95% CI: 1.001-1.011, p=0.031).

Conclusions

SLE patients have WM dysfunction as a disease-specific trait. PS dysfunction was associated with disease activity. The association PS and WM seemed to follow the Independent Consequence Model of cognition theory.

Figure & Table

Parameters		Patients with active lupus n=39	Patients with persistent remission n=32	Control subjects n=31	p-value [a]	p-value [b]	p-value [c]	p-value [d]
Demographics	Age in years	27.8 ± 8.2	27 ± 6.9	29.4 ± 7.5	0.35	ND	ND	ND
	Duration of disease in months	31.6 ± 33.7	28.9 ± 21.1		0.28	--	--	--
Tests for Attention	**Digit span forward**	**4.62 ± 0.96**	**5.22 ± 1.16**	**6.55 ± 1.09**	<0.001	<0.001	<0.001	**0.006**
	Digit span backward	**3.05 ± 1.02**	**4.19 ± 0.97**	**4.97 ± 1.2**	<0.001	<0.001	0.012	**<0.001**
Tests for Working Memory	Verbal 1-back no of hits	6.95 ± 2.36	7.66 ± 1	8.16 ± 0.9	0.027	0.012	0.045	0.425
	Verbal 1-back no of errors	2.72 ± 2.7	1.53 ± 1.02	0.94 ± 1.12	0.003	0.002	0.013	0.175
	Verbal 2-back no of hits	4.21 ± 2.54	4.34 ± 1.98	6.03 ± 1.28	0.001	0.002	0.001	0.958
	Verbal 2-back no of errors	6.38 ± 3.09	5.5 ± 2.11	3.68 ± 1.4	<0.001	<0.001	0.003	0.201
	Visual 1-back no of hits	4.33 ± 3.39	3.22 ± 3.03	8.06 ± 1.39	<0.001	<0.001	<0.001	0.119
	Visual 1-back no of errors	8.62 ± 4.72	9.59 ± 3.83	2.87 ± 2.74	<0.001	<0.001	<0.001	0.203
	Visual 2-back no of hits	1.9 ± 1.45	2 ± 1.52	4.13 ± 1.63	<0.001	<0.001	<0.001	0.885
	Visual 2-back no of errors	11.41 ± 3.61	10.44 ± 1.19	7.87 ± 2.23	<0.001	<0.001	<0.001	0.436
Tests for Processing speed	**Digit symbol substitution test**	**25.18 ± 11.61**	**43.41 ± 11.48**	**57.65 ± 17.61**	<0.001	<0.001	<0.001	**<0.001**

Cells represent mean ± standard deviation
Abbreviations: ND: not done
a Kruskal Wallis test p - value
b Mann Whitney U test p value: comparison between patients with active lupus versus control subjects
c Mann Whitney U test p value: comparison between patients with persistent remission versus control
d Mann Whitney U test p value: comparison between patients with active lupus versus patients with persistent remission

Table. Univariate association of cognitive domain test results and SLE disease activity

Keywords

Systemic lupus erythematosus, Working memory, Processing speed

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-037

Etiology of raised serum creatinine in patients with systemic lupus erythematosus at presentation and association of number of crescents in renal biopsy with rapidly progressive renal failure

RAJAT Kharbanda[1], Able Lawrence[2]

[1] Clinical Immunology and Rheumatology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Senior Resident, India
[2] Clinical Immunology and Rheumatology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Professor, India

Background

Systemic lupus erythematosus (SLE) commonly involve kidney, with increase in creatinine due to lupus related or unrelated cause. Renal biopsy remains gold standard in diagnosis of lupus nephritis (LN). Higher number of crescents had a significantly worse prognosis compared to no crescents. In this study, we analysed the causes of raised serum creatinine in patients with SLE at presentation and assessed association of number of crescents with renal failure.

Methods

This was a retrospective single centre observational study where medical records of all SLE patients visiting tertiary care hospital 2001 to 2021 was reviewed. Data was retrieved from the case sheets, clinic files and electronic records using the hospital information system. The cause of raised serum creatinine (serum creatinine >1.5) was assessed. Renal biopsy of patients with impaired renal function was compared with renal biopsy of LN patients presenting with normal renal function. Data was analyzed using Strata 15, p value of <0.5 was taken as statistically significant.

Results

1606 SLE clinic files were screened, of which 121 patients had elevated creatinine at presentation. Amongst the causes of elevated creatinine, lupus nephritis was most common (70.2%, 85/121) followed by infections (13. 2%, 16/121), Chronic kidney disease (4.9%, 6/121), cardiorenal syndrome (4.1%,5/121), drugs (3.3%, 4/121), catastrophic antiphospholipid syndrome (2.5%, 3/121), thrombotic thrombocytopenia purport (1.7%, 2/121). 68 renal biopsies of patient with elevated creatinine were compared with 319 renal biopsies with normal creatinine (Table 1). There was significant association of elevated creatinine with number of crescents in renal biopsy [p: 0.00, OR: 2.7 (1.63-4.75)].

Conclusions

Apart from lupus nephritis as cause for increased creatinine, infections should always be screened. Crescents have significant association with elevated creatinine and timely and aggressive management in such patients can give favourable outcome.

Figure & Table

Variables	Lupus nephritis with elevated creatinine (n-68)	Lupus nephritis with normal creatinine (n-319)
Disease duration (months) (median±IQR)	18 (6-24)	12 (5-30)
Age (median±IQR) (years)	26 (20-33.3)	25 (19-32)
Female n (%)	59 (86.8)	300 (94)
Creatinine at baseline (mg/dl) (median±IQR)	2 (1.8-2.8)	0.8 (0.7-1)
% patients with proteinuria and active sediments	47 (69.1)	165 (51.7)
dsDNA n (%) negative (0-30 mg/dl) positive (>30 mg/dl) 31-90mg/dl 91-300 mg/dl >300mg/dl	 5 (7.3) 8 (11.7) 28 (41.2) 27 (39.7)	26 (8.1) 49 (15.4) 145 (45.5) 99 (31)
24-hour urine protein (g/24-hour) (median±IQR)	1.75 (1.1-3.6)	2 (1.9-3)
24-hour urine protein n (%) <500 (g/ 24h) 501-1000 1.1-2.5 >2.5	 6 (8.8) 12 (17.5) 25 (36.8) 25 (36.8)	 14 (4.3) 57 (17.9) 141 (44.2) 110 (34.5)
Low C3 n (%)	46 (67.6)	206 (64.6)
Low C4 n (%)	54 (79.4)	250 (78.4)
Histologic class n (%) Class 1 Class 2 Class 3 Class 4 Class 5 Class 3+5/4+5 Crescentic	 - 2 (2.9) 16 (23.5) 38 (55.9) 4 (5.9) 5 (7.3) 3 (4.4)	 1 45 (14.1) 103 (32.3) 89 (27.9) 52 (16.3) 28 (8.8) -
Patients with crescents	35 (51.4)	88 (27.6) p: 0.00 OR:2.7 (1.63-4.75)

Table. Patient characteristics who underwent renal biopsy and comparison of crescents

Keywords

SLE, creatinine, crescents

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-038

CRP elevation in SLE pericarditis: Not all patients with SLE pericarditis have an elevated CRP value

Hyunsue Do[1], Yong-Beom Park[1]

[1] Division of Rheumatology, Severance Hospital, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul, Republic of Korea

Background

In systemic lupus erythematosus(SLE) flares, C-reactive protein(CRP) dose not increase generally. Exceptionally, in SLE with organ involvement such as SLE pericarditis, CRP have been known to be rise. There have been reports in previous studies that CRP increases a lot as in infection with CRP > 60 mg/L. So, when there is an increase in CRP, it is sometimes important to distinguish whether it is due to SLE pericarditis by cardiac invasion or infection. Differentiation is important because the treatment direction is different in clinical practice. The aim of this study was to reveal the correlation with SLE pericarditis and C-reactive protein(CRP) and CRP values in infection and SLE pericarditis.

Methods

This study included 112 patients diagnosed with SLE from 2005.1.1. to 2021.8.1. at Severance Hospital with pericardial effusion on the echocardiography with or without symptom. CRP were checked when echocardiography were performed. The results of echocardiography were mainly described as pericardial effusion amount. The possibility of infection was screened by EMR record, infection consultation, culture study.

Results

Among the target patients, a total of 27 patients had the potential for infection, and excluding them, the Median value of CRP values in the remaining patients was confirmed to be 8.86 mg/L. Not all patients with SLE pericarditis had an elevated CRP value. The number of patients with CRP > 60 mg/L higher was 20. Among them 6 patients were confirmed to have infection. As a result of the analysis of the remaining 14 patients, two of them had other reason for pericarditis such as cancer, Off-pump coronary arterial bypass grafting surgery.

Conclusions

Not all patients with SLE pericarditis had an elevated CRP value.

In some cases, CRP values were high (CRP>60mg/L) in patients with SLE pericarditis without infection, which was about 14.1%. The cause of CRP elevation was SLE pericarditis.

Figure & Table

	Number of patients
Total patients : Diagnosed with SLE 2005.1~2021.8 at severance hospital and have Pericardial effusion on Echocardiography	112
Patients without Infections	85
Patients with CRP > 60mg/L	20
Patients with CRP > 60mg/L and infections	6
Patients with CRP > 60mg/L and without infections	14
Patients with CRP > 60mg/L and without infections and have other possible cause of pericarditis	2

Table. Characteristics of subjects

Keywords

systemic lupus erythematosus(SLE), pericarditis, C-reactive protein(CRP)

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-039

Prevalence of latent tuberculosis infection and its associations with clinical and serological parameters in systemic lupus erythematosus

Gayathri Ms[1], Prakash Babu Narasimhan[1], Chengappa Kavadichanda[1], Aishwarya Gopal[1], Devender Bairwa[1], Molly Mary Thabah[1], Sonali Sarkar[2], Vir Singh Negi[3]

[1] Clinical immunology, Jawaharlal Institute of Postgraduate Medical Education and Research, India
[2] Preventive and Social Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, India
[3] Clinical Immunology, All India Institute of Medical Sciences, Bilaspur, India

Background

Systemic Lupus Erythematosus (SLE) and Tuberculosis are complicatedly related and shown increased risk of TB in SLE. Studies of Latent TB and SLE are inadequate. This study intended to assess the prevalence of latent TB and its association with disease parameters in SLE

Methods

This is a single center cross sectional study. 124 adult patients with SLE without past h/o TB were recruited. SLE demography, disease activity indices, autoantibody profile, steroid use were noted. Presence of Latent TB infection was assessed in all patients based on the IFN-g release assay (TB-IGRA). Based on the results of IGRA, SLE cases were divided into 2 groups-IGRA positive and IGRA negative

Results

Among 124 patients, 19 had latent TB resulting in a point prevalence of 15.4 %. The average disease duration was 4.3 years in IGRA positive and 4.6 in IGRA negative group(p>0.05). Among antibody profile, though no statistical significance among the groups, proportion of antibodies like anti Ku, Ro 60, Ro 52 and La were numerically higher in the IGRA positive group (21.1%, 42.1%, 42.1% and 21.1% respectively) as compared to the IGRA negative group (11.5%, 28.8%, 28.1% and 7.7% respectively). Anti nucleosome, histone, U1RNP, PCNA, aCLA IgG and IgM, beta 2 GPI IgG and LAC were numerically higher in IGRA negative group (42.3%, 40.4%, 43.3%, 8.7%, 23%, 18.3%, 28.8%, 14.4%) when compared to IGRA positive group (31.6%, 21.1%, 31.6%, 0, 15.8%, 5.3%, 15.8%, 5.3%). Mean clinical SLEDAI was 2.37 ±5.1 in IGRA positive and 3.5 ±5.77 in IGRA negative group. Comparison of organ manifestations yielded no statistically significant difference in the 2 groups at this

Conclusions

Prevalence of latent TB in SLE cases was 15.4%. Although comparison of demographic, clinical and autoantibody profile did not yield any statistically significant differences, the early turnover from this pilot study mandates further evaluation with larger sample size

Keywords

systemic lupus erythematosus, tuberculosis, IGRA

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-040

Comparison of physical functions of systemic lupus erythematosis and healthy persons and their relationship with disease activity

Yasin Baki Baydas[1]

[1] Department of internal medicine, Bezmialem University, Turkey

Background

We aimed to examine how physical function is affected in individuals with Systemic Lupus Erythematosus (SLE) and its relationship with disease activity.

Methods

112 patients diagnosed with SLE and 62 healthy individuals were included in this study. Activity classification based on SLEDAI score: Activity classification based on SLEDAI score: no activity (SLEDAI=0), mild activity (SLEDAI 1–5), moderate activity (SLEDAI 6–10), high activity (SLEDAI 11–19) , very high activity (SLEDAI ≥20). Cases in both groups filled out a questionnaire including demographic characteristics and the SF-36's Physical Function and Physical Role sub-domains, and Sit to Stand test, Timed Up and Go test were performed.

Results

112 patients with SLE (mean age: 38.11+/- 8.32 years) and 62 healthy subjects (39.28+/- 7.8 years) participated in this study. There was no significant difference between the groups in terms of age and gender.When the groups are compared; Sit to Stand test, Timed Up and Go test, SF-36's Physical Function and Physical Role subdomain scores were found to be statistically lower in patients with SLE than in healthy subjects (Respectively;, p= 0.032; p= 0.027; p= 0.046). ; p= 0.041). There were 47 patients with SLEDAI=0, 31 patients with SLEDAI 1–5, 28 patients with SLEDAI 6–10, 21 patients with SLEDAI 6–10, 18 patients with SLEDAI 11–19, and 14 patients with SLEDAI ≥20. As disease activity increased, there was a moderate negative correlation in Sit to Stand test, Timed Up and Go test scores, and a moderate positive correlation in SF-36's Physical Function and Physical Role subdomain scores (r=-0.443 p<0.001; r=-0.582) , p < 0.001; r=0.486, p<0.001; r=0.502, p<0.001).

Conclusions

According to the results obtained, it was determined that there was a significant decrease in physical capacity in patients with SLE compared to healthy individuals. In addition, as disease activity increases, there is a moderately correlated decrease in physical capacity.

E-poster Presentation

SLE-pathogenesis and animal model

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-041

Vitronectin, a novel urinary proteomic biomarker, promotes cell pyroptosis in Juvenile systemic lupus erythematosus

Zhe Cai[1,2,3], Song Zhang[1], Huasong Zeng[1]

[1] Department of Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, China., China
[2] Guangzhou Institute of Pediatrics, Guangzhou Women and Children's Medical Center, China., China
[3] Institute of Chinese Medicine and State Key Laboratory, The Chinese University of Hong Kong, Hong Kong., Hong Kong

Background

To identify the potential urine biomarkers from juvenile systemic lupus erythematosus (JSLE) patients fit for the urgent demands in clinical diagnosis. Therefore, our aim of the present study is to analyze alteration of protein expression and potential valuable biomarkers in JSLE urine.

Methods

Based on this aim, proteomics assay analyzed the changes of urinary proteins among active JSLE patients (n=10), inactive JSLE patients (n=9) and healthy controls (n=9). The correlationship between clinical pathological parameters of JSLE patients and level of urinary VTN was qualified. The effect of VTN on cell pyroptosis was verified by the results of Western blot, qPCR and ELISA assay.

Results

Herein, we have identified a group of 105 differentially expressed proteins with ≥1.3 fold up-regulation or ≤0.77 fold down-regulation in JSLE patients. We found these proteins were involved in several important biological processes such as acute phase inflammatory responses, complement activation, hemostasis, and immune system regulation in gene ontology and functional enrichment analysis. Interestingly, we found and confirmed that urinary Ephrin type-A receptor 4 (EPHA4) and Vitronectin (VTN) were significantly reduced in both inactive and active JSLE patients. Moreover, VTN treatment in THP-1 derived macrophages significantly promoted the cell pyroptosis through the activation of inflammasome NLRP3. There is an activation of Caspase-1 and an upregulated secretion of cleaved GSDMD and IL-18 in VTN treated macrophages. Most importantly, the urinary VTN was also linear correlated with clinical characteristics of JSLE, implying VTN could be a specific diagnostic biomarker to distinguish inactive and active JSLE.

Conclusions

In summary, this study provided a urinary proteomic reference profile for JSLE to assist clinical diagnoses. Patients with active and inactive JSLE have differentially obvious metabolic proteins in the urine. VTN as a novel diagnostic biomarker supplied a new insight to distinguish inactive and active JSLE.

Keywords

Vitronectin, JSLE, Pyroptosis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-042

Effect of tumor necrosis factor-α gene polymorphisms in risk of systemic lupus erythematosus patients susceptibility: Update meta-analysis

Steven Irving[1], Bastomy Eka Rezkita[1], Rabbinu Rangga Pribadi[2], Marcellus Simadibrata[2]

[1] General Medicine, Faculty of Medicine, University of Sebelas Maret, Indonesia
[2] Gastroenteroloy, Pancreatobiliary, and Digestive Endoscopy, Department of Internal Medicine, University of Indonesia, Indonesia

Background

Tumor Necrosis Factor (TNF-α) is a cytokine involved in the pathogenesis of the several inflammatory diseases, including Systematic Lupus Erythematosus (SLE). Polymorphisms in TNF-α gene have been proposed to be partly responsible for auto-antibody production in several studies. However, the results were inconsistent. We performed this meta-analysis to investigate the effect of TNF-α gene polymorphisms in risk of SLE patients susceptibility.

Methods

This meta-analysis was conducted based on the PRISMA guideline. Literature searches from Pubmed and EMBASE were conducted until December 2021 and were limited to English-only literature. Studies included in this meta-analysis were accessed using The Newcastle Ottawa Score (NOS). The primary outcome was the association between TNF α gene polymorphism and the risk of SLE. The sufficient data count is pooled by OR and 95% CI.

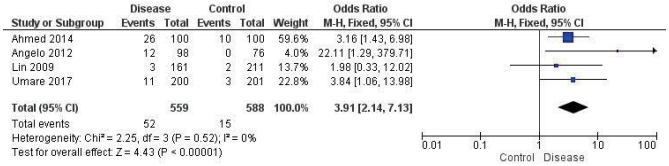
Results

Four studies (560 case / 590 control) met the inclusion criteria. G allele and GG genotype were associated with decreased risk of SLE (OR= 0.49[0.32 – 0.75], p= 0.0009 and OR= 0.52[0.40-0.69]. p= 0.0001). Meanwhile, A allele with AG and AA genotype were significantly associated with increased risk of SLE (OR= 2.05[1.34-3.13], p= 0.0009; OR=1.41 [1.05-1.87], p= 0.02 ; OR= 3.91[2.14-7.13], p= 0.00001).

Conclusions

In summary our meta-analysis suggested that G allele and GG genotype may serve as protective factor of SLE, while A allele with AG and AA genotype may act as risk factor for SLE. Further study about interaction between genetic-environment interactions with larger sample is needed.

Figure & Table



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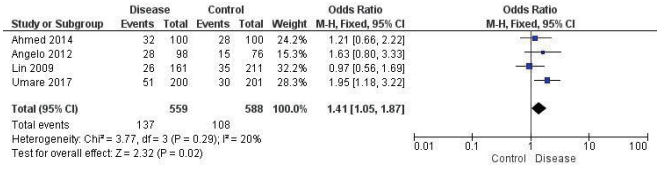

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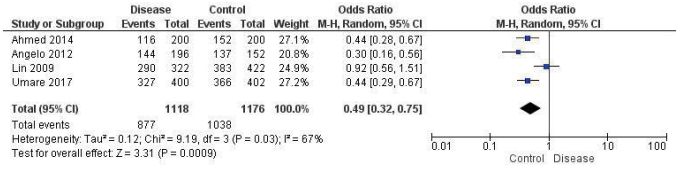

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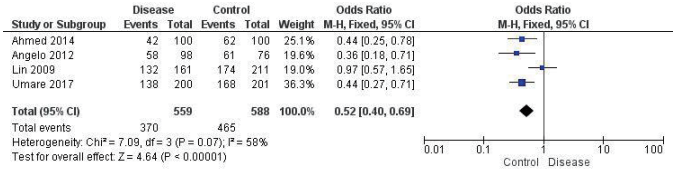

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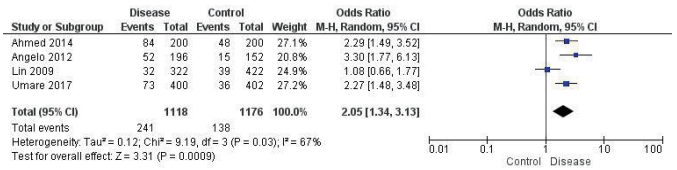


Figure. Forest plot of bassociation between TNF-α gene polymorphisms and Systemic Lupus Erythematosus A) AA vs AG + GG; B) AG vs AA + GG; C) G vs A; D) GG vs AG + AA; E) A vs G

Keywords

gene polymorphism, systemic lupus erythematosus, tumor necrosis factor α

E-poster Presentation

SLE-treatment

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-043

A retrospective single center study of the clinical response of tacrolimus treatment in patients with lupus nephritis

Ji-Won Kim[1], Ju Jung[1], Hyoun-Ah Kim[1], Chang-Hee Suh[1]

[1] Department of Rheumatology, Ajou University School of Medicine, Republic of Korea

Background

Lupus nephritis (LN) is a severe manifestation of systemic lupus erythematosus (SLE), however, current treatment for LN is still associated with severe adverse effects, treatment failures, and relapse rates. Tacrolimus (TAC) has recently become increasingly interested in its role as a potential therapeutic agent in SLE. The aim of this study was to evaluate the efficacy of TAC as a treatment for LN.

Methods

We retrospectively reviewed the medical records of patients with LN from January 1999 to December 2021. One-hundred seventy biopsy proven cases of LN were enrolled, with 92 in the TAC group and 87 in the non-TAC group. The clinical response of TAC treatment in patients with LN was evaluated by proteinuria, estimated glomerular filtration rate (eGFR), anti-double-stranded DNA (anti-dsDNA) antibody, complement 3 (C3), C4, and renal SLE disease activity index (SLEDAI). Complete renal response was defined as urine protein/creatinine <0.5, normal serum creatinine or, if normal at baseline, not increased by ≥15%, and partial renal response was defined as a normal or near-normal GFR with a ≥50% reduction in proteinuria to sub-nephrotic levels.

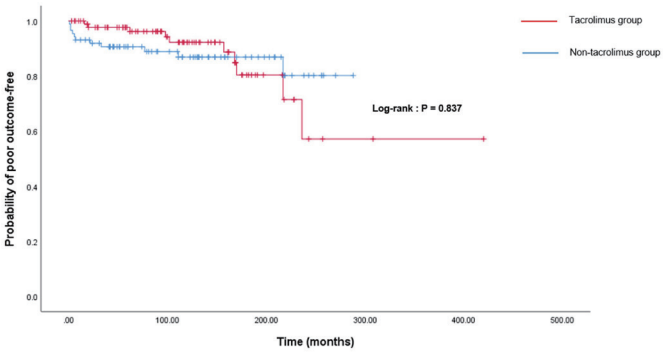
Results

The baseline clinical manifestations between the two groups showed no significant differences. Most of TAC group received combination therapy with other immunosuppressants, and only 19 (20.7%) patients maintained TAC monotherapy. After 5 years, there were no statistically significant differences in proteinuria, eGFR levels, anti-dsDNA, serum C3, C4, and renal SLEDAI. The overall (complete and partial) renal response rate was not significantly different: 72.9% of patients receiving TAC and 85.5% of patients not receiving TAC (p=0.1). The poor outcomes including end stage renal disease or death were similar in both groups.

Conclusions

Our results indicate that TAC is potentially effective in treating LN, and may be a reasonable option for patients with LN. TAC can help patients with LN achieve a renal response and slow progression.

Figure & Table



comes in patients with lupus nephritis

Keywords

Lupus nephritis, Tacrolimus, Combination therapy

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-044

Acute pancreatitis after corticosteroid pulse therapy in rheumatic disease: Acute pancreatitis is common adverse reaction after corticosteroid pulse therapy

Jinseok Kim[1], Yong-Beom Park[1]

[1] Internal medicine, Yonsei University College of Medicine, Republic of Korea

Background

Many drugs are known to cause drug-induced pancreatitis. This study investigated acute pancreatitis after corticosteroid pulse therapy in patients with rheumatic disease.

Methods

We retrospectively reviewed all patients with rheumatic disease who had received corticosteroid pulse therapy (at least methylprednisolone 500mg a day for less than 5 days) at Severance hospital, Yonsei University since electronic medical record system was set (June 2005 – December 2021). This study defined acute pancreatitis as the presence of two of three following criteria: acute onset of persistent, severe, epigastric pain often radiating to the back, elevation in serum lipase or amylase to three times or greater than the upper normal limit, and characteristic findings of acute pancreatitis on imaging (Computerized tomography (CT), Magnetic resonance imaging (MRI), or ultrasonography (USG)). Co-administered drugs that are known to be associated with drug-induced pancreatitis (Pancreatitis-associated drugs) during pulse therapy were analyzed. Autoantibodies and laboratory findings before pulse therapy were also collected in SLE patients.

Results

The total number of patients who had received corticosteroid pulse therapy due to rheumatic disease is 230 (131 patients with systemic lupus erythematosus (SLE), 63 with vasculitis, 15 with adult-onset stills' disease, 14 with inflammatory myositis, 5 with rheumatoid arthritis, 1 with relapsing polychondritis, 1 with becet disease). Seven patients (3.0%; 6 with SLE and 1 with vasculitis) had suffered from acute pancreatitis within a week after corticosteroid pulse therapy. No patients had died of acute pancreatitis. More use of pancreatitis-associatied drugs (i.e., furosemide, omeprazole, trimethoprim/sulfamethoxazole. atorvastatin, cyclophosphamide) during pulse therapy was related to high incidence of acute pancreatitis. No autoantibodies and laboratory data before pulse therapy had an impact on the events in patients with SLE.

Conclusions

Acute pancreatitis is common adverse drug reaction (ADR) after corticosteroid pulse therapy. Concomittant use of pancreatitis-associating drugs could increase the risk of acute pancreatitis after corticosteroid pulse therapy.

Figure & Table

Variables	All patients (n=230)	Patients without acute pancreatitis (n=223)	Patient with Acute pancreatitis (n= 7)	p-value
Demographic data				
Age at steroid pulse treatment	41.0 ± 26.3	41.0 ± 27.0	31.0 ± 33.0	0.277
Sex, female (%)	185 (80.4%)	178 (79.8%)	7 (100%)	0.350
Body weight	57.2 ± 13.0	57.40 ± 13.0	57.0 ± 19.9	0.325
BMI	22.1 ± 2.6	22.1 ± 2.6	22.3 ± 5.4	0.727
Type of underlying rheumatic disease				
SLE	131 (57.0%)	125 (56.1%)	6 (85.7%)	0.244
Vasculitis	63 (27.4%)	62 (27.8%)	1 (14.3%)	0.677
AOSD	15 (6.5%)	15 (6.7%)	0 (0.0%)	1.000
Inflammatory myositis	14 (6.1%)	14 (6.3%)	0 (0.0%)	1.000
Rheumatoid arthritis	5 (2.2%)	5 (2.2%)	0 (0.0%)	1.000
Relapsing polychondritis	1 (0.4%)	1 (0.4%)	0 (0.0%)	1.000
Behcet disease	1 (0.4%)	1 (0.4%)	0 (0.0%)	1.000
Corticosteroid pulse total dose (Methylprednisolone)			Linear-by-Linear Association	0.917
1500mg (500mg for 3days)	17 (7.4%)	17 (7.6%)	0 (0.0%)	
2000mg (1000mg for 2days)	1 (0.4%)	0 (0.0%)	1 (14.3%)	
2500mg (500mg for 5days)	22 (9.6%)	21 (9.4%)	1 (14.3%)	
3000mg (1000mg for 3days)	190 (82.6%)	185 (83.0%)	5 (71.4%)	
Amylase/Lipase				
Amylase level before pulse	63.0 ± 49.0	63.0 ± 49.5	88.5 ± 112.8	0.336
Lipase level before pulse	36.0 ± 30.5	36.0 ± 30.5	38.0 ± 51.8	0.854
Peak amylase level after pulse	90.0 ±80.3	86.0 ± 76.0	316.0 ± 1461.0	0.000
Peak lipase level after pulse	52.0 ± 59.3	50.0 ± 52.0	629.0 ± 1222.0	0.000
Amylase or Lipase elevation (>3 *UNL)	20 (8.7%)	14 (6.3%)	6 (85.7%)	0.000
Amylase or Lipase elevation (>2 *UNL)	32 (13.9%)	26 (11.7%)	6 (85.7%)	0.000
Amylase or Lipase elevation (>1 *UNL)	77 (33.5%)	70 (31.4%)	7 (100%)	0.000
Total number of co-administered pancreatitis-associating drugs during pulse	2.00 ± 2.00	2.00 ± 2.00	4.00 ± 1.00	0.009

Values are expressed as median ± interquartile range or n (%).
All statistical analysis was done by nonparametric test for continuous variables or by chi-square test / Fisher's exact test for categorical variables.
SLE: Systemic lupus erythematosus; AOSD: Adult-onset stills disease; UNL: Upper-normal limit
Pancreatitis-associating drugs were defined using review article *by Badalov, Nison, et al. "Drug-induced acute pancreatitis: an evidence-based review." Clinical gastroenterology and hepatology 5.6 (2007): 648-661.*
(i.e., furosemide, omeprazole, trimethoprim/sulfamethoxazole. Atorvastatin, cyclophosphamide)

Table. Comparison of variables between patients who had received corticosteroid pulse therapy with and without acute pancreatitis.

Keywords

Corticosteroid pulse therapy, acute pancreatitis, drug induced pancreatitis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-045

Myelodysplastic syndrome occurrence in post-therapeutic systemic lupus erythematosus patients

Ninda Devita[1]

[1] Biomedical Study Programme, Faculty of Medicine Public Health and Nursing, Universitas Gadjah Mada, Indonesia

Description

A 4-year-old boy comes to the hospital complaining of shortness of breath. He is a Systemic Lupus Erythematosus (SLE) patient with ongoing treatment. The history of the results of the ANA IF examination revealed a nuclear speckled pattern. Previously, the patient received Methylprednisolone 8-8-4 mg, Mycophenolate Mofetil 360-0-360, and Hydroxychloroquine 100 mg/day. Physical examination revealed rhonchi on both lungs. The results of a complete blood count revealed pancytopenia with a leukocyte count of 1.31 x 10^3 cells/uL, Hb 6.7 g/dL, and platelets 7 x 10^3 cells/uL. Follow-up examination with bone marrow aspiration revealed an increase in thrombopoiesis, erythropoiesis, and granulopoiesis accompanied by dysplasia in all three lineages showing the picture of Myelodysplastic Syndrome-Multilineage Dysplasia. The patient was then managed with the Myelodysplastic Syndrome protocol while continuing MP 8-8-4 mg therapy and discontinuing Hydroxychloroquine. Clinical improvement was found at follow-up 1 month after.

Conclusions

Systemic Lupus Erythematosus is a complex autoimmune disease, with many clinical features. Organ involvement in SLE cases often has an impact on the emergence of other diseases that have a picture of organ involvement. SLE therapy given is immunosuppressive to relieve the symptoms that arise. The incidence of Myelodysplastic Syndrome that occurs can be associated with the primary condition of this patient which is suspected to involve the bone marrow organ. However, it is undeniable that some immunosuppressive medications can trigger dysplasia. Cellular apoptosis that occurs because of treatment can trigger the development of other lineages that are not affected by the drug and eventually become dysplastic. In this case, it is not known with certainty the cause of MDS whether it is related to the pathophysiology of SLE or is the impact of treatment. This case demonstrates the need for clinician vigilance in providing SLE treatment protocols.

Figure & Table

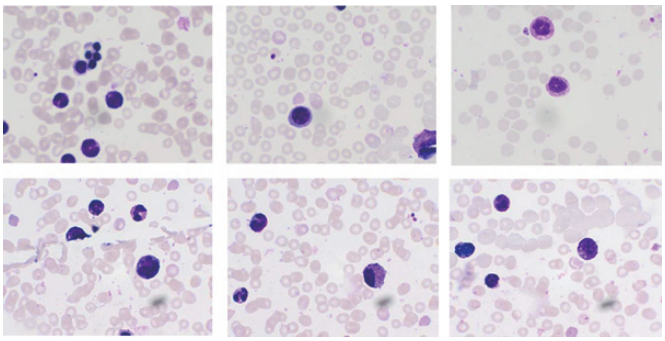


Figure. Bone marrow examination showing multi lineage dysplasia

Keywords

SLE, MDS, Dysplasia

E-poster Presentation

Spondyloarthropathies and psoriatic arthritis

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-046

Vitronectin-derived bioactive peptide prevents spondyloarthritis by modulating Th17/Treg imbalance in mice with curdlan-induced spondyloarthritis

Hong Ki Min[1], JeongWon Choi[3], Seon-Yeong Lee[3], A Ram Lee[5], Byung-Moo Min[4], Mi-La Cho[3,5], Sung-Hwan Park[2]

[1] Rheumatology, Konkuk University Medical Center, Republic of Korea
[2] Rheumatology, College of Medicine, The Catholic University of Korea, Republic of Korea
[3] Rheumatism Research Center, Catholic Research Institute of Medical Science, The Catholic University of Korea, Republic of Korea
[4] Department of Oral Biochemistry and Program in Cancer and Developmental Biology, Dental Research In, Seoul National University School of Dentistry, Republic of Korea
[5] Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea, Republic of Korea

Background

Spondyloarthritis (SpA) is a systemic inflammatory arthritis mediated mainly by interleukin (IL)-17. The vitronectin-derived bioactive peptide, VnP-16, exerts an anti-osteoporotic effect via β1 and αvβ3 integrin signaling. SpA is associated with an increased risk of osteoporosis, and we investigated the effect of VnP-16 in mice with SpA.

Methods

SpA was induced by curdlan in SKG ZAP-70W163C mice, which were treated with vehicle, celecoxib, VnP-16, or VnP-16+celecoxib. The clinical score, arthritis score, spondylitis score, and proinflammatory cytokine expression of the spine were evaluated by immunohistochemical staining. Type 17 helper T cell (Th17) and regulatory T cell (Treg) differentiation in the spleen was evaluated by flow cytometry and in the spine by confocal staining. Splenocyte expression of signal transducer and activator of transcription (STAT) 3 and pSTAT3 was evaluated by in vitro Western blotting.

Results

The clinical score was significantly reduced in the VnP16+celecoxib group. The arthritis and spondylitis scores were significantly lower in the VnP-16 and VnP16+celecoxib groups than the vehicle group. In the spine, the levels of IL-1β, IL-6, tumor necrosis factor-α, and IL-17 expression were reduced and Th17/Treg imbalance was regulated in the VnP-16 alone and VnP-16+celecoxib groups. Flow cytometry of splenocytes showed increased polarization of Tregs in the VnP-16+celecoxib group. In vitro, VnP-16 suppressed pSTAT3.

Conclusions

VnP-16 plus celecoxib prevented SpA progression in a mouse model by regulating the Th17/Treg imbalance and suppressing the expression of proinflammatory cytokines.

Figure & Table

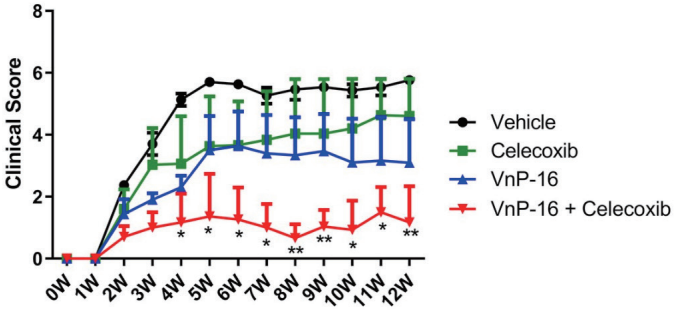


Figure. Anti-arthritic effects of vitronectin-derived bioactive peptide (VnP-16) in spondyloarthritis (SpA) mice.

Keywords

Spondyloarthritis, VnP-16, Type 17 helper T cell

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-047

The relationship between the osteoporosis and cortial index of the mandibular bone in psoriatic arthritis

Viliam Gasanova[1], Gürkan İden[2]

[1] Department of Radiology, Bahçeşehir İstinye University, Turkey
[2] orthopedics and traumatology, R. Yaşar Eryılmaz Doğubeyazıt Devlet Hastanesi, Turkey

Background

The aim of this study is to determine the detectability of systemic osteoporosis in psoriatic arthritis using mandibular radiography and indices.

Methods

In our study, 54 patients with psoriatic arthritis who had radiographs were evaluated. Data consist of DXA, mandibular radiography and rheumatological status, body mass index (BMI), and demographic values. The morphology of the mandibular inferior cortex (MCI) was determined by two observers and classified according to the Klemetti scale (1) (G1-G2-G3). Student's t-test, ANOVA, and Kappa statistics were applied. In addition, sensitivity, specificity, and positive and negative predictive values of MCI were determined in the detection of systemic bone loss.

Results

54 psoriatic arthritis patients were included in the study. Considering the lumbar spine values, 20% of the patients were found to have osteoporosis (G3), 34% to have osteopenia (G2), and 46% to be healthy (G1). Considering the femoral head values, 15% of the patients were found to have osteoporosis (G3), 21% to have osteopenia (G2), and 64% to be healthy (G1). There was no significant difference between the groups in terms of age and gender. A strong agreement (kappa: 0.784) was found between the 2 observers in the evaluation of MCI on mandibular radiography. The mean sensitivity, specificity, and positive and negative predictive values were 63.4, 84.2, 62.6, and 83.7 for the lumbar spine, while 49.5, 82.4, 76.2, and 57.9 for the femoral head.

Conclusions

As a result of this study, it has been seen that mandibular radiography and MCI can be used as an auxiliary diagnostic tool in osteoporosis resolving in psoriatic arthritis.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-048

Evaluation of the relationship between ankylosing spondylitis and its inflammation indicator calprotectin and its relationship with disease activity

Mehmet Alperen Tezcan[1], Ekin Başak Doğancı[2]

[1] Department of Radiology, Ataturk University, Turkey
[2] Physical Medicine and Rehabilitation, Rheumatology Department, Ataturk University, Turkey

Background

This study investigated whether there is a relationship between ankylosing spondylitis (AS) and calprotectin, an indicator of intestinal inflammation.

Methods

Patients who met the 1984 Modified New York criteria for AS were included in the study. Patients using infliximab, adalimumab and non-steroidal anti-inflammatory drugs for the last 8 weeks were excluded from the study. In the study, 248 AS patients and 120 healthy population without known intestinal inflammation complaints and symptoms were evaluated. Disease activity in the AS group was divided into two groups as those with Bath AS disease activity index (BASDAI) 4< and 4>. Calprotectin levels, an indirect indicator of intestinal inflammation, were measured in each patient. Patients with a fecal calprotectin level >70 ug/g were considered positive. The relationship between healthy population and AS patients and between AS disease activity and fecal calprotectin levels were examined.

Results

There was no significant difference between the groups in terms of age and gender. Calprotectin levels were high in 61 patients with ankylosing spondylitis, while high calprotectin levels were detected in two people in the healthy population. There was a significant difference in calprotectin levels between the two groups (p=0.0063). In addition, while the number of patients with BASDAI <4 was 169, the number of patients with >4 was 79. The mean fecal protein level was 24.2 ug/g in the group with high disease activity and 14.6 ug/g in the group with low activity, and there was a significant difference between the groups in fecal protein levels (p<0.001).

Conclusions

The incidence of intestinal inflammation is increased in patients with ankylosing spondylitis and the risk of bowel inflammation is associated with disease activity.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-049

Investigation of the relationship of ankylosing spondylitis and varicocele

Muhammed Emre Isıktas[1], Cafer Koçak[1], Halid Yener[1]

[1] Department of Radiology, Atatürk University, Turkey

Background

Varicocele is defined as abnormal dilatation and increased tortuosity of the veins of the pampiniform plexus and poses a risk for male infertility. We aimed to investigate the effect of sedative life developed in patients with ankylosing spondylitis on the development of varicocele with this study.

Methods

The study groups consisted of 87 AS and 51 healthy controls. Scrotal physical examination and Doppler ultrasonography were performed by two doctors who were unaware of the patient's diagnosis. Varicocele frequencies were determined and the correlation between physical examination and ultrasonographic examination was calculated. Panpiniform plexus diameter >2mm was evaluated as varicocele. In addition, reflux was evaluated with the Valsalva maneuver

Results

There was no significant difference between the groups in terms of age and gender. Varicocele was found in 26.4% (n=23) in the AS group and 23.5% (n=12) in healthy controls by physical examination. In Doppler ultrasonography, these rates were observed as 29.8% (n=26), and 27.4% (n=14), respectively. Valsalva and reflux in pampiniform plexuses were 13.8% (12) in Behçet's patients and 9.8% (5) in the healthy population. detected. While the mean pampiniform plexus diameter was 2.12 mm in BD patients, it was 1.87 mm in the healthy population. No significant difference was observed between the two groups (p=0.052). There was moderate agreement between physical examination results and Doppler ultrasonographic examination results (kappa value=0.684).

Conclusions

The incidence of varicocele in AS does not increase compared to the healthy control group. This may indicate that the sedative life in Ankylosing sponditis does not significantly affect varicocele.

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P-050

The effect of ankylosing spondylitis on carotis intima media thickness and its relationship with disease activity

Elshad İsmailov[1], Merve Polat[2], Gökhan Polat[1]

[1] Department of Radiology, Atatürk University, Turkey
[2] HEALTH PHYSICS, Karadeniz Technical University, Turkey

Background

It is known that atherosclerosis increases in ankylosing spondylitis cases. In our study, we aimed to examine the effect on carotid intima media thickness in patients followed up with AS diagnosis

Methods

244 cases (mean age: 46.2) and 124 control subjects (mean age: 42.5) followed up with the diagnosis of AS were included in the study. The clinical and demographic characteristics of the patients were recorded. Activity classification was made based on the BASDAI score: disease activity in the RA group, no activity (BASDAI =0), mild activity (BASDAI 1–2), moderate activity (BASDAI 3–5), high activity (BASDAI) according to the Bath AS disease activity index (BASDAI>5). Carotid ultrasonography was performed in all cases to evaluate subclinical atherosclerosis and intima-media thickness (IMT) was evaluated.

Results

There was no significant difference between the groups in terms of age and gender.The mean disease duration is 94.6 months. Carotid IMT of RA patients (mean 0.694mm) was significantly higher than the control (mean 0.598mm) (p=0.035). The number of patients with BASDAI =0 was 108, the number of patients with BASDAI 1–2 was 59, the number of patients with BASDAI 3–5 was 35, and the number of patients with BASDAI >5 was 40. A very high correlation was found between carotid IMT and disease activity (r=0.801, p<0.001).

Conclusions

An increase in carotid intima-media thickness is observed in patients with AS, and there is a significant correlation between disease activity and carotid intima-media thickness.

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Predictive role of neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio and platelet-to-lymphocyte ratio in the assessment of clinical response and drug persistence of tumor necrosis factor-alpha inhibitors in patients with ankylosing spondylitis

Dong Hyuk Moon[1], Seung-Geun Lee[1], Aran Kim[1], Byung Wook Song[1]

[1] Rheumatology, Pusan National University School of Medicine, Pusan National University Hospital, Republic of Korea

Background

Recently, neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR) and platelet-to-lymphocyte ratio (PLR) are recognized as surrogate markers for systemic inflammation in various disorders including ankylosing spondylitis (AS). We aimed to investigate whether baseline NLR, MLR and PLR can predict treatment response to tumor necrosis factor-alpha (TNF-α) inhibitors at 12 weeks and their long-term persistence in patients with ankylosing spondylitis (AS) in real practice.

