Dear Reader,

We are happy to present the ninth issue of the ‘Press Review and Journal Club’ newsletter that is part of a EULAR School of Rheumatology (ESOR) educational initiative, the EULAR–EMEUNET Journal Club. This newsletter includes an overview of relevant articles published both in top rheumatology journals and in major internal medicine journals during the last 4 months (January – April 2020). The article selection includes translational and clinical research papers; in case you want to read the article in more detail, a hyperlink will redirect you to the respective journal. Among the selected articles, one has been chosen by the ESOR faculty to be discussed in a few weeks in an online Twitter Journal Club. Another article, the ‘EMEUNET Paper of the Month’ has been selected by popular vote through a survey circulated among the rheumatology community. For the latter, a video interview with the first author explaining the main findings of the paper is available on our YouTube channel.

The Journal Club aims to bring together rheumatologists, clinical researchers, basic scientists, and anyone else who might be interested in the topic, to participate in an online, lively discussion. These ‘meetings’ take place on Twitter at pre-specified times and dates; the next is planned on May 19th at 8:00 PM GMT (9:00PM CET). ‘Save the date’ reminders will be sent in advance. Where possible, key authors involved in selected articles will be invited to participate. Details of the article selected and of the Journal Club are included on page 4 of this issue.

We hope that you will enjoy reading this newsletter and look forward to ‘seeing’ you soon at our Twitter JC meeting!

Paul Studenic, Richard Conway, Alessia Alunno, Elena Nikphorou, Casper Webers, Daniele Mauro, Alvise Berti, Gonçalo Boleto, George Fragoulis, Lianne Kearsley-Fleet, on behalf of the EULAR EMEUNET Journal Club team

APRIL 2020
COVID–19 AND EMEUNET/EULAR

The recent COVID–19 (coronavirus disease 2019) pandemic has had a major impact worldwide on both the personal and professional lives of many. Our rheumatology community members are involved at different levels, be it caring for infected patients, managing our own concerned and vulnerable rheumatology patients, helping with diagnostic tests in the clinical laboratories, or volunteering in any other way. The pandemic has not only put a substantial strain on healthcare systems, but also affected the health of loved ones and colleagues of many within our community. We can only applaud the huge efforts we have seen in battling this pandemic. Please, make sure to keep an eye on your own health and take rests whenever possible.

As many events have been cancelled since the outbreak, we did not include an overview of upcoming educational events in this newsletter. Please note that this includes several of the EULAR Live Courses. The EULAR 2020 Congress has been changed from a face–to–face congress to a virtual congress (more information here).

Since the outbreak, EULAR has released several statements on COVID–19. Below you will find a useful overview of this information:

• **EULAR Rheumatism and COVID–19 repository.** Overview of useful information for care providers and rheumatology patients, as well as links to many external organisations. Link: [https://www.eular.org/rheumatism_and_covid_19.cfm](https://www.eular.org/rheumatism_and_covid_19.cfm)

• **EULAR position on hydroxychloroquine shortage.** EULAR calls to incorporate independent medical expertise in the ongoing efforts to address shortages of medicines. Link to [the press release](https://www.eular.org/news/eular-position-on-hydroxychloroquine-shortage).

• **EULAR releases first reports on arthritis and COVID-19 in Italy.** Comment of EULAR on one of the first reports available regarding current RMD cases around the epidemic in Italy. Link to [the press release](https://www.eular.org/news/eular-releases-first-reports-on-arthritis-and-covid-19-in-italy).

• **EULAR Guidance for patients in the COVID–19 outbreak.** Information for patients on rheumatology care during the outbreak, as well as several simple measures to preserve their health and that of family and friends. Link: [https://www.eular.org/eular_guidance_for_patients_covid19_outbreak.cfm](https://www.eular.org/eular_guidance_for_patients_covid19_outbreak.cfm)

• **EULAR Policy statement on COVID–19.** Call by EULAR on all governments for measures to be considered to maintain appropriate care for patients with RMD. Link: [https://www.eular.org/policy_statement_on_covid_19.cfm](https://www.eular.org/policy_statement_on_covid_19.cfm)


• **EULAR Statement on events and COVID–19.** Information on status of several events organised by EULAR, such as courses and workshops. Link: [https://www.eular.org/eular_events_and_covid19.cfm](https://www.eular.org/eular_events_and_covid19.cfm)


We wish all the best for you and your loved ones, and hope you stay safe!
Sella A. Provan, Siri Lillegraven, Joe Sexton, Kristin Angel, Cathrine Austad, Espen A. Haavardsholm, Tore K. Kvien and Till Uhlig

