Early rheumatoid arthritis: Disease trajectories and pain

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People with rheumatoid arthritis (RA) tend to have different trajectories—both in how the disease evolves, and how disease states may improve over time. The frequency of pain patterns at diagnosis and

over time—and their relationship with inflammation—also represents a gap in our knowledge. EULAR—The European Alliance of Associations for Rheumatology—recommends early identification and management for people with early arthritis. But understanding disease evolution and its influencing factors is important to identify opportunities to improve management and patient outcomes.

The 2024 EULAR congress in Vienna included a clinical abstract session focusing on pain and prognosis in RA, where two groups presented their research into ways to characterize early RA.

The first looked at dissecting early RA patient trajectories through time-independent disease state patterns of inflammation in blood or joints. Presenting the work, Nils Steinz said, "Previous studies have identified smooth time trajectories of rapid, slow, or no progression of disease activity, assessed through DAS28. In real life, we observe more chaotic disease evolvements—and particularly the detours could indicate a lack of adequate treatment."

To address this, the researchers set out to discern trajectories of disease states of early RA over 1.5 years from the first outpatient clinic visit in real-world data from 1,237 patients with 5,017 visits to the Leiden rheumatology outpatient clinic. This was achieved using pseudo-time graph-based analyses of clustered visit data. Subsequently, patient trajectories were identified using a matching algorithm. To validate the findings, the pipeline was applied to data from the TACERA cohort, representing 244 patients with early seropositive RA.

The results showed eight disease states, with swollen and tender joint count, erythrocyte sedimentation rate (ESR), and leukocytes as the major discriminating factors. One cluster was the clinically optimal disease state with the least inflammation overall. The sequence of disease states experienced by patients was grouped together to form four

distinct trajectories.

Some people had high ESR clusters at start and end. Others showed rapid progression towards the ideal cluster, no disease activity. The third group transitioned through a high leucocyte state, and the fourth were classed as poor prognosis. In the TACERA analysis, the team found similar clusters and trajectories. These revealed interesting differences in age, gender, and serostatus—even though these variables were not included in the clustering.

The differences were not driven by inclusion date, follow-up duration, symptom duration, or time to methotrexate initiation. But with the exception of the people with high ESR clusters at start and end, the trajectories could not be predicted by baseline variables.

These trajectories draw a more granular picture than previously described, and show early RA patients stranded in suboptimal disease states, with inflammation and poor response the main discriminatory factors. This approach provides insights into opportunities for improving care, such as more intensive treatment at an earlier stage. Work is ongoing, and the next step will be to characterize the immune profiles of the different disease states, and discern the impact of treatment decisions.

The second work also looked at patterns, but with a focus on non-articular pain—an issue which is common in early RA, and associated with lower remission rates. "Understanding common phenotypes of regional non-articular pain and the role of RA-related joint inflammation could help better personalize RA care," said Charis Meng—presenter of the work from the Canadian Early Arthritis Cohort Study.

Data from 392 early RA patients were used to describe common non-articular pain presentations around the time of early RA diagnosis, as

well as evolution over the first year of treatment, and associations with active inflammation. Prespecified pain patterns were classified based on non-articular pain reported in the four body quadrants and axial region, excluding hands and feet, and grouped as no pain, regional, or widespread. Descriptive statistics were used to summarize the frequency and evolution of different patterns at baseline and over a 12-month follow-up.

Over half of patients reported prevalent non-articular pain at baseline, of which nearly three-quarters were classed as regional. The most frequent patterns were axial (34%), pain in both upper quadrants (20%), and both lower quadrants (10%). Of those with prevalent regional pain, it persisted or worsened in 42% over 1 year. But for those with prevalent widespread pain, 73% resolved or improved to a regional pattern.

Joint inflammation tended to be more frequently reported in corresponding locations with non-articular pain, and often persisted over follow-up. These findings suggest that non-articular pain is common in early RA and throughout the first year after diagnosis. The significantly higher frequency of tender or swollen joints within most areas of non-articular pain over time suggests RA activity may be a contributing factor

More studies are needed, but early intervention to prevent and treat non-articular pain in early RA is recommended.

More information: N. Steinz et al, OP0018 Dissecting early RA patient trajectories through time-independent disease state identification identifies distinct patterns dissected by inflammation in blood or joints, *Scientific Abstracts* (2024). DOI: 10.1136/annrheumdis-2024-eular.1512

C. Meng et al, OP0064 Characterizing Prevalent Non-Articular Pain at Early RA Diagnosis and Evolution Over the First Year of RA Treatment: Results from the Canadian Early Arthritis Cohort Study, *Scientific Abstracts* (2024). DOI: 10.1136/annrheumdis-2024-eular.5946