Abstract Highlights

Citation: EMJ Rheumatol. 2024;11[1]:36-42. https://doi.org/10.33590/emjrheumatol/HNCL8460.

The following highlights spotlight the latest research in rheumatology, featuring studies presented at this year's annual European Alliance of Associations for Rheumatology (EULAR) 2024 Congress. Ranging from predicting persistent inflammatory arthritis in patients with palindromic rheumatism to the identification of inflammatory phenotypes and systemic sclerosis, these highlights showcase the latest cutting-edge developments and most talked-about topics in the field today.

Axial Involvement in Psoriatic Arthritis and Spondyloarthritis

RESEARCH on axial involvement in psoriatic arthritis (PsA) and spondyloarthritis (SpA) presented at the annual EULAR 2024 Congress, determined the proportion of axial psoriatic arthritis (axPsA) among patients with PsA, as well as how it is diagnosed in clinical practice and the clinical and demographic characteristics associated with axPsA.

Researchers used data from the Rheumatic Diseases Portuguese Registry (Rheuma.pt) on adult patients diagnosed with PsA or axSpA, with psoriasis, who met the CASPAR criteria. Axial involvement was defined as either physician-reported spondylitis or imaging findings such as radiographic sacroiliitis (SI), SI on MRI, or syndesmophytes in axial radiography. Bivariate and multivariate analyses were performed to identify characteristics associated with axPsA.

Results showed that out of 2,304 patients, 854 (35.1%) had axPsA, with 21.8% having exclusive axPsA and 78.2% having concomitant peripheral involvement. The diagnosis of axPsA was based on suggestive imaging findings in 30.1% of the cases, with radiographic SI being the most common (75.9%). The remaining 69.9% were diagnosed based on physician reports. axPsA was associated with the male sex, positive HLA-B27, younger age at diagnosis and symptom onset, higher incidence of enthesitis, uveitis, psoriasis, inflammatory bowel disease, and a lower incidence of dactylitis and nail dystrophy, in extra-articular manifestations. Lifestyle factors such as current or previous tobacco exposure and alcohol consumption were also linked to axPsA. Patients with axPsA started biological disease-modifying antirheumatic drug (bDMARD) therapy at a younger age but had a longer time from symptom onset to the start of treatment (7 years versus 6 years; p=0.003).

> **Lifestyle factors such as current or previous tobacco exposure and alcohol consumption were also linked to axPsA**

The prevalence of exclusive axPsA among patients with PsA was 8.1%, increasing to 37.1% when including those with concomitant peripheral involvement. Radiographic sacroiliitis was the most common imaging finding in diagnosing axPsA. Patients with axPsA showed distinct clinical profiles, including higher rates of HLA-B27 positivity and enthesitis, and lower rates of dactylitis. The findings underscore the importance of thorough diagnostic evaluations to prevent underdiagnosis, particularly in subclinical cases, and highlight the need for targeted treatment strategies in managing axPsA.

New Insights into Interstitial Lung Disease Risk and Incidence in Systemic Sclerosis

RECENT research presented at EULAR 2024 has shed light on the incidence and risk factors associated with the onset of interstitial lung disease (ILD) in patients with systemic sclerosis (SSc) who initially test negative for the condition.

Although the prevalence of ILD in SSc is well-documented, little was known about the incidence of new-onset ILD following a negative high-resolution computed tomography (HRCT) at baseline. The study aimed to estimate the annual incidence of new ILD cases in patients with SSc who initially tested negative, and identify key risk factors associated with the disease's onset.

Researchers analysed data from the European Scleroderma Trials and Research group (EUSTAR) database, including patients with SSc who met the 2013 American College of Rheumatology (ACR)/EULAR criteria, had no ILD on their baseline HRCT, and had at least a 1-year follow-up visit. Patients with pulmonary hypertension, diagnosed by right heart catheterisation, were excluded from the study. Follow-up HRCT was performed, and based on the results, patients were divided into two groups: patients with new onset of ILD (incident group) and patients who remained ILD negative (negative group).

Out of 5,331 baseline ILD-negative patients, new-onset ILD was detected in 1,075 cases over a median follow-up of 3.8 years, resulting in an incidence rate of 3.7 cases per 100 person-years. The incidence rate remained stable for up to 10 years from baseline. Among patients with at least three visits within 5 years from baseline, 18.8% developed ILD, with an incidence rate of 3.6 per 100 person-years. For patients with a disease duration of 5 years or less, 21.5% developed ILD, with an incidence rate of 4.4 per 100 person-years.

Key risk factors for developing new-onset ILD included dyspnoea (New York Heart Association [NYHA] stage ≥2), male sex, older age, elevated inflammatory markers, anti-topoisomerase I antibody, and a history of digital ulcers. Protective factors included higher DLCO/SB% (single-breath carbon monoxide diffusing capacity) levels, higher haemoglobin levels, and the presence of anti-centromere antibodies.