**Trends in all-cause and cardiovascular mortality in patients with incident rheumatoid arthritis: a 20-year follow-up matched case-cohort study**


In rheumatoid arthritis (RA), an increased mortality has been observed compared to the general population. With the introduction of new treatment strategies, this risk could be lower nowadays. The authors compared all-cause and cardiovascular (CVD) mortality in 1,391 Norwegian patients with a RA diagnosis in the period 1994-2008, with matched controls (1:10 ratio), using cox regression. Patients diagnosed with RA in the earlier period (1994-2003) had increased mortality compared to controls (adjusted hazard ratio [aHR] ranged 1.37-1.42 for 10-year all-cause mortality), while no such association was observed in those diagnosed more recently (2004-2008, aHR 1.07, 95%CI 0.77-1.49). Results were similar for CVD mortality or when using contemporary mortality (2011-2015) as the outcome. It should be noted that no data on disease activity or medication use was available. The authors argue that these results suggest that modern treatment strategies for RA, which aggressively target disease activity (a known risk factor for mortality), might have a positive impact on all-cause and CVD mortality in RA.
A set of serum markers detecting systemic inflammation in psoriatic skin, enthesal, and joint disease in the absence of C-reactive protein and its link to clinical disease manifestations.


Level of CRP are often low or absent in psoriatic disease. The authors aimed to assess a selected marker panel for systemic inflammation in healthy controls and psoriatic patients with either monomorphic (skin / enthesal / joint) or polymorphic disease, with a three-step approach: (1) signal finding step (select markers by testing a broader panel in 10 patients and 10 controls), (2) validation step (assess the selected biomarkers cross-sectionally in 105 psoriatic patients and 105 controls) and (3) longitudinal step (assess the biomarker levels before and after treatment initiation with TNF- or IL-17 inhibitors in 30 patients with psoriatic arthritis). In the first step, out of 10 markers, 5 were chosen: lipocalin 2 and beta-defensin 2 (both IL-17 driven), IL-8, IL-22 and calprotectin. In the second step, patients with monomorphic skin or enthesal involvement showed increased lipocalin 2 and beta-defensin 2 levels, while those with joint involvement frequently had increased calprotectin and IL-8 levels. IL-22 was increased in all manifestations, and CRP levels were normal in the majority. In the third step, 3 months after starting a TNF- or IL-17 inhibitor, levels of all markers had significantly decreased. This set of immunological markers could possibly be used to quantify systemic inflammation and complement clinical instruments in assessing disease activity in psoriatic disease.
Recently, the 2019 ACR/EULAR criteria for IgG4–related disease (IgG4-RD) were published (pp 77–87). These are the first ACR/EULAR criteria for this clinical entity. After analyzing data from 1879 IgG4–RD cases and mimickers, 86 physicians define the criteria and the weight of 11 domains. In two validation cohorts (n=908 and n=485), the specificity and sensitivity of these criteria were 98-99% and 82-86%, respectively. In psoriatic arthritis (PsA), a head-to-head study between ixekizumab (IL−17 inhibitor) and adalimumab by Mease et al. (pp 123–131) showed that the former, at week 24, was non-inferior regarding achievement of ACR50 response (IXE 51% vs. ADA 47%), and was superior for PASI100 response (IXE 60% vs. ADA 47%; p=0.001). When both outcomes were combined (simultaneous ACR50 and PASI100 response, primary outcome), IXE was superior. Response to ixekizumab was also greater for other disease–related indices like Minimal Disease Activity and resolution of enthesitis. The safety profile was comparable between the two groups. In the field of spondyloarthopathies (SpA), one study highlighted the role of alterations in gut microbiota (dysbiosis). Yin et al. (pp 132–140), using shotgun metagenomic sequencing, analyzed stool samples form 127 radiographic axial SpA (r-axSpA) patients and 123 healthy volunteers. Microbial composition was significantly different between r-axSpA and healthy donors. Enrichment of bacterial peptides homologous to HLA-B27–presented epitopes was observed in the stools of patients with AS compared to healthy donors. Interestingly, the microbiome was significantly different in healthy volunteers compared to untreated patients, but not compared to those who were treated with anti–TNF drugs. Future studies are needed to assess whether this is a potential mechanism of action of these drugs. Data on a potential link between SpA and irritable bowel syndrome (IBS) are sparse. Wallman et al. (pp 159–161) observed a frequency of 30% of IBS in 182 consecutive axSpA patients without IBD, a