Methods

In this retrospective cohort study, we investigated 279 patients with RA who started on anti-TNF-α agents as the first-line biologic and 171 sex- and age-matched (±2 years) healthy subjects. AS patients were divided into high and low baseline NLR, MLR or PLR subgroups using median split. Response to TNF-α inhibitors at 12 weeks was defined as Bath AS Disease Activity Index (BASDAI) improvement ≥ 2 and persistence was defined as the time interval between the initiation and the first discontinuation of TNF-α inhibitors.

Results

Patients with AS had significantly higher median NLR (1.99 vs 1.45, p<0.001), MLR (0.24 vs 0.16, p<0.001) and PLR (117.29 vs 115.11, p=0.036) compared with healthy controls. One hundred and eighty-five (66.3%), 65 (23.3%) and 29 (10.4%) AS patients started with adalimumab, etanercept and infliximab, respectively, and mean BASDAI was 6.8. The frequency of non-response at 12 weeks was 3.7% and 113 (40.5%) patients stopped TNF-α inhibitors (lack of efficacy: 29, adverse events: 23 and poor health literacy: 61) during the study period. After adjusting confounding factors, high baseline NLR was related with a higher risk of non-response (OR=11.57, p=0.028) to TNF-α inhibitors at 12 weeks. In addition, high baseline NLR was independently associated with a higher risk for TNF-α inhibitors discontinuation (HR=1.66, p=0.01).

Conclusions

Our findings suggest that baseline NLR may play a predictive role for response and persistence of TNF-α inhibitors in patients with AS.

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Journal of Rheumatic Diseases
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P-052

A deep-learning-based approach for automated assessment of modified Stoke ankylosing spondylitis spine score (mSASSS) on spine radiographs: a preliminary study

Sun Yeop Lee[1], Dong Hyun Kim[2], Hee-Dong Chae[3], Hongjun Yoon[1], Hyo Jin Kim[2], Jiwoon Seo[2], Jee Won Chai[2], Sung Hwan Hong[3], Ja-Young Choi[3], Burnyoung Kim[1], Ara Seo[1], Songhwan Lim[1]

[1] Department of Medical AI, Deepnoid, Inc., Republic of Korea
[2] Department of Radiology, SMG-SNU Boramae Medical Center, Seoul National University College of Medicine, Republic of Korea
[3] Department of Radiology, Seoul National University Hospital, Seoul National University College of Medicine, Republic of Korea

Background

A deep learning (DL) algorithm is developed for the automatic detection of ankylosis in spine radiographs of patients with ankylosing spondylitis as a first step for the development of automatic mSASSS assessment.

Methods

We retrospectively collected 2,000 radiographs from 500 patients with ankylosing spondylitis from two hospitals. For each patient, lateral cervical and lumbar radiographs at baseline and follow-up were collected. Each radiograph was evaluated for mSASSS assessment, and two radiologists performed manual segmentations on the vertebra and syndesmophytes. Among 24,000 vertebral corners from 2,000 radiographs (train: 1,700, validation: 100, test: 200), 3,928 (16.4%) were ankylosis, while 873 (3.6%) were not clearly visible and excluded. A DL algorithm was developed to first segment vertebra including syndesmophytes, then extract vertebral corners to identify ankylosis. A Mask region-based convolutional neural network (R-CNN) was used in the detection and segmentation of the vertebra including syndesmophytes. Using the DL model results, ankylosis was determined if two adjacent segmented vertebral corners were overlapped.

Results

In the test set, the dice score coefficient (DSC) for the vertebra including syndesmophyte was 0.94. The sensitivity for each vertebra including syndesmophytes to be predicted with DSC higher than 0.50 was 99.66% and the precision was 99.98%. Sensitivity, specificity, precision, and accuracy for per-vertebral corner detection of ankylosis were 82.6%, 95.6%, 78.4%, and 93.3%, respectively.

Conclusions

The DL model for segmentation of vertebra including syndesmophyte showed high segmentation performance. Using this model, we develop a detection algorithm for ankylosis at the vertebra corner. Such algorithm is also helpful in future model development of automated mSASSS assessment. Further development of the classification of vertebral corner abnormalities is in progress for automated mSASSS assessment.

Figure & Table

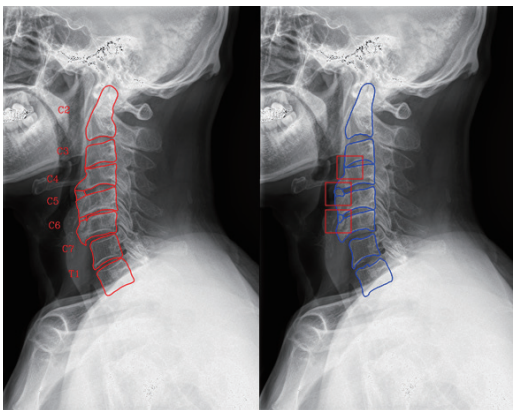

Figure. Segmentation results and identification of ankylosing spondylitis on a cervical spine
radiograph. The ground truth manual segmentations (red contour) are on the image to the left,
and the predicted segmentations (blue contour) are on the image to the right. Identified cases
of ankylosis are visualized on the predicted segmentation (red boxes).

Keywords

mSASSS, ankylosing spondylitis, deep learning

Journal of Rheumatic Diseases
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P-053

Intra-articular corticosteroids for sacroiliitis in treatment of spondyloarthritis

Pallavi Vij[1], Rudra P Goswami[1], Danveer Bhadu[1], Uma Kumar[1]

[1] Rheumatology, All India Institute of Medical Sciences, New Delhi, India

Background

Management of sacroiliitis in patients of spondyloarthritis (SpA) includes physiotherapy, NSAIDs and biologics. Intra-articular corticosteroid injection in sacroiliac (SI) joints is an underutilized procedure. The present study investigates its effectiveness among patients with SpA.

Methods

Patients with SpA attending the Department of Rheumatology, AIIMS, New Delhi were screened for inclusion using the following criteria: ASAS criteria for spondyloarthritis; predominant axial involvement; imaging evidence of active sacroiliitis; sacroiliac joint tenderness. Patients with any contraindication towards intra-articular procedure were excluded. Intra-articular triamcinolone acetonide 40 mg was administered in the sacroiliac joints with or without sonographic (USG) guidance. Baseline pain VAS and BASDAI were obtained and repeated at 7 days, 3 months and 6 months.

Results

A total of 50 SI joints (26 patients, 25 male, mean age of 26.4 ±7.7 years, mean disease duration 6.1±3.2 years) were injected (38 USG guided and 12 blind). Baseline BASDAI was 4.5±1. Mean pain VAS was reduced from baseline to all points of follow-up (baseline: 8.26 ± 0.8 (n=50), 4.8±2.2 (7th day, n=50), 4.3±1.99 (1st month, n=42) and 5.6±2.5 (3rd month, n=30), all p<0.0001 compared to baseline). Immediate response was not seen in six patients and 44 patients had a durable response (88%, 95% confidence interval (CI): 76.2-94.4) which lasted till 3-months in 20%, till 6-months in 12% and beyond six-months in 12%. Median duration of response was 75 days (95%CI: 54-96). Relapse after initial response was seen in 16 patients (36.4%, 95% CI: 23.7-51.1). In Cox regression, patients with early response had a lesser chance of relapse (Table 1). There were no significant adverse effects.

Conclusions

Intra-articular steroid injection is an effective and safe treatment alternative in spondyloarthritis with sacroiliitis and can be performed with or without USG guidance and can be tried in patients who cannot immediately afford biologics or as a bridging therapy for biologics.

Figure & Table

Independent variables	Hazard ratio	95% CI	P – value
Age	0.98	0.9–1.06	0.56
Disease duration	1.11	0.91–1.35	0.30
Baseline BASDAI	0.99	0.58–1.67	0.96
Percentage reduction of pain VAS by 7 days			0.007
<25%	Reference category		
25-50%	**0.08**	**0.02–0.39**	**0.002**
>50%	**0.27**	**0.06–1.1**	**0.06**
Method (USG versus Blind)	0.87	0.17–4.42	0.86

Table. Multivariate Cox Proportional Hazard model predicting relapse by 3 months of follow up after SI joint injection

Keywords

Sacroiliac joint, spondyloarthritis, intra-articular corticosteroids

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Journal of Rheumatic Diseases
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P-054

Drug retention of biologic agents in Korean patients with psoriatic arthritis

Ju Yeon Kim[1], Min Jung Kim[2], Sun Im Yun[2], So Young Park[2], Jiyu Sun[3], Jung Hee Koh[4], Hyoun-Ah Kim[5], Jinhyun Kim[6], Kichul Shin[2]

[1] Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Seoul Metropolitan Government-Seoul National Boramae Medical Center, Seoul, Republic of Korea
[3] Medical Research Collaborating Center, Seoul Metropolitan Government-Seoul National Boramae Medical Center, Seoul, Republic of Korea
[4] Division of Rheumatology, Department of Internal Medicine, Bucheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea
[5] Division of Rheumatology, Department of Internal Medicine, Ajou University Hospital, Suwon, Republic of Korea
[6] Division of Rheumatology, Department of Internal Medicine, Chungnam National University College of Medicine, Daejeon, Republic of Korea

Background

Clinical studies of psoriatic arthritis (PsA) in Korea are scarce than those of ankylosing spondylitis (AS), especially regarding biologic therapy. We aimed to investigate the clinical characteristics and drug retention of biologics in patients with PsA registered in a nationwide cohort.

Methods

We analyzed the data of KOBIO-PsA (Dec 2012-Jan 2022) including demographics, disease activity and concomitant medications, and drug survival of biologic therapy. Patients were divided into two groups: patients initially registered as anti-TNF users (group A) and anti-IL-17 or anti-IL-12/13 users (group B). Reasons of switching or discontinuation were also assessed . Kaplan-Meier curve for drug survival was plotted in total subjects, by group, and according to line of biologic therapy .

Results

Among a total of 107 patients, 53.2% were males and the mean age was 43.7 years. Twenty-five percent of patients had spondyloarthritis. Baseline demographic and clinical characteristics were comparable between group A and B, except for a longer disease duration in group B (p= 0.020). Psoriasis was present in 95.6% (group A), and 100% (group B). The most used first- and second-line biologic agent were Humira (46.0%) and Cosentyx (47.8%), respectively. Methotrexate was prescribed with biologics in 77.6% of cases. Oral glucocorticoid was continued in 49.5% of patients (mean daily dose of prednisolone or its equivalent 5.99 mg). The overall drug survival of biologic agents after 60 months was 41% in the study patients (Figure). The P-value of log-rank test of second- and third or more-line therapy comparing with first-line therapy was 0.5839 and 0.5022, respectively.

Conclusions

Oral glucocorticoid use is yet prevalent in PsA patients, contrary to treatment guidelines. Biologic therapy retention in Korean patients with PsA is substantially lower than what is in the literature of AS , despite the limited choice of agents in terms of mode of action.

Figure & Table

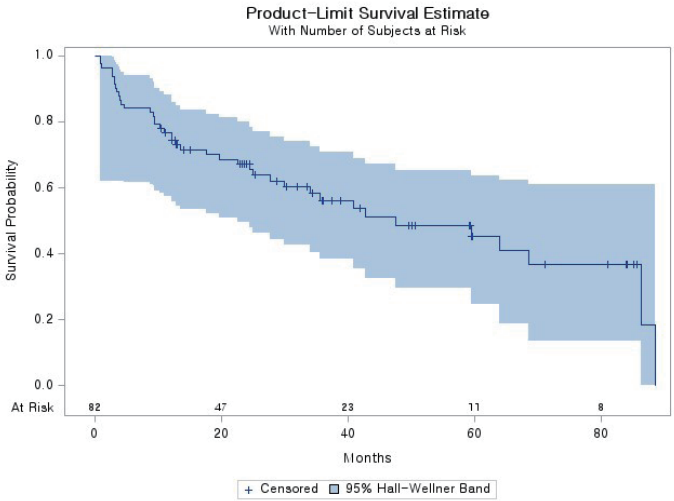

Figure. Drug survival of biologic therapy in Korean patients with PsA

Keywords

Psoriatic arthritis, KOBIO Registry

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P-055

Safety profile of Ixekizumab for the treatment of psoriatic arthritis and axial spondyloarthritis up to 3 Years: An updated integrated safety analysis

Sergio Schwartzman[1], Atul Deodhar[2], Bernard Combe[3], Ana Accioly[4], Andris Kronbergs[4], Boris Janos[4], Danting Zhu[4], David Sandoval[4], Proton Rahman[5], Denis Poddubnyy[6], Young In Eom[7]

[1] Rheumatology, The Hospital for Special Surgery, USA
[2] Rheumatology, Oregon Health & Science University, USA
[3] Rheumatology, Montpellier University, France
[4] Rheumatology, Eli Lilly and Company, USA
[5] Rheumatology, Memorial University of Newfoundland, Canada
[6] Rheumatology, Charité - Universitätsmedizin Berlin and German Rheumatism Research Centre, Germany
[7] Rheumatology, Lilly Korea Ltd, Republic of Korea

Background

We report ixekizumab (IXE) safety outcomes with over 2000patient-years (PY) of exposure up to 3years in patients with psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA).

Methods

Long-term safety of IXE was assessed from 8 randomized trials. Treatment-emergent adverse events (TEAEs) adjusted incidence rates (IRs) per 100PY within 1-year time periods through 19 March 2021 were calculated for all patients treated with ≥1 dose of IXE.

Results

Overall, 1401 PsA and 932 axSpA patients with a cumulative IXE exposure of 2247.7PY and 2096.2PY, respectively, were included in this analysis. IRs per 100PY for any TEAE were 50.3 for PsA and 38.1 for axSpA. Serious AEs were reported by 134 PsA patients (IR=6.0), and 101 axSpA patients (IR=4.8). Nine deaths were reported (6 in PsA [IR=0.3] and 3 in axSpA [IR=0.1]). IRs per 100PY of discontinuation from the study drug due to AE were 5.1 (PsA) and 3.1 (axSpA). IRs of serious infections were low (PsA: IR=1.2, axSpA: IR=1.1). IRs of opportunistic infections (PsA: IR=1.8, axSpA: IR=0.8) and Candida infections (PsA: IR=2.0, axSpA: IR=1.2) were low. There were no confirmed cases of reactivation of tuberculosis. Injection-site reactions occurred with IRs of 11.6 (PsA) and 7.4 (axSpA). IRs for allergic/hypersensitivity reactions were 4.5 (PsA) and 4.2 (axSpA). No confirmed events of anaphylaxis were reported. Across indications, IRs were low for cytopenia (≤2.5), malignancies (≤0.7), major adverse cerebro-cardiovascular event (≤0.5), depression (≤1.6), and iridocyclitis (≤2.8). Per external adjudication, 20 patients had inflammatory bowel disease (3 patients with PsA and 17 with axSpA) of which 1 was ulcerative colitis for PsA (IR=0.0) and 10 for axSpA (IR=0.5); 2 events were Crohn's disease for PsA (IR=0.1) and 7 for axSpA (IR=0.3).

Conclusions

IXE maintained a safety profile consistent to that previously reported, with no new or unexpected safety events through exposure up to 3years.

Keywords

Ixekizumab, Axial spondyloarthritis, Psoriatic arthritis

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P-056

A comparison of physical functions and its relationship with disease activity of persons with ankylosing spondilitis

Aysenur Kara[1]

[1] Department of Family Physicians, Atatürk University, Turkey

Background

We aimed to examine how physical function is affected in individuals with Ankylosing Spondylitis (AS) and its relationship with disease activity.

Methods

148 patients diagnosed with AS and 63 healthy individuals were included in this study. Activity classification was made based on the BASDAI score: disease activity in the AS group, no activity (BASDAI =0), mild activity (BASDAI 1–2), moderate activity (BASDAI 3–5), high activity (BASDAI) according to the Bath AS disease activity index (BASDAI). BASDAI >5). Cases in both groups filled out a questionnaire including demographic characteristics and the SF-36's Physical Function and Physical Role sub-domains, and Sit to Stand test, Timed Up and Go test were performed.

Results

148 patients with AS (mean age: 48.12+/- 10.52 years) and 63 healthy subjects (44.38+/- 9.8 years) participated in this study. There was no significant difference between the groups in terms of age and gender.When the groups are compared; Sit to Stand test, Timed Up and Go test, Physical Function and Physical Role subdomain scores of SF-36 were found to be statistically lower in patients with BD than healthy subjects (Respectively; t= -5.15, p< 0.0001; t= - 6.38, p< 0.0001; t=5.87, p< 0.0001; t=6.48, p< 0.0001). There were 67 patients with a BASDAI =0, 39 patients with a BASDAI 1–2, 28 patients with a BASDAI 3–5, and 14 patients with a BASDAI >5. As the disease activity increased, there was a high negative correlation in Sit to Stand test, Timed Up and Go test scores, and a highly positive correlation in SF-36's Physical Function and Physical Role subdomain scores (r=-0.743 p<0.001; r=-0.782) , p < 0.001; r=0.756, p<0.001; r=0.801, p<0.001).

Conclusions

According to the results obtained, it was determined that there was a significant decrease in physical capacity in AS patients compared to healthy individuals.

E-poster Presentation

Behçet's disease & Vasculitis

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

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P-057

Diagnostic value of 3D T1-weighted sampling perfection with application optimized contrast evolution (SPACE) magnetic resonance imaging in patients with giant cell arteritis

Recep Sade[1], Meltem Alkan melikoglu[2]

[1] Radiology, Ataturk University, Turkey
[2] Rheumatology, Ataturk University, Turkey

Background

Imaging techniques have an increasing place in the diagnosis of giant cell arteritis (GCA). Achieving a confident diagnosis of GCA is often challenging and temporal artery biopsy is still considered as the gold standard despite the delayed results. The aim is evaluate 3D T1 weighted sampling perfection with application optimized contrast evolution MRI (SPACE) sequences for diagnosis of giant cell arteritis

Methods

Ten patients with clinically suspected GCA were included and 4 had a diagnosis of GCA. We evaluated the diagnostic performance of fat-suppressed 3D T1 SPACE with 3D time of flight (TOF) coregistration

Results

Sensitivity and specificity of 3D T1 SPACE were 70% and 100% respectively. Therefore, the positive predictive value of post contrast 3D T1 SPACE was 100% and the negative predictive value was 80%. Intra- and inter-observer agreement for mural enhancement on 3D T1 SPACE was 1 and 1, respectively.

Conclusions

We demonstrate that 3D T1 SPACE is accurate for the diagnosis of GCA. The reproducibility and,short,scan duration of the technique support a wider use of MRI in the diagnosis process.

Keywords

giant cell arteritis, magnetic resonance imaging, diagnosis

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P-058

Determination of the frequency of entositis and its relationship with disease activity in Behçet's disease by ultrasonography

Serhat Kaya[1]

[1] Department of Radiology, Tunceli Devlet Hastanesi, Turkey

Background

Evaluation of the relationship between the frequency of enthesitis and disease activity in Behçet's disease by ultrasonography

Methods

86 Behçet's patients were included as the study group and 26 healthy individuals were included as the control group. Ultrasonography was performed on bilateral proximal plantar fascia, Achilles tendon, proximal and distal patellar ligament, distal quadriceps and brachial triceps tendons of all patients. Entezeal regions were evaluated according to thickness, structure, calcification, erosion, bursitis and power Doppler signals and scored according to the Madrid Sonographic Enthesitis index (MASEI). Activity classification was made based on the Behçet's Disease Instant Activity Form (BHAAF) score: no activity (BHAAF=0), mild activity (BHAAF 1–2), moderate activity (BHAAF 3–5), high activity (BHAAF 6–12).

Results

There was no significant difference between the groups in terms of age and gender.The mean total enthesitis score was found to be 18.2±9.1 in Behçet's patients and 2.0±1.8 in healthy individuals out of a maximum possible total of 136 points. According to MASEI, a significant difference was found between Behçet's patients and the control group ($p<0.001$). There were 38 patients with BHAAF=0, 23 patients with BHAAF 1–2, 17 patients with BHAAF 3–5, and 8 patients with BHAAF 6–12. MASEI scores, respectively; It was 8.6±3.8, 14.6±5.7, 19.6±8.3, 21.6±11.3. There was a significant and strong correlation between disease activity and enthetic scores ($r=0.824$, $p<0.0001$).

Conclusions

The frequency of enthesitis is significantly increased in Behçet's disease, and there is a strong linear relationship between disease activity and the frequency of enthesitis.

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-059

NeuroBehçet with spinal leptomeningeal involvement

Oğuzhan Mete[1], Gökhan Polat[2]

[1] medical faculty, Atatürk University, Turkey
[2] Department of Radiology, Ataturk University, Turkey

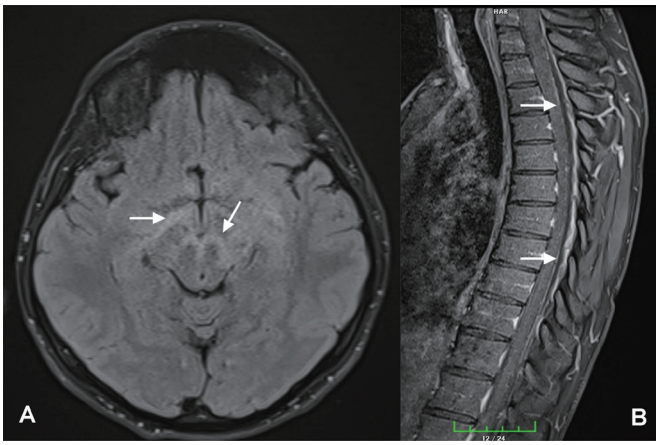
Description

A 28-year-old male patient, who was diagnosed with Behçet's disease for 2 years and followed up with uveitis, was admitted to our hospital with the complaint of severe headache. The patient was receiving adalimumab treatment. Pain increased with head and neck movements. Lumbar puncture was performed on the patient with the suspicion of meningitis. However, there was no increase in microprotein in favor of meningitis. Brain and spinal MRI was planned for Neurobehçet and methylprednisolone was started. In the MRI of the patient, there was an increase in signal on T2-weighted images in the basal ganglia and mesencephalon of the brain parenchyma. In the spinal MRI of the patient, leptomeningeal enhancement was observed. With the present findings, the patient was evaluated in favor of neurobehçet and neurobehçet spinal involvement.

Conclusions

Neurobehçet should definitely be evaluated with radiological imaging methods in the headache clinic in patients followed up for Behçet's disease. Leptomeningeal involvement should be considered in the differential diagnosis even if the LP is normal, and MRI with spinal contrast should be performed on the patient.

Figure & Table



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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-060

Investigation of the frequency of varicocele in Behçet's disease

Cafer Koçak[1], Halid Yener[1], Emre Işıktaş[1]

[1] Department of Radiology, Atatürk University, Turkey

Background

Determining the effect and relationship of Behçet's disease, which is an important cause of systemic vasculitis, with varicocele, which is an important predisposing factor in male infertility.

Methods

Study groups consisted of 67 BD and 42 healthy controls without the rheumatologic disease. Scrotal physical examination and Doppler ultrasonography were performed by two doctors, unaware of the patient's diagnosis, respectively. Varicocele frequencies were determined and the correlation between physical examination and ultrasonographic examination was calculated. Panpiniform plexus diameter >3mm was evaluated as varicocele. In addition, reflux was evaluated with the Valsalva maneuver.

Results

There was no significant difference between the groups in terms of age. Varicocele was detected by a physical examination in 41.8% (n=28) in the BD group and 19% (n=8) in healthy controls. In Doppler ultrasonography, these rates were 59.7% (n=40), and 26.1% (n=11), respectively. Valsalva and reflux in pampiniform plexuses were 26.8%(18) in Behçet's patients and 7.1%(3) in the healthy population. detected. The odds ratio for the risk of developing varicocele in BD patients compared to healthy controls was 3.42. While the mean pampiniform plexus diameter was 3.6mm in BD patients, it was 1.95mm in the healthy population. There was a significant difference between the two groups (p=0.032). A high level of agreement was found between physical examination results and Doppler ultrasonographic examination results (kappa value=0.702).

Conclusions

The frequency of varicocele in BD was found to be increased compared to the healthy control group. Considering the negative effects of this finding on male infertility, Behçet's disease may affect male infertility.

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-061

The relationship of venous involvement with disease activity in Behçet's syndrome

Muhammed Halid Yener[1], Emre Isıktas[1], Cafer Koçak[1]

[1] Department of Radiology, Atatürk University, Turkey

Background

In this study, we examined the disease activity levels of Behçet's patients with lower extremity DVT and examined the relationship.

Methods

186 patients with BS were included in the study. (163 M/23 F) Behçet's disease activity levels, Venous Clinical Severity Score (VCSS) were used. The presence of DVT of the patients was evaluated by Doppler ultrasonography. Activity classification was made based on the Behçet's Disease Instant Activity Form (BHAAF) score: no activity (BHAAF=0), mild activity (BHAAF 1–2), moderate activity (BHAAF 3–5), high activity (BHAAF 6–12).

Results

There was no significant difference between the groups in terms of age and gender. There were 76 patients with BHAAF=0, 49 patients with BHAAF 1–2, 37 patients with BHAAF 3–5, and 24 patients with BHAAF 6–12. The number of patients with DVT detected by Doppler ultrasonography in these groups, respectively; 6(7.9%), 9(18.3%), 8(21.6%), 7(29.1%). Venous Clinical severity score in patients with DVT diagnosed with BD, respectively; It was 5.4±4.9, 6.2±5.8, 5.7±5.4,6.8±6.3. There was a significant but moderate correlation between disease activity and DVT (r:0.486, P<0.01). There was no significant correlation between disease activity and venous clinical severity in patients with DVT (p=0.68).

Conclusions

Disease activity increases the risk of DVT but does not affect venous clinical severity in patients with DVT.

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Journal of Rheumatic Diseases
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P-062

Serum albumin, prealbumin, and ischemia-modified albumin levels in patients with ANCA-associated vasculitis: a prospective cohort study

Sung Soo Ahn[1], Taejun Yoon[2], Jason Jungsik Song[2], Yong-Beom Park[2], Sang-Won Lee[2]

[1] Internal Medicine, Division of Rheumatology, Yongin Severance Hospital, Yonsei University College of Medicine, Republic of Korea
[2] Internal Medicine, Division of Rheumatology, Severance Hospital, Yonsei University College of Medicine, Republic of Korea

Background

Acute phase reactants (APRs) are proteins altered by inflammation and are regarded as surrogate markers representing inflammatory status. This study evaluated changes of albumin (Alb), prealbumin (Palb), and ischemia-modified albumin (IMA) in patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in response to alterations in disease activity and the correlation between disease activity and Alb, Palb, and IMA.

Methods

Fifty-nine patients with AAV registered in the prospective SHAVE cohort, who had available serial blood samples at least three months apart were included (indicated as pre and post). Correlation analysis and linear regression were carried out to determine the relationship between continuous variables. Alb, Palb, and IMA levels in 40 healthy controls (HCs) were compared with patients with AAV.

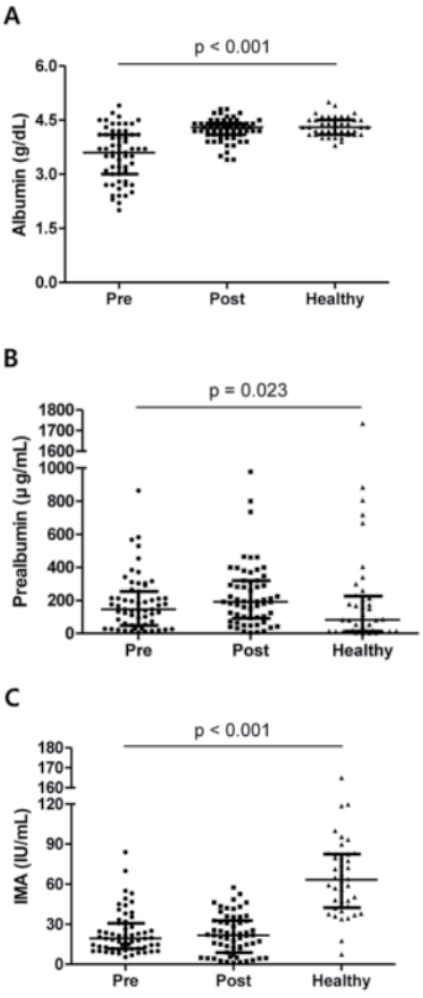
Results

Comparison of Alb, Palb, and IMA levels in HCs and in patients at initial (pre) and follow-up (post) time points revealed that Alb levels significantly increased following the improvement of disease activity and were comparable between HCs and patients at follow-up (post). Meanwhile, there was no significant difference noted in Palb and IMA levels after the decrease of disease activity. While initial (pre) Alb and Palb were significantly associated with BVAS, a subgroup analysis of patients with new-onset disease showed Palb was no longer significantly associated with Birmingham Vasculitis Activity Score (BVAS). Multivariate linear regression showed Alb level (standardized β=-0.377; 95% confidence interval: -5.623, -1.260; p=0.003) was an independent predictor of BVAS.

Conclusions

Among Alb, Palb, and IMA, we found that Alb could be a useful marker indicating disease activity.

Figure & Table



Keywords

antineutrophil cytoplasmic antibody, albumin, prealbumin

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-063

Comparison of physical functions of people with Behçet's disease and healthy and their relationship with disease activity

Yusuf Geylani[1]

[1] internal medicine department, Bitlis State Hospital, Turkey

Background

We aimed to examine how the physical function is affected in individuals with BD.

Methods

Patients diagnosed with BD and healthy individuals were included in this study. Activity classification was made based on the Behçet's Disease Instant Activity Form (BHAAF) score: no activity (BHAAF=0), mild activity (BHAAF 1–2), moderate activity (BHAAF 3–5), high activity (BHAAF 6–12). Subjects in both groups filled out a questionnaire containing questions about demographic characteristics and SF-36's Physical Function and Physical Role subdomains.

Results

There was no significant difference between the groups in terms of age and gender.82 patients with BD (mean age: 42.12+/- 9.48 years) and 36 healthy subjects (40.38+/- 9.52 years) participated in this study. Body mass index values were similar in both groups. When the groups are compared; Sit to Stand test, Timed Up and Go test, Physical Function and Physical Role subdomain scores of SF-36 were found to be statistically lower in patients with BD than healthy subjects (Respectively; t= -3.14, p= 0.00024; t = -3.39, p= 0.00018; t= 5.87, p< 0.0001; t=4.88, p< 0.0001). There were 36 patients with BHAAF=0, 22 patients with BHAAF 1–2, 14 patients with BHAAF 3–5, and 10 patients with BHAAF 6–12. As disease activity increased, there was a high negative correlation in Sit to Stand test, Timed Up and Go test scores, and a highly positive correlation in SF-36's Physical Function and Physical Role subdomain scores (r=-0.603 p<0.001; r=-0.648). , p < 0.001; r=0.678, p<0.001; r=0.634, p<0.001).

Conclusions

According to the results obtained, it was determined that there was a significant decrease in physical capacity in patients with BD compared to healthy individuals. In addition, as the disease activity increases, the decrease in physical capacity increases.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-064

COVID-19 vaccination related small vessel vasculitis with multi-organ involvement

Yunkyung Kim[1], Geun-Tae Kim[1]

[1] Division of Rheumatology, Department of Internal Medicine, Kosin University College of Medicine, Republic of Korea

Description

Since its first outbreak in 2019, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2, has been ongoing, and the pandemic is not over yet. Vaccines developed against COVID-19 have been approved and widely used since 2020; however, vaccine safety concerns need to be addressed. Autoimmune symptoms have been reported as a side effect of many COVID-19 vaccines. In particular, several cases of COVID-19 vaccine-induced vasculitis have recently been reported. We report the case of a 77-year-old woman who developed small-vessel vasculitis with multi-organ involvement after receiving the Pfizer-BioNTech COVID-19 vaccine. She experienced general weakness, dyspnea and acute renal injury after vaccination. It was diagnosed with conjunctivitis, otitis media, livedo reticularis, acute interstitial pneumonia and pauci-immune crescentic glomerulonephritis suggestive multi-organ involved small vessel vasculitis (Fig 1).

Conclusions

We believe that this case, with its radiological and histological findings, will help in the management of vaccine-induced vasculitis in the future.

Figure & Table

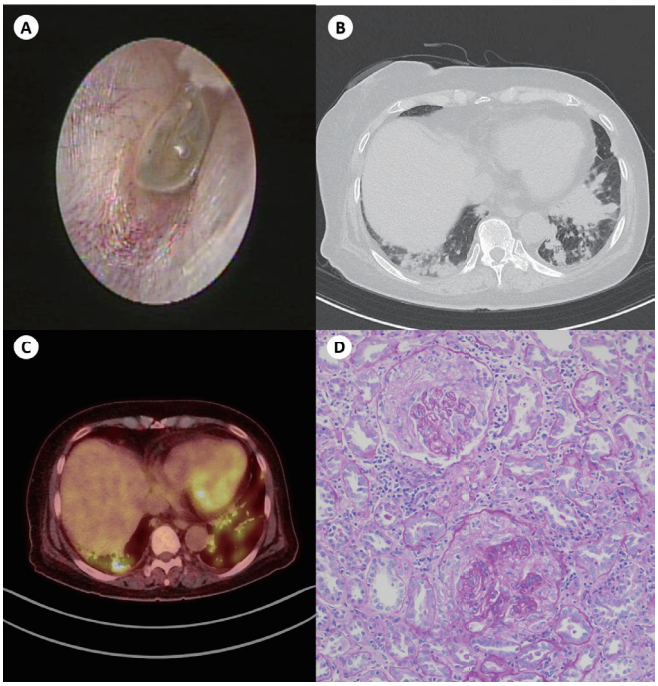


Figure. A. tympanogram of left ear B. CT image of chest C. image of PET-CT D. microscopy of glomerulus

Keywords

COVID-19 vaccine, small vessel vasculitis, multiorgan involvement

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KCR 2022
May 19(Thu) - 21(Sat), 2022

P-065

BVAS version 3 and BVAS/GPA

Jangwoo Ha[1], Sung Soo Ahn[1], Yong-Beom Park[1,2], Sang-Won Lee[1,2]

[1] Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea
[2] Institute for Immunology and Immunological Diseases, Yonsei University College of Medicine, Republic of Korea

Background

Birmingham vasculitis activity score (BVAS) version 3 (BVAS 3.0) and BVAS/Granulomatosis with polyangiitis (BVAS/GPA) are used as indicators of disease activity in anti-neutrophil cytoplasmic antibody-associated vasculitis. We evaluated the association between these indices and the significance in patients with GPA and microscopic polyangiitis (GPA/MPA).

Methods

We retrospectively reviewed the records of 203 patients with GPA/MPA in our hospital. The correlation between BVAS 3.0 and BVAS/GPA with the five-factor score (FFS) and laboratory data was investigated. The episodes of all-cause mortality, end-stage renal disease, and disease relapse were counted as adverse clinical outcomes. Multivariate Cox hazard analyses were performed to assess the relationships between both indices and patient outcomes.

Results

Sixty-five (32.0%) and 138 (68.0%) patients with GPA and MPA were included. The median BVAS 3.0 was significantly higher in patients with MPA than in those with GPA (13.0 vs. 11.0, p=0.015), whereas BVAS/GPA was higher in patients with GPA (4.0 vs. 3.0, p=0.001). BVAS 3.0 and BVAS/GPA correlated significantly (r=0.670, p<0.001); both BVAS 3.0 and BVAS/GPA were shown to be associated with the outcomes investigated in separate Cox models. However, the correlation between BVAS 3.0 and BVAS/GPA was especially higher in a subgroup of patients with MPA than in those with GPA (MPA: r=0.817, p<0.001 vs. GPA: r=0.570, p<0.001) and with renal involvement (r=0.676, p<0.001).

Conclusions

Although both BVAS 3.0 and BVAS/GPA significantly correlated and predicted outcomes well in those with GPA/MPA, a discord was observed based on disease subtypes and organ involvement.

Figure & Table

	BVAS version 3	BVAS/GPA	FFS	WBC count	Platelet count	ESR	CRP
BVAS version 3	n/a						
BVAS/GPA	0.670 (<0.001)	n/a					
FFS	0.416 (<0.001)	0.317 (<0.001)	n/a				
WBC count	0.182 (0.009)	0.248 (<0.001)	0.168 (0.017)	n/a			
Platelet count	0.062 (0.378)	0.138 (0.049)	0.031 (0.658)	0.479 (<0.001)	n/a		
ESR	0.158 (0.024)	0.129 (0.067)	0.144 (0.040)	0.287 (<0.001)	0.503 (<0.001)	n/a	
CRP	0.263 (<0.001)	0.283 (<0.001)	0.220 (0.002)	0.426 (<0.001)	0.450 (<0.001)	0.570 (<0.001)	n/a

Table. Correlation analysis between BVAS version 3, BVAS/GPA, FFS, and laboratory data
Data are presented as correlation coefficient and p-value.
BVAS: Birmingham vasculitis activity score; GPA: Granulomatosis with polyangiitis; FFS: Five-factor score; WBC: White blood cell; ESR: Erythrocyte
sedimentation rate; CRP: C-reactive protein.

Keywords

antineutrophil cytoplasmic antibody associated vasculitis, Birmingham vasculitis activity score version 3, Birmingham vasculitis activity score/Granulomatosis with polyangiitis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-066

Application of the 2022 new criteria for microscopic polyangiitis to patients with previously diagnosed microscopic polyangiitis

Jung Yoon Pyo[1], Sung Soo Ahn[1], Jason Jungsik Song[1], Yong-Beom Park[1], Sang-Won Lee[1]

[1] Internal Medicine, Yonsei University College of Medicine, Republic of Korea

Background

In 2022, the ACR and European Alliance of Associations for Rheumatology proposed new classification criteria for AAV (the 2022 ACR/EULAR criteria). This study applied the 2022 ACR/EULAR criteria to Korean patients with previously diagnosed MPA based on the old criteria to investigate the number of patients who could be reclassified as having MPA.

Methods

One-hundred seventeen patients with MPA, who met the 2007 EMA algorithm and the 2012 CHCC definitions, were included in this study. They were reclassified based on the 2022 ACR/EULAR classification criteria.

Results

Of the 117 patients, 113 patients (96.6%) were reclassified as having MPA. Of the 117 patients included in the study, there were three MPO-ANCA negative patients, all of which were not classified as MPA by the 2022 ACR/EULAR criteria. Furthermore, there were four patients having both MPO-ANCA and PR3-ANCA, three of them met both MPA and GPA criteria based on the 2022 ACR/EULAR criteria.

Conclusions

The concordance rate between the 2022 ACR/EULAR criteria and both the 2007 EMA algorithm and the 2012 CHCC definitions was 96.6%. The 2022 ACR/EULAR criteria have several issues, in particular, those regarding a too high assigned score to MPO-ANCA and ignorance of MPA-specific histopathologic findings. Therefore, we suggest that the 2007 EMA algorithm and the 2012 CHCC definitions be applied as supplementary classification criteria in these difficult cases.

Figure & Table

Variables		Values
At the time of enrolment in the cohort	Score	
Items for the 2022 ACR/EULAR criteria for MPA and assigned scores to each item (N (%))		
Clinical criteria		
Nasal involvement (discharge, ulcers, crusting, congestion, septal defect/perforation)	-3	1 (0.9)
Laboratory, imaging and biopsy criteria		
MPO-ANCA (or P-ANCA) positivity	+6	114 (97.4)
Fibrosis or interstitial lung disease on chest imaging	+3	58 (49.6)
Pauci-immune glomerulonephritis on biopsy	+3	61 (52.1)
PR3-ANCA (or C-ANCA) positivity	-1	4 (3.4)
Serum eosinophil count ≥ 1000/μL	-4	5 (4.3)
Total score for 6 items above		9.0 (3.0)
Patients with total score ≥ 5 (N (%))		113 (96.6)

Table. Frequencies of each criterion of the 2022 ACR/EULAR criteria for MPA fulfilled by patients with previously diagnosed MPA (N=117)
Values are expressed as number (percentage).
ACR: American College of Rheumatology; EULAR: European Alliance of Associations for Rheumatology; MPA: microscopic polyangiitis; MPO: myeloperoxidase; P: perinuclear; PR3: proteinase 3; C: cytoplasmic.

Keywords

Microscopic polyangiitis, 2022 ACR/EULAR classification criteria

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-067

Effect of the number of metabolic syndrome components on all-cause mortality in patients with antineutrophil cytoplasmic antibody-associated vasculitis

PIL GYU Park[1]

[1] Department of Rheumatology, Severance Hospital, Republic of Korea

Background

AAV and metabolic syndrome both are systemic inflammatory disease that can increase the incidence of all-cause mortality. Since inflammation is associated with obesity, insulin resistance, cardiovascular risks, and MetS, it can be hypothesised that patients with AAV may have an increased incidence of MetS. We recently demonstrated that the prevalence of MetS was significantly higher in Korean patients with AAV than in healthy controls. in this study, we investigated the effect of MetS severity, assessed according to the number of MetS components, on all-cause mortality in AAV patients diagnosed with MetS at the time of AAV diagnosis.

Methods

This study included 186 patients with AAV and age, sex, smoking history, and body mass index (BMI), MetS components, and MetS diagnosis were also obtained. MetS was diagnosed when three or more of the following five MetS components for Asians were present: increased waist circumference, high blood pressure, hypertriglyceridaemia, low level of high-density lipoprotein, and impaired fasting glucose or T2DM.

Results

Seven patients (3.8%) had all five MetS components, 30 (16.1%) had four components, 56 (30.1%) had three components, 26 (14.0%) had one component, and 11 (5.9%) had no MetS component. There were also no significant differences in cumulative survival rates during the follow-up among AAV patients with zero to five MetS components at baseline. Among 93 of AAV patient whom were diagnosed with MetS, as the number of MetS components increased, the cumulative patient survival rate significantly decreased. Moreover, AAV patients with MetS who had all five MetS components were approximately 62 times more susceptible to all-cause mortality than those who had only three components.

Conclusions

The presence of many MetS components at the initial diagnosis of AAV is an independent and significant predictor of all-cause mortality in AAV patients with MetS. Therefore, the presence or absence of MetS should be confirmed at diagnosis.

