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**Clinical expertise and its accuracy
in differentiating arthralgia
patients at risk for rheumatoid
arthritis from other patients
presenting with joint symptoms**

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Sir, Within RA, early initiation of treatment is associated with a higher chance of achieving DMARD-free sustained remission¹⁻³. The absolute number of RA patients achieving this beneficial condition is still low. It is hypothesised that treatment initiation in the early phase of symptoms, without clinically detectable arthritis, will be more effective in disease modulation and will reduce the persistent nature of the disease⁴. Trials are needed to study this hypothesis. For this purpose, we need to identify patients in a symptomatic phase before synovitis is clinically apparent.

The clinical presentation characterizing RA in the early symptomatic phase of this disease is unknown. A method for differentiating patients with arthralgia at risk of RA from other patients with joint symptoms is to use clinical expertise as a starting point. Rheumatologists see many patients presenting with arthralgia, but without clinically apparent arthritis. These patients fall into three categories: patients with a clear diagnosis for their arthralgia; patients without a clear diagnosis but not considered at risk for RA according to their rheumatologists (unexplained arthralgia); and patients with clinically suspect arthralgia (CSA) - based on their clinical presentation, rheumatologists suspect these patients will progress to RA⁵. This study explored the diagnostic accuracy of the clinical expertise of rheumatologists.

Between April 2012 and December 2013, 145 newly referred patients to the rheumatologic outpatient clinic in Leiden (the Netherlands) were identified as having CSA. In the same period, 1791 newly referred patients had unexplained arthralgia according to the local registry that records the diagnosis at first visit for financial purposes. Patients with arthralgia were considered to have reached the outcome when they had developed clinical arthritis within 1 year after first presentation with arthralgia and fulfilled the 1987 classification criteria for RA. For CSA patients, this was determined within the CSA cohort⁵. For the unexplained arthralgia patients, the outcome was determined by investigating which of the 1,791 patients were included in the Leiden Early Arthritis Clinic (EAC) cohort within 1 year after first presentation and also fulfilled the 1987 criteria⁶. To ensure that no converters were missed in the unexplained arthralgia group, all final diagnoses according to the mentioned registry were checked, and all files were checked for patients in whom the diagnoses remained unexplained but who had more than four visits at the outpatient clinic. These additional ways to search did not yield any additional patient with 1987 RA. All patients included in the CSA and EAC cohorts gave informed consent, and approval for these cohorts was obtained from the Medical Ethics Committee of the Leiden University Medical Center. The approval included collection of clinical and serological data and the use of these data for analyses, including this analysis.

At the 1-year follow-up, 16 of the patients identified as CSA patients had progressed to arthritis and fulfilled the 1987 criteria for RA within 1 year (11%). Likewise, 4 of the 1,791 unexplained arthralgia patients were included in the EAC and fulfilled the 1987 criteria (0.2%). The odds ratio was 55 (95% CI=18-168, $p<0.001$), the sensitivity of the clinical

expertise was 80%, the specificity was 93% and the accuracy was 93%. The four RA patients who had initially presented with arthralgia and who were not identified as having CSA had the following presentations: one patient had arthralgia with inflammatory symptoms (morning stiffness, most severe symptoms in early morning), but the rheumatologist did not label the patient as having CSA; one patient had inflammatory symptoms and psoriasis and was suspected of progressing towards psoriatic arthritis instead of RA, and therefore was not labelled as having CSA; in one person the symptoms were attributed to a recent Hepatitis B vaccination; and one person had no inflammatory symptoms or signs at all.

The performance of autoantibody testing in the diagnostic process of arthritis and RA in first-line care is not promoted by the Dutch guideline for general practitioners ⁷. More locally in the Leiden area, general practitioners are even discouraged from performing autoantibody tests before referral, and they are encouraged to refer promptly. In line with this, the large majority of patients were referred without results for ACPA or RF. Hence, the diagnosis of having CSA was essentially based on symptoms and signs. We realise that this health care system is differently organised than that in other parts in Europe. Therefore, our setting provides a unique opportunity for exploring the accuracy of clinical expertise based on symptoms and signs only. After the first visit to the outpatient clinic, autoantibody testing was carried out. Three of the four patients who were not identified as having CSA based on their clinical presentation and who did develop RA were ACPA-positive. This illustrates that the evaluation of the presence or absence of CSA was not driven by results of autoantibody status. We do not have data on ACPA-status for the patients with unexplained arthralgia who did not progress to RA. Therefore, this study does not allow us to identify the predictive value of ACPA testing in patients who are clinically not suspected of progressing towards RA.

In conclusion, the present data revealed the value of the rheumatologists' expertise in differentiating arthralgia patients based on clinical presentation (history, symptoms, signs) only. A potential disadvantage is its subjectivity. Therefore, a current EULAR taskforce is deriving criteria for CSA, using a consensus-based approach ⁸.

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