proportion twice as high as in matched controls. Of note, IBS in these patients was not associated with CRP or calprotectin levels. In systemic lupus erythematosus (SLE), a single nucleotide polymorphism (SNP) in the NCF1 gene reducing production of reactive oxygen species (ROS) has been previously associated with SLE. Linge et al. (pp 254–261) found that the existence of this SNP, compared with patients with normal–ROS genotypes, was associated with impaired neutrophil extracellular traps (NET) formation (p<0.05), increased frequency of high serum interferon activity (p<0.05) and occurrence of anti–β2 glycoprotein I (p<0.01) and anticardiolipin antibodies (p<0.05). Secondary anti–phospholipid syndrome was also more frequent (OR 1.74, 95%CI 1.19–2.55).
Immune checkpoint inhibitor (ICI)–induced inflammatory arthritis (IA) may persist even after ICI discontinuation. A prospective observational study by Braaten et al. (pp 332–338), analyzed data from 60 patients with ICI–related IA. In a median follow-up of 9 months after ICI cessation, the majority of the patients (53%) had active arthritis at their last visit. Multivariable analysis showed that the likelihood of improvement of arthritis was decreased with longer duration of ICI therapy (HR 0.82, 95%CI 0.73–0.92) and combination ICI therapy (HR 0.06, 95%CI 0.01–0.50), and in these patients close monitoring for joint-related symptoms and early referral might be warranted. In rheumatoid arthritis (RA), Ramiro et al. (pp 453–459) observed that the correct application of treat-to-target (T2T) approach in daily practice leads to better remission outcomes. In a multi-national study of 571 patients followed over a 2–year period, T2T was associated with ACR/EULAR Boolean, CDAI and SDAI remission after 3 months (OR range: 1.16–1.29). Also, sustained T2T strategy (T2T in ≥2 consecutive visits) was associated with remission according to all definitions (OR range 1.49–1.52). Disease duration did not modify this association, suggesting that results also apply to those with established RA. Finally, several sets of EULAR recommendations were published in January. The role of health–professionals in rheumatology (HPR) was highlighted by two sets of recommendations (pp 53–60 and pp 61–68). They cover the generic competencies that an HPR should have as well as the role of nurses caring for patients with inflammatory arthritis. The 2011 recommendations for vaccination in autoimmune rheumatic diseases (pp 39–52) have been update. The strength of recommendation for herpes zoster (HZ) vaccination was upgraded from C–D to B. This version confirm a more flexible approach for the live–vaccines (MMR, HZ) but highlight that live–attenuated vaccines should be avoided during the first 6 months of life in newborns of mothers treated with biologics during the second half of pregnancy. EULAR recommendations were also published for the management of Sjögren’s syndrome (pp 3–18). For systemic active disease, glucocorticoids (GCs) might be considered, while immunosuppressants might be used as GC–sparing agents or for GC–refractory cases. B–cell targeted therapies might also be considered for severe, refractory systemic disease. Finally, another set of recommendations were published for large–vessel vasculitis (LVV) (pp 19–30). High–dose glucocorticoid therapy is recommended for Takayasu or Giant Cell Arteritis. For the latter tocilizumab or methotrexate is recommended as an add–on therapy for patients who are refractory or cannot tolerate GC. Antiplatelet and/or anticoagulant treatment is no longer recommended for LVV.
The development of anti–drug antibodies in axial spondyloarthritis (axSpA) patients treated with anti-TNF has been suggested to contribute to loss of efficacy and shorter drug survival. Methotrexate (MTX) could potentially decrease this immunisation. In an RCT of adalimumab (ADA) with or without MTX by Ducourau et al. (e001047), concomitant MTX was associated with lower frequency of ADA–antibodies (25% vs 47% for MTX+ vs MTX−) and higher ADA concentrations after 26 weeks, while treatment response did not differ between groups. Currently, little is known about the course of axSpA MRI abnormalities in real–world settings. In the French prospective DESIR cohort, Madari et al. (e001093) studied changes on MRI in patients with early axSpA over time. Over 5 years, bone marrow edema on sacro–iliac joints (SIJ) decreased significantly (mean SPARCC score −1.4 [SD 6.5]), especially in patients using bDMARDs. A statistically significant yet numerically small progression in spine and SIJ fatty lesions and/or erosions was observed. This study highlights the limited value of repeated MRI in patients with early axSpA. Holland–Fischer et al. (e001102) investigated whether patients with rheumatoid arthritis (RA) have worse prognosis from pneumonia. In a population–based cohort study of over 52,000 