Editorial

Improving Outcomes in Rheumatoid Arthritis: What Determines Decisions to Change Ineffective Therapy?

Treatment of rheumatoid arthritis (RA) has been transformed greatly over the past decades from a "reactive" strategy of using disease modifying antirheumatic drugs (DMARD) only when the diagnosis was certain and damage apparent, to an aggressive strategy of "preventive" use of DMARD to control inflammation as completely as possible to slow joint damage. The new strategy has been accompanied by new DMARD, most notably methotrexate, and considerable evidence indicates that most patients with RA have better clinical status today compared with earlier periods. Availability of new biological therapies adds to the rheumatologist's armamentarium, helping many patients toward a state of low disease activity or remission.

Changes in the treatment of RA have been accompanied by increased awareness on the part of rheumatologists of a need for quantitative documentation of patient status in clinical settings. In 1983, Verna Wright pointed out that "clinicians may write 'doing well' in the notes of a patient who has become progressively crippled before their eyes"[1]. This situation is becoming rarer in contemporary care of people with RA.

A major advantage in quantitative assessment of RA patient status is the Disease Activity Score (DAS), which was developed as a composite score for disease activity in RA[2-4]. The DAS is a pooled index that includes 4 measures: tender joint count, swollen joint count, erythrocyte sedimentation rate (ESR), and patient global assessment. "High" disease activity was defined as the DAS level when a new DMARD was begun or changed from another due to lack of efficacy, while "low" disease activity was defined as a DAS level at which a new DMARD was not started or a DMARD was left unchanged for at least for one year or was stopped because of remission[5].

The DAS, which appeared in 1985, classifies patient status according to levels of "high" and "low" disease activity, reflecting decision-making concerning treatments for RA at that time. In this issue of *The Journal,* Soubrier and colleagues[6] present predictors of change of treatments for RA in the clinic supervised by Dr. Dougados. They report a lower cutoff value for "high disease activity" according to the DAS28 than has previously been reported.

Reevaluation of values of well established measures such as the DAS appears welcome at this time. Lower levels reflect improvements in patient status compared to previous decades. An improved clinical status of RA patients at this time compared to previous decades has been documented concerning disease activity[7,8], functional capacity[8–11], radiographic scores[8,12,13], and other clinical measures[8], including lower mortality rates in patients who responded to methotrexate[14,15]. Further, indirect evidence of improved patient clinical status is provided by observations that only a minority of patients in routine rheumatology care meet inclusion criteria in clinical trials[16]. The French study[6] adds indirect evidence of improved care at this time, indicating lower cutoff levels to modify a DMARD therapy of DAS28esr = 4.2 and DAS28crp = 3.6, compared to disease activity levels in the Nijmegen early RA cohort in 1985-94[5], which correspond to DAS28 > 5.1[17].

In an ideal world, disease activity as a biological phenomenon would be the most important, if not the only, determinant of decision-making concerning treatment of RA. Suppression of current disease activity would prevent future joint damage and development of functional losses. A focus on disease activity implies that clinically assessed high disease activity invariably leads to change in therapy. However, many patients seen in a regular rheumatology clinic already have developed joint damage and have problems with physical function. A decision to change RA therapy may therefore be affected also by these damage variables, in addition to currently high inflammatory activity. Development of new erosions likely increases probability of change in therapy for RA if radiographs are used in routine evaluation of patients. Good function in activities of daily living is important from the patient's perspective and

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is reflected in global health, which is included in the DAS formula. Assessment using the Health Assessment Questionnaire would have augmented the completeness of the excellent analyses of the French group[6].

From an international approach, many variables beyond DAS scores, including patient demographics and psychosocial variables, healthcare system variables, and society-associated variables, may influence a decision to change RA therapy. In the French clinic, lower age and shorter disease duration were associated with a higher likelihood of changing therapy[6]. Other patient related variables may include number and type of comorbidities, education level, and ethnic background. Local traditions may play an important role in rheumatology daily practice. In some advanced clinics in the US, methotrexate reached popularity in the early 1980s, 10–20 years before it became the drug of choice in early RA in Europe. Enormous variation was seen in DMARD "ever used" in a cross-sectional study of consecutive patients with RA from 9 Western European countries[18]. This variation likely reflects local traditions concerning the choice and availability of DMARD. Accordingly, local traditions may also affect decisions to change RA therapy.

Nowadays, many more DMARD, including biologic agents, are available compared to when the DAS was developed and definitions of "mild," "moderate," and "high" disease activity were reported. These definitions reflect the availability of DMARD and the standard of care at that time, which differs across decades. Moreover, availability of DMARD and especially biologic agents differs across countries. Further, guidelines on the use of biologic agents differ between countries and may strongly influence changes in RA therapy. The French study provides an example of a clinic where biologic agents are available for those who are regarded to need them.

A consensus statement and national guidelines for prescribing biologic agents recommend these agents for patients who have currently active disease and have received treatment with one or 2 DMARD, usually including methotrexate[19]. In some countries, guidelines additionally require a certain level of disease activity. Examples include the UK, where guidelines recommend restricting biologics to patients who have DAS28 > 5.1[20], while in The Netherlands, the activity requirement to start a biologic agent is DAS28 > 3.2. In Denmark, a patient is required to have 6 or more swollen joints. Databases that reflect clinical practice nationwide indicate that the median disease activity score ranged from 5.2 to 6.0 on DAS28 in patients who started a biologic agent in Denmark and Norway in the early years of this decade[21].

In conclusion, the Soubrier report indicates that disease activity drives changes in therapy for RA, and that lesser disease activity is tolerated compared to the past. The study raises several important questions concerning daily rheumatology practice worldwide: Does current practice regarding changes in therapy for RA reflect disease activity, as well as patient psychosocial, healthcare system, and society-related variables? What about traditions and national guidelines? What guidelines should exist for decisions to change RA therapy? These questions should be examined more widely to improve standard clinical practice in many countries.

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