Figure & Table

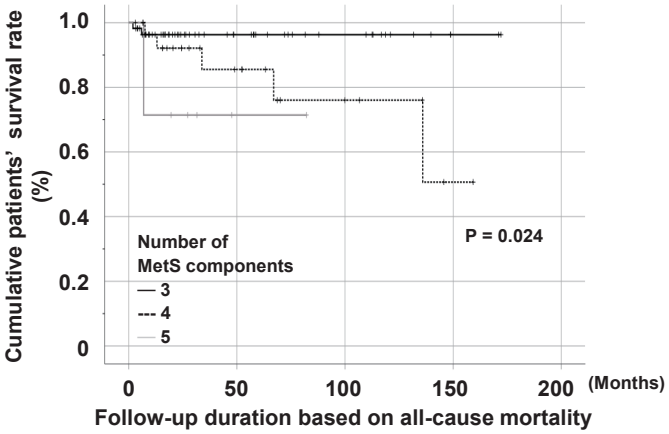

Figure. Comparison of cumulative survival rates in AAV patients with MetS

Keywords

antineutrophil cytoplasmic antibody, vasculitis, metabolic syndrome

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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KCR 2022
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P-068

Aortic involvement as a rare complication of granulomatosis with polyangiitis: a case report

Su Jin Choi[1], Doo Ho Lim1, Seung Won Choi[1]

[1] Rheumatology, Ulsan University Hospital, University of Ulsan College of Medicine, Republic of Korea

Description

Granulomatosis with polyangiitis (GPA) affects small and medium-sized vessels and rarely involves the aorta. We report a case of a 50-year-old man who presented an aortic involvement as the initial presentation of GPA along with the involvement of the upper and lower respiratory tract. He visited our hospital with pain and morning stiffness in the bilateral shoulder and hip girdle for a year. He also complained of weight loss and mild lower abdominal pain. Computed tomography (CT) scan demonstrated pulmonary nodules in both lower lobes and mildly dilated abdominal aorta with mural thrombosis. Polymyalgia rheumatica was suspected based on clinical symptoms and elevated inflammatory markers, and symptoms improved rapidly after empirical glucocorticoid treatment. However, pulmonary nodules increased with cavity formation three months later. Transbronchial lung biopsy revealed chronic lymphocytic inflammation with necrosis. The tissue polymerase chain reaction test for tuberculosis was negative, but the interferon-gamma release assays were positive. The test for anti-proteinase 3 (PR3) antibodies was positive with titers of 4.4 IU/mL. The patient was treated with anti-tuberculosis drugs over a month. However, follow-up CT scans showed an increase in the size of pulmonary nodules and an abdominal aortic aneurysm. Periaortic soft tissue thickening involving aortic arch and nasal septal perforation were also newly identified. GPA was diagnosed by video-assisted thoracoscopic surgery (VATS) wedge biopsy. He was started on high-dose glucocorticoid treatment while excluding infection conditions by blood culture, and his clinical and radiological findings improved three weeks later. Since then, improvement has been maintained with cyclophosphamide and glucocorticoid treatment.

Conclusions

This case suggests that aortic involvement can occur as an unusual complication of GPA.

Keywords

Granulomatosis with polyangiitis, Aortic aneurysm, Periaortitis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-069

ANCA sero-positivity and AAV occurrence after SARS-CoV-2 infection

Eunju Lee[1,2], Wooyong Jeong[3], Jung Yoon Pyo[1], Jason Jungsik Song[1,4], Yong-Beom Park[1,4], Su Jin Jeong[5], Sang-Won Lee[1,4]

[1] Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Dongguk University Ilsan Hospital, Republic of Korea
[3] Division of Infectious Diseases, Department of Internal Medicine, National Health Insurance Service Ilsan Hospital, Republic of Korea
[4] Institute for Immunology and Immunological Diseases, Yonsei University College of Medicine, Republic of Korea
[5] Division of Infectious Diseases, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea

Background

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been linked to the onset or worsening of autoimmune diseases (1). Previously reported cases of new-onset antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) following SARS-CoV-2 infection raised the possibility of SARS-CoV-2 infection as a trigger for AAV, by provoking the formation of autoantibodies (2, 3).

Methods

We investigated the prevalence of proteinase 3 (PR3)-ANCA and myeloperoxidase (MPO)-ANCA in 187 patients with polymerase chain reaction-confirmed SARS-CoV-2 infection who were admitted to Yonsei University Severance Hospital from June 2020 to October 2021. Blood samples were collected between 14 and 30 days after the onset of the first symptoms. PR3- and MPO-ANCA levels were measured using enzyme-linked immunosorbent assay (ELISA) kits (Euroimmun, Lübeck, Germany) according to the manufacturer's protocol. Electronic medical records of the patients were retrospectively reviewed.

Results

Overall, 18.5% of the tested patients were confirmed positive for ANCAs, with PR3 and MPO accounting for 42.4% and 66.7%, respectively. Of 33 patients who were positive for ANCAs, 31 patients were classified as GPA (12 patients) or MPA (20 patients) based on 2022 ACR/EULAR classification criteria. One patient satisfied both criteria for GPA and MPA, and no patient was classified as EGPA. There was no significant association between ANCA status and mechanical ventilation (OR: 1.11, 95% CI: 0.50–2.48, P = 0.837) or death (OR: 2.18, 95% CI: 0.53–8.14, P = 0.387).

Conclusions

A high prevalence of ANCAs among hospitalized patients with SARS-CoV-2 infection was observed. Although the ANCA-positivity is not significantly associated with the prognosis, most of the sero-positive patients were classified as AAV according to 2022 ACR/EULAR classification criteria. Long-term follow-up may be needed for the development of clinical manifestations and the levels of antibodies.

Figure & Table

Variables	GPA	MPA	EGPA	Values
At the time of first symptom				
Clinical criteria				
Nasal involvement	+3	-3		0
Cartilaginous involvement	+2			0
Conductive or sensorineural hearing loss	+1			0
Obstructive airway disease			+3	3 (9.1)
Nasal polyp			+3	0
Mononeuritis multiplex			+1	0
Laboratory criteria				
PR3-ANCA positivity	+5	-1	-3	14 (42.4)
MPO-ANCA positivity	-1	+6		22 (66.7)
Serum eosinophil ≥ 1000/μL	-4	-4	+5	2 (6.1)
Hematuria ≥ 10 RBC/HPF			-1	20 (60.6)
Biopsy criteria				
Granuloma, granulomatous inflammation, or giant cells	+2			N/A
Pauci-immune glomerulonephritis	+1	+3		N/A
Extravascular eosinophilic-predominant inflammation			+2	N/A
Imaging criteria				
Pulmonary nodules, mass, or cavitation on chest imaging	+2			3 (9.1)
Fibrosis or ILD on chest imaging		+3		4 (12.1)
Nasal/paranasal sinusitis or mastoiditis on imaging	+1			6 (18.2)
Number of patients with total score ≥ 5 for GPA/MPA or ≥ 6 for EGPA	12	20	0	Total 31

Values are expressed as number (percentage).

ACR: American College of Rheumatology; EULAR: European Alliance of Associations for Rheumatology; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis; SARS-CoV-2: severe acute respiratory syndrome coronavirus-2; ANCA: Antineutrophil cytoplasmic antibody; PR3: proteinase 3; MPO: myeloperoxidase; ILD: interstitial lung disease

Table. Application of 2022 ACR/EULAR criteria for GPA, MPA, or EGPA to patients with SARS-CoV-2 infection and ANCA positivity

Keywords

Antineutrophil cytoplasmic antibody-associated vasculitis, SARS-CoV-2, Sero-positivity

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-070

New-onset IgA vasculitis in adult patients following SARS-CoV-2 vaccines

Yunjung Choi[1], Wan-Hee Yoo[1]

[1] Internal medicine, Jeonbuk National University Hospital, Republic of Korea

Description

Recently, the occurrence of autoimmune disease after the COVID-19 vaccination has been reported. Among the autoimmune phenomena following vaccination, we herein report the three cases of new-onset IgA vasculitis.

Our first patient presented 10days after second dose of the AstraZeneca vaccine with purpuric rash on extremities. He developed the abdominal pain and melena several days after and visited our emergency room. The enteritis and mesenteric panniculitis were shown in his abdominal CT and gross hematuria and urine protein-creatinine ratio (UPCR) 3902mg/g was detected. He was started on steroid of 1mg/kg/day and resolved with the therapy. Our second patient complained with abdominal pain, purpura on both lower leg and arthralgia developed 1 day after receiving the first dose of Moderna vaccine. He showed gross hematuria, proteinuria, and elevated level of serum creatinine. He was administrated with steroid of 1mg/kg/day. A week after discharge, he presented melena due to small bowel bleeding with distal ileum wall thickening. The re-escalation dose of steroid was prescribed to the patient, he showed clinical improvement and discharged. Our third patient presented 14 days after second dose of the AstraZeneca vaccine with purpuric rash, myalgia, and melena. The overt hematuria and proteinuria were noted, and his abdominal CT showed enteritis. The empirical high dose steroid therapy was started. However, during hospitalization, he presented massive hematochezia and received small bowel resection from proximal to mid ileum. The histology of resected bowel showed vasculitis. He is being prescribed immunosuppressive agent and low dose steroid on regular-basis follow-up.

Conclusions

Although it remains unclear how the COVID vaccination leads the IgA vasculitis development, but our cases suggest that the COVID vaccination is responsible for the occurrence of IgA vasculitis. Therefore, further researches are warranted for the postvaccination monitoring setting regarding development of autoimmune phenomena such as IgA vasculitis after vaccination.

Figure & Table

Patient Characteristics	Patient 1	Patient 2	Patent 3
Age	60	63	70
Sex	M	M	M
Type of vaccination	ChAdOx1 (Oxford/AstraZeneca)	mRNA-1273 (Moderna)	ChAdOx1 (Oxford/AstraZeneca)
Time to present symptoms	10 days	1 days	14 days
Baseline Cr level (mg/dL)	0.76	0.67	0.59
Peak Cr level after COVID-19 vaccine (mg/dL)	0.98	1.29	3.34
Gross hematuria before COVID-19 vaccine	0-2/HPF	0-2/HPF	0-2/HPF
Gross hematuria after COVID-19 vaccine	21-50/HPF	21-50/HPF	21-50/HPF
Proteinuria before COVID-19 vaccine	Neg	+	+
Peak UPCR after COVID-19 vaccine (mg/g)	3902	2214	15764
UPCR 2 months after COVID-19 vaccine (mg/g)	584	454	6618
Other clinical symptoms	Purpura, Abdominal pain, Melena	Purpura, Abdominal pain, Melena, Arthralgia	Purpura, Abdominal pain, Melena, Arthralgia, Pulmonary thromboembolism
Current treatment	PD	PD	AZA, PD

Table. Characteristics of new-onset IgA vasculitis after COVID-19 vaccination

Keywords

IgA vasculitis, COVID-19, Vaccination

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-071

A case of microscopic polyangiitis with periaortitis treated with cyclophosphamide

Seoung Wan Nam[1]

[1] Rheumatology, Wonju Severance Christian Hospital, Republic of Korea

Description

Microscopic polyangiitis (MPA) is a rare autoimmune disease that involves small to medium sized vessels. The formation of a large vessel lesion in patients with MPA has been scarcely reported, and it can cause confusion in the diagnosis.

A 73-year-old woman presented with high fever and myalgia that started one month prior. She also complained of headache, dizziness, and exertional dyspnea. Initial blood test revealed increased levels of inflammatory markers. No evidence of the infection was noted despite various efforts including culture tests and imaging studies. However, CT scan showed features of periaortitis with dense aortic wall thickening in descending aorta (Figure 1-A). 18F-FDG PET/CT showed increased FDG metabolism of the aortic wall. Additional laboratory test results showed positive myeloperoxidase-ANCA. During the work-up period, her general condition deteriorated and showed progressive proteinuria and hematuria with dysmorphic cells. Accordingly, we performed renal biopsy that showed pauci-immune crescentic glomerulonephritis. Final diagnosis of MPA was made and we started cyclophosphamide pulse therapy with high dose glucocorticoid. Afterwards, she gradually showed improvements in both clinical symptoms and laboratory findings. Her proteinuria and hematuria disappeared in 3 months. Follow-up CT scan after total 8 cycles of cyclophosphamide therapy for 5-month duration showed prominently improved periaortitis with minimal periaortic soft tissue densities (Figure 1-B). Thereafter, the patient was well-maintained with azathioprine and low dose glucocorticoid which were all discontinued in 3 years.

Conclusions

Here, we present an unusual manifestation of MPA that presented with periaortitis, which was successfully treated with cyclophosphamide therapy.

Figure & Table

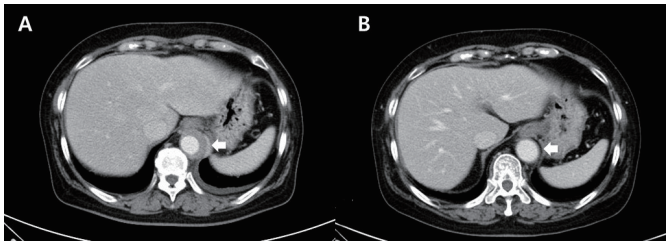

Figure. Postcontrast CT scans before and after cyclophosphamide pulse therapies

Keywords

Microscopic Polyangiitis, Periaortitis, Cyclophosphamide

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Journal of Rheumatic Diseases
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P-072

Churg-strauss syndrome presenting as acute abdomen- A case report

Subbarayudu Boda[1]

[1] General medicine, GITAM Institute of Medical Sciences and Research (GIMSR), India

Description

A 40-year-old female came to ER with pain abdomen, vomiting and loose stools for 3 days. Her past history consisted of mild intermittent asthma and hypertension. The patient had symmetric polyarthritis 6 months ago for which she was prescribed steroids. Later patient developed paranesthesia in both upper and lower limbs, right foot drop and progressive distal weakness of both upper and lower limbs. On examination, she had pallor, desquamating palpable purpuric rash over both lower limbs and extensive tinea corporis. There was tenderness on palpation in the right hypochondrium. Neurological examination revealed distal sensorimotor impairment in both upper and lower limbs without any cranial nerve involvement. Initial laboratory evaluation revealed hemoglobin, 13 g/ dL; white blood cell count, 42,300/mm3 (neutrophils 78%, lymphocytes 10%, eosinophils 10%); platelet count, 476 × 109 /L; Peripheral smear showed neutrophilic leukocytosis with shift to left. ESR- 61mm 1st hour, CRP – 48 mg/L(<5); Serum C3 was 0.3 g/L (0.9–1.8 g/L), serum C4, 0.4 g/L (0.1–0.4 g/L). The patient tested negative for human immunodeficiency virus, HbsAg and hepatitis C virus RNA. Random plasma glucose, 77 mg/dl; Serum creatinine, 0.6 mg/dl. MRCP showed cholelithiasis with prominent gall bladder walls and moderate pneumoperitoneum. The patient was operated for hollow viscous perforation. Intra-operative findings include single ileal perforation of 5mm size on the mesenteric border (2.5cm from IC junction), and multiple ulcers present all over the ileum. Histopathological examination showed vascular rich fibro collagenous tissue with perivascular eosinophilic infiltrate. p-ANCA ,c-ANCA and ANA were negative. RA Factor,494 U/L (<12 U/L); Anti-CCP was negative. We made a final diagnosis of Churg-Strauss syndrome. During follow-up, the patient was treated with cyclophosphamide pulse therapy, low dose steroid and cotrimoxazole prophylaxis.

Conclusions

To conclude, a high degree of suspicion is required for diagnosis of Churg-Strauss syndrome with GI involvement.

Figure & Table

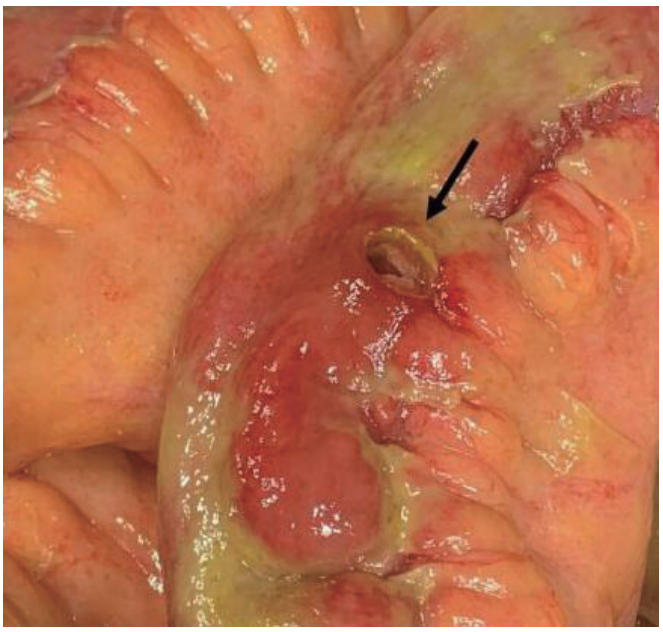

Figure. Ileal perforation in Churg-Strauss syndrome

Keywords

vasculitis, Churg-Strauss, ileal perforation

E-poster Presentation

Crystal induced arthropathies

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Seoul Dragon City, Seoul, Korea

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-073

Identification of tofuses and diagnosis of gout disease with dual-energy CT

Iraklı Tortladze[1], Giorgi Apkhazava[2], Grigol Nemsadze[1]

[1] Radiology Department, TSSU First University Clinic, Georgia
[2] Radiology Department, Tbilisi City Medical, Georgia

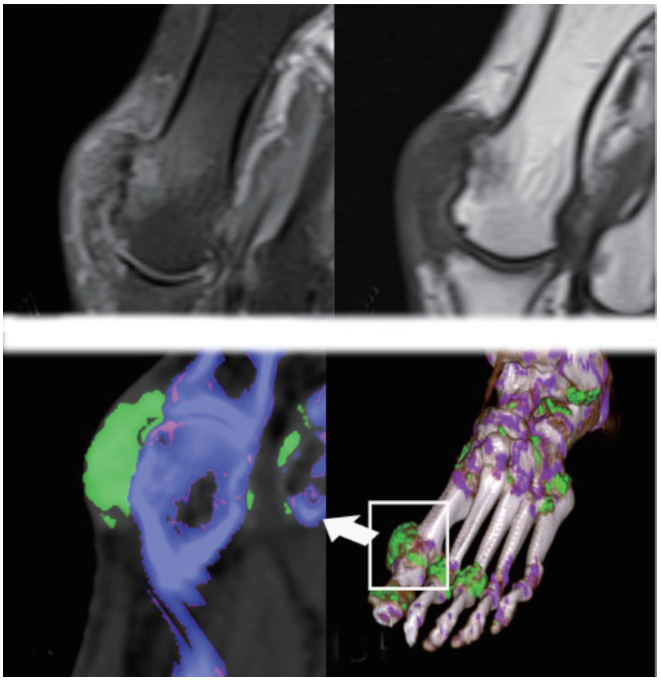
Description

A 62-year-old male patient was admitted to the emergency room with severe foot pain. Clinical examination revealed redness and swelling on the first metatarsophalangeal joint. It was seen that the patient had recurrent pain in the patient's history. The patient had old magnetic resonance(MR) imaging examination for the foot. MR images showed lesions and degenerative changes in the bone structures forming the joint(Figure 1). It was seen that the level of uric acid in the patient's laboratory tests was high. Dual-energy computed tomography(DECT) was performed in the emergency department because of the suspicion of gout disease. Multiple monosodium urate deposits (tofus) were observed around the foot in DECT(Figure 1).

Conclusions

Gout is characterized clinically by acute onset of inflammatory oligo/mono arthritis and is generally difficult to distinguish from other inflammatory arthritides (rheumatoid arthritis, septic arthritis, psoriasis, reactive arthritis etc.) without confirmation by synovial fluid analysi. Various radiological techniques can be used for diagnosis (radiography, ultrasound, computed tomography(CT), and magnetic resonance imaging). However, these methods are not specific enough to facilitate the diagnosis of gout disease. DECT is a very important technique in the noninvasive assessment of gout. It is the only technique of imaging that enables direct visualization of monosodium urate deposition. DECT has therefore emerged as a leading tool for clinicians to reliably assess and diagnose acute or early-stage gout in a noninvasive manner. Moreover, DECT can help clinicians distinguish gouty tophi from a mass or infection.

Figure & Table



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Journal of Rheumatic Diseases
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P-074

Spondylodiscitis and paravertebral abscess associated with calcium pyrophosphate dihydrate deposition disease

Burak Sarılar[1]

[1] Department of Radiology, Pamukkale University, Turkey

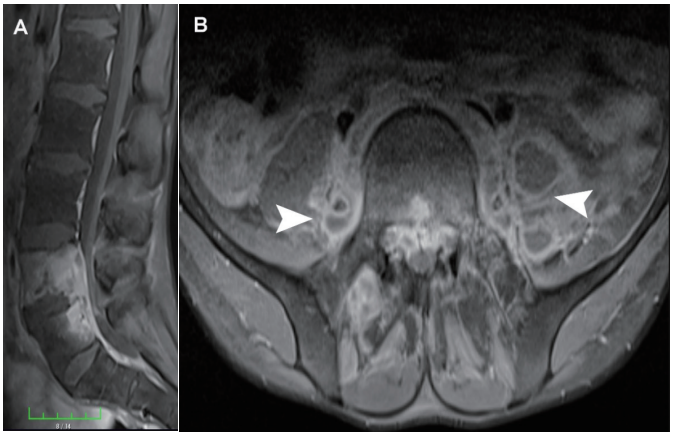
Description

A 75-year-old male patient was admitted to our clinic with back pain and limitation of movement. The patient had a synovial examination one year ago with the suspicion of acute calcium pyrophosphate (CPP) crystal arthritis. Synovial calcifications were detected by synovial histological examination and radiography evaluation. Therefore, the patient was under colchicine treatment for one year. Lumbar magnetic resonance imaging was performed for pain and limitation of movement. There were areas of spondylodiscitis and paravertebral abscess accompanied by marked contrast enhancement in the lumbar region(Figure 1). Laboratory examination revealed a high CRP level at 90 mg/L. demonstrated that Staphylococcus aureus infections, antibiotic treatment with Daptomycin was prescribed for three months and resulted in the progressive improvement of the pain and inflammatory biological tests.

Conclusions

The differential diagnosis of spondylodiscitis should be kept in mind if back pain develops in the presence of previously known peripheral CPPD disease in elderly patients.

Figure & Table



JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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P-075

Urate-lowering efficacy and renal safety of febuxostat in patients with advanced chronic kidney disease not yet on dialysis: A meta-analysis of observational studies

Changnam Son[1], Hye-Jin Jeong[1], Woo Yeong Park[2], Sang-Hyon Kim[1]

[1] Division of Rheumatology, Department of Internal Medicine, Keimyung University School of Medicine, Republic of Korea
[2] Division of Nephrology, Department of Internal Medicine, Keimyung University School of Medicine, Republic of Korea

Background

The efficacy and safety of febuxostat in patients with stage 4-5 chronic kidney disease (CKD) remain unclear, although it is commonly used in clinical practice. Clinical trials are lacking due to ethical issues related to the enrollment of advanced CKD patients. We aimed to evaluate the efficacy and safety of febuxostat in patients with stage 4-5 CKD not yet on dialysis through a meta-analysis of observational studies.

Methods

We performed a systematic search in PubMed, Ovid MEDLINE, Embase, and the Cochrane Library to find observational studies on cohorts of advanced CKD patients starting febuxostat. Articles describing changes from baseline in serum urate levels and renal function assessed by estimated the glomerular filtration rate (eGFR) were included. The articles were screened by two independent reviewers (YP and HJ). We performed a meta-analysis using a random-effects model and used R software with the 'meta' and 'Rcpp' packages for statistical analyses.

Results

Among 148 retrieved studies, five relevant observational studies involving 327 patients were included in the meta-analysis. Daily febuxostat doses of 10-120 mg were administered treatment periods of 3-12 months. The urate-lowering effect after febuxostat use was statistically significant (weighted mean difference, -1.85; 95% CI, -2.04 to -1.67; I^2; 0%, Figure 1A). Three studies involving 145 patients included eGFR assessments. Renal function as assessed by eGFR did not decrease after febuxostat use (weighted mean difference, 0.11; 95% CI, -0.25 to 0.47; I^2; 45%, Figure 1B).

Conclusions

Febuxostat has acceptable urate-lowering efficacy and renal safety in hyperuricemia patients with stage 4-5 CKD who are not yet on dialysis.

Figure & Table

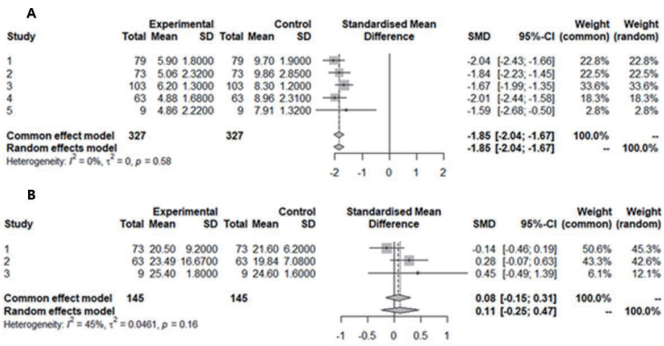

Figure. Meta-analyses of A) serum urate levels and B) eGFRs in hyperuricemia patients with stage 4-5 chronic kidney disease

Keywords

febuxostat, chronic kidney disease, meta-analysis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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P-076

A rare coexistence of quadriceps tendon calcification and patellar tendon calcification

Muhammed Eyyüp Çelik[1], Mehmet Selim Kan[1], Elshad İsmailov[2]

[1] medical faculty, Atatürk University, Turkey
[2] Department of Radiology, Ataturk University, Turkey

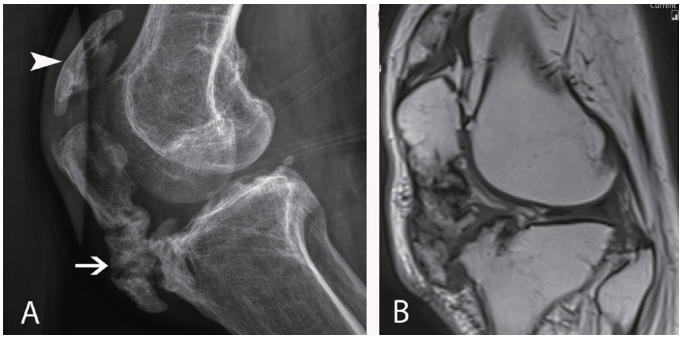
Description

A 41-year-old male patient presented with a complaint of movement restriction in his right knee. On the right knee x-ray, calcification of the patellar tendon was observed(Fig 1A, arrow). In addition, calcification was present in the right quadriceps femoris muscle tendon (Fig 1A, arrowhead). There was a significant irregularity in the patellar tendon and quadriceps femoris muscle tendon on T1-weighted magnetic resonance imaging(Fig 1B). Calcium pyrophosphate deposition in tendons was confirmed histopathologically.

Conclusions

Calcific tendinopathy (CT) calcium deposits in the substance of the tendon. CT is particularly common in the supraspinatus tendon and patellar tendon and Achilles tendon. The coexistence of quadratus femoris muscle-tendon calcification and patellar tendon calcification is very rare.

Figure & Table



Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022

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P-077

Diagnosis and treatment of gout patients at emergency room

Mi Ryoung Seo[1], Jina Yeo[1], Hyo-Jin Choi[1], Han Joo Baek[1]

[1] Division of Rheumatology, Department of IM, Gil Medical Center, Gachon University College of Medicine, Republic of Korea

Background

Gout is the most common inflammatory arthritis and is gradually increasing in Korea. Emergency room (ER) visits of patients with gout are also increasing. However, it was reported that patients with gout have not been properly managed in ER. We investigated the diagnosis and treatment of gout patients who visited the ER.

Methods

This was a retrospective study on patients with gout who visited the ER of a single tertiary center between January 2012 and December 2017. The data including demographics, clinical characteristics, diagnosis and treatment were collected.

Results

A total of 282 patients were included in this study. The number of gout patients visited the ER increased annually. Age at visit the ER was 45 years (IQR 36-62) and 90% were men. The affected areas were foot (74%) and knee (19%). Only 18% of patients had symptoms on first metatarsophalangeal joint. 39% of patients had their first gout attack at the ER visit. Patients with performed of arthrocentesis for diagnosis of gout were 20%. The patients with presumed gout in the ER were 86%. Patients without presumed gout in the ER were older age, women or patients with symptom on midfoot. They were hospitalized more, and received more MRI, antibiotic therapy and surgery. In the ER, 3% of patients were referred to a rheumatologist. 9% of patients visited the rheumatology outpatient clinic after ER visit. 36% of the patients admitted after ER visit were hospitalized in rheumatology department. Patients admitted to the rheumatology department had shorter hospital days, less magnetic resonance imaging, and fewer antibiotic therapy and surgery than those admitted to other departments.

Conclusions

Early diagnosis of gout in the ER may reduce unnecessary hospitalization, examination and treatment for patients. There is a need to improve referral or follow-up to rheumatologists for proper management of gout patients visiting the ER.

Figure & Table

	Presumed gout (n=242)	No presumed gout (n=40)	$p^{\dagger}$
Age (years)	44 (35-59)	57 (43-75)	<0.01
Male gender	225 (92.6)	31 (77.5)	<0.01
Areas affected by gout			
1st MTP	46 (18.9)	3 (7.5)	0.11
Midfoot	21 (8.7)	8 (20.0)	0.03
Precipitating factors-alcohol	29 (11.9)	0	0.02
Similar symptom before ER visit	155 (64.6)	15 (38.5)	<0.01
Gout diagnosis history before ER visit	137 (56.2)	9 (22.5)	<0.01
Treatment at ER			
NSAIDs	210 (86.4)	21 (52.5)	<0.01
Colchicine	13 (5.3)	0	0.23
Antibiotics	38 (15.6)	23 (57.5)	<0.01
Consultation	46 (18.9)	22 (55.0)	<0.01
OS/IF/RH	38/3/8	19/2/1	
Admission	53 (21.8)	27 (67.5)	<0.01
OS/IF/RH	12/15/29	12/15/2	
Hospital days	7 (5-12)	10 (7-15)	0.48
Treatment –antibiotics	19 (35.8)	20 (74.1)	<0.01
surgery	13 (5.4)	10 (25.0)	<0.01
MRI	12 (4.9)	9 (22.5)	0.02

*The data are presented as % for categorical variables and the median (interquartile range) for continuous variables; †Comparisons performed with the χ^2 test or Fisher's exact test for categorical variables and the *t*-test for continuous variables, statistical significance was $p<0.05$.

ER emergency room, *1st MTP* first metatarsophalangeal, *NSAIDs* nonsteroidal anti-inflammatory drugs, *OS* orthopedic surgery, *IF* infection, *RH* rheumatology

Table. Comparison between patients with or without presumed gout in the ER*

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P-078

Genetic analysis for inflammasome genes polymorphisms in the gout susceptibility

Denise Clavijo-cornejo[1], Alberto Lopez-reyes[2], Esteban Cruz-arenas[3], Leonor Jacobo-albavera[4], Gabriela Fuentes-moreno[1], Adriana Francisco-balderas[5], Mayra Dominguez-perez[4], Janitzia Vazquez-mellado[6], Luis H Silveira[7], Carlos Pineda[1], Gabriela Martínez-nava[2], Marwin Gutierrez[1]

[1] Division of Musculoskeletal and Rheumatic Diseases, Instituto Nacional de Rehabilitación, Mexico
[2] Geroscіences Laboratory, Instituto Nacional de Rehabilitación, Mexico
[3] Hospital Epidemiological Surveillance Unit, Instituto Nacional de Rehabilitación, Mexico
[4] Laboratory of Genomics of Cardiovascular Diseases, Instituto Nacional de Medicina Genómica, Mexico
[5] Graduate Studies Department, Instituto Politécnico Nacional, Mexico
[6] Rheumatology Department, Hospital General de México, Mexico
[7] Rheumatology Department, Instituto Nacional de Cardiología Ignacio Chávez, Mexico

Background

Recent reports have demonstrated that polymorphisms within NLRP3 inflammasome signaling pathway are key factors in the risk to develop some joint inflammatory diseases (1). To date, there is still uncertain information about the presence of these genetic variants and their association with risk of gout. The aim is to determine the association between the single nucleotide polymorphisms (SNPs), within NLRP3 inflammasome genes, and the risk of developing gout.

Methods

We included 220 gout patients and 243 healthy subjects as control group. Clinical examination was performed and laboratory including glucose concentration, total cholesterol and triglycerides were obtained. The frequency and the allelic distribution of eight SNPs from seven different genes within the NLRP3 inflammasome signaling pathway were analyzed using the Step One Plus Real-Time PCR Systems. SNPs were selected by the criterion of minor allele frequency (MAF) (above 1 %), using the 1000 Genomes Project. Genetic variation data for all the SNPs were obtained from the HapMap project (http://www.hapmap.ncbi.nlm.nih.gov/) and the public National Center for Biotechnology Information dbSNP database (http://www.ncbi.nlm.nih.gov/snp). The SNPs did not to be in linkage disequilibrium . Ancestry was analyzed using ancestry informative markers differentiating mainly Amerindian, African, and European ancestries.

Results

The missense SNP rs45520937 in PPARGC1B, showed enhanced association with the risk of developing gout when it was analyzed using the dominant model, evidencing that gout patients carried the A/G-A/A genotype have an elevated risk compared to the control group [OR (95% CI) = 2.30 (1.09-4.86), p=0.030]. The adaptor molecule CD14 rs2569190 SNP could be associated with lower risk of gout under an additive model [OR (95 % CI)= 0.41 (0.16-1.05), p= 0.064]. No significant association were identified for the remaining SNPs.

Conclusions

Our findings suggest that genetic variant rs45520937 of PPARGC1B is significantly associated with the gout susceptibility.

Figure & Table

Gene	SNP	MAF		OR (95 % CI)	*p-value*
		Controls (n=243)	Gout (n=220)		
TLR4	rs2149356	28.7	31.8	0.68 (0.33-1.40)	0.295
CD14	rs2569190	48.7	45.9	0.53 (0.25-1.13)	0.101
				0.41 (0.16-1.05)	**0.064**[&]
NLRP3	rs3806268	41.9	39.0	0.70 (0.33-1.47)	0.346
NLRP3	rs10754558	16.3	15.6	0.56 (0.26-1.22)	0.147
CARD8	rs2043211	24.7	24.1	1.35 (0.67-2.71)	0.407
IL-1β	rs1143623	44.7	37.0	1.20 (0.57-2.48)	0.632
P2RX7	rs3751142	41.0	39.3	1.12 (0.48-2.61)	0.802
PPARGC1B	rs45520937	28.3	34.9	2.30 (1.09-4.86)	**0.030**

Associations with gout were adjusted for age, sex, BMI and ancestry. *p*-values were calculated by logistic regression, using dominant model and [&]additive model . MAF, minor allele frequency; OR, Odds ratio; CI, confidence interval.

Table. Genetic analysis of 8 inflammasome genes SNPs in the gout susceptibility.

Keywords

Gout, NALP3 inflammasome, polymorphism

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Depletion, activation, and stimulation of bone destruction of innate and innate-like immune cells in gout

Ki-Jeong Park[1], Young-Nan Cho[1], Hye-Mi Jin[1], Hye-Min Jeong[1], Sung-Eun Choi[1], Ji-Hyoun Kang[1], Dong-Jin Park[1], Tae-Jong Kim[1], Shin-Seok Lee[1], Yong-Wook Park[1]

[1] Department of Rheumatology, Chonnam National University Hospital, Republic of Korea

Background

Gout is considered an autoinflammatory disease in which innate immunity is a crucial stage of disease progression. Thus, examining the behavior of innate and innate-like immune cells such as mucosal-associated invariant T (MAIT) cells, natural killer T (NKT) cells, and natural killer (NK) cells is of importance in understanding the pathophysiology of gout.

Methods

Patients with gout (n=30) and healthy controls (n=20) were enrolled, and their peripheral blood and synovial fluid samples were collected. MAIT cells, NKT cells, NK cells, cytokines, CD69, programmed death-1 (PD-1), and lymphocyte-activation gene 3 (LAG-3) levels depending on the presence of MSU crystal were analyzed by flow cytometry. In vitro osteoclastogenesis experiments were performed using peripheral blood mononuclear cells in the presence of M-CSF and RANK ligand.

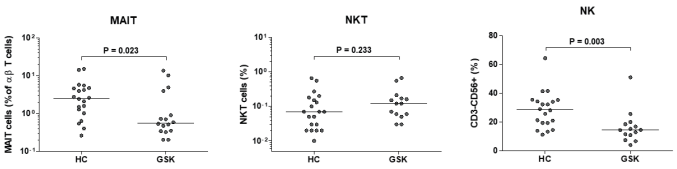
Results

The frequency analysis revealed that MAIT cells and NK cells decreased in the peripheral blood of gout patients, but NKT cells frequency showed no difference. For the circulating MAIT cells, activation markers such as CD69, PD-1, and LAG3 were increased in the gout patients. For the NK cells of gout patients, the expression of CD69 was more prominent in the synovial fluid, but their level in the synovial fluid was lower than that of peripheral blood. Of note, CD69 expression of both MAIT cells and NK cells in the PBMC were increased in the presence of MSU crystal, suggesting that their activation might be triggered by the MSU crystal deposition. Furthermore, activated MAIT cells secreted pro-resorptive cytokines (i.e. IL-6, IL-17, and TNF-a) that contribute to osteoclastogenesis.

Conclusions

Circulating MAIT cells and NK cells are numerically reduced but functionally activated in gout patients. Besides, activated MAIT cells and NK cells could potentially induce bone resorption and damage. These findings imply that these immune cells could be critical contributors in amplifying and controlling the inflammation in gout.

Figure & Table



Keywords

Gout, Innate immunity, Osteoclastogenesis

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P-080

Gout disease modification: Proposal for a definition

Jasvinder Singh[1]

[1] Medicine/Rheumatology, University of Alabama at Birmingham, USA

Background

Our objective was to identify a provisional set of domains for disease modification in gout with an aim to develop a provisional definition of disease modification in gout in the future.

Methods

We performed qualitative nominal group (NG) study with 19 gout experts (15 were authors/expert panel members of the 2012 and/or 2020 ACR gout guidelines, and/or 2015 ACR/EULAR gout classification criteria) about what constitutes “disease modification” in gout.

Results

Decrease in gout flares was rated #1 rank in all six NGs as indicative of disease modification in gout, followed by serum urate (SU) lowering, which was rated #1 rank in 1 of the 6 NGs (tied score with flares in one NG). Other components of gout disease modification were to improve quality of life/productivity; restore function; reduce/eliminate pain; reduce tophi burden; and joint preservation or resolution of joint damage. Potential addition components that were not ranked in the top 3 votes within each NG were: Decrease healthcare cost/utilization; cardiovascular/renal morbidity/mortality reduction; and stop urate crystals formation.

Conclusions

Our qualitative study provides a provisional set of domains for disease modification in gout. Future studies for the development of thresholds for disease modification domains are needed.

Keywords

gout, disease modification

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P-081

Predictors of increased vascular stiffness in gout patients

Wooseong Jeong[1], Jinseok Kim[1], Joon Hyouk Choi[2]

[1] Internal medicine, Division of Rheumatology, Jeju National University School of Medicine, Republic of Korea
[2] Internal medicine, Division of Cardiology, Jeju National University School of Medicine, Republic of Korea

Background

There are many reports that gout and hyperuricemia increase vascular stiffness. It is also well known that gout and hyperuricemia are significantly correlated with the occurrence of cardiovascular disease. Arterial stiffness is an independent prognostic indicator in coronary heart disease. Therefore, we conducted this study to find out what factors increase vascular stiffness in gout patients.

Methods

Augmentation index (AIx) was measured in gout patients without a history of uric acid lowering treatment who visited Jeju National University Hospital from March 2019 to March 2021.

Results

One hundred ninety nine patients participated in this study and AIx was measured. The average age of patients was 48.1±14.77 years, the mean gout duration was 4.63±6.3 years, the average of uric acid level was 8.9±1.1 mg/dL, the average of AIx was 21.2±9.4% which was higher than the reference value (16.9%). When comparing the high and low groups based on the AIx reference value, the high AIx group had a younger age (42.3 vs 59.8 years, p<0.001), had fewer DM (6.0 vs 19.7 %, p=0.003), had fewer HTN (16.5 vs 57.6 %, p<0.001), had fewer hyperlipidemia patients (16.5 vs 33.3%, p=0.007), had a higher CCr (111.6 vs 80.4mL/min, p<0.001), and had a higher uric acid level (9.0 vs 8.6 mg/dL, p=0.012). But there was no significant difference in disease duration, total cholesterol, BMI, tophi, between the two groups. Multivariate linear regression analysis showed that age (b=0.355, 95% CI 0.186-0.518), CCr (b=0.058, 95% CI 0.001-0.115, p=0.046), uric acid level (b=1.997, 95% CI 0.747-3.247) and BMI (0.730, 95% CI 0.355-1.104, p<0.001) are the predictor of increased vascular stiffness.

Conclusions

Based on the results of our study, there is a possibility that managing the uric acid level, CCr, and BMI can prevent the increase in vascular stiffness in gout patients.

Keywords

gout, vascular stiffness, predictor

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-082

Clinical features of Korean patients with calcium pyrophosphate crystal deposition disease: A retrospective multicenter study

Eun Hye Park[1], Ji Hyoun Kim[2], Sang Wan Chung[3], You-Jung Ha[4], Eun Ha Kang[4], Yun Jong Lee[4], Jong Jin Yoo[5]

[1] Division of Rheumatology, Department of Internal Medicine, Chung-Ang University College of Medicine, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Chungbuk National University Hospital, Republic of Korea
[3] Division of Rheumatology, Department of Internal Medicine, Kyung Hee University Medical Center, Republic of Korea
[4] Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Republic of Korea
[5] Division of Rheumatology, Department of Internal Medicine, Kangdong Sacred Heart Hospital, Republic of Korea

Background

To assess the clinical features of Korean patients with calcium pyrophosphate crystal deposition disease (CPPD).

Methods

Clinical data of 283 patients with CPPD from five university hospitals between January 2000 and September 2020 were reviewed. Patients with arthritis and the presence of CPP crystals in synovial fluid or tissue, typical x-ray chondrocalcinosis (CC), or CPP crystal deposits identified by ultrasonography or computed tomography were included; those with asymptomatic CPPD were excluded.

Results

The median age at diagnosis of CPPD was 82.0 (IQR 76.2-87.3) years, and 214 (75.6%) were female. Acute CPP crystal arthritis was the most common form of CPPD (60.4%), followed by osteoarthritis with CPPD (37.1%), and chronic CPP crystal inflammatory arthritis (2.5%). Most patients presented with monoarticular (57.2%) or oligoarticular (37.9%) arthritis [median 1.0 (1.0-2.0) joint]. Knee (73.1%) was the most common joint, followed by wrist (22.3%), shoulder (3.2%), spine (2.8%), metacarpophalangeal (2.8%), and acromioclavicular (1.1%) joints, symphysis pubis (0.7%) and hip joint (0.4%). Systemic symptoms including fever (48.4%) and confusion (5.3%) occurred. The median duration of first symptom to resolve was 8.0 (5.0-13.0) days. Recurred CPPD attacks were observed in 37 (13.1%); the median interval among the attacks was 173.5 (56.5-739.5) days. 207 (73.9%) had undergone synovial fluid examination; CPP crystals were identified in the synovial fluid of 157 (75.8%) patients. Radiographic CC was observed among 209 (73.9%); sonographic evidence of CPP crystal deposit was found in 24 (8.5%). The majority (83.0%) of patients have received nonsteroidal anti-inflammatory drugs for CPPD. Colchicine and systemic glucocorticoids were given to 159 (56.2%) and 140 (49.5%) patients, respectively. 101 (35.7%) have received intra-articular glucocorticoid injection, mostly in the knee joint (71.3%). 17 (6.0%) used conventional synthetic disease-modifying anti-rheumatic drugs, including methotrexate (4.2%), hydroxychloroquine (4.6%), sulfasalazine (0.7%), and leflunomide (0.4%).

Conclusions

This is the largest study on clinical findings among Korean patients with CPPD.