patients with pneumonia (1220 with RA), they observed that 90–day mortality was similar in RA and non–RA patients (19.9% vs 18.9%; adjusted HR 1.05, 95%CI 0.92–1.19). On the other hand, CRP levels >20mg/L 30–90 days prior to admission predicted mortality in patients with RA (HR 4.98, 95%CI 2.19–11.36; compared to CRP <8mg/L), regardless of prednisolone use. bDMARD and csDMARD use were not associated with mortality, suggesting high RA disease activity rather than RA medication predicts pneumonia mortality. Ultrasound (US) is a validated tool for the diagnosis of gout. However, data on the sensitivity to change of US gout lesions is scarce. In this prospective study of 50 gout patients initiating or increasing urate–lowering therapy, Christiansen et al. (e001144) found a significant decrease in double–contour and tophus sum scores on US from months 0 to 6 (3.16 and 2.68 to 1.34 and 1.83, respectively, p<0.002), showing sensitivity to change. Erosion sum scores remained almost unchanged. MTP1–4 and knees were the locations with most pronounced changes in scores. Pain is the most common patient–reported symptom in patients with rheumatic and musculoskeletal diseases. Ogdie et al. (e001042) conducted a post–hoc analysis of 3330 patients in seven tofacitinib (TOFA) studies in RA, psoriatic arthritis (PsA) and SpA. Compared with placebo, pain improvements in TOFA–treated patients were observed in all disease populations. Rapid improvement was observed, irrespective of prior treatment.
Inflammatory biomarkers have had limited success in predicting disease progression in rheumatoid arthritis (RA). Bach et al. (pp. 47–56) investigated markers of neutrophil activation (calprotectin) and cell death (neutrophil extracellular traps, NETs) in three cohorts of (in total) 441 patients with RA, who were age- and sex-matched with healthy controls. Calprotectin and NETs were significantly increased in RA patients, and calprotectin levels correlated with CDAI. Patients positive for both ACPA and calprotectin had higher odds of developing joint erosions and joint space narrowing (OR 7.5 and 4.9, respectively), compared to those with only positive ACPA (OR 6.0 and 2.0, respectively) or calprotectin (OR 5.6 and 3.5, respectively), suggesting neutrophil biomarkers provide additional prognostic value in RA. Hanly et al. (pp. 67–77) investigated nervous system disease in a longitudinal cohort of 1827 patients affected by systemic lupus erythematosus (SLE). Over a mean follow-up of 7.6 years, 52% of patients experienced any neuropsychiatric event, whilst 7.6% of patients experienced peripheral nervous system (PNS) neuropsychiatric events (e.g. peripheral neuropathy or mononeuropathy), the majority of which were attributed to SLE. Although PNS events were associated with lower quality of life, their outcome was favourable as most events resolved or improved over time. Hinze et al. (pp. 499–505) investigated the association between IL1RN polymorphisms and response to interleukin−1 blockade in 61 systemic juvenile idiopathic arthritis (JIA) patients. Six of the seven reported SNPs (IL1RN) thought to be associated with response to anakinra were analysed. Response was assessed within 6 months of IL−1 blockade using various outcomes, including clinical response, switch to other therapy (IL−6 blockade), achievement of inactive disease and reaching a glucocorticoid−free state. However, the authors were unable to confirm any associations of these six IL1RN gene polymorphisms, or the IL1RN haplotype, with various definitions of an adequate treatment response. In osteoarthritis (OA), Sueishi et al. (pp. 620–631) hypothesised that G protein–coupled receptor kinase 5 (GRK5) plays an important role in the pathogenesis through its ubiquitous expression and ability to regulate NF-κB signalling. GRK5 protein expression was increased in human OA cartilage compared with normal chondrocytes of healthy patients. In addition, on Western blot analysis, GRK5 depletion reduced IκBα phosphorylation (≤4.4-fold decrease [p<0.05]) and decreased p65 nuclear translocation (≤6.4-fold decrease [p<0.01]) in mouse chondrocytes. These results suggest that GRK5 regulates cartilage degradation through a catabolic response mediated by NF-κB signaling, and could be a potential treatment target in OA.
In primary Sjögren’s syndrome, hydroxychloroquine (HCQ) was shown to downregulate systemic interferon (IFN) activation in the peripheral blood of 77 patients in a RCT of 24 weeks with 400mg/d HCQ versus placebo by Bodewes et al. (pp 107–111). HCQ reduced IFN–stimulated gene expression compared with placebo, with a significant reduction in type-I–IFN (adjusted difference in change from baseline [95%CI], 5.24 [−7.76 to −2.72]), TLR9 (−0.09 [−0.16 to −0.03]) and MyD88 (~3.99 [−7.64 to −0.35]), but not TLR7 (~0.05 [−0.13 to 0.03]), but failed to improve disease activity scores.