The study highlights the importance of continued screening for ILD in patients with SSc, regardless of disease duration. Identifying these risk factors is crucial for early diagnosis and prompt treatment initiation, potentially improving patient outcomes. The findings emphasise that ILD can develop at any stage after SSc diagnosis, underscoring the need for vigilant monitoring over time.

> **The incidence rate remained stable for up to 10 years from baseline**

Predicting Persistent Inflammatory Arthritis in Patients with Palindromic Rheumatism

PALINDROMIC rheumatism (PR) is a precursor to rheumatoid arthritis (RA), with up to 50% of patients with PR progressing to persistent inflammatory arthritis (PIA), predominantly RA.

Identifying and studying PR longitudinally is challenging, and the risk factors for progression are not well understood. This study aimed to develop the first risk stratification tool for predicting PIA progression in patients with PR, using data from a large UK prospective PR cohort. Results of this study were presented at EULAR 2024.

The Leeds PR cohort included patients recruited from primary and secondary care, defined by episodic joint pain and swelling with no alternative diagnosis. Baseline assessments of clinical, serological, and immunogenetic parameters were conducted, followed by regular evaluations. PIA progression was identified by clinical synovitis persisting for over 3 weeks.

The study followed 161 patients with PR from July 2008–January 2023, with 90% DMARD-naïve at baseline. Of these, 33% (53/161) developed PIA, and 91% met RA criteria. Key predictive factors identified through LASSO and Cox regression analysis included female gender, anti-cyclic citrullinated peptide positivity, rheumatoid factor positivity, age over 40 years, smoking history, and flare intervals of less than 1 month. Significant associations were found for female gender (hazard ratio: 2.2) and high anti-CCP levels (hazard ratio: 5.9).

The study developed 'Ever' and 'Two-year' prediction models, stratifying patients into low-, moderate-, and high-risk groups. High-risk patients had progression rates of 53% and 37% for the 'Ever' and 'Two-year' models, respectively, while no low-risk patients progressed. The findings suggest that combining these predictive factors allows effective risk stratification, enabling better monitoring and potential intervention for high- and moderate-risk groups in clinical practice.

Assessing Infections in Patients with Rheumatoid Arthritis

NEW research presented at EULAR 2024 aimed to address the safety profile of JAK inhibitors (JAKi), particularly with regard to infection risk.

The safety profile of JAKi remains a critical concern amongst patients with rheumatoid arthritis (RA), as real-world data on the incidence and severity of opportunistic infections and herpes zoster (HZ) remains an area of active study.

In order to shed more light on the topic, lead author Romain Aymon, Geneva University Hospital, Switzerland, and colleagues studied patients from 14 RA registries across Europe and Québec, that were starting JAKi, TNF-inhibitors (TNFi), or bDMARDs with other modes of action (OMA). The outcomes being measured included all infections, serious infections (requiring hospitalisation, intravenous treatment, or resulting in death), all infections excluding HZ, and HZ. Infections were linked to treatments within 3 months of cessation (1 year after initiation for rituximab) or until follow-up loss, death, or study end. Incidence rates (IR) per 100 patient-years (PY) with 95% CI were computed. Poisson regressions with propensity score weighting (including country, disease, patient characteristics, and comorbidities) were performed within each individual register and combined using random-effect meta-analysis to obtain adjusted incidence rate ratios (aIRR) with 95% CI.

Overall, 54,905 treatment initiations were considered in 36,838 patients with a mean patient follow-up of 2.8 years. Amongst these patients, 7,070 incident infections were reported, of which 1,379 were considered as serious, and 352 were HZ. Crude incidence of any infection was lower for TNFi (7.0/100 PY) than for JAKi (9.0/100 PY) and OMA (10.6/100 PY). The adjusted Poisson regression found no significant difference in the incidence of any infections (aIRR: 1.13; 95% CI: 0.91; 1.40) or serious infections (aIRR: 0.99; 95% CI: 0.71; 1.39) between JAKi versus TNFi. However, the incidence of any infection was higher for OMA versus TNFi (aIRR: 1.20; 95% CI: 1.09; 1.32). Compared to TNFi, the incidence of HZ was significantly higher for JAKi (aIRR: 2.27; 95% CI: 1.71; 3.02), but not for OMA (aIRR: 1.07; 95% CI: 0.74; 1.55).

The team found that there was no significantly higher risk of infections, either any or serious, in patients with RA treated with JAKi compared to TNFi. However, they reported that there was a higher risk of any infections with OMA. Compared to TNFi, the incidence of HZ was significantly higher in patients receiving JAKi. The authors elaborated, explaining that future planned subgroup analyses will focus on at-risk populations, specific medications, and infection types to guide treatment choices.