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-083

Effect of lifestyle change on incident gout: a nationwide population-based cohort of young men

Yeonghee Eun[1], Kyungdo Han[2], Seung Woo Lee[3], Seonyoung Kang[4], Seulkee Lee[4], Hoon-Suk Cha[4], Eun-Mi Koh[4], Jaejoon Lee[4], Hyungjin Kim[4,5]

[1] Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Republic of Korea
[2] Department of Statistics and Actuarial Science, Soongsil University, Republic of Korea
[3] Department of Biomedicine & Health Science, College of Medicine, Catholic University of Korea,, Republic of Korea
[4] Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea
[5] Department of Medical Humanities, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea

Background

Although gout in young people is increasing, studies on the risk factors for gout in these people are lacking. In this study, we explored the risk factors of gout and effect of lifestyle change on the development of gout in large nationwide population-based cohort of young men.

Methods

Between 2009–2012, men aged 20–39 years who participated in two national health examinations at 2-year intervals were included in the study. The outcome was occurrence of gout, which was defined using the diagnosis code of gout (ICD-10 code M10) in the claims database. Cox proportional hazard model was used to evaluate the association between incident gout and baseline factors or lifestyle change.

Results

A total of 1,977,849 subjects were included in the study, and the mean follow-up period was 5.5 ± 4.3 years. Gout occurred in 38,839 subjects (incidence rate = 3.59/1,000 person-years). A high body mass index, alcohol drinking, and comorbidities such as hypertension, diabetes mellitus, and hyperlipidemia were associated with an increased risk of gout. Among lifestyle factors, change in obesity had the greatest impact on gout, followed by drinking. Development of obesity increased the risk of gout by 1.75 times (95% CI 1.68–1.81), and recovery from obesity decreased the risk of gout by 40% (aHR 0.60, 95% CI 0.57–0.64). Heavy drinking increased the risk of gout by 38% (aHR 1.38, 95% CI 1.33–1.43), and stopping heavy drinking decreased the risk of gout by 11% (aHR 0.89, 95% CI 0.85–0.94). The effect of obesity on gout was evident in the younger age group, and the effect of heavy drinking on gout was weak in the severely obese group.

Conclusions

Obesity and heavy drinking in young men are important modifiable risk factors for gout. Therefore, the management of these risk factors in young men should be emphasized.

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KCR 2022
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P-084

Gout is associated with the risk of osteoporosis: a population-based study

Jihyoun Kim[1], So Rae Kim[2], Gilwon Kang[3], In Ah Choi[4]

[1] Division of Rheumatology, Department of internal medicine, Chungbuk National University Hospital, Republic of Korea
[2] Internal medicine, Chungbuk National University Hospital, Republic of Korea
[3] Department of Health Information and Management, College of Medicine, Chungbuk National University, Republic of Korea
[4] Division of Rheumatology, College of Medicine, Chungbuk National University, Republic of Korea

Background

It is known that uric acid has both role as an antioxidant effect and a pre-oxidant that induces oxidative stress related to inflammation. Inflammatory cytokines can stimulate osteoclast bone resorption. The effects of gout on osteoporosis due to paradoxical function of uric acid also showed conflicting results in the previous studies. This study aimed to investigate the association between gout, which is considered the hallmark disease of hyperuricemia, and osteoporosis.

Methods

This retrospective cohort study used data from the Korean National Health Insurance Service (NHIS) database. In total, 628,565 participants with a diagnosis of gout (ICD-10, M10) who were prescribed medications for gout, such as colchicine, allopurinol, febuxostat, and benzbromarone for at least 90 days were selected from the NHIS database. Patients with osteoporosis were assigned thorough a diagnosis code for osteoporosis with or without pathologic facture (ICD M80, M81). The control cohort was defined as patients who had never had a gout diagnostic code and had never been administered any gout medication. Age and sex 1:1 propensity score matching was performed in the selected control cohort.

Results

Finally, total of 305,810 patients with gout met the study criteria. Compared with the control group, both male (incidence rate ratio: IRR 1.38; 95% CI: 1.35-1.40), and female patient (IRR 1.21; 95% CI: 1.16-1.27) with gout showed increased IRR of osteoporosis. In stratified analysis by age, gout patients showed an increased IRR of osteoporosis in all age groups except for those over 80 years old (p<0.001). In cox proportional hazard model analysis, gout showed increased Hazard ratio (HR) 1.48 (95% CI; 1.45–1.51, p<0.001). Female sex and old age were risk factors for osteoporosis (HR was 4.49,95% CI; 4.38–4.61 in female group, 20.93, 95% CI; 19.55–22.41 in 70's, respectively).

Conclusions

Gout is significantly associated with the risk of osteoporosis in Korean patients.

Figure & Table

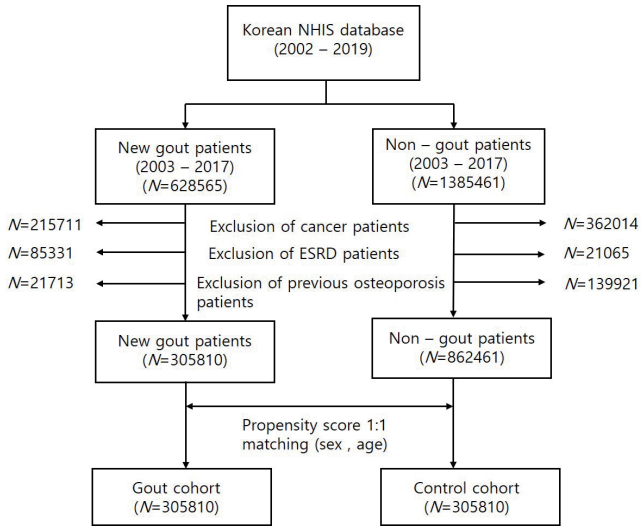

Figure. Flow chart for the selection of the study population from the National Health Insurance Service database. In total, 305,810 patients with gout and 305,810 control participants were compared via propensity score matching.

Keywords

gout, uric acid, osteoporosis

E-poster Presentation

Pediatric rheumatology

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-085

Vascular imaging findings with high-pitch low-dose dual-source CT in atypical Kawasaki disease

Mecit Kantarci[1], Elif Güven[1], Naci Ceviz2, Hayri Oğul[1], Recep Sade[1]

[1] Radiology, Ataturk University, Turkey
[2] Pediatric Cardiology, Ataturk University, Turkey

Description

Determining the presence of aneurysms, thrombosis, and stenosis is very important for the diagnosis of atypical Kawasaki disease (AKD) and in the follow-up of AKD patients with aneurysms. We aimed to demonstrate high-pitch low-dose dual-source computed tomography (CT) angiography findings in pediatric patients with AKD.

Methods

Over a 5-year period, high-pitch low-dose CT angiography was performed to determine vascular aneurysms or occlusions in 17 patients who had suspected AKD. The patients ranged from 2 months of age to 11.3 years, with a mean age of 3 years. The American Heart Association's criteria were used to diagnose AKD.

Results

We did not detect any vascular problems in 6 of the patients, and they were not included in our study. Arterial aneurysms were present in 11 patients (aged 2 months to 11.3 years; mean age, 4.2 years; 7 males). In one patient, there was also a thrombus at an arterial aneurysm. Coronary artery aneurysms were detected in 7 patients and systemic artery aneurysms were detected in 7 patients. Three patients had both systemic and coronary aneurysms.

Conclusions

Our results suggest that high-pitch low-dose dual-source CT can detect all types of aneurysms, stenosis and occlusions of vessels in patients with AKD who were not previously diagnosed. This useful, easy, robust and fast technique may be preferred to diagnose AKD.

Figure & Table

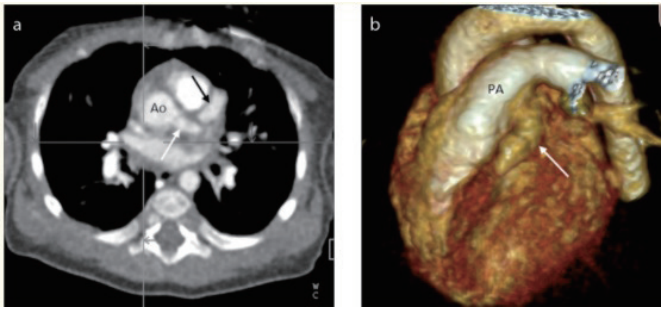

Figure. Left main coronary artery (LMCA) and left anterior descending (LAD) artery aneurysms in a 6-month-old male with unexplained f

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Bilateral calcification of ear cartilage

Gökhan Polat[1], Recep Sade[1]

[1] Radiology, Atatürk University, Turkey

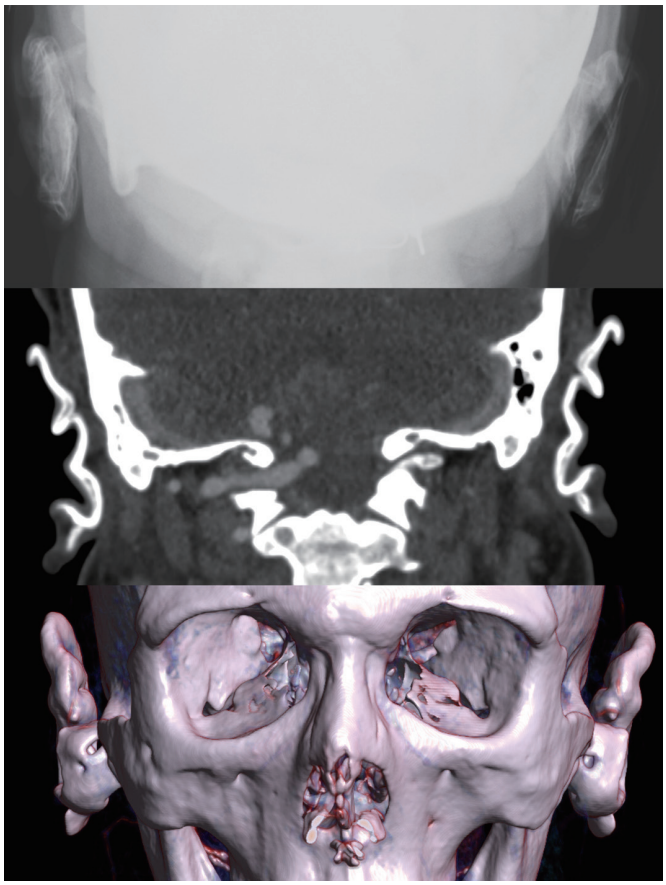
Description

A 17-year-old boy children presented to rheumatology clinic complaining of intermittent hearing loss, dyspnea, swelling of the joints, hardening of the ear. The patient is followed up with the diagnosis of rheumatoid arthritis. On physical examination, the auriculars were of normal appearance, with no visible changes in the derm. Radiography and computed tomography(CT) was performed. Radiography, coronal CT and three-dimensional volume rendering CT images showed bilateral auricular cartilage calcification (Figure 1A,1B, and 1C).

Conclusions

Rheumatoid arthritis is a systemic disorder affecting mesenchymatous tissues, It seems possible that change in the connective tissue may be a predisposing agent in its development. For this reason, rheumatoid arthritis may cause calcification in structures such as the vertebral disc and costal cartilage. Ear cartilage calcification was most commonly caused by adrenal insufficiency. However, rheumatoid arthritic secondary ear cartilage calcification has not been reported in the literature. Ear cartilage calcification is important for the clinician to be able to diagnosis this pathological disorder as it may sometimes be the only indicator of an underlying endocrinologic, immunologic and metabolic disorder that can generally be subclinical.

Figure & Table



Keywords

rheumatoid arthritis, CALCİFİCATİON, young boy

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The treatment effect of tofacitinib on Blau syndrome: A case series of Chinese pediatric patients

Zhe Cai[1,2,3], Song Zhang[1], Huasong Zeng[1]

[1] Department of Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, China., China
[2] Guangzhou Institute of Pediatrics, Guangzhou Women and Children's Medical Center, China., China
[3] Institute of Chinese Medicine and State Key Laboratory, The Chinese University of Hong Kong, Hong Kong., Hong Kong

Description

Blau syndrome (BS) is characterized by the autoinflammatory syndromes of granulomatous recurrent uveitis, dermatitis and symmetric arthritis. It is associated with the nucleotide-binding oligomerization domain containing 2 (NOD2) gene mutations. Therefore, the missense heterozygous mutation in NOD2 gene could cause an activation of NF-κB pathway that could cause a secretion of the pro-inflammatory cytokines like IL-1β, IL-6 and TNF-α. While the biologic agent tocilizumab, a Janus kinase (JAK) inhibitor, can prevent inflammatory cytokines from increasing in rheumatoid arthritis patients. However, whether tofacitinib has a similar effectiveness in child patients with BS is not clear. Our aim is to assess the efficacy of tofacitinib in these patients. Tofacitinib was regularly given to thee BS patients (termed as Patient-1, -2, and -3) in different dosage: 1.7 mg/day (0.11 mg/kg), 2.5 mg/day (0.12 mg/kg), and 2.5 mg/day (0.33 mg/kg), respectively. The clinical manifestations of patients, magnetic resonance imaging, serological diagnosis, and therapeutic measures and outcomes of treatments were recorded. The inflammatory cytokines (IL-1β, IL-2, IL-4, IL-6, IL-10, TNF-α, IFN-γ) were measured by ELISA assay. The clinical characteristics and serological diagnosis of all BS patients were drastically improved after they received tofacitinib treatment such as the relieved joint pain and swelling. All mutations were located on exon 4 of the NOD2 gene in these patients, and a novel unreported mutation (p.M513K) in NOD2 was found in Patient-3. All the patients have reached clinical remission of polyarthritis and improvements in erythrocyte sedimentation rate, levels of C-reactive protein and inflammatory cytokines after 12 month treatment with tofacitinib. Most importantly, no side effects were seen during tofacitinib treatments.

Conclusions

The improvement of inflammatory symptoms in BS suggests that tofacitinib treatment is a promising and effective therapeutic approach for BS patients who have an unsatisfactory response to the corticosteroids, biological reagents and traditional disease-modifying antirheumatic drugs like tocilizumab.

Keywords

Blau syndrome, tofacitinib, pediatric patients

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The evaluation of MRI findings of sacroiliitis in patients with Juvenile idopathic arthritis for detection of active and structural damage lesions according to updated preliminary OMERACT pediatric JAMRIS scoring system

Berhan Pirimoglu[1], Alperen Tezcan[1], Cagatay Engin[2], Gokhan Polat[1], Ahmet Yalcin[1], Recep Sade[1]

[1] Radiology, Ataturk University School of Medicine, Erzurum/TURKEY, Turkey
[2] Pediatric Orthopedics, Ataturk University School of Medicine, Erzurum/TURKEY, Turkey

Background

Magnetic resonance imaging (MRI) is the best imaging technique for detection of sacroiliac joint (SIJ) involvement in juvenile idiopathic arthritis (JIA). Therefore, we aimed to evaluate the active and structural damage lesions in patients with juvenile idiopathic arthritis on sacroiliac joint MRI examinations according to updated pediatric JAMRIS (Juvenile Idiopathic Arthritis MRI Score) scoring system.

Methods

The acquired MRI examinations between January 2018 and December 2021 of children ≤18 years with confirmed imaging and clinical diagnosis of JIA. Patients with comorbidities such as primary or metastatic bone cancer, SIJ fractures and not containing the minimum imaging protocol for this study were excluded. The study sacroiliac joint MRI examinations were reviewed for presence of SIJ pathologies by two radiologists with consensus (BP and AT) who were blinded to the clinical history and other imaging findings. The final 22 cases included in the study were randomly selected. They were evaluated by using the JAMRIS-SIJ scoring methods.

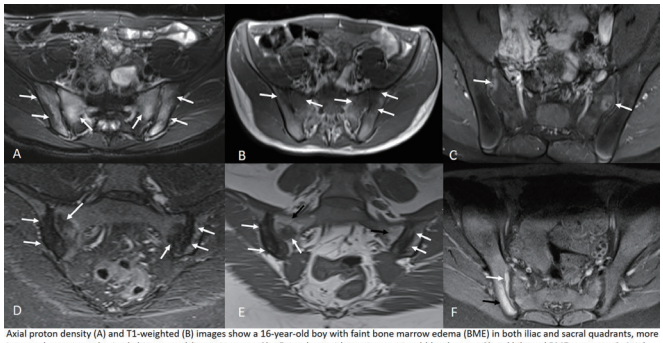
Results

Out of the 22 patients who had MRI examinations selected for the study 12 (54.5%) were males. The median age of the patients was 12 years (8.4–16.4, range 6–18 years). The incidence of JAMRIS-SIJ pathologies among the study MRI examinations were 14 (63.6%) BME, 9 (40.9%) osteitis, 5 (22.7%) erosions, 5 (22.7%) sclerosis, 4 (18.1%) joint space enhancement, 3 (13.6%) fat lesions, 2 (9.1%) inflammation in erosion cavity, 1 (4.5%) capsulitis, 1 (4.5%) enthesitis and 1 (4.5%) backfill. Four (18.1%) of the MRI examinations were normal for patient's age, exhibiting varying normal growth and age-related variants of the bone marrow signal in the SIJ region.

Conclusions

Multiple features of imaging findings are visible on sacroiliac joint MRI examinations. We suggest the updated pediatric JAMRIS scoring system can be widely used for evaluation the active and structural damage lesions in juvenile idiopathic arthritis on SIJ MRI examinations.

Figure & Table



Axial proton density (A) and T1-weighted (B) images show a 16-year-old boy with faint bone marrow edema (BME) in both iliac and sacral quadrants, more intense than presacral veins (white arrows) (intensity score=2), ≥5mm deep with continuous signal (depth score=2) and bilateral BME score was 8. Axial contrast-enhanced T1-weighted image (C) shows a 14-year-old boy with bilateral osteitis in both sacral quadrants (white arrows, osteitis score=2). The semicoronal STIR (D) and T1-weighted (E) images show a 11-year-old boy with bilateral sclerosis (white arrows) and fat lesions (black arrows) in both iliac and sacral quadrants (scleoris score=8 and fat metaplasia score=2). Axial contrast-enhanced T1-weighted image shows an 8-year-old girl with joint space enhancement (white arrow) and osteitis (black arrow) in right iliac quadrant (joint space enhancement score=1 and osteitis score=1).

Keywords

Juvenile idiopathic arthritis, JAMRIS, Magnetic resonance imaging

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P-089

The clinical characteristics of 15 IgG4 related disease in pediatric patients

Zheng Liu[1], Wen Zhang[1]

[1] Department of Rheumatology, Peking Union Medical College Hospital, China

Description

To investigate the clinical characteristics and treatment efficacy of IgG4 related disease (IgG4-RD) in pediatrics.

Methods

A total of 15 patients newly diagnosed with IgG4-RD in pediatric were enrolled from prospective IgG4-RD cohort of Peking Union Medical College Hospital between January 2010 and January 2021. The patients' demographic characteristics, baseline laboratory parameters, clinical symptoms onset, organs involvement and treatment efficacy were analysed.

Results

Fifteen IgG4-RD in pediatric patients accounted for 1.6% of the total number of IgG4-RD patients in our cohort, including 9 males (60%) and 6 females(40%).The mean age of disease onset was (13.3±3.9) years old, 9 males (60%) and 6 females (40%). The average number of organs involvement was (2.8±1.6), 86.7% patients had more than one organ involvement. The most common involved organs were lymph nodes and submandibular glands (53.3%) Other affected organs include lacrimal glands (46.7%), pancreatitis (26.7%), parotid gland (20%), bile duct and lung (13.3%) and sinus, liver, pituitary gland, kidney skin, periaortitis, gastrointestinal tract, thyroid gland (6.7%). 33.3%, 80%, and 86.7% of patients had an elevation of serum IgG IgG4 and total IgE, respectively. 3(20%) patients who had normal serum IgG4 level at baseline suffered from serum IgG4 elevation in follow-up. The serum IgG4 level of the remaining patients decreased after treatment. 9 53.3% patients received glucocorticoids combined with immunosuppressive agents treatment 1(6.7% patients treated with glucocorticoids alone 2 (13.3% patients received immunosuppressant only and 3 20% patients with surgical treatment and symptomatic treatment. 4(26.7%) patients suffered clinical relapse, which may relate to the high number of organs involved at baseline, high IgG4 level at baseline, glucocorticoids treatment alone, or re-elevation of IgG4 during maintenance therapy and follow-up.

Conclusions

Lymph nodes and submandibular glands are the most commonly involved organs in IgG4-RD in pediatric patients. The clinical characteristics and treatment response of pediatric patients were similar to IgG4-RD of adult patients.

Keywords

IgG4 related disease in pediatric, Rare disease, Cohort study

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Predictors of long-term functional outcomes of enthesitis related arthritis (ERA) category of Juvenile idiopathic arthritis (JIA) in adulthood: A single centre experience from a tertiary care hospital

Naveen R[1], Shivika Guleria[1], Anu Balakrishnan[1], Sanjukta Majumder[1], Amita Aggarwal[1]

[1] Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, India

Background

Long term functional outcomes in JIA-ERA (the commonest category of JIA) is scant. This study assessed the long-term functional outcomes of JIA-ERA in adulthood and the factors (clinical and genetic) predicting the same.

Methods

Patients with ERA (ILAR classification) having >5 years of disease and above the age of 16 years were included. Data on clinical features, Bath indices (BASMI, BASDAI, BASFI), health assessment questionnaire disability index (HAQ-DI) was collected. Clinical features within 6 months of disease onset was recorded. Poor functional outcome was defined as BASFI>0.9 or HAQ-DI>0.5. Genetic factors looked for were HLA-B27, ERAP polymorphisms (rs27044, rs27037), and IL23R. All data were expressed as median (IQR) or as frequency.

Results

135 patients (127-male) with age of disease onset 13(10-15) years and disease duration 7(5-11) years were recruited. There was delay in diagnosis of 3(1-6) years. Most had active disease (81%-ASDAS-ESR>1.3). Ninety-two (68%) had functional disability with median HAQ-DI of 0.43(0-1), BASFI of 1.8(0.37-3.12).

Poor functional outcome was seen in three-fourths (n=92, 68%). Those with poor functional outcomes had longer delay in diagnosis (4 vs 1 years, p<0.001), higher school years lost (p=0.01). They also had higher Bath indices now. ERAP (rs27044) polymorphism heterozygous state was also more frequent in them [OR 4.8 (1.2-19)]. HLA-B27, ERAP rs23037 and IL23R polymorphisms were similar. None of the clinical features at disease onset predicted poor functional outcomes. In multivariate analysis, those with poor outcomes had higher BASDAI [OR 3.14 (1.5-6.2)](Table 1).

Conclusions

Poor functional outcome was seen in 68% of adults with JIA-ERA 7 years into disease. Longer delay in diagnosis and school years lost characterised those with poor functional outcomes. ERAP rs27044 heterozygous state was more frequent in those with poor outcomes. None of the clinical features at disease onset predicted long term functional outcomes in adulthood.

Figure & Table

Table 1. Differences in baseline characteristics between those with and without poor functional outcomes (BASFI≥0.9 or HAQ≥0.5)

	Poor functional outcome (n=92)	No poor functional outcome (n=43)	OR (CI) (U/M)	P
Age in years	20 (18-23)	19 (17-22)		NS
Age of onset of disease (years)	13 (10-15)	12 (11-15)		NS
Gender (M:F)	88:4	39:4		NS
Delay in diagnosis (years)	4 (2-6)	1 (1-4)		<0.001
School years lost (in years)	0 (0-2)	0 (0-0)		0.010
Clinical features at onset (within 6 months) n (%)				
Arthritis	79 (86)	41 (95)		NS
Clinical Hip joint involvement	17 (71)	7 (16)		NS
IBP	48 (44)	23 (59)		NS
Tarsitis	42 (45)	18 (42)		NS
Uveitis	2 (2)	4 (9)		NS
Enthesitis	77 (83)	36 (83)		NS
Tendoachilles enthesitis	59 (64)	27 (63)		NS
Axial site enthesitis	44 (48)	19 (44)		NS
Peripheral site enthesitis	71 (77)	34 (79)		NS
Radiological features at onset (within 1 year)				
X-ray sacroiliitis at onset	55 (64)	20 (60)		NS
X-ray hip arthritis at onset	21 (25)	3 (9)		NS
Genetic markers				
ERAP 1 (rs 27044) Homozygous (out of 103)	24 (33)	10 (33)		NS
ERAP 1 (rs 27044) Heterozygous (out of 103)	45 (92)	14 (70)	4.8 (1.2-19)	0.019
ERAP 1 (rs 27044) at least one variant gene	69 (94)	24 (80)	4.3 (1.1-16)	0.024
ERAP 1 (rs 27037) Homozygous (out of 101)	26 (36)	11 (37)		NS
ERAP 1 (rs 27037) Heterozygous (out of 101)	39 (55)	15 (50)		NS
ERAP 1 (rs 27037) at least one variant gene	65 (91)	26 (87)		NS
IL-23R Homozygous (out of 100)	15 (21)	4 (13)		NS
IL23R Heterozygous (out of 100)	28 (40)	15 (50)		NS
IL23R at least one variant gene	43 (61)	19 (63)		NS
HLA B27 positivity (out of 122)	79 (86)	36 (84)		NS
Outcome measures				
BASDAI	**4.9 (3.1-6.5)**	**1 (1-2)**	**3.14 (1.5-6.2)#**	**0.001@**
BASMI	1.6 (1-2.15)	1 (0-1.6)		0.002
BASFI	2.9 (1.6-4)	0 (0-0.4)		<0.001
HAQ DI	0.87 (0.28-1)	0 (0-0)		<0.001
BASDAI ≥ 4 (%)	61 (67)	3 (7)	27 (7.7-95)	<0.001
ASDAS-ESR	3 (2.5-7)	1.6 (1.3-2.3)		<0.001
ASDAS-CRP	3.35 (2.4-3.8)	2.2 (1.3-2.9)		<0.001
Treatment received				
NSAIDS alone	27 (29)	13 (30)		NS
DMARDS+ NSAIDS	64 (69)	28 (65)		NS

IQR Interquartile range, BASDAI Bath ankylosing spondylitis disease activity index, BASMI Bath ankylosing spondylitis metrological index, BASFI Bath ankylosing spondylitis functional index, HAQ DI Health assessment questionnaire disability index, NSAIDS Non-steroidal anti-inflammatory drugs, DMARDS Disease modifying anti rheumatoid drugs
P<0.05 is significant
OR (CI) in significant in binary logistic regression, @ P value as per Binary logistic regression

Table. Differences in baseline characteristics between those with and without poor functional outcomes

Keywords

Functional outcomes, juvenile idiopathic arthritis, Enthesitis related arthritis

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P-091

Secondary hemophagocytic lymphohistiocytosis: overwhelming clinical manifestations may cause more chemotherapy than necessary

Hye Yeon Choi[1], Jung Woo Rhim[1], Dae Chul Jeong[1], Soo-Young Lee[1]

[1] Department of Pediatrics, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Background

Secondary hemophagocytic lymphohistiocytosis (HLH) is a rare but fatal disease, so early recognition and aggressive chemotherapy are essential to achieve a good prognosis. However, overwhelming clinical manifestations that meet the HLH-2004 diagnostic criteria may lead to overtreatment. Here, we report an experience of the 40-week intensive chemotherapy including etoposide in secondary HLH patients that could have been replaced by the 8-week immune modulators.

Methods

In this retrospective study, medical records were reviewed for patients who were diagnosed with secondary HLH at the study hospital over the past 5 years. Diagnosis of HLH was based on HLH-2004 criteria. Six patients met the diagnostic criteria and were included in this study.

Results

Of the 6 patients with secondary HLH, 2 had juvenile idiopathic arthritis (JIA), 1 had Kawasaki disease, and the remaining 3 had no underlying disease. There was an important difference in treatment modalities among the patients: 3 patients were treated with the 8-week immune modulators (i.e., corticosteroids and cyclosporine A), while the remaining 3 patients were treated with the 40-week chemotherapy (i.e., the HLH-2004 therapeutic protocol). Regardless of treatment modality, all recovered without sequelae. When medical records were compared in detail between 2 patients with JIA and between 2 patients without underlying disease, we noted that 1 patient with JIA and 1 patient without underlying disease could have received the 8-week immune modulators instead of the 40-week chemotherapy and would have obtained similar outcomes.

Conclusions

Prompt initiation of adequate treatment for secondary HLH is very important. It is also necessary to avoid overtreatment in the subset of secondary HLH patients. Many patients with secondary HLH can be successfully treated with short-term immune modulators. The choice of treatment modalities should be determined on the basis of therapeutic response, in addition to initial clinical and laboratory features.

Keywords

Hemophagocytic lymphohistiocytosis, HLH-2004 guidelines, Overtreatment

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-092

Interstitial lung disease in pediatric systemic lupus erythematosus: A case report

Soo-Young Lee[1], Hye Yeon Choi[1], Jung Woo Rhim[1],
Hye Jin Lee[1], Hyun Mi Kang[1], Dae-Chul Jeong[1]

[1] Pediatrics, College of Medicine, The Catholic University of Korea, Republic of Korea

Description

Systemic lupus erythematosus (SLE) is multisystem autoimmune disease. Clinical presentations are variable according to the involved organs. Interstitial lung disease (ILD) is rarely presented in pediatric SLE and limited data exist on treatment of the patients with ILD in SLE. Here, we reported a 13-year old girl with exertional dyspnea without fever during the treatment with oral steroid and hydroxychloroquine after diagnosed of SLE. At initial diagnosis of SLE, she presented skin rash, hair loss with thrombocytopenia in spite of intravenous immunoglobulin and steroid therapy, and did not complain any respiratory symptoms. Chest radiologic finding showed bilateral infiltration of lung fields and high resolution chest CT showed bilateral diffuse ground glass attenuation with lower lobe predominance, and ill-defined small nodules with variable sized cysts in both lungs. Pulmonary function test showed restrictive pattern compatible with ILD. We identified high level of KL-6 such as surrogate marker of ILD. Lung biopsy revealed subpleural fibrosis with bulla formation, and focal interstitial thickening with fibrosis, edema and lymphoid aggregates. She received oral prednisolone with mycophenolate mofetil (MMF) after methylprednisolone pulse therapy. Her respiratory symptom and pulmonary function test and the level of KL-6 were showed improvement after treatment.

Conclusions

We emphasize that careful evaluation for respiratory involvement should be considered in pediatric SLE patient, especially when the patient shows respiratory symptoms such as dyspnea on exertion and cough. And MMF combined with corticosteroids could be the useful treatment options for pediatric ILD-SLE.

Keywords

Systemic lupus erythematosus, Pediatric, Interstitial lung disease

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-093

A20 Haploinsufficiency identified in a girl presented with systemic juvenile idiopathic arthritis: A case report

Jung-Woo Rhim[1], Hye Yeon Choi[1], In Hyuk Yoo[1], Soo Youn Lee[1], Dae-Chul Jeong[1]

[1] Pediatrics, College of Medicine, The Catholic University of Korea, Republic of Korea

Description

Haploinsufficiency of A20 (HA20) is a newly described autoinflammatory disease caused by mutations in tumor necrosis factor-α-induced protein 3 (TNFAIP3) gene. Patients present wide spectrum of manifestations with early-onset systemic inflammation like Behcet's disease or other autoimmune features. Here, we report the case of HA20 initially diagnosed with systemic juvenile idiopathic arthritis (sJIA).

An 11-year-old girl has presented recurrent episodes of fever with vomiting, diarrhea since 11-month of age. She was diagnosed with sJIA presenting fever with skin rash, lymphadenopathy and arthritis when she was 27-month-old. The patient developed fever with gastrointestinal symptoms including abdominal pain with vomiting about five times per year in spite of disease-modifying anti-rheumatic drugs (DMARDs) therapy. Acute phase reactants were markedly increased during the period of her symptoms and improved by conservative treatment with hydration, but still showed elevated levels when she was well-being state. At the age of 7, familial genetic study for Mediterranean fever (MEF) syndrome identified that the patient and her father had two heterozygous mutations regarding variant of uncertain significance in MEFV gene by Sanger method.

At the age of 11, she admitted due to the recurrent gastrointestinal symptoms with high acute phase reactants. Colonoscopy showed multiple ulcers on intestinal mucosa compatible with Crohn's disease. The next generation sequencing identified the pathogenic heterozygous mutation (c.427C>T) at TNFAIP3 gene, leading to HA20. This genetic mutation presents to fail to the negative feedback mechanism for nuclear factor kappa B (NF-κB) activation, developing autoinflammatory features such as fever and systemic inflammation.

Conclusions

HA20 should be considered in the patient with recurrent inflammatory disease that presented with fever and gastrointestinal symptoms which might be regarded as respective episodes of acute infections.

Keywords

Tumor necrosis factor alpha-induced protein 3, autoinflammatory disease, acute phase reactants

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-095

Flare-up of juvenile idiopathic arthritis (JIA) the day after receiving a booster shot of BNT162b2 mRNA vaccine

Kwang Nam Kim[1], Hyong Suk Park[1]

[1] Pediatrics, Myongji Hospital, Republic of Korea

Description

Vaccine is an effective public health measurement to control the global COVID-19 pandemic. Patients with rheumatoid arthritis (RA) are twofold more vulnerable to infections that result in hospitalization and impaired quality of life. So, with consideration to the benefits of vaccination outweighing the risks, EULAR recommends that patients with RA should receive COVID-19 vaccines without needing major adjustment to their ongoing treatment regimens.

However, concerns about the safety of the vaccines are a major hurdle to widespread vaccination to the adolescent and children. Here, we report a JIA flare patient the day after receiving the booster shot of BNT162b2 mRNA vaccine.

A 18-year-old male, previously completely remission state of JIA, developed right knee joint swollen the day after 3rd dose of BNT162b2 mRNA vaccine. He is on medication state, MTX 3tab weekly, Folic Acid 1tab daily and Enbrel 1.0 twice/week since May 2019. He was given the third vaccination on Dec. 16, 2021. The next day after the vaccination, his right knee was swollen and felt pain on Dec. 17, 2021. The swollen joint was not improved with NSAID. So, prednisolone 15mg (3tab) was added on Jan. 3, 2022.

US of right knee showed large amount of joint effusion on right knee and US guided aspiration and IntraArticular steroid injection on Jan. 5, 2022.

Physical examination revealed that right knee swollen joint was aggravated on Jan. 26, 2022, nevertheless IA steroid injection on Jan 5, 2022. It is still swollen and painful on Feb. 10, 2022.

Conclusions

We experienced that after full vaccination with BNT162b2 patient with JIA, showed an increased risk of possible arthritis flare. So, to understand the association between arthritis flare and vaccination is important to overcome vaccine hesitancy.

Figure & Table

	12/20/2021	12/27/2021	12/29/2021	1/17/2022	1/26/2022	2/10/2022
D-dimer	1.79	1.73	1.85			
Troponin	0.16	2.51				
CK-MB	0.79	0.18				
Hs-CRP	2.38 mg/dL	6.51 mg/dL	8.54 mg/dL	1.44 mg/dL	2.32 mg/dL	1.72 mg/dL
ESR	12 mm/hr	32 mm/hr	41 mm/hr	32 mm/hr	37 mm/hr	38 mm/hr

Table. ESR and hs-CRP change

Keywords

Juvenile Idiopathic Arthritis, BNT162b2 vaccine, Flare-up JIA

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Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-096

Challenges and management for pediatric rheumatology patient's in the COVID-19 era: Perspectives from several countries

Putri Ayu[1]

[1] Economics, Andalas University, Indonesia

Background

A global public health problem that threatens millions of lives around the world today is the COVID-19 pandemic This pandemic can have severe clinical manifestations such as acute respiratory distress syndrome or a cytokine storm that causes death. Pediatric rheumatology doctors during the Covid-19 pandemic have gone the extra mile to protect patients from COVID-19 infection without compromising disease prognosis. The management of cancer patients has so far been carried out mainly on rheumatology patients, including pediatric rheumatology because they have the risk of getting infections when they are children and it is very difficult to treat immunosuppression. This study aims to analyze the management of health workers in pediatric rheumatology patients in the era of the COVID-19 pandemic in various countries.

Methods

This study uses published international journals such as MEDLINE/PubMed and Scopus databases on the management of pediatric rheumatology health workers during the COVID-19 pandemic in patients using comparative analysis methods and descriptive studies. The countries taken in this study were France, Italy, India, the United States, Europe, and Germany.

Results

The results of the study concluded several categories in the health management of pediatric rheumatology patients during the COVID-19 pandemic. First, management of outpatient visits using teleconsultation, Favor Home Hospitalization or home care, telemedicine. Second, clinical trials for patients whose visits must be replaced by teleconsultation. Clinical and New patient registration is temporarily suspended. Third, Supportive Care is given for pediatric rheumatology, and vaccination is highly recommended.

Conclusions

During the COVID-19 pandemic, it was concluded that there were several non-evidence-based practices in institutions to reduce the risk of exposure to COVID-19 for both pediatric rheumatology patients. The results show the need to test patients for SARS-CoV-2 infection, Pharmacists should be able to prescribe doses during treatment at once, Support hospitalization at home.

Keywords

Pediatric Rheumatologists, Challenges, Managements

E-poster Presentation

Fibromyalgia and soft tissue disorders

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-097

The use of shear-wave elastography for myofascial pain syndrome's severity

Recep Sade[1], Meltem Alkan melikoglu[2]

[1] Radiology, Ataturk University, Turkey
[2] Rheumatology, Ataturk University, Turkey

Background

Manual palpation is a subjective procedure for identifying and differentiate Myofascial Trigger Points (MTrPs), the use of Shear Wave Elastography (SWE) as an objective alternative is increasing. This study aimed to analyze pain pressure thresholds (PPTs) and SWE differences.

For analysis between active MTrPs, latent MTrPs and control points located in the upper trapezius Association of SWE features with clinical severity indicators (eg, area of pain expansion, PPTs, and neck pain).

Methods

This study was conducted to calculate the correlation. and to analyze the differences in sociodemographic, clinical and SWE characteristics in 24 asymptomatic patients subjects with latent MTrPs and 16 patients with neck pain and active MTrPs.

Results

Significant PPT differences between active with latent MTrPs ($p < 0.001$) and control points ($p < 0.001$) were found, but no differences between latent MTrPs and control points ($p > 0.05$). There were no stiffness differences between active MTrPs with latent MTrPs or control points ($p > 0.05$). However, significant control point stiffness differences between-samples were found ($p < 0.05$). SWE showed no significant correlation with clinical severity indicators ($p > 0.05$). No stiffness differences between active and latent MTrPs were found.

Conclusions

Neck pain patients showed increased control point stiffness compared with asymptomatic subjects. SWE showed no association with clinical severity indicators.

Figure & Table

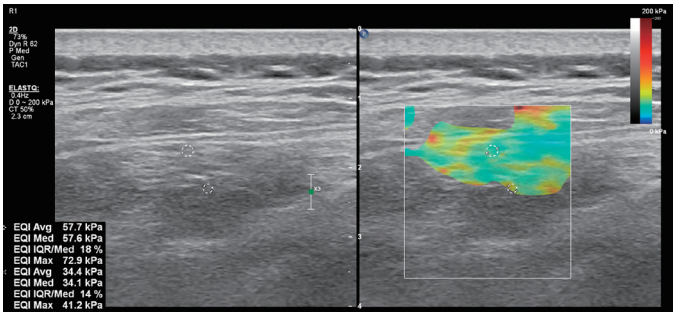

Figure. Shear Wave Elastography image of 39-year old females shows Myofascial Trigger Point and its elasticity score

Keywords

elasticity imaging techniques, myofascial pain syndromes, trigger points

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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P-098

Amigos de fibro (Fibro Friends): Validation of an educational program for health promotion in fibromyalgia

Mateus Antunes[1], Ana Carolina Schmitt[1], Amélia Marques[1]

[1] Department of Physiotherapy, Speech Therapy and Oc, University of São Paulo (USP), Brazil

Background

Health education is one of the main items to enable the health promotion of patients with fibromyalgia and should prepare them to assume control and responsibility for their own health and the health of their territory, as well as prepare them for empowerment. decision-making, participation, social control and acting on the conditions and determinants of their health and quality of life. Therefore, the "Amigos de Fibro" was created in Brazil, an educational program to promote the health of patients with fibromyalgia. The objective was to validate a health promotion program focused on health education for patients with fibromyalgia in Brazil.

Methods

A study with a methodological approach was carried out with the participation of health professionals (n=23) (specialist judges) and patients with fibromyalgia (target audience) (n=45) who answered an instrument to assess the objectives, themes and proposed actions, relevance, writing style and program structure using the Delphi technique. Content Validity Index (CVI) ≥ 0.78 and Kappa Coefficient ≥ 0.61 were used for data analysis.

Results

All items evaluated in both groups had a considerable minimum CVI by CVI and Kappa Coefficient. The Kappa Coefficient of expert judges was 0.90 and that of target audience judges was 0.85. Finally, in the global assessment of "Amigos de Fibro", the CVI of the expert judges was 0.90, whereas the values of the target audience judges were 0.95.

Conclusions

"Amigos de Fibro"was considered adequate when its content and internal consistency were evaluated, in this sense, it can be used by health professionals with patients who have fibromyalgia, allowing them to act as agents that promote their health. New studies are being carried out to show more positive effects of "Amigos de Fibro".

Keywords

Fibromyalgia, Health education, Health Promotion

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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P-099

Amigos de fibro (Fibro Friends): Validation of an educational E-book to promote the health of patients with fibromyalgia in Brazil

Mateus Antunes[1], Ana Carolina Schmitt[1], Amélia Marques[1]

[1] Department of Physiotherapy, Speech Therapy and Oc, University of São Paulo (USP), Brazil

Background

Promoting the health of fibromyalgia patients is very important and recommended by leading health bodies and researchers. Patient education is the primary tool for managing symptoms. In Brazil, "Friends of Fibro" was created, an educational program that will promote the health of patients with fibromyalgia. In addition, an e-book was developed to be offered to patients using the public health system in Brazil. The aim of the study was to develop and validate an e-book to promote the health of individuals with fibromyalgia.

Methods

This is a methodological study, which through a bibliographic survey, the available publications on the subject were analyzed. Then, this knowledge was used to build the theoretical content addressed and the art and layout of the e-book was elaborated. In the last stage, the validation of the constructed material was carried out, by content specialists (n=23), technicians (n=23) and design (n=23) and fibromyalgia patients (n=45) evaluated the e-book through qualitative (Delphi methodology). For data collection, different questionnaires were used, according to the focus of evaluation of each group of participants, analyzed for agreement using the Content Validity Index (CVI) and reliability using Cronbach's Alpha (αC).

Results

In reliability, all groups also had an acceptable αC: content (0.960), technical (0.963), design (0.977), and target audience (1.08). In the global assessment of the agreement of all groups of judges, the CVI presented a considerable minimum, being: content (0.79), technical (0.89), design (0.92), and target audience (0.97).

Conclusions

The e-book was developed and validated in terms of content and relevance, and can be used to promote the health of individuals with fibromyalgia. New studies are being carried out to show more positive effects of "Amigos de Fibro".