Over 70% of patients with autoinflammatory diseases do not receive a molecular diagnosis, and are classified as undifferentiated or undefined SAID (uSAID). Papa et al. (pp 344–360) tested a cohort of 50 patients (86% paediatric) with uSAID with a novel 41 genes’ next generation sequencing panel: 4% received a definite diagnosis (atypical form of Mevalonate–Kinase deficiency), 54% had possible pathogenic variants (not consistent with clinical phenotype) and the remainder was genetically negative. Of the latter, those with recurrent fevers typically had gastrointestinal, skin and articular involvement, depicting a novel subset of uSAID responsive to steroids and colchicine. Obesity is a risk factor for rheumatoid arthritis (RA). Maglio et al. studied the incidence of RA in 2002 Swedish subjects with obesity that underwent bariatric surgery and 2034 matched controls (pp 303–309). None of these had RA at baseline; 92 participants developed RA during 21 years of follow–up. Neither bariatric surgery (HR 0.92, 95%CI 0.59–1.46) nor change in BMI from baseline at 2 years follow–up (HR 0.96, 95%CI 0.82–1.12) were associated with incidence of RA, which might be due to the low number of RA cases. Non–adherence to urate lowering treatment (ULT), due to lack of disease knowledge among physicians and prevalent misconceptions of gout in patients, is a major cause of gout flares. In a large trial (n=438) by Fuller et al. (pp 575–579), patients with nurse–led care, compared to GP–led care, reported better adherence to ULT (adjusted RR 1.19, 95%CI 1.09–1.30) and less self–reported flares in the last 12 months (median 0 [IQR 0.0] vs 1 [IQR 0.3]), and showed greater satisfaction and gout knowledge. Salivary glands (SG) are frequently involved in IgG4–related disease (IgG4–RD). A recent study by Liu et al (pp 634–640) showed IgG4–RD patients with SG involvement (SG+) were younger, mostly female, more frequently allergic, and had higher eosinophil count, IgG4/IgG ratio and IgG4 and IgE levels. IgG4–RD SG–patients had more frequent systemic involvement, were more frequently ANA positive and had more often elevated ESR and CRP levels. These differences suggest distinct clinical phenotypes, possibly reflecting differences in pathogenesis.
Currently, specific biomarkers are lacking in osteoarthritis (OA). Rousseau et al. (22:2) examined the possible association of circulating miRNA with knee OA, using next generation sequencing followed by confirmatory PCR. After comparing 43 women with prevalent OA, 23 women with incident knee OA over a 4-year follow-up and 67 healthy subjects, they found that serum miR−146a−5p was significantly increased in the group of prevalent knee OA compared with controls (p = 0.015). A significant association between the baseline level of serum miR−186−5p and the risk of incident knee OA was also observed. In psoriatic arthritis (PsA), Combe et al. (22:14) assessed safety data for the anti−IL17 drug ixekizumab, obtaining data from 3 trials (SPIRIT−P1/P2/P3). In 1118 patients with a total exposure of 1822 patient−years (PY), no unexpected adverse events were recorded. The most common were upper respiratory tract infection, nasopharyngitis, and injection−site reactions. Opportunistic infections included oral and esophageal candida and localized herpes zoster. The incidence rate for inflammatory bowel disease was 0.1/100 PY. In many PsA patients, CRP is normal despite active disease. A selection of serum biomarkers was examined by Sokolova et al. (22:26) in 105 PsA patients and in 105 healthy controls. Although CRP was normal in patients with skin or enthesal involvement, beta−defensin 2 and lipocalin−2 levels were increased. This was not the case for patients who had only joint involvement, who more frequently had elevated calprotectin and IL−8. The majority of patients with at least 2 manifestations (skin/enthesal/joint) had widespread marker elevation. Noteworthy, treatment with TNF or IL−17 inhibitors led to decrease of all inflammation markers. In systemic sclerosis (SSc), gastrointestinal (GI) dysmotility is difficult to treat. Nakane et al. (22:32) measured biomarkers and antibodies against 2 subunits (α3 and β4) of the nicotinic acetylcholine receptor at autonomic ganglia (gAChR) in SSc patients with and without GI involvement. Patients with SSc and gastrointestinal manifestations displayed increased expression of VEGF and higher mean levels of anti−gAChRα3 autoantibodies, compared to SSc patients without GI involvement (p<0.001). Scleroderma Renal crisis (SRC) is one of the major complications of SSc. EUSTAR−investigators analysed the influence of ACE inhibitors, other anti−hypertensive drugs and hypertension on SRC (22:59). In data from 14,524 patients, they observed an SRC incidence of 3.72/1000PY. Use of ACE inhibitors was associated with increased risk of SRC, even after adjusting for arterial hypertension (HR: 2.04, 95%CI: 1.29−3.24). In contrast, other antihypertensives and glucocorticoids (prednisolone<15 mg) did not affect SRC hazard. ACE inhibitors, however, remain the first choice in the treatment of SRC.
