

IN BRIEF

SPONDYLOARTHRITIS

Polygenic risk scores outperform other tests in AS

Polygenic risk scores (PRSs) can better discriminate patients with ankylosing spondylitis (AS) from healthy individuals and individuals with chronic back pain than other standard diagnostic tests, according to a receiver operator characteristic analysis. A PRS developed for individuals of European descent had a higher discriminatory capacity (area under the curve (AUC)=0.924) than *HLA-B27* testing (AUC=0.869), MRI (AUC=0.885) or C-reactive protein (AUC=0.700) in this population. Similarly, a PRS that had been developed specifically for East Asian populations had a better discriminatory capacity than *HLA-B27* testing in individuals of East Asian descent.

ORIGINAL ARTICLE Li, Z. et al. Polygenic risk scores have high diagnostic capacity in ankylosing spondylitis. *Ann. Rheum. Dis.* <https://doi.org/10.1136/annrheumdis-2020-219446> (2021)

OSTEOARTHRITIS

Osteoarthritis risk factors differ between sexes

According to an analysis of the Rotterdam Study, the prevalence and strength of various risk factors for knee osteoarthritis differs between men and women. These findings might inform the development of sex-specific risk tools. The majority of the risk factors assessed had a higher prevalence in women than in men, with the exception of alcohol intake and smoking, which were higher in men, and high BMI, which was equal for both sexes. The relative risk associated with high physical activity or a Kellgren–Lawrence score of 1 at baseline was higher for men than for women, whereas the relative risk associated with a BMI ≥ 27 was higher for women.

ORIGINAL ARTICLE Szilagy, I. A. et al. Towards sex-specific osteoarthritis risk models: evaluation of risk factors for knee osteoarthritis in males and females. *Rheumatology* <https://doi.org/10.1093/rheumatology/keab378> (2021)

SJÖGREN SYNDROME

Ultrasound scoring system shows promise in pSS

Findings from a cross-sectional, single-centre, observational study support the use of the OMERACT ultrasound scoring system in the diagnosis of primary Sjögren syndrome (pSS). Of 134 patients suspected of having pSS, those patients who fulfilled the ACR–EULAR pSS classification criteria more often had a score of ≥ 2 in ≥ 1 gland than those patients who did not fulfil the criteria (72% versus 13%; $P < 0.001$). At this scoring cut-off point, the scoring system had a good sensitivity (72%) and specificity (91%) for diagnosing pSS when using the 2016 ACR–EULAR criteria as a reference standard.

ORIGINAL ARTICLE Fana, V. et al. Application of the OMERACT Grey-scale Ultrasound Scoring System for salivary glands in a single-centre cohort of patients with suspected Sjögren's syndrome. *RMD Open* **7**, e001516 (2021)

PAEDIATRICS

MIS-C is a risk factor for thrombotic events

In a multicentre retrospective cohort study of children and adolescents hospitalized with COVID-19 or multi-system inflammatory syndrome in children (MIS-C), thrombotic events occurred in 9/426 patients (2.1%) with COVID-19 and 9/138 patients (6.5%) with MIS-C. In addition to MIS-C, risk factors for thrombosis in these patients included age ≥ 12 years, cancer and the presence of a central venous catheter. In those patients who developed thrombosis, the mortality was high (28%).

ORIGINAL ARTICLE Whitworth, H. B. et al. Rate of thrombosis in children and adolescents hospitalized with COVID-19 or MIS-C. *Blood* <https://doi.org/10.1182/blood.2020010218> (2021)

AUTOINFLAMMATORY DISEASES

Pathogenic *UBA1* variants define a subset of relapsing polychondritis

Vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic (VEXAS) syndrome is a newly discovered condition caused by somatic mutations in *UBA1* and is characterized by systemic inflammation that affects multiple tissues. Because of its wide range of phenotypes, this condition often meets criteria for other rheumatic diseases, including relapsing polychondritis. Two new studies have identified *UBA1* variants in a subgroup of patients with relapsing polychondritis, supporting the concept that relapsing polychondritis is more than one disease.

Relapsing polychondritis is a rare idiopathic inflammatory disease characterized by inflammation of the cartilage in various tissues. Given the discovery of VEXAS syndrome and the heterogeneity of relapsing polychondritis, two teams of researchers independently sought to identify and characterize patients with VEXAS-associated *UBA1* mutations among cohorts of patients with relapsing polychondritis.

In a prospective observational cohort of 92 patients with relapsing polychondritis (72 female and 20 male), Ferrada et al. identified seven patients with somatic mutations in *UBA1* using exome and targeted sequencing. These patients were exclusively male and were also characterized by older age, ear and nose chondritis and haematologic abnormalities.

“We derived an evidence-based clinical algorithm that identified every patient with VEXAS syndrome within our cohort with near perfect accuracy based on male sex and two common laboratory tests,” says corresponding author Marcela Ferrada. This algorithm had a 100% sensitivity and 96% specificity.

In a separate study, Tsuchida et al. identified eight patients with VEXAS-associated *UBA1* mutations among a group of 13 patients (11 male and two female) using Sanger sequencing. All of the patients were male and

skin inflammation was a prominent feature. “Because low prevalence somatic mutation can be missed with Sanger sequencing, we then performed droplet digital PCR and peptide nucleic acid-clamping PCR to identify low-frequency mutations,” explains Yohei Kirino, corresponding author on the Tsuchida et al. study. They identified for the first time a female patient with a somatic variant in *UBA1* (that had a low allele prevalence of 0.14%).

The clinical observations across both studies were similar, with a few differences. Some of the patients with VEXAS syndrome in the Tsuchida et al. study had airway involvement, which was not observed in the other study. “We are not sure why this difference occurred, but we believe it might be due to ethnicity differences,” remarks Kirino.

“The data suggest that *UBA1* genetic screening of patients with relapsing polychondritis, especially in men with skin lesions, might be useful in the development of precision medicine for relapsing polychondritis. Further collaborations to determine the specific clinical features of this disease and the optimal strategy for *UBA1* screening, including which specimens and cut-off values to use, are needed,” says Kirino.

“We are currently trying to better understand the natural history and clinical features of patients with VEXAS syndrome,” explains David Beck, co-senior author on the Ferrada et al. study. “Our ultimate goal is to use these studies to find effective therapies for patients with VEXAS syndrome.”

Jessica McHugh

ORIGINAL ARTICLES Ferrada, M. A. et al. Somatic mutations in *UBA1* define a distinct subset of relapsing polychondritis patients with VEXAS syndrome. *Arthritis Rheumatol.* <https://doi.org/10.1002/art.41743> (2021) | Tsuchida, N. et al. Pathogenic *UBA1* variants associated with VEXAS syndrome in Japanese patients with relapsing polychondritis. *Ann. Rheum. Dis.* <https://doi.org/10.1136/annrheumdis-2021-220089> (2021)