Keywords

Fibromyalgia, Health education, Health Promotion

E-poster Presentation

Idiopathic inflammatory myositis and muscle biology

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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P-101

Erdheim-Chester disease mimicking coronary artery disease in a systemic lupus erythematosus patient

Grigol Nemsadze[1], Megi Kurtanidze[2], Tamar Melkadze[1]

[1] Radiology Department, TSSU First University Clinic, Georgia
[2] Radiology Department, Tbilisi City Medical, Georgia

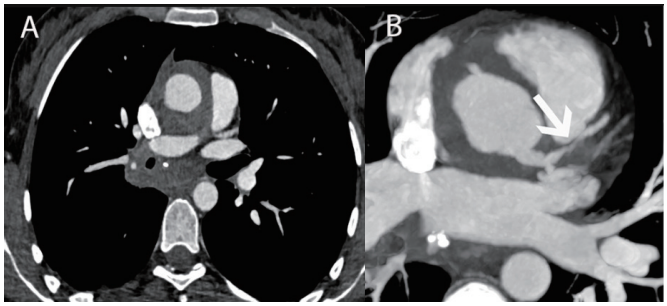
Description

A 38-year-old male patient presented to the emergency clinic with progressive atypical chest pain suggestive of unstable angina. The patient had been followed up and treated for systemic lupus erythematosus for 6 years. His elevated cardiac troponin biomarker. For this reason, we suspected coronary artery disease. A physical examination revealed a heart rate of 80 beats per minute and blood pressure of 130/60mm Hg. Electrocardiographic findings were unremarkable. It was seen that the patient occasionally referred to our hospital with these complaints. A Cardiac computed tomography (CT) scan revealed soft tissue surrounding the aorta and coronary artery (Figure 1A (asterisks) and 1B). It showed decreased coronary artery calibration (Figure 1B, white arrow). Rheumatologic and immunological diseases were investigated for the reason CT findings. Urine protein electrophoresis, Serum IgG4 level, and hepatitis panel were normal. Autoimmune workup, including antinuclear antibody, rheumatoid factor, anti-double-stranded DNA antibodies, complement levels, and antitopoisomerase, was similarly unremarkable. Fibroadipose tissue with exceeding histiocytes, highlighted by CD68-PGM1 and CD163 immunostaining, was evidenced from a biopsy of the left paravertebral tissue mass surrounding the descending aorta. He was treated with interferon alpha.

Conclusions

Erdheim-Chester disease (ECD) is an uncommon multisystem non-Langerhans cell histiocytosi. ECD cardiovascular involvement is usually asymptomatic and therefore under-diagnosed but linked to poor prognosi. As a conclusion, Erdheim-Chester's disease with coronary artery involvement is extremely uncommon. Due to the narrowing of coronary arteries, Erdheim-Chester disease should be kept in mind as atypical chest pain reason.

Figure & Table



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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-102

New onset clinically amyopathic dermatomyositis following SARS-CoV-2 vaccine: A case report

Eric Ranniel Guevarra[1], Sandra Teresa Navarra[1]

[1] Section of Rheumatology, Department of Internal Medicine, University of Santo Tomas Hospital, Manila, Philippines, Philippines

Description

Amyopathic dermatomyositis is a rare autoimmune skin disease with similar cutaneous manifestations as classic dermatomyositis (CDM), but with absent or subclinical muscle involvement i.e. Clinically Amyopathic Dermatomyositis (CADM). Inciting agents including vaccines have been linked to CADM. We describe a case of new-onset CADM associated with COVID-19 vaccine.

To illustrate the occurrence of new-onset Clinically Amyopathic Dermatomyositis (CADM) in a 27-year-old male following COVID-19 immunization.

A previously well 27-year-old male developed joint and muscle aches accompanied by scattered erythematous patches on the face and both upper and lower extremities, a week after receiving first dose of viral vector SARS-CoV-2 vaccine. He took an anti-histamine and paracetamol with some relief of pains and slight clearing of the rashes. He proceeded to receive a second dose of the same vaccine 2 months later. A few days following the second dose, there was exacerbation of the skin lesions and was referred to Rheumatology clinics. Physical exam disclosed an ambulatory well-built male with normal vital signs and no objective muscle weakness. Skin involvement included facial rash, and the characteristic Heliotrope rash, Gottron's papules, and Holster sign. Complete blood counts, chemistries and muscle enzymes were within normal. Antinuclear antibody (ANA), erythrocyte sedimentation rate (ESR) and Smith/ribonucleoprotein (Sm/RNP) antibody were positive. He was managed with tapering prednisone and maintained on methotrexate and folic acid with significant improvement at time of this report.

Conclusions

This is the first reported case of adverse reaction to COVID-19 vaccine that had studied in detail the skin and systemic autoimmune reaction. Development of autoimmune reaction following SARS-CoV-2 vaccine has been described extensively; however, evidence of autoimmunity following vaccination is still relatively scant. Our case suggests that in predisposed subjects' vaccination could trigger an autoimmune reaction similar to the natural infection.

Figure & Table

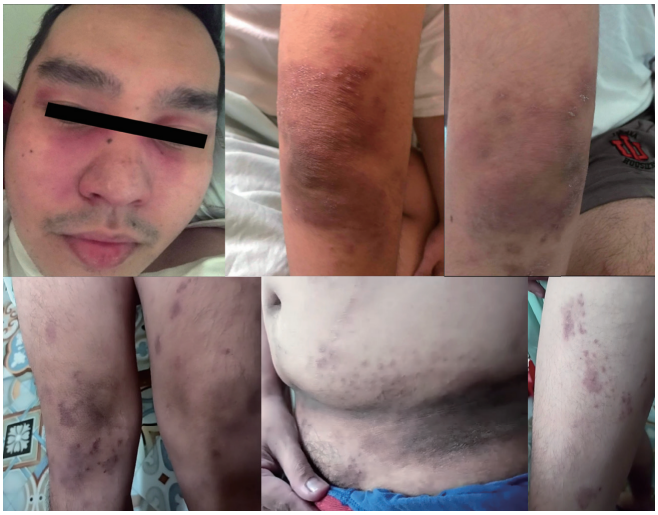

Figure. Skin lesions showing heliotrope and malar rash, Gottron's papules, hyperpigmentation and Holster sign

Keywords

Clinically amyopathic dermatomyositis, COVID-19 vaccine

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-103

Rare case of dermatomyositis following SARS-CoV-2 vaccination

Mark Andrian Yano[1], Geraldine Zamora[1]

[1] Division of Rheumatology, Department of Medicine, Philippine General Hospital, Philippines

Description

We report a case of 51-year-old male who developed erythematous maculopapular rash on the upper anterior chest and upper back along with symmetric proximal muscle weakness two months after receiving his second dose of Sinovac (CoronaVac) COVID 19 vaccine. His symptoms were followed by periorbital edema which eventually involved the upper and lower extremities. He also had dysphagia and unintentional weight loss. His medical history was notable for hypertension which was well controlled and a 15-pack year smoking history. He had no family history of autoimmune diseases.

Physical examination revealed areas of poikiloderma on the lower anterior neck (V sign), upper back (shawl sign), heliotrope rash and hyperkeratotic pink ill-defined papules with scale on bilateral lateral second digits (mechanic's hands). Symmetric proximal muscle weakness in the upper and lower extremities was objectified. Onychoscopy revealed erythema on the proximal nailfold with no telangiectasias.

Blood tests revealed elevated muscle enzymes (total CK 3899 U/L, CK MB mass 15.4 ng/mL, LDH 683, AST 232 U/L and ALT 66 IU/L) elevated ESR (36) and normal CRP. Anti Jo 1 and anti U1 RNP were negative. Work up for systemic infection, thyroid function and malignancy were unremarkable. Chest and abdominal CT scan revealed diffuse subcutaneous edema with no evidence of intrathoracic or intraabdominal mass lesions.

Patient was started on hydrocortisone 1 mg/kg/day and later shifted to prednisone 80 mg per day. Azathioprine was introduced on the 3rd hospital day. Gradual subjective improvement of muscle strength was noted.

Conclusions

We hypothesize that among patients with genetic predisposition, the possibility of vaccines triggering dermatomyositis and other autoimmune event is possible and as vaccine inoculation increases, data will accumulate, and comparisons will become possible.

Figure & Table

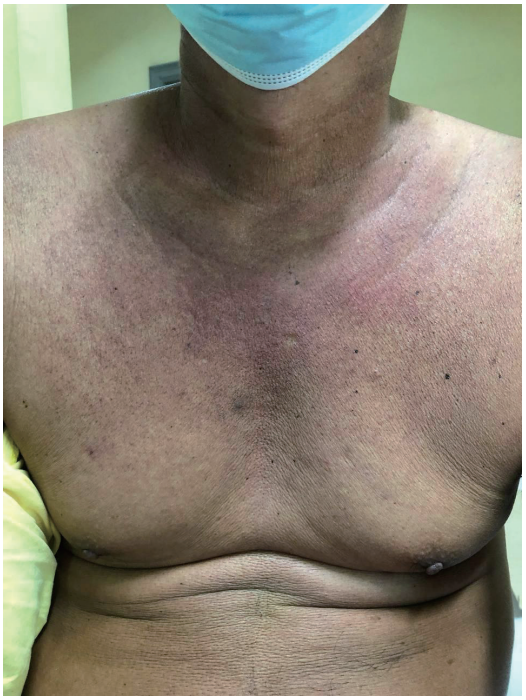

Figure. V sign in the upper anterior chest of the patient

Keywords

Dermatomyositis, COVID 19 vaccine

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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P-104

Clinical characteristics and outcomes of adult patients with anti-MDA5 dermatomyositis- A single centre experience from South India

Shivraj Padiyar[1], Aswin Nair[1], Prathyusha Manikuppam[1], Avanish Jha[1], Abhilasha Manwatkar[1], John Mathew[1]

[1] Clinical Immunology and Rheumatology, Christian medical College, Velore, India

Background

To study the demographic, clinical characteristics, and treatment outcomes of patients with anti-MDA5 dermatomyositis

Methods

This is a retrospective study done between 2019 and 2021 in a tertiary care centre from South India. All consecutive patients, presenting to the adult rheumatology department, classified as idiopathic inflammatory myositis (IIM), and positive for anti-MDA5 antibody were included in the study. Baseline characteristics of anti-MDA5 patients were compared with the data of non-MDA5 patients over the last 10 years. Clinical, biochemical, and treatment responses were assessed on follow-up. Complete and partial responders were identified using predefined criteria. Factors predicting mortality were determined by logistic regression analysis. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 20.

Results

A total of 29 adult patients of dermatomyositis were positive for anti-MDA5 antibody during the study period. The mean (±SD) age of the patients was 40.3 (±13.02) yrs with the female: male ratio of 1.4:1. Panniculitis, calcinosis, palmar papules, and ulcerated gottron's were the specific cutaneous manifestations, seen in 3(10 %), 7(24 %), 4(13.4%), and 7(24%) patients respectively. 14 patients (48.1%) had clinically amyopathic dermatomyositis. 17 patients (60.7%) had interstitial lung disease by CT scan, of which organizing pneumonia was the predominant pattern. Complete response was seen in 10 patients (43%), while the partial response was seen in 8 patients (34%). Five patients died on follow-up, accounting for a mortality of 21%. Age >50 yrs was significantly associated with mortality (p=0.025)

Conclusions

Anti-MDA5 dermatomyositis represents a distinct and unique subset of Idiopathic inflammatory myositis with characteristic clinical manifestations. A combination of high-dose steroids with mycophenolate led to improvement in all the patients with anti-MDA5 antibodies with non-RP-ILD presentations. Elderly age is a poor prognostic factor of mortality.

Figure & Table

Parameter	Anti-MDA5 DM (N-29)	Non Anti-MDA5 DM (N=421)	P value
Age, mean (± SD), yrs	40.3(±13.02)	38.4(±13.5)	0.45
Duration of disease, months mean (± SD),	15.6(±22.79)	14.04(±22.18)	0.71
Female/Male	17/12	292/129	0.22
Cutaneous lesions			
Gottron's sign	20(69%)	109 (25.9%)	**<0.001**
Heliotrope rash	13(44.8%)	153(36.3%)	0.36
Panniculitis	3(10.3%)	9(2.1%)	**<0.001**
Calcinosis	6(20.7%)	53(12.7%)	**<0.001**
Mechanics Hands	4(13.8%)	40(9.5%)	0.45
Cutaneous ulcers	9 (31%)	18(4.3%)	**<0.001**
Ulcerated Gottron's	7(24.1%)	0	**<0.001**
Cutaneous vasculitis	4(13.8%)	28(6.9%)	0.16
Raynauds phenomenon	5(17.2%)	43(10.2%)	0.23
Systemic manifestations			
Fever	7(24.1%)	150(35.6%)	0.209
Dysphagia	4(13.8%)	112(26.7%)	0.19
Arthritis	24(82.8%)	139(33%)	**<0.001**
Clinical Muscle weakness	14(48.3%)	380(90.5%)	**<0.001**
ILD	17(60.7%)	158(37.5%)	**0.015**
Type of ILD			
NSIP	3(17.6%)	94(59%)	
OP	6(35.2%)	19(11.9%)	
NSIP-OP	6(35.2%)	4(2.5%)	
UIP	0	4(2.5%)	
Unclassified	2(11.7%)	38(24%)	
CPK levels, units/L, mean (± SD)	244(±623.8)	2375(±5520)	**<0.001**
LDH, units/L, mean (± SD)	780(±364)	1156(±783)	**<0.001**
Anti-Ro52 positivity *	7(24.1%)	71(16.9%)	0.21

* Done using EUROIMMUNE assay, a titre of 2+ or more is considered positive

ILD- Interstitial lung disease, NSIP- Non specific Interstitial pneumonitis,OP-Organizing pneumonia, RP-ILD- Rapidly progressive ILD, CPK- Creatinine phosphokinase, LDH- lactate dehydrogenase, ANA- antinuclear antibody, IIF- Indirect Immunofluorescence,

Table. Clinical and demographic characteristics of individuals with anti-MDA-5 antibody dermatomyositis

Keywords

Anti-MDA5, Ulcerated Gottron's, Rapidly progressive ILD, panniculitis, Palmar papules

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Changes in quantitative interstitial lung disease scores on high-resolution CT in idiopathic inflammatory myositis

Jina Yeo[1], Soon Ho Yoon[2], Ju Yeon Kim[3], Jeong Seok Lee[4], Eun Young Lee[3], Jin Mo Koo[2], Lila Pourzand[5], Jonathan G Goldin[5], Grace-Hyun J Kim[5], You-Jung Ha[6]

[1] Rheumatology, Gil Medical Center, Gachon University College of Medicine, Republic of Korea
[2] Radiology, Seoul National University Hospital and College of Medicine, Republic of Korea
[3] Rheumatology, Seoul National University Hospital and College of Medicine, Republic of Korea
[4] Clinic Pappalardo Center, Korea Advanced Institute of Science and Technology (KAIST), Republic of Korea
[5] Radiology, David Geffen School of Medicine, University of California, Los Angeles (UCLA), USA
[6] Rheumatology, Seoul National University Bundang Hospital, Republic of Korea

Background

To investigate longitudinal changes of the quantitative interstitial lung disease (QILD) scores and their clinical impact in idiopathic inflammatory myositis (IIM) associated ILD.

Methods

A total of 80 patients with IIM-ILD who underwent at least 2 times of serial HRCT scans were included. Quantitative analysis of HRCT was presented as total extent of QILD scores (%) in whole lung (WL) and most severe zone (MSZ). Individual time-estimated yearly ΔQILD score between first 2 visits was derived using a linear approximation.

Results

Baseline median score of WL-QILD and MSZ-QILD were 28.1% (19.1-43.8) and 68.0% (45.5-81.8), respectively, and QILD score showed significant correlations with %FVC (r=-0.349) and %DLCO (r=-0.381), (p<0.05). The ΔQILD score presented that approximately half of the patients showed improvement in QILD scores; however, when patients were sorted by visual assessment in ILD subtype on HRCT, approximately two-thirds of the patients with usual interstitial pneumonia (UIP) pattern were aggravated in QILD scores and <50% of subjects with nonspecific interstitial pneumonia and organizing pneumonia were aggravated (Figure 1, UIP 80% vs. Non-UIP 44.4%, p=0.013). While there was no immunosuppressive drugs related to meaningful improvement in QILD scores during first 2 visits, significant aggravation was observed in tacrolimus users (n=7) compared with tacrolimus non-users (n=73) (+20.3 (2.7-38.4) vs. -1.2 (-8.3-6.5), p=0.013). Higher baseline QILD scores were noted in deaths (n=6) than survivors (n=74) (45.4 (32.9-56.5) vs. 26.9 (19.0-42.4), p=ns) and poor survival rate was observed in patients with high grade of ground glass opacity by visual assessment in right upper lobe (p=0.042). In patients with 3 serial HRCT scans (n=41), dynamic changes of four distinct patterns (improving/worsening/convex/concave) were observed.

Conclusions

The changes in QILD score in IIM-ILD are dynamic and present different by visual assessment. QILD score has the potential for evaluation of the severity changes, prognosis and medication response in patients with IIM-ILD.

Figure & Table

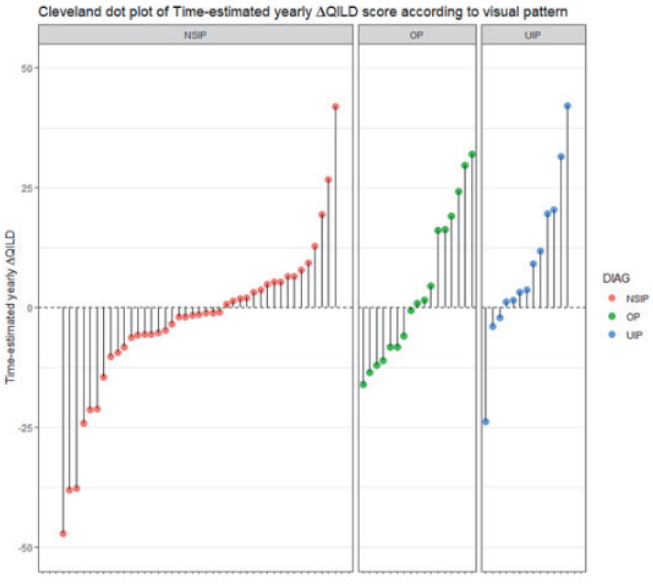

Figure. Cleveland dot plot of individual time-estimated yearly ΔQILD during fist 2 visits

Keywords

quantitative score, interstitial lung disease, idiopathic inflammatory myositis

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Time-dependent changes in rapidly progressive-interstitial lung disease and mortality risk in anti-MDA5 antibody positive dermatomyositis patients: A cohort study of 272 cases in China

Hanxiao You[1], Lingxiao Xu[1], Lei Wang[1], Chengyin Lv[1], Fenghong Yuan[2], Ju Li[3], Min Wu[4], Shiliang Zhou[4], Zhanyun Da[5], Jie Qian[5], Hua Wei[6], Wei Yan[6], Lei Zhou[7], Yan Wang[7], Songlou Yin[8], Dongmei Zhou[8], Jian Wu[9], Yan Lu[10], Dinglei Su[11], Zhichun Liu[12], Lin Liu[13], Longxin Ma[14], Xiaoyan Xu[15], Yinshan Zang[16], Huijie Liu[17], Tianli Ren[18], Fang Wang[19], Miaojia Zhang[1], Wenfeng Tan[1]

[1] Department of Rheumatology, The First Affiliated Hospital of Nanjing Medical University, China
[2] Department of Rheumatology, the Affiliated Wuxi People's Hospital of Nanjing Medical University, China
[3] Department of Rheumatology, Huai'an First People's Hospital, China
[4] Department of Rheumatology, The First People's Hospital of Changzhou, China
[5] Department of Rheumatology, Affiliated Hospital of Nantong University, China
[6] Department of Rheumatology, Northern Jiangsu People's Hospital, China
[7] Department of Rheumatology, Changzhou No.2 People's Hospital, China
[8] Department of Rheumatology, Affiliated hospital of Xuzhou Medical University, China
[9] Department of Rheumatology, The First Affiliated Hospital of Soochow University, China
[10] Department of Rheumatology, Jiangsu Province Hospital of Chinese Medicine, China
[11] Department of Rheumatology, Nanjing First Hospital, China
[12] Department of Rheumatology, The Second Affiliated Hospital of Soochow University, China
[13] Department of Rheumatology, Xuzhou Central Hospital, China
[14] Department of Rheumatology, Yancheng No.1 People's Hospital, China
[15] Department of Rheumatology, Zhongda Hospital Southeast University, China
[16] Department of Rheumatology, The Affiliated Suqian First People's Hospital of Nanjing Medical University, China
[17] Department of Rheumatology, The First People's Hospital of Lianyungang, China
[18] Department of Rheumatology, Wuxi No.2 People's Hospital, China
[19] Department of Cardiology, The First Affiliated Hospital of Nanjing Medical University, China

Background

Anti-melanoma differentiation-associated gene 5 (MDA5) positive dermatomyositis (DM) is a rare but distinct subtype of DM with a poor prognosis. We conducted this study to investigate the clinical characteristics and outcomes in anti-MDA5 antibody positive dermatomyositis and whether the risk of RP-ILD and death were time-dependent or not.

Methods

We assessed a cohort of 272 patients with anti-MDA5-positive DM. We summarized the clinical characteristics of patients with MDA5+ DM, and used COX regression to analyze independent risk factors for RPILD and death. We also described changes in risk of RPILD and death over time and their potential clinical implications.

Results

There were 272 anti-MDA5+ DM patients enrolled in this historical prospective clinical study. According to the multivariate cox regression analysis, short disease course, high ESR level, anti-Ro52 positive and anti-MDA5 titer (++~+++) were independent risk factors of RP-ILD. Arthritis, high CK level, high CRP level and RPILD were independent risk factors of death. Hazards regarding RPILD and mortality diminished over time from diagnosis, declined faster in the first six months.

Conclusions

Short disease course, high levels of muscle enzymes and high inflammation state are risk factors for poor prognosis. Our data regarding time-dependent hazards of RPILD and death reflect the disparate change of risks and this change of risk should be considered in clinical decision making.

Figure & Table

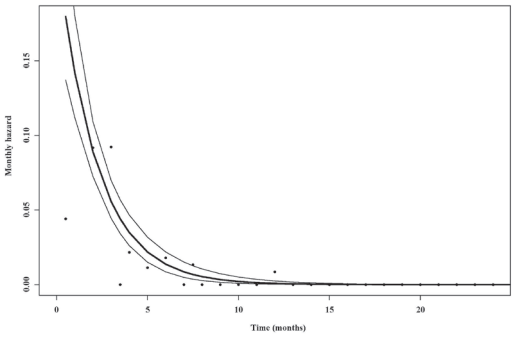

Figure. The survival of RP-ILD in anti MDA5+ DM patients smoothed hazard plots. Smoothed hazard plots more clearly demonstrate changes in risk at different time intervals than Kaplan-Meier plots do.

Keywords

Dermatomyositis, MDA5, Interstitial lung disease

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Coexisting of anti-Ro52 autoantibodies on anti-MDA5 autoantibodies-positive dermatomyositis is highly associated with rapidly progressive interstitial lung disease and mortality risk

Hanxiao You[1], Chengyin Lv[1], Lingxiao Xu[1], Lei Wang[1], Fenghong Yuan[2], Ju Li[3], Min Wu[4], Shiliang Zhou[4], Zhanyun Da[5], Jie Qian[5], Hua Wei[6], Wei Yan[6], Lei Zhou[7], Yan Wang[7], Songlou Yin[8], Dongmei Zhou[8], Jian Wu[9], Yan Lu[10], Dinglei Su[11], Zhichun Liu[12], Lin Liu[13], Longxin Ma[14], Xiaoyan Xu[15], Yinshan Zang[16], Huijie Liu[17], Tianli Ren[18], Fang Wang[19], Miaojia Zhang[1], Wenfeng Tan[1]

[1] Department of Rheumatology, The First Affiliated Hospital of Nanjing Medical University, China
[2] Department of Rheumatology, the Affiliated Wuxi People's Hospital of Nanjing Medical University, China
[3] Department of Rheumatology, Huai'an First People's Hospital, China
[4] Department of Rheumatology, The First People's Hospital of Changzhou, China
[5] Department of Rheumatology, Affiliated Hospital of Nantong University, China
[6] Department of Rheumatology, Northern Jiangsu People's Hospital, China
[7] Department of Rheumatology, Changzhou No.2 People's Hospital, China
[8] Department of Rheumatology, Affiliated hospital of Xuzhou Medical University, China
[9] Department of Rheumatology, The First Affiliated Hospital of Soochow University, China
[10] Department of Rheumatology, Jiangsu Province Hospital of Chinese Medicine, China
[11] Department of Rheumatology, Nanjing First Hospital, China
[12] Department of Rheumatology, The Second Affiliated Hospital of Soochow University, China
[13] Department of Rheumatology, Xuzhou Central Hospital, China
[14] Department of Rheumatology, Yancheng No.1 People's Hospital, China
[15] Department of Rheumatology, Zhongda Hospital Southeast University, China
[16] Department of Rheumatology, The Affiliated Suqian First People's Hospital of Nanjing Medical University, China
[17] Department of Rheumatology, The First People's Hospital of Lianyungang, China
[18] Department of Rheumatology, Wuxi No.2 People's Hospital, China
[19] Department of Cardiology, The First Affiliated Hospital of Nanjing Medical University, China

Background

Interstitial lung disease (ILD) is a common extramuscular complication contributing to significant morbidity and mortality in anti-melanoma differentiation associated gene five dermatomyositis (anti-MDA5+ DM). We conducted this study to investigate the association of anti-Ro52 antibodies with clinical characteristics and prognosis in anti-MDA5 + DM patients.

Methods

We assessed a cohort of 246 patients with anti-MDA5-positive DM. To calculate hazard ratios (HRs) and 95% confidence intervals (95% CIs) for RP-ILD and death while controlling for potential confounders, variables selected by univariate COX regression analysis were included in a multivariate COX regression model with the stepwise forward selection method. A 2-tailed P value <0.05 was considered to indicate statistical significance.

Results

246 anti-MDA5+ DM patients enrolled, 70 cases male, with an average age of 53.1±12.35 years. Anti-Ro52 coexisted in 64.22% (158/246) patients. Anti-Ro52 autoantibodies positive anti-MDA5+ DM patients had a higher rate of RP-ILD (log-rank p<0.001) and a higher mortality rate (log-rank p=0.01). For anti-MDA5+ DM patients with positive anti-Ro52 antibodies, patients with short disease course, high inflammation are at high risk of RP-ILD and death. The appearance of the active rash is an independent protective factor of death.

Conclusions

Anti-Ro52 antibodies is highly prevalent in anti-MDA5-positive DM patients and their coexistence correlates with a higher rate of RP-ILD and mortality. Patients with a short disease course, increased inflammation and without rash are more likely to have a poor prognosis.

Figure & Table

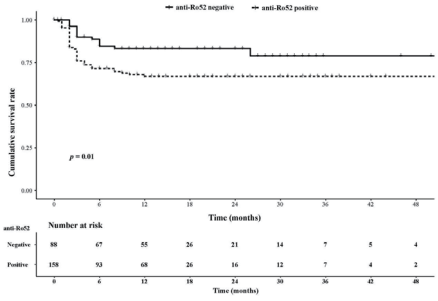

Figure. Difference of cumulative survival rate anti-MDA5+ DM patients with versus without anti-Ro52 autoantibodies. Patients with anti- Ro52 antibodies positive had a significant higher mortality rate (log-rank p =0.01).

Keywords

Dermatomyositis, MDA5, anti-Ro52

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Galectin-9 and CXCL-10 as biomarkers in assessing disease activity in Dermatomyositis and Polymyositis - A single centre cohort study

SAI KUMAR Dunga[1,2], Chengappa Kavadichanda[1], Devender Bairwa[1], Molly Mary Thabah[1], Vir Singh Negi[1]

[1] Department of Clinical Immunology, Jawaharlal institute of postgraduate medical education and research, India
[2] Department of Clinical Immunology and Rheumatology, Apollo Hospitals, Vishakapatnam, India

Background

Biomarkers are important in diagnosing, treating and prognostication of Idiopathic inflammatory myositis (IIM). Traditional biomarkers have a great extent of variability in their levels and poor correlation with disease activity. Hence there is a dire need for new biomarkers.

Methods

This cohort study included 42 IIM patients satisfying 2017 EULAR/ACR criteria. Patients were classified as active (n=18) and inactive disease (n=24) based on clinical status at baseline. Apart from routine investigations, serum samples (5 ml of peripheral venous blood) were collected at enrollment and at 3 months and 6 months for biomarker analysis. Galectin-9, CXCL-10, IL-10, TNFRII, BAFF and APRIL, were measured at baseline, at 3 months and at 6 months using ELISA. Data were analysed using SPSS version 19.0.

Results

All patients followed up at 3 months and 39 completed 6 months follow-up. There was a significant change($p<0.05$) in the Galectin-9, CXCL10, APRIL, TNFRII levels in the active disease subgroup at 3 months and 6 months from baseline. Upon posthoc analysis of the significant variables, the change between baseline and at 3 months as well as change between 3 months and at 6 months was also significant($p<0.001$). Galectin-9, CXCL10, APRIL, TNFRII were able to differentiate($p<0.05$) between patients with active disease and inactive disease at baseline. Based on the coordinates of the ROC curve we obtained a cut-off value of 1455.47pg/ml for galectin-9 (with a sensitivity of 69% and specificity 0f 76%), 86 pg/ml for CXCL10 (with a sensitivity of 87.5% and specificity 0f 66%). Change in galectin-9 ($r=0.534$), CXCL-10 ($r=0.409$) and BAFF ($r=0.534$) showed moderate correlation with change in MMT8 at 6 months.

Conclusions

Galectin-9, CXCL10, APRIL, TNFRII are reliable markers for assessing treatment response and differentiating patients with active and inactive disease. Galectin-9 was more specific and CXCL10 was more sensitive in differentiating active versus inactive patients with IIM.

Figure & Table

	Baseline (n=18)	3 months (n=18)	6 months (n=16)	P value
Galectin-9 pg/ml	1849.67 (699-6735)	937.49 (486-6174)	616.95 (287-4407)	**0.001**
CXCL10 pg/ml	460.52 (109-460.5)	80.58 (18-460.5)	73.81 (12-460.5)	**0.001**
APRIL ng/ml	0.78 (0.194-4.15)	0.23 (0.01-2.87)	0.03 (0.01-0.475)	**0.005**
TNFRII ng/ml	13.34 (2.7-25.2)	6 (3.5 – 19.3)	4.43 (0.9-16)	**0.001**
BAFF ng/ml	0.017 (0.01-1.1)	0.01 (0.01-0.34)	0.01 (0.01-0.05)	0.204
IL-10 pg/ml	0.01 (0.01-24.7)	0.01 (0.01-14.3)	0.01 (0.01-12.2)	0.343

APRIL, A proliferation inducing ligand, BAFF, B cell–activating factor, CXCL, (C-X-C motif) ligand; IL-10, interleukin 10, TNFRII, Tumour necrosis factor receptor II

Table. Comparison of biomarker levels among the active disease subgroup at baseline, 3 months and 6 months

Keywords

Biomarkers, Inflammatory myopathy, Disease activity

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Role of Semiquantitative thigh Magnetic Resonance Imaging (tMRI) in determining skeletal muscle outcomes at baseline and on follow up in idiopathic inflammatory myopathies (IIMs)

Mamatha Gorijavolu[1], Devender Bairwa[1], Chengappa Kavadichanda[1], Aishwarya Gopal[1], Sai Kumar Dunga[1], Molly Mary Thabah[1], Vir Negi[1]

[1] Clinical Immunology, Jawaharlal institute of postgraduate medical education and research, India

Background

Idiopathic Inflammatory Myopathies (IIMs) are characterized by muscle inflammation and associated muscle weakness. Semiquantitative scoring of thigh Magnetic Resonance Imaging (tMRI) has shown contradictory results in associating muscle inflammation, damage, and clinically assessed muscle weakness. Moreover, there are no studies assessing the role of tMRI detected muscle damage in determining long-term recovery of muscle strength and endurance.

Objectives: To correlate baseline tMRI scores with consecutively collected manual muscle testing 8 (MMT-8) scores.

Methods

This is a retrospective analysis of a single-center myositis cohort. Baseline demographic, clinical, and serological parameters of IIM patients (n=55) who underwent baseline tMRI (STIR and T1 sequences) at the time of diagnosis were noted. MRI images were assessed for intramuscular and fascial edema, atrophy and fatty replacement using a semiquantitative score. MMT-8 values and muscle enzyme levels which remained unchanged at least for 6 months during follow-up were noted for 42 patients. For statistical analysis, Spearman correlation and multiple linear regression were performed .

Results

The median age was 36 (27.25-44.75) years, median duration of disease at presentation was 4 months (2-10), median duration of follow up was 24 months (6.75-38.25). Baseline muscle enzymes CPK(r=0.531), AST(r=0.535) and ALT(r=0.442) showed significant positive correlation($p<0.01$) with muscle edema. Baseline MMT-8 showed significant negative correlation with muscle edema(r=-0.657) and fascial edema(r=-0.522) ($p<0.01$). Follow up MMT-8 showed significant negative correlation with muscle edema(r=-0.359), muscle atrophy (r=-0.319) and fatty infiltration(r=-0.308) ($p<0.05$) . Baseline MMT-8 and MRI fatty infiltration were significantly different between patients who achieved and did not achieve MMT-8 of ≥74 on follow-up . Multiple regression analysis revealed adjusted R^2 value of 0.386. Baseline MMT-8(β=0.372) and muscle atrophy(β=-0.459) significantly predicted MMT-8 on follow-up.

Conclusions

Low baseline MMT-8 and presence of muscle atrophy at baseline are predictors of poor outcome. Hence performing a baseline MRI will help in the prognosis.

Figure & Table

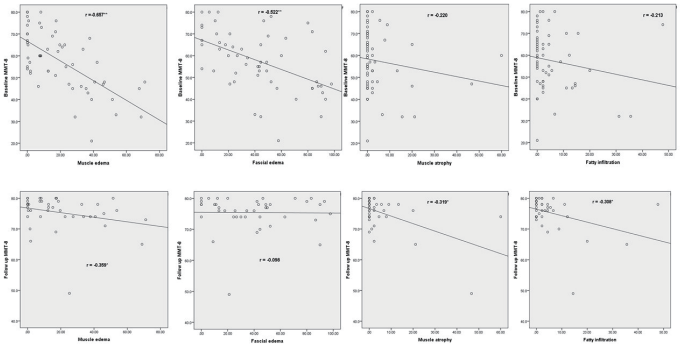

Figure. Correlation between baseline and Follow up MMT-8 with tMRI scores.

Keywords

Idiopathic inflammatory myositis, Thigh Magnetic Resonance Imaging, MMT-8

E-poster Presentation

Sjögren's syndrome

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Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Hyperglobulinemia in primary Sjögren's syndrome predicts the poor outcome: From multicenter registration study

Hui Zhong[1], Yanhong Wang[2], Pingting Yang[3], Xinwang Duan[4], Yongfu Wang[5], Jian Xu[6], Lijun Wu[7], Qin Li[8], Xiaodan Kong[9], Liyun Zhang[10], Xiaomei Li[11], Dong Xu[1], Mengtao Li[1], Yan Zhao[1], Xiaofeng Zeng[1]

[1] Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, China
[2] Department of Epidemiology and Biostatistics, Institute of Basic Medical Sciences Chinese Academy of Medical Sciences, China
[3] Department of Rheumatology and Immunology, The First Affiliated Hospital, China Medical University, China
[4] Department of Rheumatology and Immunology, The Second Affiliated Hospital Nanchang University, China
[5] Department of Rheumatology, First Affiliated Hospital of Baotou Medical College, Inner Mongolia University of Science&Technology, China
[6] Department of Rheumatology and Immunology, The First Affiliated Hospital of Kunming Medical University, China
[7] Department of Rheumatology and Immunology, Xinjiang Uygur Autonomous Region People's Hospital, China
[8] Department of Rheumatology, The First People's Hospital of Yunnan Province, China
[9] Department of Rheumatology and Immunology, The Second Affiliated Hospital, Dalian Medical University, China
[10] Department of Rheumatology and Immunology, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, China
[11] Department of Rheumatology and Immunology, the first affiliated hospital of USTC(Anhui Province Hospital), China

Background

Primary Sjogren's syndrome(pSS) is an autoimmune disease characterized by exocrine gland involvements and B cell hyperactivity. About half of pSS patients have hyperglobulinemia, and whether treatment should be initiated for hyperglobulinemia is still controversial. The aim of this study to investigate the all-cause mortality of pSS with hyperglobulinemia, based on a multicenter cohort.

Methods

Patients who met 2002 AECG criteria or 2016 ACR/EULAR classification criteria for SS and did not overlap other connective tissue diseases in Chinese Rheumatism Data Center from May 2016 to July 2021 were included in this study. Data of demographic and clinical characteristics, laboratory results, disease activity and damage scores were used. Hyperglobulinemia was defined as IgG>17.0g/L, or IgA>4.0g/L, or IgM>2.6g/L. The primary outcome is all-cause death until July 15, 2021.

Results

A total of 9527 pSS patients were included in the study, and 4236(44.5%) pSS had at least one kind of elevated immunoglobulin levels among IgG, IgA and IgM. Patients with hyperglobulinemia had significantly increased risk of death, with crude HR 2.6(95%CI 1.91-3.55). After adjustment for sex, age, disease course, ILD and PAH, pSS patients with hyperglobulinemia still had significant increased risk of all-cause death (adjusted HR 1.87 95%CI 1.36-2.57) than those without. The 5-year and 10-year survival rates of patients with hyperglobulinemia were 96.9%, 92.3%, which were significantly lower than those with normal immunoglobulin level. In subgroup analysis, pSS patient with both elevated IgG and IgA had the highest risk of death (HR 3.88, 95%CI 2.766-5.44). Death risk positively correlated with IgG levels (P for trend <0.001).

Conclusions

hyperglobulinemia is an independent risk factor for increased all-cause mortality in pSS patients. Therefore, treatments should be given to pSS patients with hyperglobulinemia, especially to those with both increased IgG and IgA.

Keywords

Sjogren's syndrome, hyperglobulinemia, prognosis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
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Primary Sjögren's syndrome is associated with increased risks of not just lymphoma: a systematic review and meta-analysis

Hui Zhong[1], Siyao Liu[1], Yanhong Wang[2], Dong Xu[1], Mengtao Li[1], Yan Zhao[1], Xiaofeng Zeng[1]

[1] Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, China
[2] Department of Epidemiology and Biostatistics, Institute of Basic Medical Sciences Chinese Academy of Medical Sciences, China

Background

To investigate the association between primary Sjogren's syndrome(pSS) and the risks of malignancy, with a focus on solid tumors and hematological malignancies other than non-Hodgkin lymphoma (NHL) through a systematic review and meta-analysis.

Methods

We searched PubMed and EMBASE by March 21st 2021. Inclusion criteria were as follows: (1) pSS was the exposure of interest; (2) newly developed malignancies were the outcome of interest; (3) standardized incidence ratio or relative risk with 95% confidence interval or essential data to calculate them were reported. (4) Study design was cohort study. Patient with other connective diseases were excluded. Quality assessment was conducted according to Newcastle-Ottawa Scale for cohort study. Random or fixed effect models were used to calculate the pooled SIR according to the heterogeneity.

Results

A total of 1003 articles were found by a comprehensive search in PubMed and EMBASE. Twenty-eight articles were eligible. Since 4 of them were from the same database, the one with longest observational span was chosen. Therefore, twenty-five articles were included for final analysis, which involved more than 47607 pSS patients with the follow-up of more than 452468 person-year. We found that pSS was associated with increased risks of overall malignancy(pooled SIR 2.17, 95%1.57-3.00), hematological malignancy(pooled SIR 11.55, 95%CI 4.32-30.90) including NHL(pooled SIR 13.71, 95%CI 8.83-21.29), Hodgkin lymphoma(pooled SIR 8.84, 95%CI 5.00-15.61), multiple myeloma(pooled SIR 8.27, 95%CI 3.08-22.24), leukemia(pooled SIR 2.56, 95%CI 1.78-3.69) and solid tumors(pooled SIR 1.39, 95%CI 0.90-2.13) including lung cancer(pooled SIR 1.55, 95%CI 1.29-1.85), thyroid cancer(pooled SIR 2.05, 95%CI 1.20-3.48), non-melanoma skin cancer(pooled SIR 1.71, 95%CI 1.08-2.72), kidney/urinary tract cancer(pooled SIR 1.36, 95%CI 1.03; 1.80), liver cancer(pooled SIR 1.70, 95%CI 1.13-2.57) and prostate cancer(pooled SIR 1.50, 95%CI 1.02-2.22).

Conclusions

This meta-analysis shows that pSS patients have increased overall cancer risk, which not only contributed by NHL, but also by other hematological malignancies and solid tumors.

Keywords

Sjogren's syndrome, malignancy, prognosis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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Salivary ultrasonography and histopathologic evaluation of secondary Sjögren's syndrome in rheumatoid arthritis patients

Minae Oh[1], Youngjae Park[1], Youn Soo Lee[2], Wan-Uk Kim[1]

[1] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's hospital, The Catholic University of Korea, Republic of Korea
[2] Department of Hospital Pathology, Seoul St. Mary's Hospital, The Catholic University of Korea, Republic of Korea

Background

Sjogren's syndrome (SS) is one of the most frequent autoimmune conditions overlapped in rheumatoid arthritis (RA). Recently, novel modalities such as salivary ultrasonography (SGUS) and shear wave elastography (SWE) are introduced for evaluating SS. However, in patients with secondary SS, diagnostic performance of SGUS and its relationship with clinicopathological characteristics have not been clearly defined. In this study, we aimed to investigate prevalence of secondary SS in RA patients using new modalities and clarify their clinicopathological features.

Methods

Thirty-one RA patients presented with sicca symptoms were included for being evaluated on SS, and were compared with 18 primary SS (pSS) patients as a control. All subjects were assessed through SGUS and SWE as well as conventional diagnostic approaches for SS, including minor salivary gland biopsy (MSGB). In SGUS evaluation, two separate scoring systems were used. MSGB specimens were digitally scanned and evaluated by a specialized pathologist.

Results

Among 31 RA patients with sicca symptoms, 19 (61.2%) were diagnosed as secondary SS according to the 2016 classification criteria for SS. Interestingly, secondary SS patients had significantly lower positivity for anti-Ro antibody and anti-La antibody than pSS patients. Both SGUS scoring systems demonstrated good diagnostic performance in differentiating secondary SS from RA patients with sicca symptoms. As expected, in histopathologic assessment of MSGB, secondary SS and pSS patients exhibited significantly higher lymphocytic infiltration areas than RA patients without SS. Focus score and lymphocytic infiltration areas in were correlated well with sonographic severity by the two scoring systems. The pathologic severity of fibrosis was positively correlated with SWE, but failed to have correlations with SGUS findings.

Conclusions

Secondary SS is more frequent in RA patients than reported earlier and presents less positivity for anti-Ro/La antibodies. Similar to for pSS, SGUS shows good diagnostic performance for secondary SS, reflecting well histopathologic severity on MSGB.

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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STAT4 gene polymorphisms in risk of Sjögren's syndrome patients susceptibility: Update systematic review and meta-analysis

Rendra Ristian wibowo[1], Bastomy Eka rezkita[1], Ambar Mudigdo[2], Dyah Ratna[2]

[1] Internal Medicine, Sebelas Maret University, Indonesia
[2] Pathological Anatomy, Sebelas Maret University, Indonesia

Background

Sjögren's syndrome (SS) is chronic autoimmune condition typically known by autoantibody generation, sicca syndrome, and periepithelial lymphocytic lesions in target tissues. STAT4 genes encode transcription factor that transmits signal induced by interleukin 12(IL-12) IL-23, and type 1 interferon. STAT4 also play important role in developing IL-17 secreting Th cells in response to IL-23. Both lineages are key role in developing SS. Objectives of this paper is to investigate the possible association of the polymorphism of the STAT4 with susceptibility to SS and with phenotypic disease features.