In an observational study of 209 patients with **rheumatoid arthritis (RA)**, enrolled at time of bDMARD initiation and followed for 12 months, Hammer et al. (pp.27–35) observed that those with predominantly tender joints (tender joint count [TJC] > swollen joint count, 40% of sample) had higher clinical composite disease activity score levels but similar laboratory markers and actually lower (better) ultrasound scores compared to patients with predominantly swollen joints (60% of sample). These findings suggest that inclusion of TJC in composite disease activity scores could contribute to misleading information about inflammatory activity, and highlight why composite scores should be interpreted carefully. In semi-structured interviews with 21 health care professionals who manage children and young people with **juvenile idiopathic arthritis (JIA)** in the UK, Lee et al. (pp.69–77) identified six themes regarding their beliefs about the role of pain and prioritization of its assessment in JIA. These included lack of training and low confidence in pain assessment, reluctance to engage in pain discussions, low prioritization of pain assessment, specific beliefs about the nature of pain in JIA, treatment of pain in JIA, and undervaluing pain reports. Assessment of pain symptoms was regarded as a low priority and some actively avoided conversations about pain. A shift in perceptions about pain management in JIA may be helpful for professionals. Stewart et al. (pp.122–130) investigated foot and ankle characteristics in 54 patients with **systemic lupus erythematosus (SLE)** compared with 56 age- and sex-matched controls. Participants with SLE had lower muscle force for foot and ankle movement as measured with a dynamometer, higher self-reported foot problem scores, and more frequently an abnormal ankle–brachial index and higher vibration perception thresholds, suggesting neurovascular involvement. While walking, participants with SLE also had altered gait patterns, which included reduced gait velocity, and this association persisted after adjusting for foot pain. The authors argue for further research on foot-specific interventions in SLE. Studies on the cardiovascular risk of patients with **primary Sjögren’s syndrome (SS)** are limited and report conflicting results. Beltai et al. (pp.131–139) conducted a meta-analysis of 14 studies and observed that primary SS was associated with increased cardiovascular morbidity (RR 1.34, 95%CI 1.06–1.38), cerebrovascular morbidity (RR 1.46, 95%CI 1.43–1.49), heart failure rate (OR 2.54, 95%CI 1.30–4.97), and thromboembolic morbidity (RR 1.78, 95%CI 1.41–2.25) compared to the general population. Interestingly, there was no increased risk of cardiovascular mortality (RR 1.48, 95%CI 0.77–2.85). Patients with primary SS might benefit from screening for cardiovascular comorbidities and preventive interventions.
It remains unclear if a premature atherosclerosis and macrovascular disease occur in systemic sclerosis as in other well-characterized rheumatic conditions. In a large US database, Ying et al. (pp.82–88) observed an increased incidence rate of stroke among 4545 individuals with systemic sclerosis (15.3 per 1000 person-years, PY) compared to matched controls (12.2 per 1000PY), resulting in a HR of 1.21 (95%CI 1.05–1.40) when adjusted for baseline cardiovascular comorbidities, medication use, and Medicare enrolment. Infections in chronically immunosuppressed patients with systemic lupus erythematosus (SLE) can be a major problem in the management of these patients. Rúa−Figueroa et al. (pp.234–240) analysed the incidence and risk factors of bacteremia in a large multicentric cohort of SLE patients. The incidence rate was 2.7/1000PY. At the time of bacteremia, 89% were on corticosteroids (69% >10mg/day) and 57% on immunosuppressive drugs. Gram−negatives, especially E. coli, caused 53% of the episodes. Bacteremia was recurrent in 27% of cases and carried a mortality of 14%. Elevated creatinine (OR 1.31, 95%CI 1.01−1.70), diabetes (OR 6.01, 95%CI 2.26−15.95), cancer (OR 5.32, 95%CI 