Determinants of physical function in rheumatoid arthritis: association with the disease process

J. M. W. Hazes

Rheumatoid arthritis (RA) is a chronic, debilitating disease that follows a progressive course characterized by persistent inflammation and erosive joint damage leading to functional disability. The Health Assessment Questionnaire is now viewed as a key instrument to measure physical function, based on its reliability and ease of use. It has been demonstrated that multiple variables affect physical function, of which those most frequently indicated are disease activity, joint damage and the psychosocial characteristics of the patient. When these variables are pooled together the variation observed in a patient’s physical function over the long term can be explained mainly by disease activity, partially by joint damage and additionally by psychosocial factors. Therefore, to maintain or improve physical function in long-standing RA, it is imperative to control disease activity and joint damage by early initiation of treatment.

KEY WORDS: Disease activity, Disease Activity Score, Function, Health Assessment Questionnaire, Joint damage, Rheumatoid arthritis.

The course and outcome of physical function

The HAQ assesses function and disability in patients with RA based on their ability to perform customary daily life activities [3]. Responses are scored on a 4-point scale, where 0 is the best and 3 the worst. HAQ scores have only become widely used in the assessment of physical function in RA within the last two decades. The majority of initial studies conducted using the HAQ were cross-sectional and most longitudinal studies have provided prospective data only on the short-term (2–3 yr) and on the middle- to long-term (5–8 yr) course of RA [4–6].

A recent long-term longitudinal study evaluated the course and outcome of physical function (as determined by the HAQ) over a median of 12 yr (range 10–14 yr) in 132 women with RA [7]. In this patient cohort, physical function decreased with disease duration at a rate that was fairly constant in early and late disease: the median HAQ score at baseline was 0.63, at year 3 and at year 6 it was 0.75 and at year 12 it was 0.87. Over 12 yr the median HAQ score deteriorated by 0.24, which is considered a clinically relevant change [8]. However, when the HAQ score was assessed in individual cases, outcomes were different, with evidence of large intra-individual variation. This was thought to be associated with the variable changes in pain and inflammation seen in individual patients over the disease course. The consequence of this variability in HAQ score at the individual patient level is that the true gradual increase in disability over time is often obscured.
Determinants of physical function in RA

Several recent studies have confirmed that physical function is affected by multiple variables, of which those most frequently indicated are disease activity, joint damage and the psychosocial characteristics of the patient [6, 8–10].

Disease activity is associated with the number of swollen and tender joints, duration of morning stiffness, erythrocyte sedimentation rate (ESR), fatigue, pain and depression. The Disease Activity Score (DAS)—a standard measurement of the activity of a patient’s disease—is a pooled index of the ESR, the number of swollen joints, the Ritchie Articular Index and the general health of the patient measured by a visual analogue scale [11]. Long-term RA studies show that the mean level of disease activity is maintained at a relatively constant level over the course of RA [7].

Joint damage is measured radiographically and evaluated by either the Larsen or Sharp scoring methods, or modifications of these [1, 7]. A number of studies have followed the progression of joint damage in patients with RA over the long term. Analysis of the results from pooled data from six studies showed that, in patients receiving conventional therapy, the mean damage up to 5 yr from disease onset was 16% of the maximal damage, while after 20 yr it was 40% [12]. The mean annual increase over 20 yr was between 1.6 and 1.9% of the maximal possible damage [13–18]. Psychosocial functioning is most widely measured with the Arthritis Impact Measurement Scale, which assesses all aspects of physical health, psychological health, symptoms, social interaction and work [19]. As arthritis is a debilitating, chronic disease that has a substantial effect on all daily activities, this arthritis-specific measure of HRQOL is important and provides a good indicator of both the global effects of arthritis on a patient’s life, as well as the effects of treatment.

The relationship between physical function, disease activity and joint damage

Several studies have reported the relationship between functionality, disease activity and joint damage in RA [7, 18, 20, 21]. These studies have investigated the association of the disease activity and joint damage variables with physical function and how this differs in the early and late course of the disease.

A recent study that followed 132 patients with RA for 12 yr demonstrated that disease activity is the most influential determinant of the loss of physical function [7]. At the start of the study there was a strong correlation between the HAQ score and the DAS ($r = 0.68$), with a weaker correlation between the HAQ score and the Sharp score ($r = 0.22$). On evaluation of the patients at 3 yr, the DAS score was still more strongly correlated with functionality than the Sharp score ($r = 0.51$ and $r = 0.29$, respectively). As time progressed, however, the contribution of joint damage to loss of functionality increased, becoming particularly important in the later stages of the disease. At study completion, the effects of DAS on functionality remained consistent ($r = 0.61$), while the correlation between Sharp score and functionality had increased ($r = 0.57$). When the variables were pooled, the variation in physical function at 12 yr as measured by the HAQ could be explained largely by disease activity (51%), additionally by joint destruction (12%) and by psychosocial factors (9%; Fig. 1). The investigators concluded that disease activity is the most important determinant in the loss of functionality in RA patients during the first 12 yr of RA.