Methods

This meta-analysis was conducted based on the PRISMA guideline. Literature searches from Cochrane, Pubmed and EMBASE were conducted until December 2021 and were limited to English-only literature. Inclusion criteria of these meta-analysis include case control and cohort study. Studies included in this meta-analysis were accessed using The Newcastle Ottawa Score (NOS). The primary outcome was the association between STAT4 gene polymorphism and the risk of SS. The sufficient data count is pooled by OR and 95% CI.

Results

Four studies (652 case / 1052 control) met the inclusion criteria. G allele and GG genotype were associated with decreased risk of SS (OR= 0.65[0.56 – 0.76], p= 0.0001 and OR= 0.59[0.48-0.73]. p= 0.0001). Meanwhile, T allele and GT genotype were significantly associated with increased risk of SS (OR= 1.53[1.31-1.79], p= 0.0001 and OR=1.38 [1.12-1.69], p= 0.002).

Conclusions

Our meta-analysis suggested that G allele and GG genotype may serve as protective factor of SS, while A allele and GT genotype may increase risk factor for SS. Further study about interaction between genetic-environment interactions with larger sample is needed

Figure & Table

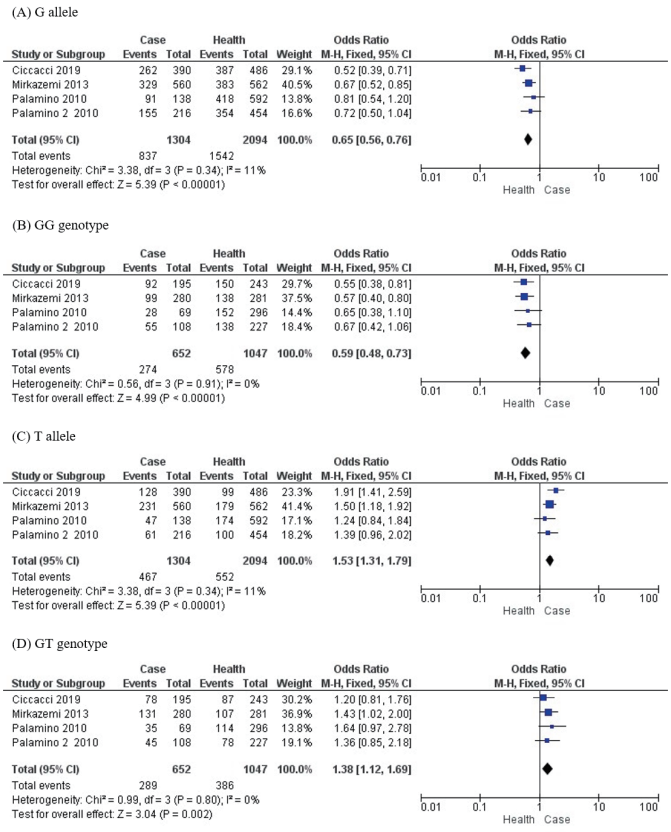

Table. Forest Plot from 4 studies.

Keywords

Gene polymorphism, Sjögren's syndrome, STAT4

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-114

Interstitial lung disease in Sjögren's syndrome: Prevalence, Patterns, Treatment, and prognosis

Jung Hee Koh[1], Su-Jin Moon[1], Yong Hyun Kim[2], Jun-Ki Min[1]

[1] Division of Rheumatology, Department of Internal medicine, College of Medicine, The Catholic university of Korea, Republic of Korea
[2] Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Bucheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Republic of Korea

Background

Interstitial lung disease (ILD) is a potentially serious yet underdiagnosed manifestation of primary Sjogren's syndrome (pSS). This observational study aimed to investigate the clinical, functional, and imaging characteristics of ILD in pSS, together with treatment and prognosis.

Methods

Longitudinal clinical and laboratory data for patients with pSS at a single center between January 1, 2010, and December 31, 2021, were collected from the clinical data warehouse (CDW). Predisposing factors for the development of ILD and acute exacerbation were identified using a logistic regression model.

Results

In total, 284 patients with pSS were included in this study (Female, 96%; median age, 53 years). Among them, 32 patients with pSS (11%) were comorbid with ILD (13 biopsy-proven cases). Age, immunoglobulin G level, and C-reactive protein (CRP) level were associated with ILD. Usual interstitial pneumonia (UIP) or fibrosing nonspecific interstitial pneumonia (NSIP) was the most prevalent CT pattern in pSS-ILD (44%), followed organizing pneumonia (22%). Three-quarters of patients showed reduced diffusion capacity, and 35% of patients with pSS-ILD showed a restrictive functional pattern. The median follow-up period was 2.2 years. During follow-up, one patient died (3%), 13 patients (41%) experienced acute exacerbation (AE), and 4 patients (13%) were progressed. Patients with AE were treated with a high-dose steroids-based regimen and 64% of them presented improvement in the CT scan after at least 6 months. The pulmonary function was stationary in all patients with SS-ILD.

Conclusions

ILD was prevalent in pSS patients. Elder age and higher CRP and immunoglobulin G levels were associated with pSS-ILD. Most pSS-ILD patients responded to high-dose steroids, however, a few patients progressed. Our data highlighted the importance of screening for ILD in high-risk pSS patients.

Keywords

Sjogren's syndrome, Interstitial lung disease, prevalence

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Distinct metabolic biomarkers to distinguish immunoglobulin G4-related disease from Sjögren's syndrome and pancreatic cancer and predict disease prognosis

Yu Peng[1], Wen Zhang[1]

[1] Rheumatology, Peking Union Medical College Hospital, China

Background

The pathogenesis of immunoglobulin G4-related disease (IgG4-RD) remains unclear. IgG4-RD often mimics other diseases, including pancreatic cancer (PC) and Sjogren's syndrome (SS), which may easily lead to misdiagnosis. This study was performed to explore the underlying mechanisms and potential biomarkers of IgG4-RD and other misdiagnosed diseases.

Methods

Untargeted liquid chromatography–tandem mass spectrometry metabolomics profiling of plasma samples from a cohort comprising healthy controls (HCs) and patients with IgG4-RD, PC, and SS was performed. A random forest machine learning model was used to verify the relevance of the identified metabolites in the diagnosis of different diseases and the prediction of disease prognosis.

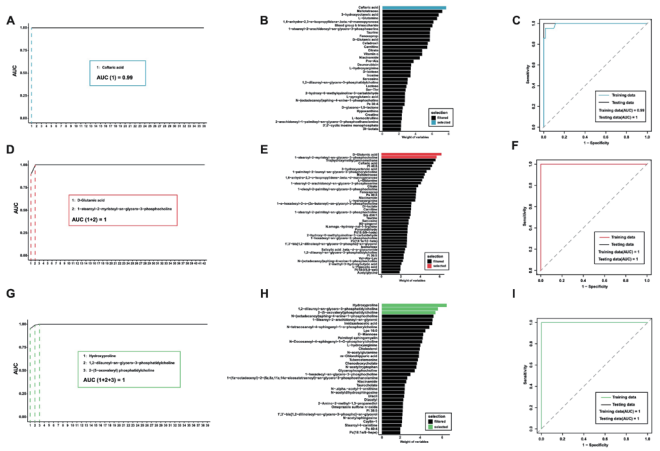
Results

The ATP-binding cassette transporters pathway was found to be most closely related to IgG4-RD, which was significantly upregulated in the IgG4-RD group than in all the paired groups. Six metabolites were proved to be valuable biomarkers for IgG4-RD. Caftaric acid, D-glutamic acid, 1-stearoyl-2-myristoyl-sn-glycero-3-phosphocholine, hydroxyproline, 1,2-dilauroyl-sn-glycero-3-phosphatidylcholine, and 2-(5-oxovaleryl) phosphatidylcholine were useful in distinguishing between IgG4-RD, PC, SS, and HC (AUC = 1). A combination of Ps 40:4, 3-methyl-2-oxopentanoate, 1-palmitoyl-2-lauroyl-sn-glycerol-3-phosphorylcholine, and Pc(16:0e/13-hode) showed a moderate value in predicting relapse in patients with IgG4-RD (AUC = 0.72).

Conclusions

Our findings revealed the underlying mechanisms of IgG4-RD and provide new insights for deepening our understanding of IgG4-RD. Metabolomic biomarkers have significance in the clinical diagnosis and disease prognosis of IgG4-RD.

Figure & Table



JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Predictors of the future development of systemic lupus erythematosus (SLE) in Korean primary Sjögren's syndrome (pSS) patients with anti-DNA antibody (+) by the Farr method.

Bong-Woo Lee[1], Youngjae Park[2], Jennifer Lee[2], Sung-Hwan Park[2], Seung-Ki Kwok[2]

[1] Division of Rheumatology, Department of Internal Medicine, Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Background

Primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE) can coexist and pSS can precede SLE. Some pSS patients are positive for anti-DNA antibody, but SLE is not diagnosed at that time. Therefore, we aimed to clarify the predictors of the future development of SLE in pSS patients with anti-DNA antibody (+).

Methods

This retrospective study assessed 174 pSS patients with positive for anti-DNA antibody by the Farr method, who regularly visited Seoul St. Mary's Hospital between 2013 and 2021. All patients did not meet the 2019 EULAR/ACR Classification Criteria for SLE at baseline. 174 patients were classified into a group that later developed SLE and a group that did not. Data were compared between the two groups, including demographic features, extra-glandular manifestations (EGMs), clinical indices, and laboratory values at baseline. Additionally, predictors of the onset of SLE were analyzed.

Results

Among 174 pSS patients with positive for anti-DNA antibody by the Farr method, 47 patients met the 2019 EULAR/ACR Classification Criteria for SLE in the future from the baseline. In the future SLE development group, lower Schirmer test positive proportion, higher ESSDAI score in biological and hematological domain, and higher frequency of autoimmune thyroiditis were found. In addition, that group showed lower WBC counts, C3, and C4 at baseline. The multivariate logistic regression analysis revealed leukopenia (<4000/mm3) (OR: 7.43 (2.75-20.6) p = <0.001), low C3 (OR: 16.71 (6.00-46.56) p = <0.001) and low C4 (OR: 16.71 (6.00-46.56) p = <0.001) at baseline to be associated with the development of SLE in anti-DNA (+) pSS patients.

Conclusions

Leukopenia and low C3/C4 at baseline were associated with the future development of SLE in anti-DNA (+) pSS patients. For the anti-DNA (+) pSS patients with those predictors, it is necessary to periodically check the symptoms and laboratory tests included in the SLE classification criteria.

Figure & Table

	Future SLE development (+) anti-DNA (+) pSS (n=47)	Future SLE development (-) anti-DNA (+) pSS (n=127)	p value
Baseline characteristics			
Age (at baseline)	47.38 (±1.85)	53.24 (±1.16)	0.009
Age (at diagonsis)	42.49 (±1.64)	48.38 (±1.15)	0.006
Disease duration (month)	57.81 (±7.83)	58.21 (±5.20)	0.967
Female sex	46 (97.9%)	126 (99.2%)	0.468
Ocular dryness	42 (89.4%)	114 (89.8%)	1.000
Oral dryness	46 (97.9%)	114 (89.8%)	0.116
Schirmer test (<5mm/5min)	21 (44.7%)	82 (64.6%)	0.024
No. of EGM	1.47 (±0.17)	1.34 (±0.096)	0.496
OSS by SICCA method (≥ 5)	11 (23.4%)	46 (36.2%)	0.145
Unstimulated salivary flow rate (< 0.1 mL/min)	40.40%	47.20%	0.602
EGMs			
Articular involvement	22 (46.8%)	52 (40.9%)	0.495
Raynaud's phenomenon	6 (12.8%)	24 (18.9%)	0.498
Lymphadenopathy	9 (19.1%)	17 (13.4%)	0.346
Pulmonary involvement	4 (8.5%)	16 (12.6%)	0.596
Cutaneous involvement	5 (10.6%)	18 (14.2%)	0.623
Liver involvement	1 (2.1%)	10 (7.9%)	0.292
Splenomegaly	0	0	-
Lymphoma	1 (2.1%)	3 (2.4%)	1.000
Renal involvement	3 (6.4%)	5 (3.9%)	0.447
Myositis	0	0	-
Peripheral neuropathy	2 (4.3%)	5 (3.9%)	1.000
Central nerve system	2 (4.3%)	3 (2.4%)	0.613
Autoimmune thyroiditis	14 (29.8%)	17 (13.4%)	0.024
ESSDAI (by domain)			
Total score	6.96 (±0.805)	5.51 (±0.488)	0.123
Constitutional	0.21 (±0.07)	0.12 (±0.03)	0.149
Lymphadenopathy	0.23 (±0.10)	0.27 (±0.14)	0.884
Glandular	0.23 (±0.1)	0.17 (±0.06)	0.599
Articular	0.38 (±0.08)	0.29 (±0.05)	0.308
Cutaneous	0.49 (±0.22)	0.24 (±0.07)	0.156
Pulmonary	0.3 (±0.22)	0.35 (±0.11)	0.798
Renal	0	0.05 (±0.04)	0.475
Muscular	0	0	-
Peripheral nerve system	0.02 (±0.02)	0.03 (±0.02)	0.722
Central nerve system	0.21 (±0.21)	0.06 (±0.04)	0.294
Hematological	0.87 (±0.14)	0.4 (±0.06)	<0.001
Biological	1.3 (±0.11)	0.97 (±0.08)	0.021
Laboratory data			
WBC count	3.85 (±0.20)	4.98 (±0.15)	<0.001
Leukopenia (< 4000/mm3)	31 (66%)	36 (28.3%)	<0.001
ANC count	2.02 (±0.17)	2.75 (±0.12)	0.001
Neutropenia (< 1500/mm3)	16 (34%)	14 (11%)	0.001
Hb	12.46 (±0.18)	12.65 (±0.1)	0.329
Anemia, < 12 g/dL	17 (36.2%)	34 (26.8%)	0.262
Platelet count	205.51 (±10.52)	225.06 (±5.18)	0.068
Thrombocytopenia, < 150,000/mm3	7 (14.9%)	9 (7.1%)	0.14
Immunoglobulin G	2177.06 (±132.35)	2068.54 (±75.24)	0.463
Elevation of Immunoglobulin G (>1,600 mg/dl)	34 (72.3%)	80 (63.0%)	0.285
C3	79.68 (±2.69)	97.46 (±1.303)	<0.001
C4	16.73 (±0.88)	21.34 (±0.51)	<0.001
Cryoglobulin	1 (2.1%)	0 (0%)	0.27
Rheumatoid factor positivity	25 (53.2%)	80 (60.0%)	0.295
Anti-CCP positivity	1 (2.1%)	4 (3.1%)	1
Anti-Ro/SSA antibody positivity	46 (97.9%)	115 (90.6%)	0.19
Anti-La/SSB antibody positivity	26 (55.3%)	66 (52%)	0.735
Anti-RNP antibody positivity	5 (10.6%)	12 (9.4%)	0.78

Table. Basal demographics , secretory function-related values, EGMs, ESSDAI and laboratory data

Keywords

pSS, SLE, Anti-DNA antibody

E-poster Presentation

Systemic sclerosis and Raynaud's phenomenon

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Analysis of clinical features of myocardial involvement in systemic sclerosis

Huilin He[1]

[1] Rheumatology, Peking Union Medical College Hospital,Beijing,China, China

Background

To analyze the clinical characteristics of systemic sclerosis (SSc) with myocardial involvement.

Methods

Data of SSc patients with myocardial involvement who admitted in Peking Union Medical College Hospital from 2012 to 2021 were retrospectively collected. SSc patients without myocardial involvement were randomly selected as control according to 1:3 matched age and sex during the same time. Clinical characteristics, laboratory, imaging examinations and treatment data were analyzed.

Results

There were 26 patients with SSc with myocardial involvement, including 21 females (80.8%). The onset age of SSc was 44.8±15.1 years. Patients with SSc with myocardial involvement had fewer puffy finger(15.4% vs. 56.4%, P<0.001), loss of finger pad substance(11.5% vs. 34.6%, P=0.024), pulmonary arterial hypertension(7.7% vs. 32.1%, P=0.017), gastroesophageal reflux(19.2% vs. 52.6%, P=0.003), and interstitial lung disease(61.5% vs. 83.6%, P=0.020) compared with controls, but more myositis(38.5% vs. 9.0%, P=0.001) and renal crisis(11.5% vs. 1.3%, P=0.047). In terms of laboratory examination, patients combined with cardiac involvement had more elavated CK (30.8% vs. 6.9%, P=0.006) and positive anti-SCL70 antibody (65.4% vs. 37.2%, P=0.012). The age of cardiac involvement in SSc patients was 48.0±15.2 years, and the median duration of cardiac involvement was 22.0 (5.8, 56.5) months. Among the 26 patients, 16 (61.5%) had cardiovascular symptoms. Among the 10 patients (38.4%) without cardiovascular symptoms, 6 had elevated CTnI, 7 had elevated NT-proBNP and 7 presented with cardiomyopathy or myocardial fibrosis in UCG or cardiac MRI. Four patients underwent methylprednisolone pulse therapy, and cardiac radionuclide TATE showed diffuse inflammation in two of them. Thirteen patients with a median follow-up time of 13.4 (6.15, 29.2)/month, and four patients developed new-happened LVEF＜50%.

Conclusions

Nearly half of patients are subclinical, SRC and myositis were more common in these patients. These patients usually have poor prognosis. Regular monitoring of CTnI, NT-proBNP and UCG is helpful for patients.

Keywords

Systemic sclerosis, Myocardial involvement, Treatment

E-poster Presentation

Miscellaneous rheumatic and inflammatory diseases

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-118

Brain magnetic resonance imaging finding in autoimmune rheumatic disease

Recep Sade[1], Meltem Alkan melikoglu[2]

[1] Radiology, Ataturk University, Turkey
[2] Rheumatology, Ataturk University, Turkey

Background

Autoimmune rheumatic diseases (ARDs) may affect the brain. We evaluate and compare brain magnetic resonance imaging (MRI) findings of patients with ARD and non-ARD patients.

Methods

Retrospectively, 30 patients with ARD and 30 age and gender-matched controls with non-ARD, were evaluated and compared brain MRI findings.

Results

25 (83,3%) ARD patients and 20 (66,6%) controls had white matter hyperintensities ($p < 0.001$) in at least one brain area (subcortical/deep/periventricular white matter, basal ganglia, pons, brainstem, or mesial temporal lobe). Only the frequency and number of subcortical and deep white matter lesions were significantly greater in ARD patients ($p < 0.012$ and 0.032, respectively). ARD vs. control status was the only independent predictor of having any brain lesion. Penalized logistic regression selected only ARD vs. control status as the most important feature for predicting whether brain lesions were present on brain MRI (odds ratio: 4.32, marginal false discovery rate = 0.021).

Conclusions

Subclinical brain involvement of ARD patients was highly prevalent in this study. However, further research is required to determine the clinical relevance of these findings.

Keywords

Autoimmune rheumatic disease, magnetic resonance imaging, diagnosis

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Spontaneous knee hemarthrosis associated with enoxaparin treatment in a post COVID-19 patient

Mark Andrian Yano[1], Geraldine Zamora[1], Karen Anne Claridad[2], Ralph Elvi Villalobos[2]

[1] Division of Rheumatology, Department of Medicine, Philippine General Hospital, Philippines
[2] Division of Pulmonary Medicine, Department of Medicine, Philippine General Hospital, Philippines

Description

We report a case of a 66-year-old Filipino male who developed spontaneous hemarthrosis of the left knee following enoxaparin use as venous thromboembolism prophylaxis. Pertinent in the medical history was the diagnosis of chronic kidney disease and chronic respiratory failure as sequelae of COVID 19 infection. During the course of admission, the patient developed acute pain and swelling of the left knee. The patient was bedridden and no prior traumatic events were noted. Coagulation parameters were within normal range. Arthrocentesis revealed viscous hemorrhagic synovial fluid (25 ml) with fluid analysis showing predominance of red blood cells (RBC 680,000 WBC 7200) with no crystals seen on polarizing microscopy. Microbial cultures did not reveal any growth. Methylprednisolone was given and enoxaparin continued. One day post arthrocentesis, there was improvement of pain and joint function. Joint swelling resolved. Patient had no recurrence of joint pain and swelling.

Conclusions

This is an elderly patient with chronic kidney disease who recently recovered from COVID 19 infection. He received prophylactic dose of enoxaparin at 40 mg every 24 hours. No other drugs that can affect hemostasis were given. The patient's bleeding parameters were within normal limits during admission and at the onset of hemarthrosis. We hypothesize that elderly patients with chronic kidney disease may be prone to bleeding and can present with hemarthrosis even with low dose enoxaparin. Whether the association between history of COVID-19 infection and hemarthrosis is co incidental or causal remains to be elucidated. Prompt aspiration can provide early diagnosis and facilitate proper treatment.

Figure & Table

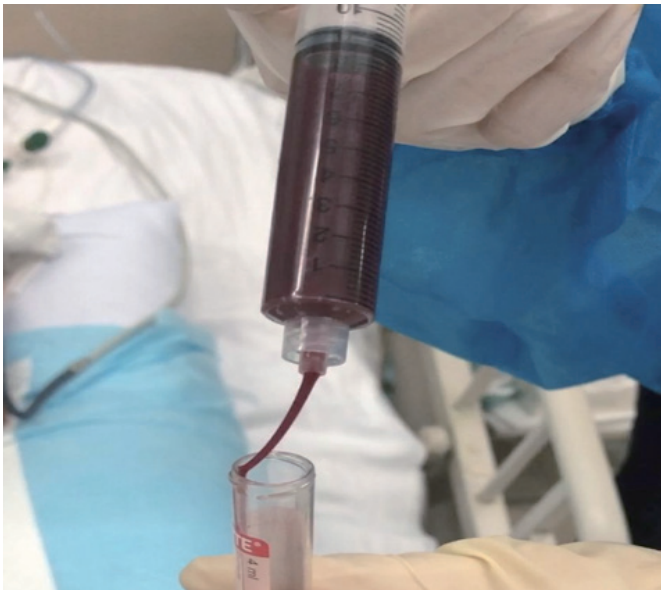

Figure. Viscous hemorrhagic synovial fluid

Keywords

Hemarthrosis, COVID 19, Enoxaparin

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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May 19(Thu) - 21(Sat), 2022

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Clinical profile and outcome of adult Filipino patients with septic arthritis in a tertiary hospital in the Philippines

Mark Andrian Yano[1], Alfonso Juan Miranda[2]

[1] Department of Internal Medicine, Chong Hua Hospital, Philippines
[2] Division of Rheumatology, Department of Internal Medicine, Chong Hua Hospital, Philippines

Background

Septic arthritis is the invasion of a joint by an infectious agent resulting in joint inflammation. Considered a medical emergency, it requires prompt diagnosis followed by rapid and aggressive treatment. However, recent local data of septic arthritis among Filipinos is still limited despite medical advancement.

Methods

This is a retrospective descriptive study. The medical records of admitted patients diagnosed with pyogenic arthritis, septic or infectious arthritis, and tuberculous arthritis at Chong Hua Hospital, Cebu City, Philippines from January 1, 2012 to December 31, 2019 were identified and reviewed. Epidemiological, clinical and laboratory data regarding septic arthritis were gathered. Descriptive statistics such as frequency and percentage distribution were used in expressing the data.

Results

Fifty-seven patients were identified as having septic arthritis based on discharge diagnoses. Twenty-five of the patients (43.86%) were between the ages of 45 to 64 years old. Comorbidities such as diabetes mellitus (49.12%, n=28) and hypertension (43.86%, n= 25) were commonly identified. Twenty (35%) of the patients had primary joint disease, with gout (21%) as the most prevalent. Majority of the patients (94%) patients presented with monoarthritis. Gram negative bacilli was the most common pathogen isolated in eighteen (31.5%) cases. Ceftriaxone was the most commonly used empiric antibiotic in eighteen (31.5%) cases. The empiric antibiotic treatment was adequate in 66.67% (n=38) of the cases with identified septic arthritis.

Conclusions

This study highlights the unique characteristics of septic arthritis in this population such as its prevalence in the middle-aged population, isolation of gram-negative bacilli as the most common isolate, and normal initial of levels of WBC, CRP, and ESR. Thus, maintaining a high clinical suspicion and being cognizant of predisposing risk factors, adequate treatment and care may be provided to septic arthritis patients.

Figure & Table

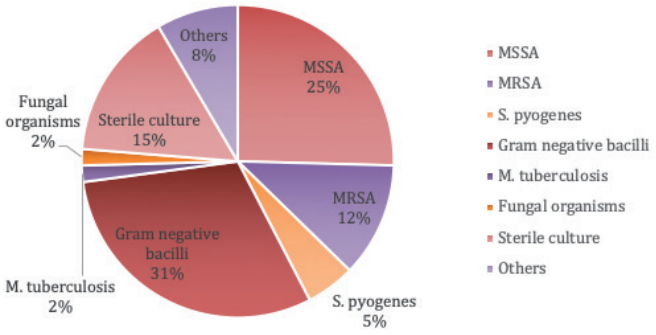

Figure. Causative organisms of septic arthritis

Keywords

Septic arthritis, Filipino

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Tuberculosis fasciitis of the neck in Behçet's patient

Yunus Fersan[1], Mehmet Aksit[1], Gökhan Polat[2]

[1] medical faculty, Atatürk University, Turkey
[2] Department of Radiology, Ataturk University, Turkey

Description

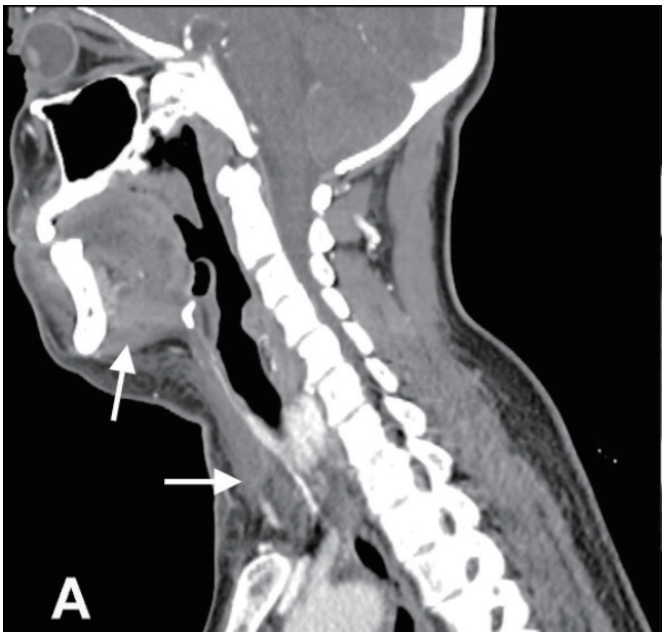
A 44-year-old male patient had complaints of widespread pain and erythema in the floor of the mouth in the neck. The patient has a known 16-year-old diagnosis of Behçet's disease. He was administered 110 mg of methylprednisolone acetate, intramuscularly for immediate pain relief. He was prescribed azathioprine, 145 mg/d, and adalimumab, 40 mg subcutaneously every other week. Computed tomography was performed on the patient and there was an increase in density in favor of inflammation in the superficial fascia and subcutaneous areas(Figure 1). The patient was diagnosed with superficial fasciitis by imaging.

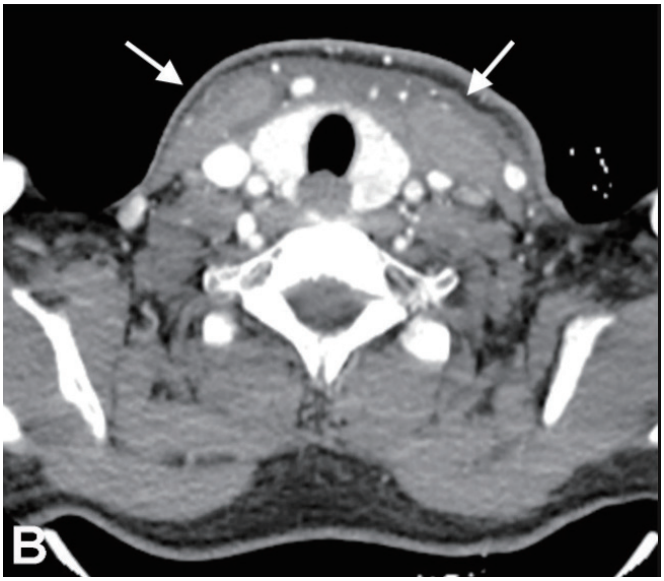
Histopathological examination of the biopsy taken from the fascia revealed diffuse necrosis without epithelioid cell granuloma. Acid-fast bacilli were seen by acid-fast staining and Mycobacterium tuberculosis was detected in cell culture. Therefore, the patient was diagnosed with tuberculous fasciitis. The patient was treated with antituberculosis for 12 months.

Conclusions

It can mimic tuberculous fasciitis, cellulitis, and autoimmune fasciitis; therefore diagnosis may be delayed. Although rare, it has also been reported in patients receiving immunosuppressive therapy for rheumatic disease, including polymyositis and rheumatoid arthritis. To our knowledge, this is the first documented case of tuberculous fasciitis in a patient with BD.

Figure & Table





JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Chronic inflammatory demyelinating polyneuropathy (CIDP) in polyangiitis granulomatosis with cyclophosphamide

Kadem Tüysüz[1], Mehmet Aksit[1], Gökhan Polat[2]

[1] medical faculty, Atatürk University, Turkey
[2] Department of Radiology, Ataturk University, Turkey

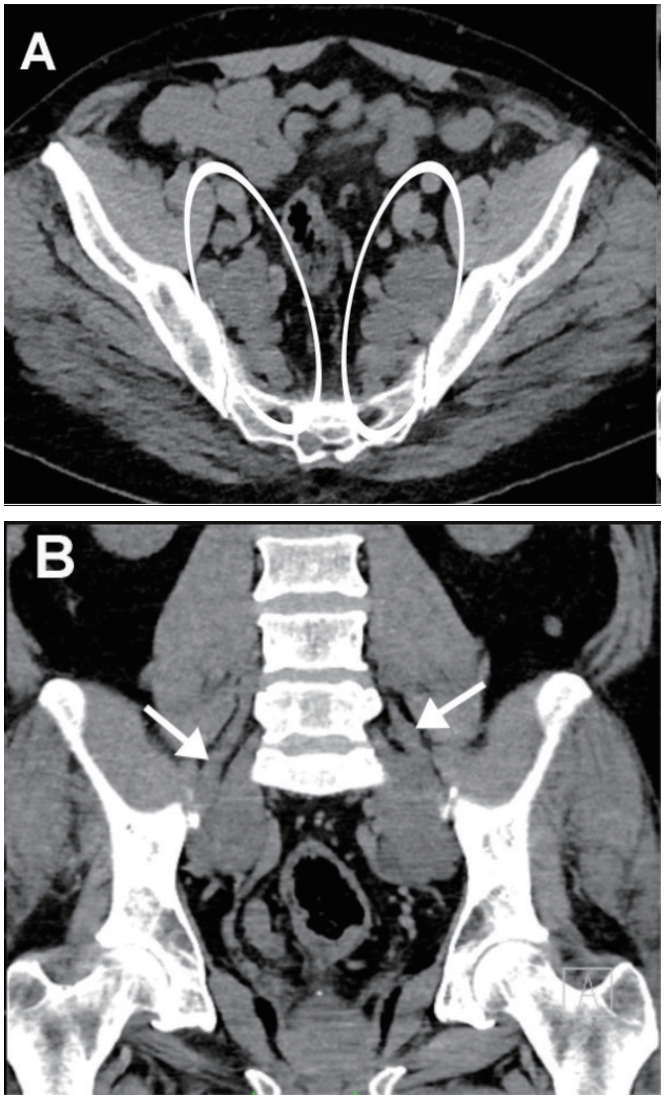
Description

A 49-year-old male patient was being followed up and treated with the diagnosis of Polyangiitis Granulomatosis. The patient was receiving oral Cyclophosphamide therapy. The patient presented with abdominal pain and stool incontinence. In addition, the patient had a complaint of weakness in his legs, which had started for two months. On examination, the patient had 3/5 motor weakness in the legs. A progressive loss of sensation was also observed. Abdominal CT was first performed on the patient. There was increased thickness and diffuse nodularity in the bilateral lumbar peripheral nerves(Figure 1). The diagnosis of CIDP was considered based on clinical findings and radiological images. Electromyography (EMG) confirmed the diagnosis of CIDP. The patient's neuropathy and muscle weakness improved on treatment with intravenous immunoglobulin (IVIG) and high-dose steroids.

Conclusions

The diagnosis of CIDP should be considered in the differential diagnosis of motor and sensory loss that starts in the lower extremities in rheumatological diseases under immunosuppressive therapy.

Figure & Table



JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

P-123

A rare combination of autoimmune pancreatitis and focal cranial eosinophilic granuloma

Tamar Melkadze[1], Iraklı Tortladze[1], Giorgi Apkhazava[2]

[1] Radiology Department, TSSU First University Clinic, Georgia
[2] Radiology Department, Tbilisi City Medical, Georgia

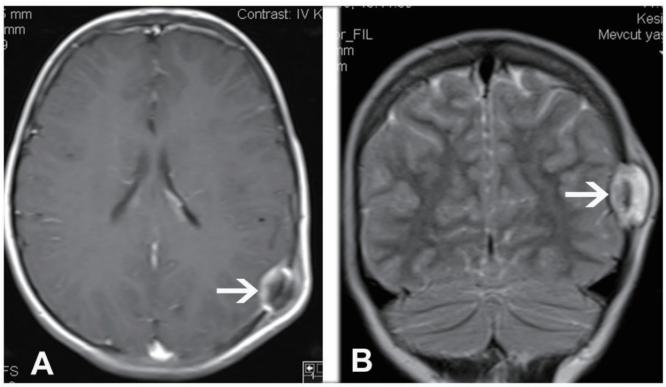
Description

A 35-year-old male patient was admitted to our hospital 1 year ago with complaints of severe abdominal pain and jaundice. Computed tomography performed on the patient revealed pancreatic diameter increase, edematous density loss, and peripancreatic mesenteric inflammation findings. The patient was diagnosed with acute pancreatitis with these findings. In the process, no specific finding to explain pancreatitis was detected, and the patient was followed up with the diagnosis of autoimmune pancreatitis due to the high Ig G4 level and response to steroids. The patient was admitted to our hospital with complaints of swelling and pain in his head that had been growing steadily for the last 1 month and could be palpated by hand. Cranial magnetic resonance imaging(MRI) was performed on the patient. On MRI, there was a focal bone-destroying lesion in the parietal bone(Figure 1). Because of its invasion in the form of a target, eosinophilic granuloma was first considered radiologically. The diagnosis was confirmed immunohistochemically with CD1a and S100 positivity.

Conclusions

Autoimmune pancreatitis is a chronic disease characterized by acute necrosis and inflammation. Autoimmune pancreatitis and eosinophilic granuloma are two independent entities. Co-occurrence is rare and has not been described in the literature.

Figure & Table



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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Diagnostic value of the inflammatory scores in polymyalgia rheumatica

Ji-Won Kim[1], Hyoun-Ah Kim[1], Ju-Yang Jung[1], Chang-Hee Suh[1]

[1] Department of Rheumatology, Ajou University School of Medicine, Republic of Korea

Background

Polymyalgia rheumatica (PMR) is a chronic inflammatory rheumatic disease in the elderly, characterized by bilateral shoulder and hip stiffness and elevated inflammatory markers, however, there are no specific diagnostic features. This study aimed to investigate the value of various serological inflammatory scores, including the systemic immune-inflammation index (SII), C-reactive protein/albumin ratio (CAR), albumin/globulin ratio (AGR), and prognostic nutritional index (PNI), as diagnostic markers in PMR.

Methods

We reviewed medical records of 156 patients diagnosed with PMR and 408 patients diagnosed with rheumatoid arthritis as a control group between January 1999 and September 2020. For each individual inflammatory scores, we estimated the sensitivity, specificity, and the area under the curve (AUC) with 95% confidence intervals for PMR diagnosis using receiver operating characteristic (ROC) curve analysis.

Results

A total of 156 patients with PMR had higher values of SII, and CAR, as well as lower values of AGR and PNI, than RA patients. The CAR showed the best value for diagnosis with an AUC of 0.823 (95% confidence interval [CI], 0.784-0.861) with a cutoff value of 0.75, and had diagnostic value in the order of SII (AUC 0.797 [95% CI 0.757-0.837], cutoff value 877.8), AGR (AUC 0.696 [95% CI 0.648-0.743], cutoff value 1.33), and PNI (AUC 0.691 [95% CI 0.641-0.741], cutoff value 12.5). Furthermore, elevated levels of SII or CAR, and decreased levels of AGR or PNI were associated with fever, weight loss, and headache.

Conclusions

Serological inflammatory scores, such as SII, CAR, AGR, and PNI, were useful as a diagnostic laboratory marker for PMR, and among these markers, CAR had the highest value.

Figure & Table

	AUC	P-value	Cut-off	Sensitivity	Specificity
SII	0.797	< 0.001	877.8	72.4	72.5
CAR	0.823	< 0.001	0.75	70.5	80.6
AGR	0.696	< 0.001	1.33	60.5	69.2
PNI	0.691	< 0.001	12.5	72.5	60.9

Table. Utility of serological inflammatory scores for diagnosing polymyalgia rheumatica
SII, systemic immune-inflammation index; CAR, C-reactive protein/albumin ratio; AGR, albumin/globulin ratio; PNI, prognostic nutritional index

Keywords

Polymyalgia rheumatica, Diagnostic marker, Inflammatory scores

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A short long way from juvenile idiopathic arthritis to pachydermoperiostosis (Touraine–Solente–Gole syndrome)

Bogdan Ion Gavrila[1], Ioan Ancuta[1], Mihai Bojinca[1], Claudia Silvia Ciofu[1]

[1] Bucharest, University of Medicine and Pharmacy „Carol Davila", Romania

Description

We present the case of a 19-year-old man, presented in April 2021 in our Clinic for polyarticular painless swellings, especially in the knees.

In 2018 he was diagnosed with Juvenile idiopathic arthritis(JIA) and treatment with Methotrexate started (15mg/wk), stopped becauase of nausea by the patient after 6 months.

At the time of evaluation we found multiple skin lesions - facial seborrhea,acnee,highly marked skin creases in the forehead,thickened eyelids,skin ankles sweating.

Osteoarticular system with clubbing of the fingers and toes,enlergement of bilateral forearm and legs,effusion of bilateral knee joints.

Biologically mild anemia with biologic inflammatory syndrome.Immunology RF,anti-CCP, ANA negative,normal levels of IgA,M,G

X rays of the hands and forearms showed enlargement of distal ulna and radius with cortical thickening,carpitis.Pelvis x rays with cortical thickening of the femur.Knee x rays decreased joints space.

Diagnostic and therapeutic arthrocentesis was perfromed with intraarticular Betamethasone administration.Results showed negative cultures,exsudates characteristics,citology negative for the presence of ragocytes.

At that time were considered the following diagnoses:Pachydermoperiostosis,SAPHO syndrome,acromegaly,thyroid acropachy,secondary hypertrophic osteoarthropathy.

The patient is discharged with the following treatment:Methylprednisolone 16mg/day,potassium and Vitamin D 3 supplements colchicine 1 mg/day,Sulfasalazine 3 mg/day.

Endocrinological evaluation was performed with Somatomedin C (IGF-I), thyroid hormone within normal limits.

CT scan was performed with pericardic fluid blade,gynecomastia.

He returns to our clinic after 6 months,and at the time of the evaluation we find in addition to the previous evaluation the appearance of a typical skin manifestation - tick transversely folded skin of the scalp-cutis verticis gyrate. Also he had significant effusion of bilateral knee joins and pronounced biological inflammatory syndrome.

The imaging investigations are completed with skull x ray-skull.

The final diagnosis was established: pahidermoperiostosis –complete form.

Conclusions

What therapeutic options should we take into consideration for this rare case, considering only few cases reported using NSAIDs, cortisone, colchicine and bisphosphonates?

Figure & Table

Keywords

Pachydermoperiostosis, Rare disease, Juvenile idiopathic arthritis

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Allopurinol and febuxostat hypersensitivity in a patient with young onset gout

Mark Andrian Yano[1]

[1] Division of Rheumatology, Department of Medicine, Philippine General Hospital, Philippines

Description

We report a case of a 29-year-old Filipino male with young onset gout. Patient had a typical gout history which started since he was 18 years old with joint pain and swelling initially involving the 1st MTP joint and later progressed to arthritis involving the ankles and knees. He has multiple tophi in both hands and toes causing deformity and limitation of movement. His laboratory tests consistently showed elevated uric acid at a range of 12-14 mg/dL. His creatinine was elevated at 1.6 mg/dL (eGFR 59 ml/min). He was initially started on allopurinol 100 mg daily, however, after seven days of allopurinol intake, he developed generalized pruritus, facial swelling, painful erythematous papules and vesicles along with mucosal involvement. He was admitted as a case of Steven Johnsons Syndrome. Allopurinol was withdrawn and he was given corticosteroid with noted relief of symptoms.

The frequency of gout flares increased up to ten times a year necessitating monthly intake of prednisone. Thus, febuxostat was commenced at a dose of 40 mg daily, but after 5 days, he developed generalized pruritus and angioedema. Febuxostat was discontinued and IV corticosteroids was given with relief of symptoms.

In view of the persistently elevated uric acid and recurrent gout flares, febuxostat was restarted at a dose of 20 mg daily. However, the patient had recurrence of generalized urticaria a week after intake. Discontinuation of febuxostat and a short course of prednisone led to resolution of symptoms.

Considering the limited therapeutic options, the patient was referred to an allergy specialist for febuxostat desensitization.

Conclusions

Although rare, febuxostat hypersensitivity has been reported and can be severe. It is unclear whether a previous allopurinol adverse reaction might have a role in the subsequent development of hypersensitivity to febuxostat.

