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EDITORIAL

Are prognostic factors in rheumatoid arthritis of any use in daily clinical practice?

P. van Riel

Department of Rheumatology, University Medical Centre St Radboud, Geert Grooteplein 8, 6525 GA Nijmegen, the Netherlands, tel.: +31 (0)24-361 45 80, fax: +31 (0)24-354 14 33, e-mail: P.vanRiel@reuma.umcn.nl

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown origin with a highly variable presentation. Its main manifestation is synovitis of the peripheral joints. The disease usually starts in the small joints of the hands and then gradually develops in the feet; all the other, larger joints may become involved as well. This does not only cause the patient a great deal of discomfort, like pain and stiffness, but also has a huge impact on mobility and psychosocial wellbeing. The course of RA is very heterogeneous. Some patients undergo a mild course that may resolve within months or years, often without any structural damage while others have severe, erosive disease with extra-articular manifestations and decreased life expectancy. Pharmacotherapy is still the cornerstone in the management of RA, a distinction being made between first- and second-line treatment. First-line treatment, i.e. non-steroidal anti-inflammatory drugs (NSAIDs), is given as soon as the symptoms of pain and stiffness appear, while second-line agents are usually given only after the diagnosis RA has been confirmed.

In the past decade many new treatments have become available for the management of RA, including leflunomide and the biological agents.[1,2] This has changed the treatment strategy dramatically: patients are now being treated earlier and more aggressively. Some of these treatments are very toxic and/or expensive. In order to improve the risk/benefit ratio of the pharmacotherapy, many attempts have been made to find factors which could predict the course of the disease.[3] If that were possible, only those patients in whom the disease is expected to run a severe course would be offered the most effective treatment, which is often also more toxic and/or expensive.

Many factors have been described that predict joint destruction and functional disability in patients with RA. Probably the most useful are those factors that are independent of disease activity, such as the presence of rheumatoid factor and the so-called shared epitope of HLA-DRB1. The early presence of bony erosions is another important prognostic marker. In addition, clinical indicators such as many affected joints, the presence of extra-articular features and a considerable degree of physical disability at onset are associated with poor prognosis, as are sociodemographic markers such as older age at onset and a lower level of formal education.

In this issue Van Venrooij and colleagues discuss the properties of a new specific autoantibody: the anticyclic citrullinated antibody (anti-CCP).[4] In a long-term follow-up study of patients with recent onset RA it was shown that patients positive for this antibody had significantly more severe joint destruction than the anti-CCP negative patients.[5] However the additional predictive value over the IgM rheumatoid factor test was only modest.

In conclusion: although several factors have been shown to be able to predict a more severe disease course, their positive predictive value is still not strong enough to be useful in daily clinical practice.

Another characteristic of the anti-CCP test is a higher specificity compared with the IgM rheumatoid factor test. As the IgM rheumatoid factor, anti-CCP antibodies are frequently present many years before the diagnosis of RA can be made. Due to these two features the anti-CCP test may have an important role in the early diagnosis of RA. As many studies have shown that therapeutic interventions early in the course of the disease lead to earlier disease control and therefore less joint damage, it is

important to make the diagnosis of RA in a patient with joint symptoms as soon as possible.[6] The classification criteria developed by the American College of Rheumatology have been used to do this, although they were not designed for this purpose.[7] These criteria were originally developed in an established patient population to classify RA in order to be able to compare different patient populations. So, these criteria are not the optimal instrument to distinguish early RA from undifferentiated polyarthritis. Van Venrooij and colleagues demonstrate that it is possible to discriminate erosive versus non-erosive arthritis or self-limiting from persistent arthritis using the anti-CCP test in a prediction model including six other variables. The discriminative ability of the same model without the anti-CCP test was significantly lower. The differences, however, were remarkably small.

Although these findings are of great importance for basic and clinical research in RA, the question remains what the consequences are for our daily clinical practice. Should we test all our patients with an early undifferentiated arthritis and rheumatoid arthritis and treat them aggressively in case of a positive anti-CCP test? Is there still a need for clinical joint examination, laboratory tests as the acute-phase response and imaging of the joints by regular X-rays of hands and feet? Yes, certainly there is!

One baseline assessment of disease activity is not sufficient to predict the future course of the disease, although several studies have shown that time-integrated disease process variables do reflect the outcome of the disease. We all know that persistent high disease activity causes many immediate problems to the patient, but it has also been shown that this is more likely to eventually lead to irreversible joint damage,[8] a higher probability of developing secondary lymphomas[9] and even a reduction in life expectancy.[10] Disease-controlling antirheumatic therapies do influence the disease activity,[11] therefore to guide treatment decisions it is important to follow the fluctuating course of the disease activity as accurately as possible.[12] In fact, this is no different from monitoring the glucose level in patients with diabetes mellitus and the blood pressure in patients with hypertension.

Due to the heterogeneity of the disease expression, it is not possible to assess disease activity in all patients with rheumatoid arthritis with one single variable. Disease activity should be represented by a set of variables, which can be reported and analysed either separately or as part of an index of disease activity like the DAS28.[13] Serial measurements of the DAS28 have shown to be strong predictors of physical disability and radiological progression. Beside variables assessing disease activity, which should be measured frequently, joint damage should be monitored periodically with X-rays, and possibly also functional capacity with a patient questionnaire, to follow the disease process in the long term. The anti-CCP test has a role in the early detection of the disease. The decision to start or change antirheumatic therapies, however, is still based on the complete clinical picture of the patient. The role of prognostic factors in this respect is only modest.

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