2.23−12.70), use of immunosuppressive drugs (OR 6.35, 95%CI 3.42−11.77) and SLE organ damage (OR 1.65, 95%CI 1.31−2.09) were independently associated with bacteremia. The genetic component in the pathogenesis of radiographic axial spondyloarthritis (formerly ankylosing spondylitis [AS]) is estimated to be 90%. Of the known heritability, ~20% is explained by HLA−B27, and 113 identified AS−associated single−nucleotide polymorphisms (SNP) account for ~7%. Rostami et al. (pp.204–210) constructed a weighted genetic risk score (wGRS) using currently known genome−wide susceptibility SNP, and evaluated its predictive ability for AS in a population−based study. Among 164 cases and 49,032 controls, wGRS had low discrimination (area under the curve [AUC] 0.62, 95%CI 0.58−0.67) compared to HLA−B27 (AUC 0.88, 95%CI 0.85−0.90) and addition of the wGRS to HLA−B27 resulted in a minor improvement of limited clinical value (AUC 0.90, 95%CI 0.87−0.92). The evolution of interstitial lung disease (ILD) secondary to antisynthetase syndrome is heterogeneous and has not been characterized well. González−Pérez et al. (pp.415–423) assessed the evolution of pulmonary function in 118 patients with ILD and antisynthetase antibody positivity (i.e. anti−Jo1, anti−PL7, anti−PL12, anti−EJ, anti−OJ). After a median 2 years follow−up, 67% had improved pulmonary function. This improvement occurred within the first 6 months after initiating medical treatment; thereafter, pulmonary function remained stable. No difference was observed among the different antibody−subsets in proportions of patients who improved or in survival.
Plasma-exchange (PE) is commonly used in patients with severe ANCA-vasculitis. However, its added value to immunospressive (IS) therapy is uncertain. In the PEXIVAS trial of 704 patients, Walsh et al. (N Engl J Med. 2020 Feb 13;382(7):622–631) observed similar mortality/end-stage kidney disease (ESKD) rates in ‘PE + IS’ versus ‘IS alone’ groups after up to 7 years of follow-up (28.4% vs 31.0%; HR 0.86, 95%CI 0.65–1.13). Interestingly, the authors showed that reduced–dose of glucocorticoids (50% reduction) was non–inferior to standard dose in terms of mortality/ESKD (30.3% vs 29.1%; HR 1.00, 95%CI 0.76–1.31). Data on the efficacy of disectomy in patients with chronic sciatica caused by lumbar disk herniation are scarce. In an RCT, Bailey et al. (N Engl J Med. 2020 Mar 19;382(12):1093–1102) assigned patients with sciatica lasting >4 months to undergo microdisketomy or standardized nonoperative care. Among 790 patients, the authors showed that pain intensity at 6 months was 2.8±0.4 in the surgical group and 5.2±0.4 in the nonsurgical group (difference 2.4; 95%CI 1.4–3.4). Patients with rheumatoid arthritis (RA) have reduced vaccine-induced protective responses against influenza. Colmegna et al. (Lancet Rheumatol 2020 Jan; 2(1), Pe14–e23) investigated the immunogenicity of a high–dose influenza vaccine (HDIV), compared to a standard–dose vaccine (SDIV), in 279 patients with RA. Patients receiving HDIV were more likely to seroconvert than those who received SDIV (OR 2.99 [95%CI 1.46–6.11] for strain A/H3N2; 1.95 [1.19–3.22] for strain B/Bris and 3.21 [1.57–6.56] and 2.44 [1.18–5.06] for strain A/H1N1 2016/2017 and 2017–2018, respectively). Several studies suggested efficacy of abatacept in primary Sjögren’s syndrome (pSS). In this single–centre RCT, van Nimwegen et al. (Lancet Rheumatol 2020 Mar; 2(3), Pe153–e163) assessed the efficacy of abatacept versus placebo in 80 pSS patients. The primary outcome, EULAR SS Disease Activity Index (ESSDAI) at 24 weeks, did not differ between the treatment groups (mean difference −1.3 [95%CI −4.1 to 1.6]. Mycophenolate mofetil (MMF) has been shown to halt the progression of diffuse cutaneous systemic sclerosis (dcSSc). However, defining the optimal MMF therapy duration can be challenging. In a follow–up extension of a prospective open–label trial, Mendoza et al. (Semin Arthritis Rheum. 2020 Feb;50(1):135–139) assessed the clinical evolution of rapidly progressive dcSSc following MMF discontinuation or dose reduction (<1000mg/day). Of 19 patients who had received full–dose MMF for an average of 22.9 months, 5 (26%) showed an ≥20% increase of the Modified Rodnan skin score, requiring to resume full–dose MMF within an average of 6.9 (3–14) months. Skin involvement rapidly stabilized after resumption of full–dose MMF.
In light of the COVID-19 (coronavirus) pandemic, most live educational events have been postponed. Fortunately, there are many alternatives to keep up to date on recent developments in rheumatology.