Figure & Table

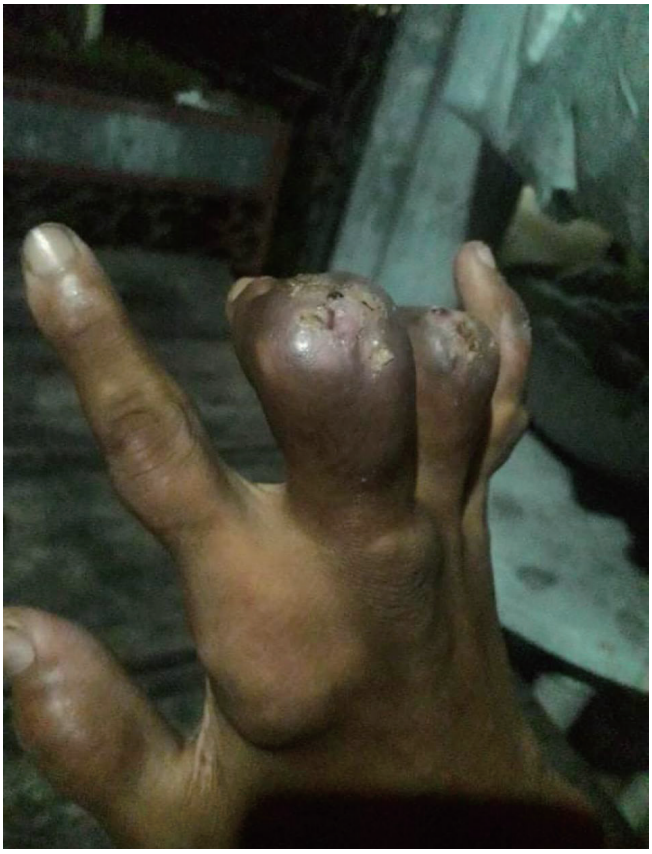

Figure. A photograph of the patient's right hand showing multiple tophi formation

Keywords

Febuxostat hypersensitivity, Steven Johnsons syndrome, Young onset gout

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Curative-intent resection is a strong indicator of steroid-free remission in IgG4-related disease

Jung Gon Kim[1], Sunhee Jang[2], Jennifer Lee[1], Ji Hyeon Ju[1], Wan-Uk Kim[1], Sung-Hwan Park[1], Seung-Ki Kwok[1]

[1] Department of Internal Medicine, Division of Rheumatology, Seoul St. Mary's Hospital, College of Medicine, Seoul, Republic of Korea
[2] Department of Internal Medicine, Yonsei Hangang Hospital, 25 Mapodaero, Mapogu, Seoul, Republic of Korea

Background

Long-term prescription of corticosteroids is common for IgG4-related disease (IgG4-RD) despite corticosteroid-related adverse reactions. To the best of our knowledge, studies on determinants of steroid-free remission (SFR) in IgG4-RD have not been reported yet. Thus, we examined various clinical factors affecting achievement of SFR in IgG4-RD.

Methods

A total of 155 patients had newly diagnosed IgG4-RD, autoimmune pancreatitis, or idiopathic retroperitoneal fibrosis at our unit between 2005 and 2021. Among them, 58 patients who met the 2019 ACR/EULAR criteria for IgG4-RD were finally included. SFR was defined as meeting all of the followings: 1) clinically asymptomatic state; 2) disappearance or > 50% reduction in the size of IgG4-RD lesion without occurrence of a lesion in a different site; 3) being free of glucocorticoids for six months or more. Patient demographics, laboratory parameters, early use of steroid-sparing agents within three months, and curative-intent resection of IgG4-RD lesions were examined regarding SFR from the date of diagnosis using Cox regression analysis.

Results

Sixteen (27.6%) of 58 patients with IgG4-RD achieved SFR during the follow-up period (median: 38.2 months). Univariable Cox regression analysis showed that curative-intent resection (hazard ratio (HR): 5.11 [95% confidence interval (CI): 2.13–12.23]), and multiple organ involvement (≥ 2) (HR: 0.39 [95% CI: 0.17-0.90]) were significantly associated with SFR in the opposite way. In the univariable Cox regression analysis, age, sex, head and neck phenotype, elevated inflammatory markers, elevated serum IgG4, and early use of steroid-sparing agents did not have any significant associations with SFR. In the multivariable Cox regression analysis, curative-intent resection (HR: 4.26 [95% CI: 1.5–12.14]) was the only predictor of SFR. Multiple organ involvement (≥ 2) did not show meaningful prediction (HR: 0.73 [95% CI: 0.26-2.01]).

Conclusions

Curative-intent resection of IgG4-RD lesions was the only strong predictor of SFR in IgG4-RD in our study.

Figure & Table

	Unadjusted HR (95% CI)	*P*	Adjusted HR† (95% CI)	*P*
Demographics				
Male	0.66 (0.28-1.52)	ns	-	-
Elderly (≥ 65 year)	0.65 (0.22-1.23)	ns	--	-
Phenotype of IgG4-RD				
Multiple organs involved (≥ 2),	0.39 (0.17-0.90)	<0.05	0.73 (0.26-2.01)	ns
Head and neck limited phenotype	0.62 (0.23-1.69)	ns	-	-
Laboratory markers				
Elevated ESR (≥ 20 mm/hour)	0.52 (0.22-1.23)	ns	-	-
Elevated CRP (≥ 6 mg/L)	0.84 (0.33-2.15)	ns	-	-
Serum IgG4 > 1 ULN	0.95 (0.35-2.59)	ns	-	-
Treatment modality				
*Early use of steroid-sparing agents	0.98 (0.38-2.51)	ns	-	-
Curative-intent surgery	5.11 (2.13-12.23)	<0.001	4.26 (1.5-12.14)	<0.01

*Prescription of azathioprine, methotrexate, or hydroxychloroquine within 3 months after diagnosis of IgG4-RD.

†Variables of the multivariable Cox regression model=multiple organs involved (≥ 2), and curative-intent resection.

HR, hazard ratio; CI, confidence interval; IgG4-RD, IgG4-related disease; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ULN, upper limit normal.

Table. Cox regression analysis for steroid-free remission

Keywords

IgG4-related disease, steroid-free remission, surgical treatment

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Application of HScore and MS score in diagnosis of macrophage activation syndrome associated with adult onset Still's disease

Zhao Peng[1,2,3], Shuang Zhou[1,2,3], Qian Wang[1,2,3], Xinping Tian[1,2,3], Mengtao Li[1,2,3], Yan Zhao[1,2,3], Xiaofeng Zeng[1,2,3]

[1] Department of Rheumatology and Clinical Immunology, Chinese Academy of Medical Sciences & Peking Union Medical College,Beijing, China
[2] National Clinical Research Center for Dermatologic and Immunologic Diseases (NCRC-DID), Ministry of Science & Technology, Beijing, China
[3] State Key Laboratory of Complex Severe and Rare Diseases, Peking Union Medical College Hospital, Beijing, China

Background

AOSD-associated MAS is traditionally identified based on the HLH-2004 criteria. Due to the different pathogenesis and clinical manifestations between MAS and primary HLH, HLH-2004 could not diagnosis MAS timely, particularly in the early stage. The sensitivity of diagnosing MAS using HLH-2004 criteria was only 56.6%. In order to diagnosis MAS timely, Study developed and validated weighted scores, named Hemophagocytic syndrome diagnostic (H) score and MAS/ juvenile idiopathic arthritis(MS)Score. However, there are no criteria that are specific for AOSD-associated MAS, It is also unclear whether the HScore and MS-Score were more timely than HLH-2004 criteria in diagnosis AOSD-associated MAS. The purpose of our study was to compare whether the HScore and MScore are more timely than the HLH-2004 criteria in diagnosing AOSD-associated MAS.

Methods

The demographic, clinical and laboratory features, pathological findings of patients with AOSD-associated MAS were collected in Peking Union Medical College Hospital (PUMCH) from January 2013 to December 2020. HLH-2004 criteria, MS-Score and HScore were used to diagnosis of AOSD-associated MAS. And compare the different time points in diagnosis of AOSD-associated MAS between these methods.

Results

33 patients with AOSD-associated MAS were identified. 27 (81.8%) were female, the median duration of AOSD-associated MAS was 49 (31, 157) days, and 3 (9.1%) died. The median time of diagnosis AOSD-associated MAS was 46 (27.5, 57.0) days by HLH-2004, 31 (19.0, 54.0) days by HScore, and 20.0 (10.5, 44.5) days by MS-Score(χ=31.147, P<0.001). The median time of diagnosis AOSD-associated MAS by MS-Score was 19.0 (4.5, 31.0) days earlier than by HLH-2004 criteria(χ=-1.344, P<0.001), And 13.5 (0.5, 21.5) days earlier than HScore (χ=-0.766, P=0.007). The median time of diagnosis AOSD-associated MAS by HScore was 4.5 (0.0, 10.5) days earlier than by HLH-2004 criteria (χ=-0.578, P=0.062).

Conclusions

MS-Score could identification of AOSD-associated MAS earlier than HLH-2004 criteria, while HScore can not.

Keywords

Macrophage activatin syndrome, adult onset Still's disease, MS score; HScore

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The role of interleukin-18 as a diagnostic biomarker to differentiate active adult-onset Still's diseas from COVID-19

Roland Helmizar[1]

[1] Internal Medicine, Indonesian University, Indonesia

Background

The coronavirus disease 2019 (COVID-19) outbreak has rapidly extended globally within a short period. Adult Onset Still's Disease (AOSD) is a rare systemic inflammatory disease with various manifestations and can mimic other diseases. Hyperinflammation and cytokine storm play an important role in the pathogenesis of both COVID-19 and AOSD. Interleukin (IL)-18 is one of the leading cytokines markedly elevated in systemic inflammatory diseases that cause the 'cytokine storm' in both diseases. Given the similar clinical features, it is necessary to identify potential biomarkers that can differentiate COVID-19 from AOSD.

Methods

A systematic search through Pubmed/MEDLINE, Cochrane Library, EBSCO, and EMBASE was conducted to find studies about the role of IL-18 as a diagnostic biomarker to differentiate active Adult-Onset Still's Disease from COVID-19. Two studies were selected and critically appraised. Data were then summarized descriptively.

Results

The two studies included consist of cross-sectional and single-arm meta-analysis. A cross-sectional study stated active AOSD patients had 68-fold higher IL-18 levels than severe COVID-19 patients ($p<0.001$). IL-18 levels at the cut-off value 190.5 pg/mL had the highest discriminative power for active AOSD and severe COVID-19, with AUC 0.948, sensitivity 91.3%, specificity 95.8%, and accuracy of 91.5% ($p<0.005$). Multivariate regression analysis revealed IL-18 as a significant predictor of active AOSD ($p<0.05$). Single-arm meta-analysis stated fold changes of IL-18 were defined as the mean expression level ratio of severe COVID-19 and AOSD to healthy controls. Noteworthy, the fold change of IL-18 in patients with active AOSD was approximately 594, which was much higher than that in severe COVID-19 (fold change 2.17), without statistical comparability.

Conclusions

IL-18 is a potential biomarker discriminator between AOSD and COVID-19 and may significantly predict active AOSD. Further studies with good quality evidence are still needed to confirm these findings.

Keywords

interleukin-18, Adult-Onset Still's Disease, COVID 19

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Journal of Rheumatic Diseases
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Cancer-associated vasculitis: A single-centre pilot study

Hyunsue Do[1], Sangwon Lee[1]

[1] Division of Rheumatology, Severance Hospital, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul, Republic of Korea

Background

This study investigated the clinical features of cancer-associated vasculitis within 3 years before and after the diagnosis of the corresponding underlying cancer in 73 Korean patients.

Methods

Based on the inclusion criteria, 73 patients with cancer-associated vasculitis were included in this study, and their medical records were retrospectively reviewed. The time gap between cancer and vasculitis was set as within 3 years before and after the diagnosis of the corresponding underlying cancer, and was partitioned into 90-day increments and included 25 time-compartments.

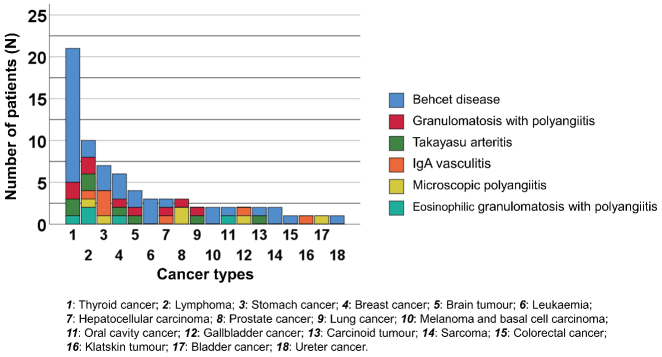
Results

The median age was 53.0 years and 42.5% were male. The incidence rate of cancer-associated vasculitis was 0.034%. The most frequently observed cancer was thyroid cancer (28.8%), followed by lymphoma (13.7%) and stomach cancer (9.6%). Whereas, the most common cancer-associated vasculitis was Behcet disease (52.1%), followed by granulomatosis with polyangiitis (12.3%), and Takayasu arteritis (11.0%). Behcet disease exhibited a tendency of association with several cancers but granulomatosis with polyangiitis and Takayasu arteritis exhibited no predominant association with the types of the corresponding underlying cancer. Forty-two (57.5%), 7 (9.6%) and 24 (32.9%) patients had vasculitis before, at the time of, and after the diagnosis of the corresponding underlying cancer, respectively. The time compartment with the largest distribution of patients was between 1 day and 90 days after the diagnosis of cancer.

Conclusions

The incidence rate of cancer-associated vasculitis was 0.034%. The most common cancer-associated vasculitis was Behcet disease, and the types of cancer-associated vasculitis and each underlying cancer seemed to be dependent on ethnic and geographic differences.

Figure & Table



1: Thyroid cancer; ***2***: Lymphoma; ***3***: Stomach cancer; ***4***: Breast cancer; ***5***: Brain tumour; ***6***: Leukaemia; ***7***: Hepatocellular carcinoma; ***8***: Prostate cancer; ***9***: Lung cancer; ***10***: Melanoma and basal cell carcinoma; ***11***: Oral cavity cancer; ***12***: Gallbladder cancer; ***13***: Carcinoid tumour; ***14***: Sarcoma; ***15***: Colorectal cancer; ***16***: Klatskin tumour; ***17***: Bladder cancer; ***18***: Ureter cancer.

Figure. Frequency of vasculitis according to each underlying cancer

Keywords

cancer, vasculitis, ethnicity

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Journal of Rheumatic Diseases
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Cerebellar infarction as the initial presentation of IgG4-Related Disease

Gaurav Nepal[1], Vikash Jaiswal[2]

[1] Internal Medicine, Tribhuvan University Institute of Medicine, Nepal
[2] Internal Medicine, Larkin Community Hospital, USA

Description

A 60-year-old man came to the ER with dizziness and blurred vision. He also mentioned numbness and discomfort in his right hand that started months ago. His right finger was likewise discolored. A little purple discoloration of the right fingertip was noted on the physical exam. Inpatient treatment was given. Initial ESR 48 mm/hr and CRP 13.9 mg/L. Initial lab work showed an ESR of 48 mm/hr and CRP of 13.9 mg/L. His basic metabolic panel, complete blood count, and autoimmune tests were all unremarkable. MRI brain revealed a small, acute right cerebellar infarct, subacute left cerebellar infarct, and mild bifrontal chronic microvascular ischemic changes. Echocardiogram was normal. CT chest, abdomen, and pelvis showed a solid partially calcified right retroperitoneal mass arising from the pancreatic head/duodenum. Associated mild retroperitoneal lymphadenopathy was noted. Endoscopic-ultrasound with biopsy showed lymph-node tissue with plasmacytosis and >40% plasma-cells positive for IgG4, compatible with IgG4-lymphadenopathy. The specimen was composed of lymphoid tissue lacking germinal-centers with plasmacytosis. Immunohistochemical staining was performed. The sample was negative for epithelial malignancy. CD20 demonstrated an increase in B-cells, and CD138 showed an increase in plasma cells. Kappa and lambda in situ hybridization showed polytypic expression. CD3 and CD43 highlighted background T cells. The stroke team discharged the patient on apixaban, clopidogrel, and aspirin prior to the pathology results. As stroke was thought to be caused by cardiovascular risk factors or pancreatic CA, hence steroids were not provided initially. The patient was then lost to follow-up.

Conclusions

Cerebellar symptoms in IgG4-RD are a rare initial manifestation. The early start of corticosteroids has been shown to result in significant improvement. While the disease's exact cause is unknown, practitioners should be aware of its unusual presentation and have a high clinical index of suspicion.

Figure & Table

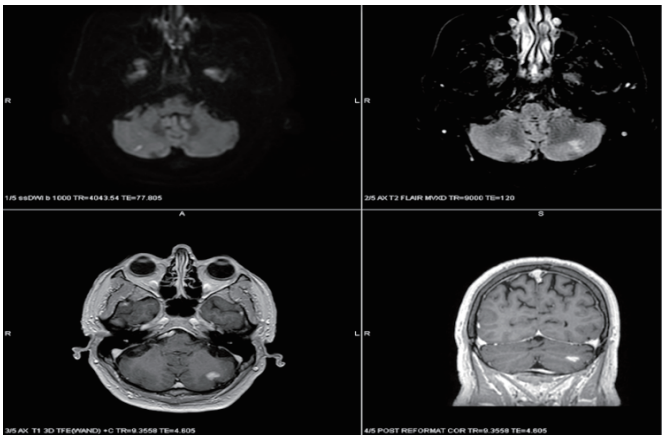

Figure. Magnetic resonance (MR) imaging of the brain with and without contrast revealed a small, acute right cerebellar infarct, subacute left cerebellar infarct, and mild bifrontal chronic microvascular ischemic changes.

Keywords

IgG4-Related Disease, IgG4-RD, IgG4RD

E-poster Presentation

Epidemiology & Public health

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

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Relationship between Lung Involvement and Gout in Covid-19 disease

Fatih Işık[1], Zeynep Tüzün[2], Fatma Beyza Isık[3]

[1] Department of Radiology, Atatürk University, Turkey
[2] Internal Medicine , Rheumatology Department, Ataturk University, Turkey
[3] health practice and research center, Ataturk University, Turkey

Background

We aimed to evaluate the joint deposit accumulation of covid-19 infection with dual-energy CT in patients followed up for gout disease.

Methods

Thirty-four patients who were followed up for gout and who had COVID-19 infection were evaluated in the study. Of these patients, 18 patients whose joint uric acid accumulation was examined with dual-energy up to 1 year before the COVID-19 infection were included in the study. A radiologist examined the accumulation of uric acid in the dual-energy CT images of the patients. Covid radiological severity classification in patients was made according to the percentage of radiological involvement on CT imaging. Mild radiological findings were classified as = 0-50%, severe radiological findings = 51-100%.

Results

5 of 18 patients had acute joint pain attacks during the Covid-19 infection process. An increase in the amount of joint uric acid was observed in 5 of 18 patients. There was no difference in 13 of them. Of the 5 patients with increased uric acid content, 3 patients had severe pulmonary involvement and 2 patients had mild lung involvement. Of the 13 patients with increased uric acid content, 3 patients had severe pulmonary involvement and 10 patient had mild lung involvement. There was a weak inverse correlation between uric acid deposition and lung involvement (P = 0.047, r = -0.3924). While the radiological findings of 3 patients who had acute joint attacks during Covid infection were severe, 2 of them were observed in the mild severity classification. Of the 13 patients who did not have an acute attack, 3 had severe pulmonary involvement and 10 had mild pulmonary involvement. There was a weak inverse relationship between radiological findings and acute joint pain (P = 0.04950, r = -0.4082).

Conclusions

Although Covid-19 radiological involvement does not significantly change the gout disease attack and joint deposit accumulation.

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Post-COVID mesial temporal sclerosis

Megi Kurtanidze[1], Tamar Melkadze[2], Iraklı Tortladze[2]

[1] Department of Radiology, Tbilisi City Medical, Georgia
[2] Radiology Department, TSSU First University, Georgia

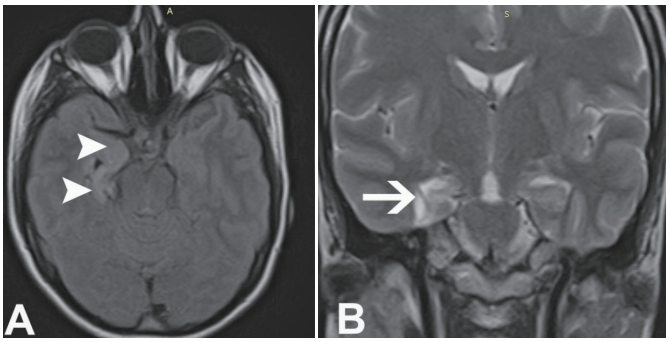
Description

A 29-year-old young patient was admitted to our hospital with seizures. In her history, she had a history of covid 19 that had been passed 20 days ago. Due to severe lung involvement in Covid-19 infection, the patient was treated as an inpatient. After the Covid infection, the patient's complaints such as bad odor perception and dizziness continued. Brain magnetic resonance imaging(MRI) was performed because of the seizure. There was an increase in edematous signal at the level of the right temporal lobe (Figure 1A). The patient was first evaluated in favor of encephalitis. The patient was started on treatment for encephalitis and epilepsy. As the patient's epilepsy complaints continued during the process, a control MRI was performed 3 months later. Control MRI showed volume loss consistent with sclerosis in the temporal lobe hippocampal region (Figure 1B).

Conclusions

Covid infection is a viral infection that causes the activation of cytokines. Mesial temporal sclerosis was found to be associated with cytokines, especially interleukin 1beta (IL-1β), IL-6, tumor necrosis factor-alpha (TNF-a). Therefore, the immune response seen in Covid patients may cause limbic encephalitis in the mesial temporal region and cause mesial temporal sclerosis by creating an autoantibody response in the process.

Figure & Table



JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Incidence of rheumatic diseases during the COVID-19 pandemic in Korea: A nationwide claims study

Soo Min Ahn[1], Seongho Eun[2], Seokchan Hong[1], Chang-Keun Lee[1], Bin Yoo[1], Ji Seon Oh[3], Yong-Gil Kim[1]

[1] Department of Rheumatology, Asan Medical Center, Republic of Korea
[2] Department of Management Engineering, College of Business, KAIST, Republic of Korea
[3] Department of Information Medicine, Big Data Research Center, Asan Medical Center, Republic of Korea

Background

The recent COVID-19 pandemic has been reported to change the epidemiology of not only infectious or respiratory diseases but also several non-infectious diseases such as Kawasaki disease. This study investigated the change in the incidence of various rheumatic diseases during the COVID-19 pandemic.

Methods

The number of patients for each disease from January 2016 to December 2020 was obtained from the Korea Health Insurance Review and Assessment Service database. We compared the incidence of nine rheumatic diseases [systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), ankylosing spondylitis (AS), Sjogren syndrome (SJS), Behçet disease (BD), idiopathic inflammatory myositis (IIM), systemic sclerosis (SSc), polymyalgia rheumatica (PMR), and gout] and hypertension before and after the COVID-19 outbreak. The incidence before and after the COVID-19 outbreak was compared using the ARIMA analysis and quasi-Poisson analysis.

Results

Compared with the predicted incidence in 2020 by the ARIMA model, the monthly incidence of SLE, BD, AS, SJS, IIM, and SSc temporarily and significantly decreased, while the monthly incidences of gout, RA, PMR, and hypertension were within the 95% confidence interval (CI) of predicted values in the first half of 2020, the early stage of COVID-19 outbreak. In age and sex-adjusted quasi-Poisson regression analysis, the annual incidences of IIM (Rate ratio [RR]: 0.473, 95% CI: 0.307–0.697), SLE (RR: 0.845, 95% CI: 0.798–0.895), and BD (RR: 0.850, 95% CI: 0.796–0.906) were significantly decreased compared with the previous 4 years.

Conclusions

In conclusion, we found that the annual incidence of some rheumatic diseases including IIM, SLE, and BD decreased during the COVID-19 pandemic.

Figure & Table

Diseases	Mean (2016–2019)	Observed (2020)	Rate ratio (95% CI)
IIM	839.8	397	0.473 (0.307–0.697)
SLE	5371.3	4541	0.845 (0.798–0.895)
BD	3598.3	3057	0.850 (0.796–0.906)
SJS	7913.5	7280	0.920 (0.839–1.007)
AS	11679.5	10934	0.936 (0.848–1.031)
SSc	592.8	557	0.940 (0.806–1.090)
RA	17490.3	17342	0.992 (0.944–1.041)
Gout	129543	131133	1.012 (0.916–1.117)
PMR	1072	1152	1.075 (0.928–1.239)
HTN	680943.2	696391	1.023 (0.929–1.124)

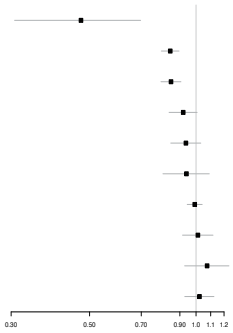

Table. Annual incidence of various diseases in 2020 versus 2016-2019

Keywords

Incidence, COVID-19, Rheumatic disease

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Changes in the lungs that develop with COVID-19 in patients with rheumatoid arthritis

Eugenia Aronova[1], Galina Gridneva[1], Boris Belov[1]

[1] department of comorbid infections, V.A. Nasonova Research Institute of Rheumatology, Russian Federation

Background

The aim of our study was to analyze the severity of changes in the lungs obtained with computed tomography (CT) in patients with COVID-19 and rheumatoid arthritis

Methods

We studied the data of discharge reports after inpatient treatment of COVID-19, verified by RT-PCR to SARS-CoV-2 RNA, in patients with RA. The results of the correlation analysis were considered reliable at $p<0.05$.

Results

The study included 42 adult (over 18 years old) patients (38 women, 90.5%) with a reliable diagnosis of RA (ACR/EULAR). The mean age of the patients was 51.17±15.78 years. In 14 patients, RA proceeded with extra-articular manifestations in the form of Sjögren's syndrome. High RA activity at the time of COVID-19 disease was in 10 patients (23.8%), moderate - in 19 (45.2%), low - in 10 (23.8%). During the COVID-19 period, CT scan was performed in 26 patients. When assessed according to the "empirical visual scale", CT-0 was noted in 2 patients (7.7%), CT-1 - in 12 (46.2%), CT-2 - in 7 (26.9%), CT- 3 - in 4 (15.4%), CT-4 - in 1 (3.8%). There were no statistically significant correlations between the severity of changes in the lungs and RA activity, as well as the presence of extra-articular manifestations.

27 patients (64.3%) underwent COVID-19 on an outpatient basis. For the treatment of COVID-19, 26 cases were prescribed antibacterial drugs, 13 cases - injectable and 20 - oral anticoagulants, 20 cases - glucocorticoids, also 20 - antiviral drugs, 4 patients required IL-6 inhibitors and 2 - janus inhibitors -kinase. Three patients did not require any therapy other than standard care.

Conclusions

In the study group, COVID-19 proceeded predominantly with moderate lung involvement. No statistically significant correlations were found between the severity of changes in the lungs and RA activity, as well as the presence of extra-articular manifestations.

Keywords

rheumatoid arthritis, COVID-19, lung involvement

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Incidence, prevalence, and clinical characteristics in ANCA-associated vasculitis: A National Health Insurance Service Database (2002-2018)

Sung Ahn[1], Hyunsun Lim[2], Chan Hee Lee[3], Young-Beom Park[4], Sang-Won Lee[4], Jinsu Park[3]

[1] Department of Internal Medicine, Yongin Severance Hospital, Yonsei University College of Medicine, Republic of Korea
[2] Research and Analysis Team, National Health Insurance Service Ilsal Hospital, Republic of Korea
[3] Department of Internal Medicine, National Health Insurance Service Ilsal Hospital, Republic of Korea
[4] Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea

Background

To evaluate the incidence and prevalence of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) by analyzing the nationwide healthcare administrative database.

Methods

Patients with claim data from a general or tertiary hospital with ICD-10 code for AAV (microscopic polyangiitis [MPA], granulomatosis with polyangiitis [GPA], and eosinophilic granulomatosis with polyangiitis [EGPA]) were identified from the National Health Insurance Service Database (2002-2018). A patient with AAV was defined when at least one of the following criteria was satisfied; i) registered in the individual copayment beneficiaries program with the corresponding code of AAV; ii) prescribed with glucocorticoids. We calculated the incidence of AAV after applying a 2-year washout period.

Results

A total of 2,113 patients had AAV, of which 708 had MPA, 638 had GPA, and 767 had EGPA. The overall incidence and prevalence of AAV tended to increase continuously during the observed years. The highest incidence of AAV was reported as 0.48/100,000 people year (PY) in 2017 and the prevalence of 2.40/100,000 PY in 2018 (Figure 1). The proportion of females in patients with AAV was 53.9%, and AAV was the most common in those aged 60–69 years. At the time of onset, patients with MPA were the oldest at 64.3 ± 14.1, patients with GPA were 57.5 ± 15.2, and patients with EGPA were the youngest at 52.9 ± 15.9. In addition, patients with MPA had the highest mean CCI (3.3 ± 1.62) compared to patients with GPA (2.83 ± 1.58) and EGPA (2.75 ± 1.43).

Conclusions

By searching through the national healthcare database, the following results were obtained: i) even though AAV is still rare, the annual incidence of AAV in South Korea is increasing, with the highest incidence of 0.48/100,000 persons reported in 2017; ii) MPA patients are the oldest at the time of diagnosis and have more comorbidities.

Keywords

vasculitis, ANCA, healthcare claim data

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Association between sarcopenia and rheumatoid arthritis in the Korean population: A nationwide cross-sectional study

Jae Hyun Jung[1], Yu Jin Lee[1], Eui Seop Song[1], Gwan Gyu Song[1]

[1] Internal Medicine, Korea University College of Medicine, Republic of Korea

Background

Rheumatoid arthritis (RA) includes musculoskeletal symptoms and leads to disuse atrophy of skeletal muscles and change in body composition. The musculoskeletal symptoms and loss of physical function in may be associated with the prevalence of sarcopenia, which is characterized by muscle loss. This study aimed to investigate the prevalence of sarcopenia and its association with RA in the general Korean population.

Methods

We conducted a nationwide cross-sectional study using data from the Korea National Health and Nutrition Examination Survey and included 7,389 men and 9,798 women. Binominal logistic regression models were used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for sarcopenia prevalence in RA patients.

Results

The prevalence of sarcopenia was 23.0% in men, 25.0% in women, 61.5% in men with RA, 32.3% in women with RA, 22.8% in men without RA, and 24.9% in women without RA. After adjusting for potential confounding variables, the prevalence of sarcopenia was significantly higher in men with RA than in men without RA (OR, 3.11; 95% CI, 1.29–7.46), but this was not seen in women.

Conclusions

The presence of sarcopenia was more than three-fold in Korean men with RA than in those without RA.

Figure & Table

	Men			Women		
	OR	95% CI	*P*	OR	95% CI	*P*
Crude	5.41	2.45–11.95	<0.001	1.44	0.99–2.08	0.054
Model I	2.95	1.25–6.97	0.014	1.32	0.88–1.97	0.183
Model II	3.15	1.32–7.50	0.010	1.32	0.88–1.98	0.174
Model III	3.02	1.26–7.20	0.013	1.32	0.88–1.97	0.184
Model IV	3.11	1.29–7.46	0.011	1.36	0.91–2.04	1.139

Model I has been adjusted for age, BMI, and current menstrual status especially in women

Model II has been adjusted for Model I + DM, HTN, and dyslipidemia

Model III has been adjusted for Model II + alcohol consumption and smoking status

Model IV has been adjusted for Model III + household income and education

OR, odds ratio; CI, confidence interval; BMI, body mass index; DM, diabetes mellitus; HTN, hypertension

Table. Odds ratios and 95% confidence intervals for sarcopena in patients with rheumatoid arthritis

Keywords

Rheumatoid arthritis, Sarcopenia, Prevalence

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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Psychometric properties of the PHQ-8 in individuals with osteoarthritis

Patrick Brzoska[1]

[1] Health Services Research, Witten/Herdecke University, Faculty of Health, School of Medicine, Germany

Background

Osteoarthritis is one of the most common musculoskeletal illnesses. It may affect quality of life and is associated with limitations in daily activities and depressive symptoms, which may severely impair patients' capacity to cope with the disease. Frequently used instruments to study depressive symptoms among individuals with osteoarthritis and other musculoskeletal disorders are the CES-D und PHQ-8. While the psychometric properties of the CES-D have been studied among patients with musculoskeletal diseases, including osteoarthritis, little is known about the PHQ-8 in this respect. The present study investigates the psychometric properties of the PHQ-8 in a sample of people with osteoarthritis in Austria.

Methods

Data from a representative population-based survey conducted in Austria in 2018/2019 on 15,461 men and women was used, of which 2,206 (14.3%) reported to have been diagnosed with osteoarthritis. The psychometric properties of the PHQ-8 were examined by means of confirmatory factor analysis (CFA) and multiple indicators multiple causes (MIMIC) models.

Results

The baseline 8-item, one-factor measurement model of the PHQ-8, most often proposed in previous studies, showed an acceptable fit (RMSEA=0.06, TLI=0.92, CFI=0.95, SRMR=0.04); however, some factor loadings were only moderate in size (see Fig. 1). Measurement non-invariance related to sex was observed in items 3 and 4, measurement non-invariance related to age was observed in items 2, 6, 7 and 8. Effects of sex and age slightly differed between analyzes adjusted (beta=0.059 and beta=0.075, respectively) and not-adjusted (beta=0.136 and beta=0.118, respectively) for measurement non-invariance.

Conclusions

While the PHQ-8 shows an acceptable validity in the assessment of depression in patients with osteoarthritis, comparisons between sociodemographic categories such as sex and age may be biased by measurement non-invariance. As the findings show, this may either over- or underestimate the true effects. Instead of the comparison of manifested means, therefore, latent variable modeling should be employed to obtain valid estimates.

Figure & Table

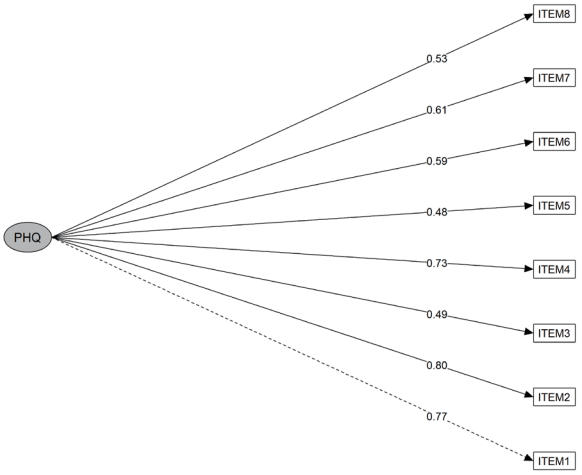

Figure. Factor structure of the PHQ-8 in individuals with osteoarthritis in Austria

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The Barriers Of Patients With Osteoporosis In Various Countries During The COVID-19 Pandemic

Nuraliah Nuraliah[1]

[1] Public Health, West Sulawesi Research and Empowerment Center, Indonesia

Description

During the Covid-19 pandemic, it is very difficult for patients to access good health services. This situation has affected the management of many long-term conditions including patients with osteoporosis as resources are diverted to cover urgent care. Drawing on literature review research, the author analyzed the information on how the COVID-19 pandemic has impacted the diagnosis and management of osteoporosis in some countries. Data were collected through a comprehensive review of the literature using suitable keywords on the search engines of PubMed, SCOPUS, Google Scholar and Research Gate in the first week of May 2020 on developments and guidance during the current COVID-19 pandemic. This study found two main the barriers of patien with osteoporosis during the COVID-19 pandemic, namely (1) process of care, (2) the governance and strategy. The osteoporosis care stagnated and lower quality of care was provided. During the initial phase of the COVID-19 pandemic, there was no guidance of professional societies or guidelines on the organization of osteoporosis care in case of such a crisis, and treatment relied on local ad hoc strategies.

Conclusions

This review has provided information that the COVID-19 pandemic was impacting the diagnosis and management of osteoporosis patients. Therefore, a comprehensive approach is needed for future improvement to osteoporosis service by managing the standardization of osteoporosis care delivery in situations of crisis.

Keywords

Osteopororis, COVID-19, Osteoporosis Management,

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Use of telemedicine for follow-up of lupus nephritis in the COVID-19 outbreak: A randomized controlled trial

Ho So[1], Everlyn Chow[1], Isaac Cheng[1], Xerox Chow[1], Tena Li[1], Cheuk Chun Szeto[1], Lai Shan Tam[1]

[1] Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong

Background

Patients with SLE are at increased risk of severe COVID-19. An alternative option would be to adopt telemedicine (TM) to maintain medical care while minimizing exposure. Despite being widely adopted during the pandemic, the evidence supporting the use of TM in rheumatology has been limited.

Methods

This was a 1-year, single-center, RCT. From May 2020, adult patients with SLE according followed up at the LN clinic were invited to participate in the study. Participants were randomized 1:1 to either TM (TM group) or standard FU (SF group). Patients randomized to receive TM FU were scheduled for a video consultation. Patients in the SF group received standard in-person outpatient care.

Results

A total of 141 patients with LN completed the study. There were no baseline differences, including demographics, SLEDAI-2k and SLE damage index, between the 2 groups. At one year, 80.0% and 80.2% of the patients in the TM group and SF group were in LLDAS or remission respectively. SLE disease activity indices including SLEDAI-2k, PGA, proteinuria amount and serum anti-ds-DNA level remained similar between the 2 groups. The overall patient satisfaction score was higher in the TM group with a significantly shorter waiting time before seeing doctors. The mean indirect costs of illness and the out-of-pocket costs for health care services were similar between the 2 groups in one year. The total number of FU was similar. However, significantly more patients in the TM group requested change mode of FU. The proportion of patients requiring hospitalization during the study period was also higher in the TM group. After adjustment, not being in not being in LLDAS at baseline was the predictor of hospitalization.

Conclusions

TM FU resulted in similar disease activity control and better satisfaction in patients with LN but needs to be complemented by physical visits, particularly in those with unstable disease.

Keywords

SLE, COVID, telemedicine

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Immunopathological process in the Chronic arthritis and Rheumatic Heart Diseases caused by streptococcus of Group A

Nazgul Omurzakova[1], Akpay Sarybaev[1]

[1] Rheumatology and High Mountain Diseases, National Center of Cardiology and Internal Medicine, Kyrgyzstan

Description

Antigens of cell wall of Group A streptococcus (GAS) and (or) their antibodies has an effect in the development of immunopathological conditions, which differs by their characteristics.

For the last years we observe trends of the heavy invasive streptococcal infection proceeding with a hypotension, coagulopathy and multiple functional insufficiencies of a «streptococcal toxic shock syndrome ». This syndrome presents as a toxic and toxic septic conditions with elements of SLE-like eruption, connected with ability of GAS cross-reaction with DNA, forming like lupus reactions.

SGA promotes development of chronic arthritis variant, which debut has clinical lines rheumatic fever and developed stage (after decades) – RA. This form of disease begins from childhood (arthritis of small joints, carditis) as the rheumatic fever with repeated acute attack of arthritis without deformations of joints and following exacerbation (women usually after childbirth). Rheumatic heart diseases is revealed in more advanced age - 20 years old (that is in 14 years) and at a mature age (45 years) there are symptoms of chronic arthritis on seronegative type.

It is necessary to understand, why in one cases SGA causes development rheumatic fever with or without heart disease but in other cases there is arthritis exhibit tendency to synchronisation.

Conclusions

At patients with chronic arthritis (ChA), joints are organs of the maximum accumulation of fragments of peptidoglycan (PPG)- polysaccharide (PSH). Long-lasting not biodegraded cytodermes can induce synthesis of RF and cause development of chronic arthritis.

Though rheumatic fever (RF) and chronic arthritis (ChA) very much differ from each other and have nosologic independence, but at fundamental level they can have general pathogenetic ways. Probably, this general level consists in a trigger role of the same component of streptococcus of group A.

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Comparison of renal outcomes and mortality in early and delayed onset lupus nephritis

Soo-Kyung Cho[1,2], Hyoungyoung Kim[1,2], Jungyong Han[1,2], Yena Jeon[3], Sun-Young Jung[4], Eun Jin Jang[5], Yoon-Kyoung Sung[1,2]

[1] Department of rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea
[2] Hanyang University Institute for Rheumatology Research, Seoul, Republic of Korea
[3] Department of statistics, Kyungpook National University, Daegu, Republic of Korea
[4] College of Pharmacy, Chung-Ang University, Republic of Korea
[5] Department of information statistics, Andong National University, Andong, Republic of Korea

Background

To compare the renal outcomes and mortality in patients with early and delayed onset lupus nephritis (LN).

Methods

We constructed a retrospective cohort of incident cases of Systemic Lupus Erythematosus (SLE) using the nationwide Korean National Health Insurance Service databases between 2008 and 2018. Then we selected LN patients according to our operational definitions; renal biopsy after urine analysis and creatinine test. Patients who developed LN within 12 months of diagnosis (Early LN group) were compared with patients in whom LN was diagnosed after 12 months of SLE diagnosis (Delayed LN). The hazard ratio (HR) of progression to end-stage renal disease (ESRD) was estimated by the Kaplan-Meier and the Cox model, and by the Fine-Gray model when deaths present as competing events.

Results

We identified 3,779 incident SLE patients who developed LN; 2,291 early LN patients and 1,489 delayed LN patients. The median duration from SLE diagnosis to the development of LN in early LN and delayed LN groups were 0.23 months and 34 months, respectively. Early LN patients showed a similar risk of progression to ESRD compared with the delayed LN group [HR 1.14, 95% confidence interval (CI); 059 to 2.21] after adjusting the confounders such as age, sex, lupus severity, type of insurance, comorbidity, and medications. However, early LN patients had a nearly two-fold increased risk of mortality than the late LN group (HR 1.94, 95% CI; 1.85 to 2.03].

Conclusions

The mortality of early LN patients was higher compared with the delayed LN patients, while their risk of progression to ESRD was comparable.

Keywords

systemic lupus erythematosus, lupus nephritis, mortality

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Level of knowledge on systemic lupus erythematosus among nursing students in selected universities in the Philippines

Cherry Ann Garcia Durante[1,2], Jeeno Jay Frani[2]

[1] Center for Research and Publication, Emilio Aguinaldo College - Manila, Philippines
[2] School of Nursing, Emilio Aguinaldo College - Manila, Philippines

Background

Systemic Lupus Erythematosus (SLE) is estimated to affect approximately 1.5 million individuals. As future nurses, it is vital that students would know about its pathogenesis and clinical manifestation to appropriate relevant nursing interventions to the patients. This study aimed to describe the level of knowledge of student nurses about SLE.

Methods

Among 250 nursing students, 231 consented to be respondents (response rate: 92.4%) from three universities in the Philippines. A self-administered online questionnaire was used to gather data on level of knowledge about SLE from January to February 2022. Informed consent was secured from the participants.

Results

Among the study participants, 28.14% had low knowledge on SLE, while 10.82% had high knowledge. 88% of those with high knowledge were female participants. In the 34-item knowledge questions, the average score was 21. 49, ranging from a score of 3-31 points. Low scores were noted on manifestations of SLE with correct responses of only 12.5%, diagnosis of SLE (16.88%), and risk factors and co-morbidities (26%). A one-way ANOVA was conducted to determine if knowledge was different for different year levels. There was a statistically significant difference between groups as determined by one-way ANOVA ($F=5.41$, $p = 0.001$). Higher year level was associated with higher level of knowledge.

Conclusions

Based on the results of the study, almost 3 out of 10 students nurses had low knowledge about SLE. There is a need to educate the student nurses about SLE and its manifestations, diagnostic tests, risk factors and co-morbidities to ensure appropriate nursing interventions will be provided to future patients.

Keywords

SLE, Knowledge level on Systemic Lupus Erythematosus, Nursing Students

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Journal of Rheumatic Diseases
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Comparative safety of tofacitinib and TNF inhibitor in Korean patients with rheumatoid arthritis: A prospective, single-center cohort study

Yeo-Jin Song[1,2], Soo-Kyung Cho[1,2], Hyoungyoung Kim[1,2], Hye Won Kim[2], Eunwoo Nam[2], Ja-Young Jeon[3], Hyun-Jeong Yoo[3], Chan-Bum Choi[1,2], Tae-Hwan Kim[1,2], Jae-Bum Jun[1,2], Sang-Cheol Bae[1,2], Dae Hyun Yoo[1,2], Yoon-Kyoung Sung[1,2]

[1] Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea
[2] Hanyang University Institute for Rheumatology Research, Seoul, Republic of Korea
[3] Pfizer Pharmaceuticals Korea Ltd., Seoul, Republic of Korea

Background

To evaluate the safety of tofacitinib compared with tumor necrosis inhibitor (TNFi) treatment in Korean patients with rheumatoid arthritis (RA).