Risk of Mortality in Patients with Tophaceous Versus Non-tophaceous Gout

PATIENTS with tophaceous gout face significantly higher risks of mortality, acute myocardial infarction (MI), and end-stage renal disease (ESRD) compared to those with non-tophaceous gout, according to recent research presented at EULAR 2024.

The study, which analysed data from a cohort of 213 million patients using the TriNetX Diamond network, included 284,241 individuals with tophaceous gout and 73,569 with non-tophaceous gout. Through rigorous propensity score matching, the researchers balanced the baseline characteristics of 73,495 patients in each group, ensuring a robust comparison.

Results highlighted that after 1 year, 5.0% of patients with tophaceous gout had died, compared to 4.2% of those with non-tophaceous gout, reflecting a 20% higher risk (hazard ratio [HR]: 1.20; 95% CI: 1.15–1.26). The disparity widened over 5 years, with mortality rates at 14.1% for tophaceous gout patients versus 11.4% for those with non-tophaceous gout (HR: 1.24; 95% CI: 1.20–1.27).

The risks of acute MI and ESRD also increased significantly in the tophaceous gout group. At 1 year, the incidence of acute MI was 1.7% in tophaceous gout group, compared to 1.4% in the non-tophaceous group (HR: 1.20; 95% CI: 1.10–1.31). Over 5 years, these rates escalated to 4.4% and 3.7%, respectively (HR: 1.21; 95% CI: 1.15–1.28). Similarly, ESRD risk was 1.2% at 1 year for patients with tophaceous gout versus 1.1% for the others (HR: 1.12; 95% CI: 1.02–1.24), and 3.2% at 5 years compared to 2.8% (HR: 1.16; 95% CI: 1.09–1.23).

These findings confirm that tophaceous gout is associated with an increased risk of mortality, acute MI, and ESRD. The authors highlight that these risks may relate to increased total urate burden, inflammation, and cumulative cardio-renal adverse effects of non-steroidal anti-inflammatory drugs or glucocorticoid use. They call for further investigation into intensive urate-lowering therapies, such as uricase, to mitigate these critical health risks.

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Identification of Inflammatory Phenotypes and Prognoses in Systemic Sclerosis

C-REACTIVE protein (CRP)-associated inflammatory phenotypes in systemic sclerosis (SSc) have been identified by researchers, in addition to their association with increased risk of all-cause mortality and interstitial lung disease, according to research presented at EULAR 2024.

SSc has a complex pathology consisting of immune system dysregulation, tissue fibrosis, and vascular dysfunction, which results in inflammatory, fibrotic, and vascular alterations in patients. Previously in the field, a link between elevated CRP levels and inflammation in early disease onset has been established, but there is a lack of data to elucidate this association. Researchers from the Department of Rheumatology, León University Hospital Complex, Spain, aimed to identify CRP-associated inflammatory phenotypes and prognostic implications in patients with SSc.

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The research identified 133 patients with SSc, according to the 2013 American College of Rheumatology (ACR)/EULAR criteria. With CRP levels above 5 mg/L at their first clinic visit, patients were classified as having an inflammatory phenotype. Compared to patients with a non-inflammatory phenotype (CRP <5mg/L), patients with inflammation at SSc onset demonstrated higher serum levels of KL-6 (p=0.002) and IL-18 (p=0.040) at baseline.

Assessment of clinical parameters revealed that diffuse-cutaneous disease (p=0.020), anti-Scl-70 autoantibodies (p=0.020), interstitial lung disease (p=0.020), lower diffusing capacity for carbon monoxide (p=0.010), and myositis (p=0.040), were more frequently associated with an inflammatory phenotype. Additionally, logistic regression analysis revealed that inflammation at SSc onset was linked to mortality (β: 0.65, p=0.004), interstitial lung disease (β: 0.45, p=0.007), arthritis (β: 0.40, p=0.040), myositis (β: 0.23, p=0.040), IL-18 levels (β: 0.32, p=0.002), and anti-Scl70 positivity (β: 0.21, p=0.040).

In 53 (39%) patients, elevated CRP levels continued for over 80% of visits (classed as a persistent inflammatory phenotype). Analysis with Cox regression models revealed that persistent inflammation was associated with a 4.6 times higher risk of all-cause mortality (hazard ratio: 4.61; 95% CI 1.2–15.2; p=0.04) and 5.6 times higher risk of interstitial lung disease (hazard ratio: 5.41; 95% CI: 2.4–16.4; p=0.02).

The results of the study demonstrate that CRP-associated inflammation at disease onset is linked to specific clinical and immunological features in patients with SSc, which may aid in diagnosis. Additionally, the finding that persistent inflammation increases the risk of all-cause mortality and interstitial lung disease highlights the need for personalised treatment strategies focused on CRP-associated inflammation.