The COBRA (Combinatietherapie Bij Reumaatodo Artritis) multicentre study investigated the association between clinical signs of disease in individual joints in patients with RA and their tendency to develop progressive damage, concluding that there is a strong relationship between these variables [22]. At baseline, 3% of small joints showed damage; after 1 yr disease had progressed in 10% of these joints. Signs of disease activity in a joint, such as damage, swelling or pain, independently and strongly predicted progression of damage in that joint ($P < 0.001$). Because joint damage is an outcome parameter of long-term RA and, ultimately, functional disability, these findings have important implications.

Loss of physical function as determined by small joint damage

Radiographs of joint damage are often used clinically as measures of destruction and disability. Generally, this assessment is restricted to radiographs of the small joints, specifically the hands and feet. It has been well documented that radiographic damage in the hands and

![Fig. 1. Disease activity, joint destruction, and psychosocial factors all contribute to the HAQ score. The contribution of the pooled variables of disease activity, destruction and psychosocial function to the variation in physical function at 12 yr of disease duration as measured by the HAQ in a cohort of patients with RA [7]. Figure reproduced with permission of John Wiley & Sons Inc. ©1999 American College of Rheumatology.]
feet appears early in RA and progresses steadily throughout the course of the disease [5, 15]. However, it is likely that radiographic damage of the large joints also contributes considerably to disability.

A limited number of studies have investigated the radiographic damage of the large joints and showed that the pattern of damage is similar to that seen in the small joints; it should be noted, however, that these studies had methodological flaws, such as bias in patient selection [23–25]. Confirmation was seen in a recent study investigating the extent of radiographic damage of large joints over 12 yr in 105 patients with RA and the relationship between such damage, small joint involvement and physical function [26]. When radiographs of the shoulders, elbows, hips, knees, ankles and subtalar joints were assessed using the Larsen scoring method, erosive large joints were observed in 54% of patients (Larsen score ≥2) and abnormal large joints in 70% of patients (Larsen score ≥1). The large joints most frequently affected were the elbows, shoulders and knees (32, 31 and 27%, respectively), significantly more often bilaterally than unilaterally (P < 0.05). The Larsen score of large joint damage was highly correlated with the modified Sharp score of small joint damage (r = 0.76; P < 0.01) and with disability as measured by the HAQ (r = 0.60; P < 0.01). Furthermore, the radiographic damage of both the large and small joints explained 40% of the variance of HAQ at 12 yr. However, the most important contributor to the HAQ was the DAS (r = 0.61; P < 0.01), which confirms that disease activity is still the main determinant of disability. In clinical practice, the strong correlation that exists between the small and large joints means that radiographs of hands and feet can be used as a substitute parameter for all joint damage. The benefits of using radiographs of the small joints are that they are cost-effective and easily obtained with regular uniformity [26].

**Rationale for the early treatment of RA**

To maintain or improve physical function in longstanding RA, joint damage should be delayed or prevented. Psychosocial aspects also need appropriate attention. Most importantly, however, disease activity must be controlled. Therefore, early treatment is recommended to reduce or prevent loss of physical function in the later stage of disease resulting from disease activity and joint destruction [27, 28]. Particularly important is attaining rapid control of disease activity, which is associated with loss of function in all phases of the disease [7].

Results from a recent study have shown that early treatment of patients with recent-onset RA using disease-modifying anti-rheumatic drugs (DMARDs) is associated with a better disease outcome after 2 yr, when compared with patients in whom treatment was delayed [27]. Patients who received DMARD treatment after a median lag time of 15 days (n = 97) had less radiological joint damage compared with those who received treatment after a median lag time of 123 days (n = 109), with median Sharp scores of 3.5 and 10, respectively (P < 0.05; Fig. 2). Greater improvements in HAQ were also seen with early treatment (Fig. 3).

The results from this study and other previous studies that have evaluated the early introduction of DMARDs found that such treatment leads to earlier disease control and reduced joint damage [28–31]. The investigators concluded that the early diagnosis and referral of patients with RA is crucial for optimal medical care.
Conclusions
A number of studies have been conducted on the course and outcome of physical function in RA patients in view of the importance of maintaining effective functionality to ensure the continued performance of common daily activities. Throughout the course of the disease, the loss of physical function is mainly attributed to disease activity—specifically pain and inflammatory synovitis—while later in the disease course, joint damage becomes an important determinant. Early treatment is recommended to prevent structural joint damage, which progresses over the disease course and is irreversible once joint erosion occurs. The progression of large joint damage correlates strongly with that of the small joints and, therefore, the related scoring methods may be interchangeable in clinical practice. Early treatment is also necessary to optimally suppress disease activity, which has been clearly demonstrated as the most important determinant in the loss of physical function in the early stages of RA.

References