Methods

Data were extracted from prospective cohorts of RA patients starting tofacitinib or TNFi in Hanyang University Hospital for Rheumatic Diseases between March 2017 and May 2021. Data on adverse events (AEs) were collected through interviews and medical records and classified by Common Terminology Criteria for AEs. The observation started from enrollment until discontinuation of each agent or November 2021. Among overall AEs, we estimated the crude incidence rate (IR) and incidence rate ratio (IRR) of each treatment-related AEs (TAEs) between tofacitinib and TNFi users. Serious AEs (SAEs) were also presented.

Results

This study included 200 tofacitinib users (474.2 person-years [PYs], mean 2.4 years) and 223 TNFi users (473.8 PYs, mean 2.1 years). Tofacitinib users were older and had a longer disease duration than TNFi users. Disease activity at enrollment was also higher in tofacitinib users. In the tofacitinib group, infection including herpes zoster was the most common TAE (9.07/100 PYs), and in the TNFi group, infection (5.49/100 PYs) and injection site reaction (5.28/100 PYs) were most common. The incidences of AE leading to drug discontinuation (IRR 0.70, 95% CI 0.27–1.84) and SAEs (IRR 2.00, 95% CI 0.81–4.95) were similar in both groups. As AEs of special interest, there were 4 cases of acute coronary syndrome and 1 case of venous thromboembolism only in the tofacitinib group, of which 1 case each was of TAE. We observed 2 cases of malignancy in the tofacitinib group and 1 case of malignancy in the TNFi group.

Conclusions

Our unmatched cohort study showed a similar incidence of SAEs in Korean RA patients treated with either tofacitinib or TNFi, while their baseline characteristics or patterns of AE differed between the two groups.

Figure & Table

Category	Tofacitinib (n=200)			TNF inhibitor (n=223)			Incidence rate ratio (95% CI)	*P*
	Number of cases	Number of patients (%)	Incidence rate*	Number of cases	Number of patients (%)	Incidence rate*		
Total	72	52 (26.0)	15.18	96	68 (30.5)	20.26	0.75 (0.55–1.02)	0.064
Blood and lymphatic system disorders	1	1 (0.5)	0.21	0	0 (0.0)	0.00		
Cardiac disorders	1	1 (0.5)	0.21	0	0 (0.0)	0.00		
Endocrine disorders	0	0 (0.0)	0.00	1	1 (0.4)	0.21		
Eye disorders	2	2 (1.0)	0.42	1	1 (0.4)	0.21	2.00 (0.18–22.04)	0.572
Gastrointestinal disorders	11	9 (4.5)	2.32	6	6 (2.7)	1.27	1.83 (0.68–4.95)	0.233
General disorders and administration site conditions	0	0 (0.0)	0.00	25	25 (11.2)	5.28		
Hepatobiliary disorders	0	0 (0.0)	0.00	1	1 (0.4)	0.21		
Infections and infestations	43	34 (17.0)	9.07	26	22 (9.9)	5.49	1.65 (1.02–2.69)	0.043
Injury, poisoning and procedural complications	1	1 (0.5)	0.21	1	1 (0.4)	0.21	1.00 (0.06–15.97)	1.000
Investigations	0	0 (0.0)	0.00	6	4 (1.8)	1.27		
Musculoskeletal and connective tissue disorders	1	1 (0.5)	0.21	3	3 (1.3)	0.63	0.33 (0.03–3.20)	0.341
Neoplasms benign, malignant and unspecified	0	0 (0.0)	0.00	1	1 (0.4)	0.21		
Nervous system disorders	2	1 (0.5)	0.42	1	1 (0.4)	0.21	2.00 (0.18–22.04)	0.572
Renal and urinary disorders	0	0 (0.0)	0.00	1	1 (0.4)	0.21		
Reproductive system and breast disorders	0	0 (0.0)	0.00	3	3 (1.3)	0.63		
Respiratory, thoracic and mediastinal disorders	3	3 (1.5)	0.63	2	2 (0.9)	0.42	1.50 (0.25–8.97)	0.658
Skin and subcutaneous tissue disorders	6	5 (2.5)	1.27	18	17 (7.6)	3.80	0.33 (0.13–0.84)	0.020
Vascular disorders	1	1 (0.5)	0.21	0	0 (0.0)	0.00		
Serious adverse event	14	11 (5.5)	2.95	7	7 (3.1)	1.48	2.00 (0.81–4.95)	0.135
Adverse event leading to discontinuation	7	3 (1.5)	1.48	10	8 (3.6)	2.11	0.70 (0.27–1.84)	0.468

* Observation periods were 474.2 person-years (PYs) for tofacitinib users and 473.8 PYs for TNF inhibitor users, and incidence rate was calculated as cases per 100 person-years.

RA, rheumatoid arthritis; TNF, tumor necrosis factor; CI, confidence interval.

Table. Treatment-related adverse events in RA patients who used tofacitinib or TNF inhibitor

Keywords

safety, rheumatoid arthritis, tofacitinib

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Vol. 29, Suppl. 1, May, 2022
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A tale of three paths: Singaporean patient journeys from initial symptoms of gout to presentation for health care

Aloysius Chow[1], Laurie J. Goldsmith[1], Delfinn Tan[1], Madelynn Chan[2], Richard Lee[3], Christian Mallen[4], Bernadette Bartlam[4], Helen Elizabeth Smith[1]

[1] Family Medicine and Primary Care, Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore
[2] Rheumatology, Allergy and Immunology, Tan Tock Seng Hospital, Singapore
[3] Woodlands Polyclinics, National Healthcare Group Polyclinics, Singapore
[4] School of Medicine, Keele University, United Kingdom

Background

Gout is a common form of arthritis with a rising incidence worldwide. Early intervention is important, yet there is evidence from many countries that gout is inadequately treated. To address this issue, we conducted a qualitative study of patients' experiences of gout diagnosis and initial treatment in Singapore.

Methods

Our study consisted of semi-structured interviews with adults with gout about their initial symptoms and journey to receiving a diagnosis from a provider of Western medicine. Interviewees were recruited from healthcare and non-healthcare settings and snowball techniques. Data were analyzed using thematic analysis by multiple analysts.

Results

Fifty-six participants varied by age, gender, ethnicity, and time since getting diagnosed. The interviewees' experiences of receiving their diagnoses were grouped into three major pathways. Pain is the main driver of the first two pathways. The more intense the pain, the less the individual needs to be aware of or know about gout to immediately seek out healthcare. The delay and duration of delay of presentation to healthcare can be due to assumptions that the pain resulted from a sprain/injury and that adequate rest was sufficient. Other interviewees first visit an alternative medicine provider before arriving at a provider of Western medicine. The third pathway was driven by individual health beliefs that prioritize self-care and self-management over seeking care from a healthcare provider.

Conclusions

Patients' understandings of gout and the need for timely presentation can be facilitators of seeking diagnosis and treatment early. Not all patients prioritize seeking healthcare even when their symptoms of gout disrupted their daily activities. Improved patient education has potential to accelerate some pathways of presentation to healthcare (i.e., Pathways #1 and #2). Other pathways (i.e., Pathway #3) are likely more resistant to a change despite patient education, and may require other interventions.

Keywords

Gout, Patient experience, Qualitative research

E-poster Presentation

Osteoporosis and metabolic bone diseases

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022

KCR 2022
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Two novel mutations in TCIRG1 induced infantile malignant osteopetrosis: A case report

Ping Wu[1]

[1] Department of Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, Guangdong, China., China

Description

We present the case of a 4-month-old male infant with abnormal skull development, hypocalcemia and premature closure of the cranial sutures. Due to the hyper bone density showed by his radiographic examination, which are characteristic patterns of IMO, we speculated that he might be an IMO patient. In order to confirm this diagnosis, a high-precision whole exome sequencing of the infant and his parents was performed. The analysis of high-precision whole exome sequencing results lead to the identification of two novel heterozygous mutations c.504-1G > C (a splicing site mutation) and c.1371delC (p.G458Afs*70, a frameshift mutation) in gene TCIRG1 derived from his parents. Therefore, we propose that there is a close association between these two mutations and the onset of IMO.

Conclusions

To date, these two novel mutations in gene TCIRG1 have not been reported in the reference gene database of Chinese population. These variants have likewise not been reported outside of China in the Genome Aggregation Database (gnomAD). Our case suggests that the use of whole exome sequencing to detect these two mutations will improve the identification and early diagnosis of IMO, and more specifically, the identification of homozygous individuals with TCIRG1 gene mutation. We propose that these mutations in gene TCIRG1 could be a novel therapeutic target for the IMO in the future.

Figure & Table

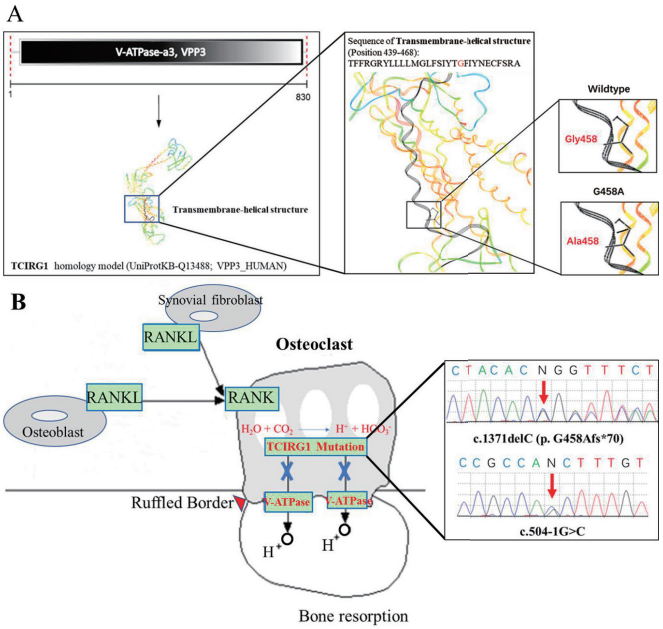

Figure. The pathogenesis mechanism of infantile malignant osteopetrosis.

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Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Relationship between vitamin d, body mass index with bone mineral density of Mongolian miners

Garamjav Khishigdavaa[1], Tuvshinjargal Dashdavaa[2], Agiimaa Ulziibadrakh[1], Buyankhishig Lhagvatogoo[1], Uuriintuya Altankhuyg[1], Ariuntungalag Khishigbadrakh[3]

[1] Radiology, Medipas hospital, Mongolia
[2] Radiology, Mongolian National University of Medical Science, Mongolia
[3] Rheumatology, Medipas hospital, Mongolia

Background

Osteoporosis is a worldwide health problem and is considered as the most common bone disease. Body mass index (BMI) and vitamin D level are being risk factors to bone mineral density (BMD). However, there are very few studies on BMD and its associated factors among miners in Mongolia. Our study aimed to investigate the relationships between serum 25-hydroxyvitamin D (25(OH) D) levels, BMI and BMD among Mongolian miners.

Methods

Included were 120 miners (60 males and 60 females) were recruited for this cross-sectional study at Medipas hospital. Miners body mass index was calculated. Serum 25OHD tests were performed. BMD was determined by quantitative ultrasound. Bivariate regression models were used to investigate the relationships between serum 25(OH) D, BMI and BMD.

Results

Total of 120 miners with a mean age of 45.8 ± 8.5 years were included in the study. Thirty two participants had osteopenia. Osteoporosis was present in 9 miners. The mean BMI of subjects was 27.6±4.3 kg m2. The mean values for serum 25(OH) D levels were 21.0 ± 9.1 ng/ml. In 86.7% of participants, serum 25(OH) D levels were below 30 ng/ml, confirming vitamin D deficiency. The BMI significantly negative correlated with BMD (r = -0.313, p = 0.012). There was no association between 25(OH) D levels and BMD (r = 0.102, p=0.430).

Conclusions

This study showed that the BMI significantly influences BMD in survey participants miners. However, there was no direct relationship between vitamin D level and BMD among miners.

Keywords

Body mass index, Bone mineral density, Vitamin D

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Application of Machine Learning to identify osteoporosis based on the extreme learning machine (ELM) model algorithm

Rifaldy Fajar[1,2], Asfirani Umar[2], Sahnaz Vivinda Putri[2]

[1] Applied and Interdisciplinary Mathematics, University of L'Aquila, Italy, Italy
[2] Computational Biology and Medicine Laboratory, Yogyakarta State University, Indonesia

Background

Osteoporosis is a condition in which bones lose strength and are prone to fractures. Osteoporosis has no external symptoms and the first sign of osteoporosis is often broken bone. Broken and broken bones are the same thing. The bones that most often fracture due to osteoporosis are the wrists, hips, and spine. Osteoporosis cannot be seen with the naked eye. Therefore, in this study, osteoporosis identification was carried out using x-ray images (bone radiograph) based on machine learning.

Methods

In this study, the bone radiograph dataset was used. Bone radiographs were obtained from IEEE-ISBI 2014 competition dataset. The method used to identify is the extreme learning machine, in which previously the feature values in the image were taken using invariant moment feature extraction. The characteristic value of the bone radiograph image will go through the classification stage using ELM, then the results of normal or osteoporosis images will be obtained. Regarding classification, the stages are determining the number of nodes in the hidden layer, determining the activation function, the training process, the testing process, and the output calculation.

Results

This study uses 86 images as training data and 30 images as testing data. Image testing using several parameters such as epoch 1000, hidden node 50, threshold 170, and a learning rate of 0.2 has the ability to be quite successful in identifying osteoporosis to get a system accuracy of 90%.

Conclusions

Through several tests, it can be concluded that hidden nodes affect system accuracy. If the hidden node is the greater the value, the better the accuracy, if the hidden node is the smaller the value, the more error the image will get. The accuracy value obtained is quite good at 90% so the osteoporosis identification system can help make it easier to see osteoporosis and normal bone radiograph images.

Keywords

ELM Algorithm, Osteoporosis, Machine Learning

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FRAX model is useful for prediction of major fractures in RA patients with glucocorticoid-induced osteoporosis

Yoon-Kyoung Sung[1,2], Hyoungyoung Kim[1,2], Yeo-Jin Song[1,2], Tae-Han Lee[3], Hye Won Kim[2], Eunwoo Nam[2], Soo-Kyung Cho[1,2]

[1] Department of rheumatology, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea
[2] Hanyang University Institute for Rheumatology Research, Seoul, Republic of Korea
[3] Department of rheumatology, Keimyung University Dongsan Medical Center, Daegu, Republic of Korea

Background

To evaluate the fracture risk in patients with rheumatoid arthritis (RA) according to Korean clinical practice guidelines for glucocorticoid-induced osteoporosis (GIOP)

Methods

A retrospective study was conducted on a cohort of RA patients ≥ 40 years old receiving glucocorticoids for more than 3 months in a single academic hospital from 2008 to 2019. Patients who could be assessed with the fracture risk assessment (FRAX) tool were selected and further divided into two groups according to the presence of bone mineral density (BMD). After categorizing the patients according to WHO criteria and Korean guidelines for GIOP, we observed the patients from their first visit to the last visit or the development of fracture, until September 2021. The incidence rate (IR) of major osteoporotic fracture per 100 person-year (PY) was calculated in each risk group.

Results

Among the 753 patients included in this study, 428 patients (56.8%) had BMD and the other 325 patients (43.2%) did not for 2 years after first visit. Among the patients having BMD, 30% (n=129, 769.74 PYs) were osteoporosis and they were also included in moderate/high fracture risk group based on FRAX. Although they had received anti-osteoporotic treatment, their IR of major fracture was 1.95/100 PYs. The other patients without osteoporosis (n=299), 285 patients (1728.47 PYs) are in moderate/high-risk group based on FRAX and their IR of major fracture was 0.42/100 PYs. In patients without BMD, 80.3% of them (n=261, 1706.90 PYs) were categorized as moderate/high-risk group based on FRAX, and their IR of major fracture was 0.41/100PYs. No fracture was observed in patients who were low-risk group based on FRAX (n=64, 412.52 PYs).

Conclusions

In RA patients who are using glucocorticoids, especially who had osteopenia/normal BMD or not available BMD, fracture risk assessment by FRAX might be a good indicator for fracture prevention.

Keywords

Fracture risk assessment, glucocorticoid-induced osteoporosis, bone mineral density

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May 19(Thu) - 21(Sat), 2022

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Genetic variation of susceptibility gene of osteoporosis, measuring method of oste- oporosis risk

Ahmad Ahmad[1]

[1] Govermental Science, Universitas Al Asyariah Mandar, Indonesia

Description

Osteoporosis is a bone disorder characterized by reduced bone strength, increasing the risk of fracture. Osteoporosis occurs due to an imbalance between the formation of new bone and the resorption of old bone. Osteoporosis usually has no specific signs or symptoms until a fracture occurs. Genetic variation is the variation that occurs in the genome of an organism, either in nucleotide bases, genes or chromosomes. Genetic variation at the elementary level is indicated by differences in the sequence of the nucleotide bases that make up DNA in cells. Genes can be used as markers for cell recruitment and activation molecules. This study aims to evaluate the genetic variation of susceptibility gene of osteoporosis, measuring method of osteoporosis risk.

Data obtained from 27 nucleotide sequences of susceptibility gene of osteoporosis, measuring method of osteoporosis risk on secondary data form on https://www.ncbi.nlm.nih.gov/. The phylogeny analysis of DNA sequences was inferred using the UPGMA method, the evolutionary history (Neighbor-Joining method), the evolutionary distances (Maximum Composite Likelihood method) using MEGA 7.0 software.

The result shown that on the phylogenetic tree (Figure 1.) 27 sequences were divided into 3 main groups, namely group I consisting of 10 sequence, group II consisting of 6 sequence, and the group III consisting of 11 sequence. The optimal tree with the sum of branch length = 131.14792886 is shown. The tree is drawn to scale, with branch lengths in the same units as those of the evolutionary distances used to infer the phylogenetic tree. The proportion of sites where at least 1 unambiguous base is present in at least 1 sequence for each descendent clade is shown next to each internal node in the tree.

Conclusions

The genetic variation of susceptibility gene of osteoporosis, measuring method of osteoporosis risk sequence have highly variation.

Figure & Table

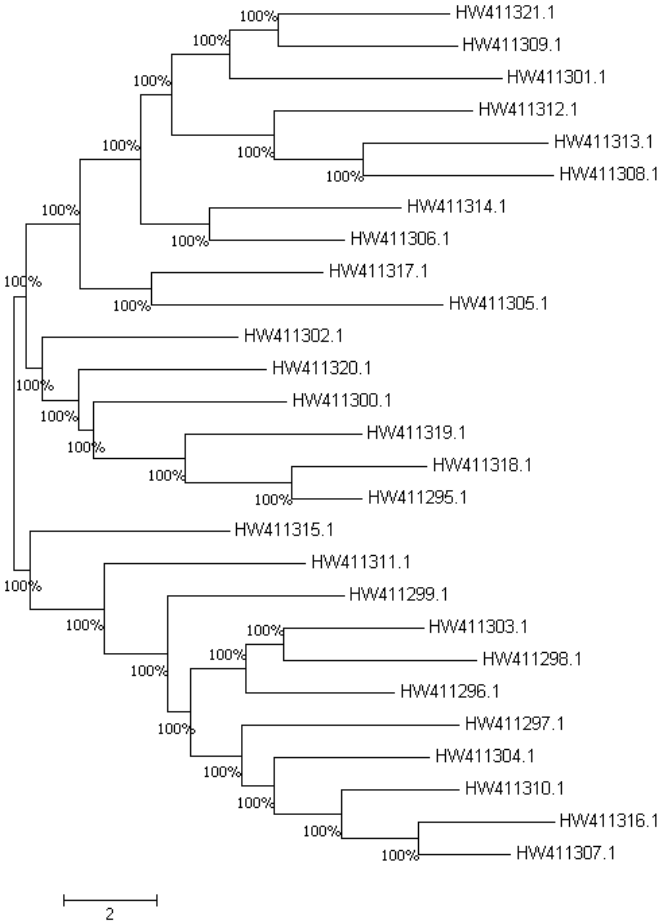

Figure. Phylogenetic tree of Osteophorosis

Keywords

Genetic Variation, Susceptibility Gene, Osteoporosis

JRD Journal of Rheumatic Diseases
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Patient preference and efficacy of zoledronic acid in the treatment of glucocorticoid-induced osteoporosis in patients with autoimmune diseases

Ji-Won Kim[1], Ju-Yang Jung[1], Hyoun-Ah Kim[1], Chang-Hee Suh[1]

[1] Department of Rheumatology, Ajou University School of Medicine, Republic of Korea

Background

The most commonly used drugs for glucocorticoid-induced osteoporosis (GIOP) is bisphosphonate (oral alendronate and risedronate, and intravenous zoledronic acid). Zoledronic acid is a convenient treatment option that allows compliance to be advantageous over other bisphosphonates. Our aim is to evaluate the efficacy compared to other bisphosphonates as well as the preference and patient satisfaction of zoledronic acid.

Methods

We recruited 50 patients with new fractures or osteoporosis found in follow-up bone densitometry after taking oral bisphosphonates for at least 1 year in patients diagnosed with GIOP during treatment for autoimmune diseases. After 1 year of treatment with zoledronic acid, patients completed the survey to rate their preference and satisfaction. The treatment efficacy was analyzed by comparing the changes in bone density and fractures with patients maintaining oral bisphosphonates as controls.

Results

Mean age was 64.1 years, 96% were female, and the mean duration of GIOP was 5.5 years. There was no difference in the cumulative glucocorticoid doses of the two groups. Thirty-nine patients (78%) preferred and were more satisfied with intravenous zoledronic acid over oral bisphosphonates, and satisfaction was strongly affected by the administration interval and convenient regimen. The infusion-related adverse events of zoledronic acid were only 2 patients (4%). In addition, there were no significant differences in annualized percentage change in bone density in the lumbar spine (1.9±3.91g/cm2 vs. 1±5.3g/cm2, p=0.355), femur neck (-0.91±6.31g/cm2 vs. 0.41±5.07g/cm2, p=0.264), and hip (0.29±2.91g/cm2 vs. 0.41±5.07g/cm2, p=0.888) between patients who received zoledronic acid and those who took oral bisphosphonates. The occurrence of new fractures was two in each of the two groups, showing no difference.

Conclusions

Zoledronic acid was preferred and more satisfactory by patients, and the treatment efficacy for osteoporosis was similar to oral bisphosphonates. Therefore, zoledronic acid is recommended as an appropriate treatment for GIOP in patients with autoimmune disease.

E-poster Presentation

Osteoarthritis and biology of bone and joint

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
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The potential targets of San-Miao-San in the treatment of osteoarthritis

Zhe Cai[1,2], Ping Wu[1], Yu Feng[3]

[1] Department of Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, China., China
[2] Institute of Chinese Medicine and State Key Laboratory, The Chinese University of Hong Kong, Hong Kong., Hong Kong
[3] Department of Sports Medicine and Arthroscopy, General Hospital of Ningxia Medical University, China., China

Background

To examine the potential therapeutic targets of Chinese medicine formula San-Miao-San (SMS) in the treatment of osteoarthritis (OA), we analyzed the active compounds of SMS and key targets of OA, and investigated the interacting pathways using network pharmacological approaches and molecular docking analysis.

Methods

The active compounds of SMS and OA-related targets were searched and screened by TCMSP, Drugbank, Genecards, OMIM, DisGeNet, TTD, and PharmGKB databases. Venn analysis and PPI were performed for evaluating the interaction of the targets. The topological analysis and molecular docking were used to confirm the sub-networks and binding affinity between active compounds and key targets, respectively. The GO and KEGG functional enrichment analysis for all targets of each sub-network were conducted.

Results

A total of 57 active compounds and 203 targets of SMS were identified by the TCMSP and Drugbank database; while 1791 OA-related targets were collected from the Genecards, OMIM, DisGeNet, TTD, and PharmGKB databases. By Venn analysis, 108 intersection targets between SMS-targets and OA-targets were obtained. Most of these intersecting targets involve quercetin, kaempferol and wogonin. Moreover, intersecting targets identified by PPI analysis were introduced into Cytoscape plug-in CytoNCA for topological analysis. Hence, nine key targets of SMS for OA treatment were obtained. Furthermore, the potential binding conformations between active compounds and key targets were found through molecular docking analysis. According to the DAVID enrichment analysis, the main biological processes of SMS in the treatment of OA include oxidative stress, response to reactive oxygen species and apoptotic signaling pathways. Finally, we found wogonin, the key compound in SMS, might play a pivotal role on Toll-like receptor, IL-17, TNF, osteoclast differentiation, and apoptosis signaling pathways through interacting with four key targets.

Conclusions

Therefore, this study elucidated the potential active compounds and key targets of SMS in the treatment of OA based on network pharmacology.

Keywords

San-Miao-San, Osteoarthritis, Network pharmacology

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Journal of Rheumatic Diseases
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Serum, synovial visfatin level during flare-up and remission of primary knee OA

Haytham Abd elaal[1]

[1] Rheumatology, MOH, Egypt

Background

Osteoarthritis (OA) causes pain and dysfunction and is the leading cause of disability in elderly people in industrialized countries . Several epidemiologic studies have shown a positive association between obesity and hip and knee OA, highlighting the key role of mechanical loading on Cartilage metabolism . fat cells secrete a variety of proteins with the functional and structural properties of cytokines; these are termed “adipokines.” Adiponectin, leptin, and resistin are the most abundant adipokines produced by Adipose tissue, and production of leptin and resistin is increased in obese individuals. One recently described adipokine is visfatin. It is secreted by mature adipocytes, and its plasma concentration markedly increases in parallel with the amount of visceral fat. Visfatin exerts insulin-mimetic effects in vivo and in vitro. results in breakdown of articular cartilage.

Methods

in order to achieve the target of our study which was to measure serum and synovial fluid Visfatin in patients with primary OA in two clinical settings, 20 patients with primary OA of the knee in flare-up, were selected from the out-patients clinic. The patients were followed up every two weeks after the first setting until they entered into remission i.e. returned to the base line before the last flare up. Twenty normal controls age, sex and body mass index (BMI) matched were recruited.

Results

We could demonstrate from our results that the serum level of Visfatin in OA patients were higher than the control group with high significant difference.

Conclusions

1-Visfatin was elevated both systemically and locally in the patients with primary knee OA

2-Visfatin was elevated during OA flare ups and decrease during OA remission.

3-The level of visfatin was higher in serum in comparison to synovial fluid in OA patients.

4-There was no difference in the level of visfatin in relation to aging or gender difference.

Figure & Table

	group	Number	Mean	Std. Deviation	t	P
age	1.00	20	53.8500	5.36509	1.71	0.096
	2.00	20	50.8000	5.93473		
weight	1.00	20	89.1500	13.02336	0.63	0.534
	2.00	20	86.6500	12.14507		
height	1.00	20	163.8500	10.44421	3.28	0.002
	2.00	20	154.6500	6.93029		
BMI	1.00	20	33.6018	6.69692	1.39	0.172
	2.00	20	36.3591	5.78994		
waist_circ	1.00	20	92.6000	11.60943	0.151	0.138
	2.00	20	99.1000	15.28639		
hip_circ	1.00	20	105.5000	11.42251	2.98	0.005
	2.00	20	119.1500	16.98382		
w/h_ratio	1.00	20	.8832	.11957	1.86	0.071
	2.00	20	.8312	.03739		

Group1= cases group2=control

There was significant difference between cases and control in height (cases were taller) and hip circumference (control group had wider waist circumference).

Table. Demography and patient characteristics in both groups.

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Influence of metabolic syndrome in patients with knee osteoarthritis

Jamol Uzokov[1], Anis Alyavi[1], Bakhromkhon Alyavi[1]

[1] Internal Medicine, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Uzbekistan

Background

Metabolic syndrome (MetS) is a cluster of several risk factors and risk for future type 2 diabetes mellitus and cardiovascular disease. Knee osteoarthritis is a degenerative disorder and widespread in older generation. Aim of the study was to evaluate the influence of metabolic syndrome and its components in patients with knee osteoarthritis

Methods

One hundred and twenty patients with knee osteoarthritis were enrolled in this study (Mean age-58.12±12.6 years; male-41%). Patients were divided into two groups by sixty whether diagnosed with concomitant MetS or not. Group I consisted of 60 patients with knee osteoarthritis whilst Group II made up 60 patients with knee osteoarthritis and MetS. All anthropometry, laboratory and instrumental data were collected for the assessment and all statistical analysis were performed by STATA.

Results

Patients with knee osteoarthritis and MetS significantly affected with varus deformity, tenderness over knee joint and flexion deformation than those without MetS (P<0.05). Kellgren and Lawrence radiological score were significantly higher in Group II than Group I participants (P<0.001). Even though, Lequesne functional score was higher in Group II there were not statistically significant changess between groups (P>0.05). Among MetS components abdominal obesity (AO, 2.2; CI 95%; 1.7-3.6; P<0.05), hypertension (1.8; CI 95%; 1.4-2.5; P<0.05), dyslipidemia (1.4; CI 95%; 1.1-2.2; P<0.05) were positively associated with knee osteoarthritis.

Conclusions

MetS is associated with more severe clinical picture and radiological changes in knee osteoarthritis. Among MetS components, AO, hypertension, dyslipidemia might influence course of action of the knee osteoarthritis. Further studies are required with large amount of participants.

Keywords

knee osteoarthritis, metabolic syndrome, dyslipidemia

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Efficacy of joint treatment with metformin and NSAIDS in patients with knee osteoarthritis and metabolic syndrome

Bakzod Karimov[1], Jamol Uzokov[1], Anis Alyavi[1]

[1] Rheumatology, Republican specialized scientific practical medical center of therapy and medical rehabilitation, Uzbekistan

Background

Knee osteoarthritis is widespread among older population. Co-incidence of knee osteoarthritis and metabolic syndrome exaggerates the course of disease and was associated with poor long-term prognosis. Aim of the study was to evaluate the combined therapy with metformin and NSAIDs in patients with knee osteoarthritis and MetS.

Methods

82 patients with knee osteoarthritis and metabolic syndrome were enrolled in the study (Mean age-60.22±14.8 years; male-39%). Patients were divided into two groups by 60. Group I were assigned additional metformin to NSAIDs whereas Group II were assigned only NSAIDs. Anthropometry, laboratory and instrumental data (including MRI) were assessed at baseline and in 3 years period for the follow-up. All statistical analysis were performed using STATA.

Results

Group I patients tended to have lower BMI (27.2 vs. 29.4, P<0.05), less knee pain (4.6 vs. 7.2, P<0.05) and less severe knee osteoarthritis (K-L grade 3.2 vs 4.3, P<0.05) than Group II. The medium rate of medial cartilage volume loss was significantly lower in patients with metformin and NSAIDs users than those without metformin users (P<0.05). Even though, the medium rate of lateral cartilage volume loss were lower in metformin group, there were not any statistically significant changes between groups (P>0.05). Risk of total knee replacement was higher in Group II than Group I over the period of 3 years (OR 0.45; CI 95%; 0.12-0.74; P<0.05).

Conclusions

Combination therapy with metformin and NSAIDs may be beneficial in long-term prognosis in patients with knee osteoarthritis and metabolic syndrome. Further studies are needed to clarify.

Keywords

knee osteoarthritis, metabolic syndrome, metformin

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Detection of the sesamoid bone of the metacarpal joint in patients with osteoarthritis using the deep learning model

Bon San Koo[1], Wonjung Kim[2], Gaeun Lee[2], Seunghun Lee[3], June-Goo Lee[2], Jae-Bum Jun[4]

[1] Internal medicine, Inje University Seoul Paik Hospital, Inje University College of Medicine, Republic of Korea
[2] Biomedical Engineering Research Center, Asan Institute for Life Sciences, Asan Medical Center, Republic of Korea
[3] Department of Radiology, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea
[4] Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Republic of Korea

Background

The purpose of this study is to develop a deep learning model to detect sesamoid bone using previous digital tomosynthesis and radiograph images, and to find out the distribution and characteristics of sesamoid bone in the metacarpo-phalangeal (MCP) joint on hand radiographs in patients with osteoarthritis.

Methods

The model to detect sesamoid bone using the deep learning algorithm (Mask R-CNN) were developed. Hand radiograph images and distribution information of sesamoid bones of 5 MCP joints found on tomosynthesis in previous study were used for training (180 hand radiograph) and test set (50 hand radiograph). The accuracy of sesamoid bone detection was determined in test set. The sesamoid bone was detected on the radiograph in patients with osteoarthritis using the deep learning model, and the difference in the number of sesamoid bone according to the age, sex, and time was investigated with statistical analysis.

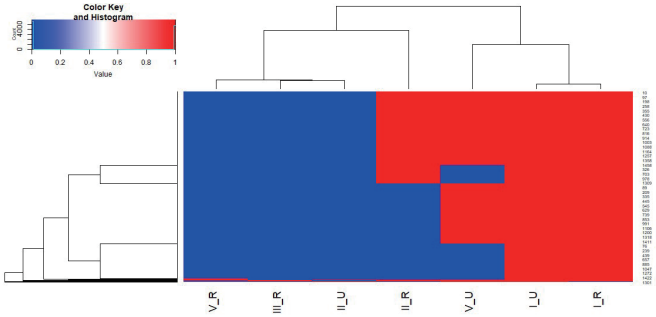
Results

In test set, accuracy, recall, precision, and F1 score were 0.84, 0.74, 0.76, and 0.75, respective. Using this model, sesamoid bones were analyzed on 1,474 hand radiographs and a total of 4,754 sesamoid bones were detected. The number of sesamoid bone in radial and ulnar side was 1,472 (99.9%) and 1,471 (99.8%) in first finger, 727 (49.3%) and 8 (0.5%) in second finger, 7 (0.5%) and 0 in third finger, 12 (0.8%) and 1057 (71.7%) in fifth finger, respectively. Most of the sesamoid bones are found at the first, second, and fifth MCP joints, and they are largely clustered into two groups. Group 1 includes the ulnar

Conclusions

The sesamoid bone, which is difficult to confirm in the radiograph, was detected using a deep learning model. In addition, more sesamoid bone was identified in osteoarthritis patients than reported in previous studies and found particularly in MCPs that are primarily stressed in the hands.

Figure & Table



Keywords

sesamoid bone, osteoarthritis, metacarpophalangeal joint

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
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Blood D-dimer level after COVID-19 in patients with knee osteoarthritis

Zumrad Ubaydullaeva[1], Jamol Uzokov[1], Anis Alyavi[1], Daler Orziev[1], Omina Mukhitdinova[1]

[1] Internal Medicine, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Uzbekistan

Background

Covid-19 was emerged in Wuhan and disseminated to the rest of the world. The virus may impact any kind of human organs. Aim of the study was to estimate the blood D-dimer level after Covid-19 in patients with knee osteoarthritis.

Methods

72 patients who were undergone Covid-19 (mild to moderate severity) without knee osteoarthritis (Group 1; aged 44-75 years, mean age 57.6±12.6 years) and 72 patients with knee osteoarthritis who was influenced by Covid-19 (Group 2; aged 44-73 years, mean age 56.8±12.4 years) have been enrolled in this prospective study. Baseline characteristics were collected when first admitted to the hospital due to Covid-19, and follow-up characteristics were collected when they admitted to our hospital for the rehabilitation after undergoing Covid-19 in 3 months. Baseline and follow-up anthropometric, laboratory and instrumental data were assessed. All statistical analysis were performed by STATA software.

Results

Mean blood D-dimer level significantly reduced in both groups (from 856 ng/mL to 482 ng/mL in the first group, $P<0.05$ vs. from 823 ng/mL to 463 ng/mL in the Group 2, $P<0.05$), however there were not observed statistically significant changes when compared to groups, $P>0.05$. In the first group mean D-dimer level tended to be higher in men, with high fibrinogen level, and older patients. In the second group, D-dimer level tended to be higher in patients with higher body mass index (BMI) with high fibrinogen level and in men. In the first group in 29% of patients was observed high level of D-dimer (>500 ng/mL) after 3 months whereas in the second group elevated D-dimer level maintained in 38% of patients.

Conclusions

Elevated blood D-dimer level are common after Covid-19, however concomitant knee osteoarthritis does not effect on it. Further studies are required to clarify exact mechanisms.

Keywords

knee osteoarthritis, Covid-19, D-dimer

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Lactobacillus (LA-1) and butyrate inhibit osteoarthritis by controlling autophagy and inflammatory cell death of chondrocytes

Keun-Hyung Cho[1], JooYeon Jhun[1], Hyun Sik Na[1,2], Jin Seok Woo[1], A Ram Lee[1,2]
Seon-Yeong Lee[1], JeongWon Choi[1], Sung-Hwan Park[3], Mi-La Cho[1,4]

[1] Rheumatism research center, The catholic university of Korea, Republic of Korea
[2] Department of Biomedicine & Health Sciences, College of Medicine, The catholic university of Korea, Republic of Korea
[3] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Med, Catholic University of Korea, Republic of Korea
[4] Department of Medical Lifescience, College of Medicine, Catholic University of Korea, Republic of Korea

Background

Osteoarthritis (OA) reduces quality of life as a result of the pain caused by continuous joint destruction. Inactivated Lactobacillus (LA-1) ameliorated osteoarthritis and protected cartilage by modulating inflammation.

Methods

In this study, we evaluated the mechanism by which live LA-1 ameliorated OA. To investigate the effect of live LA-1 on OA progression, we administered LA-1 into MIA-induced OA animals.

Results

The pain threshold, cartilage damage, and inflammation of the joint synovial membrane were improved by live LA-1. Furthermore, the analysis of intestinal tissues and feces in disease model has been shown to affect the systems of the intestinal system and improve the microbiome environment. Interestingly, inflammation of the intestinal tissue was reduced, and the intestinal microbiome was altered by live LA-1. The number of short-chain fatty acid (SCFA)-producing bacteria was increased by live LA-1. In addition, daily supply of butyrate, a bacterial SCFA, showed a tendency to decrease necroptosis, a type of abnormal cell death, by inducing autophagy and reversing impaired autophagy by the inflammatory environment. These results suggest that OA is modulated by changes in the gut microbiome, suggesting that activation of autophagy can reduce aberrant cell death.

Conclusions

In summary, live LA-1 or butyrate ameliorates OA progression by modulating the gut environment and autophagic flux. Our findings suggest regulation of the gut microenvironment as a therapeutic target for OA.

Keywords

Osteoarthritis, Inflammation, Microbiota

E-poster Presentation

Orthopedics & Rehabilitation

KCR 2022 May 19(Thu) - 21(Sat), 2022
Seoul Dragon City, Seoul, Korea

JRD Journal of Rheumatic Diseases
Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022
KCR 2022
May 19(Thu) - 21(Sat), 2022

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Effects of conventional rehabilitative and aerobic training in patients with idiopathic inflammatory myopathy

Guangyu Zhang[2], Mingwei Tang[1], Xiao Zhang[1], Shuang Zhou[1], Chanyuan Wu[1], Jiuliang Zhao[1], Dong Xu[1], Qian Wang[1], Mengtao Li[1], Lixia Chen[2], Xiaofeng Zeng[1]

[1] Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Chinese Academy of Medical Science, China
[2] Department of Physical Medicine and Rehabilitation, Peking Union Medical College Hospital, Chinese Academy of Medical Science, China

Background

Idiopathic inflammatory myopathies (IIMs) are a group of chronic autoimmune diseases mainly involving the muscular tissue. Physical therapy has recently become major means of intervention to help IIM patients regain muscle strength and the physical capacity in addition to conventional medications. This research is to investigate the efficacy of conventional rehabilitation alone and conventional rehabilitation combined with aerobic training on muscle strength and function, health condition, and quality of life for patients with stable idiopathic inflammatory myopathy.

Methods

This is a historical retrospective cohort study, in which the medical records of IIM patients who received the combination of conventional rehabilitative therapy and aerobic training (combined training group, CTG), from February 2015 to December 2017 were reviewed. IIM patients who received conventional therapy alone were matched based on their age, gender, and disease activity as the control group (CG). Manual Muscle Testing (MMT8) was the primary outcome, and Myositis Functional Index (FI-2), Health Assessment Questionnaire (HAQ), and Short Form 36 (SF-36) scores at 12 weeks during training were the secondary outcomes.

Results

56 patients were included in this analysis: 28 in CTG, 28 in CG. Patients in both groups had improved MMT8, FI-2, HAQ, and SF-36 scores after 12 weeks' physical therapy. There was a significantly higher score of MMT8 and HAQ in CTG than CG at the 12th week. FI-2 scores were significantly higher in the CTG in 4 items ($P<0.05$) of hip flexion, step test, heel lift, and toe lift. SF-36 scores of the CTG were also higher than CG in 5 items ($P<0.05$) of physical functioning, general health, vitality, social functioning, and mental health.

Conclusions

Physical exercise training including conventional rehabilitation and aerobic training improved muscle function, health condition, and quality of life. Conventional rehabilitative training combined with aerobic training achieved better improvement compared with conventional rehabilitation training alone.

Figure & Table

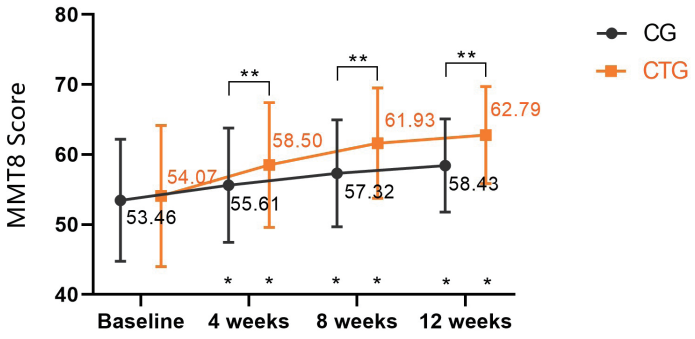

Figure. Mean Manual Muscle Test (MMT8) scores of the combined training group(CTG) and control group(CG) before and after training

Keywords

myositis, rehabilitation, aerobic Training

Journal of Rheumatic Diseases
Vol. 29, Suppl. 1, May, 2022

2022년 5월 19일 발행

발 행 인 이상헌 **편 집 인** 이영호 **기 획 인** 성윤경

발 행 대한류마티스학회
(우: 04378) 서울특별시 용산구 한강대로 95
래미안 용산 오피스텔 A동 1917호
Tel: 02-794-2630, Fax: 02-794-2631
E-mail: webmaster@rheum.com
Homepage: www.rheum.or.kr

편집제작 (주)엠씨아이코리아
(우 : 06154) 서울특별시 강남구 봉은사로 460
금척타워 8층
Tel: 02-6263-2060, Fax: 02-579-2662
E-mail: seoul@mci-group.com

〈pISSN 2093-940X〉
〈eISSN 2233-4718〉

Publisher Sang-Heon Lee **Editor in Chief** Young-Ho Lee

Published by
Korean College of Rheumatology

Office of Executive Secretary
Raemian Yongsan A Building 1917,
95 Hangang-daero, Yongsan-gu, Seoul 04378, Korea
Tel 82-2-794-2630 | **Fax** 82-2-794-2631
E-mail webmaster@rheum.com
Homepage www.rheum.or.kr

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This work was supported by the Korean Federation of Science and Technology Societies (KOFST) Grant funded by the Korean Government.