An overview of several useful online resources:

- **EMEUNET “What Is New” initiative.** Discussion of recent papers in the field of Rheumatology, aimed at helping EMEUNET members up to date with the latest scientific and clinical findings in different areas of rheumatology. Sorted by disease topic. Link: [https://emeunet.eular.org/what_is_new.cfm](https://emeunet.eular.org/what_is_new.cfm)

- **EMEUNET Podcast.** Recently launched, this podcast is meant for clinicians and researchers in the field of rheumatology who want to keep up to date on recent publications and events. The latest addition covers COVID-19 and features key people involved in the COVID-19 Rheumatology Alliance. Link: Anchor and [Spotify](https://emeunet.eular.org/what_is_new.cfm)

- **EULAR Imaging Library.** An online gallery of a wide spectrum of imaging modalities and rheumatic and musculoskeletal diseases in adults and children. Link: [https://www.eular.org/eular_imaging_library_portal.cfm](https://www.eular.org/eular_imaging_library_portal.cfm)

- **EULAR Ultrasound Scanning App.** A comprehensive digital technical manual of ultrasound (US) in rheumatology. Designed as an illustrated tool for use on tablets and smartphones, it displays the procedures for US assessment of the principal joint areas and other relevant anatomic regions. Link: [http://ultrasound.eular.org/#/home](http://ultrasound.eular.org/#/home)

- **EULAR Outcome Measures Library.** A comprehensive database of validated instruments (indices, questionnaires, scales, or others) that are used in rheumatology, with an emphasis on Patient Reported Outcomes. Instruments are categorized by disease or by topic. Link: [http://oml.eular.org/](http://oml.eular.org/)

- **ACR Virtual Rheumatology Learning Collaborative.** A free 8-week lecture series of over 20 live lectures on a variety of topics in rheumatology. Previous recordings are available to watch as well. Link: [https://www.rheumatology.org/I-Am-A/Fellow-in-Training/Lecture-Archives](https://www.rheumatology.org/I-Am-A/Fellow-in-Training/Lecture-Archives)
A NEW PUBLICATION FROM EMEUNET:
THE EMEUNET POST-DOC MENTORING PROGRAM

EMEUNET launched a survey in 2017 to evaluate the need of a mentoring program for the post-doc career stage. The survey also evaluated the expectations of such a program, including potential priorities in topics to be addressed and the desired mentors’ profiles.

Informed by the results of the survey (> 270 participants, with 99% reporting a need in post-doc mentoring)), a program was developed to cover the unmet need of mentoring in early career researchers in Europe: the EMEUNET Post-Doc Mentoring Program. The program was based on remote mentoring with international renowned experts who mentor young rheumatologists and researchers following a well-defined structure. The pilot edition, with a duration of one year, was launched at EULAR 2018 by the EMEUNET Peer Mentoring subgroup. The evaluation of the program after completion revealed that such a mentoring initiative was feasible and useful.

The experience with this pioneering program has been recently published in RMD Open by members of the EMEUNET Peer Mentoring subgroup and the Steering Committee. The publication can be accessed here.

From EMEUNET, we invite you not to miss this publication and contribute to its dissemination among your networks.

Do not miss the opportunity to learn more about this original project from EMEUNET and stay tuned for future editions!
JOIN EULAR TASK FORCES AND COMMITTEES

Young investigators of EMEUNET are an integral part of all task forces and committees working on new EULAR recommendations. This is a wonderful chance for EMEUNET to increase its visibility and for you to accelerate your academic career.

EMEUNET members with interest in methodology and previous experience in EULAR Task Forces can also have the opportunity to become junior methodologists. For further information, please contact emeunet.education@gmail.com

Take a look at emails from EMEUNET and find the opportunity most suitable for you!

SHARE YOUR IDEAS!

Over the years EMEUNET has developed several projects covering different topics and areas of interest. However, we always appreciate any suggestions and welcome new ideas to expand on what we currently offer to EMEUNET members. Make your voice heard and share your ideas with us!

For suggestions and ideas, just write down some lines to summarize your proposal and send it either via email at emeunet@eular.ch or contact us through our website (http://emeunet.eular.org/contact_us.cfm). Don’t forget to provide your contacts so we can come back to you for additional details!

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