Abstract

The major objectives in treating patients with rheumatoid arthritis are managing the symptoms of disease and preserving joint structure, with the ultimate goal of disease remission. Several independent studies have shown that treatment decisions driven by quantitative rather than subjective monitoring of disease activity result in significantly improved patient outcomes. Various assessment tools are available that measure both clinical and patient-reported outcomes. While some measurement tools may be more appropriate for use in clinical trials, several have been developed that are simple and practical to use, even in a busy clinic. As pivotal members of the multidisciplinary rheumatology healthcare provider team, the nurse and the rheumatologist play key roles in managing a patient’s progress by closely monitoring their response to treatment. Here, we discuss optimal disease management founded on a multidisciplinary approach and provide an overview of some key measures for assessing patient response to treatment.

Rheumatoid arthritis (RA) is a debilitating inflammatory disease with clinical signs and symptoms that include swollen joints, cartilage and bone damage, morning stiffness, and loss of physical function. Consequently, patients with severe disease face significant disability, deformity, and irreversible joint damage. This chronic condition can also have a significant negative impact on patients’ health-related quality of life (HRQoL), with many patients experiencing fatigue, decreased sleep quality, depression, and reduced work productivity. Taken together, these symptoms have a detrimental impact on the patient’s physical, social, psychological, and economic well-being.

There are two main goals for the treatment of RA by rheumatology healthcare practitioners (HCPs). The first is to make the patient feel better by managing the symptoms of the disease, and the second is to secure the patient’s future by preserving their joint function, with the ultimate goal of remission. Disease-modifying antirheumatic drugs (DMARDs) used in the treatment of RA have the potential to reduce and prevent joint damage, as well as to preserve joint integrity and function in patients. Nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids are often used as supplemental therapies to help manage the symptoms of the disease. Of the currently available DMARDs, traditional nonbiologic therapies include methotrexate, hydroxychloroquine, sulfasalazine, and leflunomide, and biologic therapies include the tumor necrosis factor antagonists etanercept, infliximab, and adalimumab. Other biologic agents include the selective T-cell modulator abatacept, the B-cell depleting therapy rituximab, and the interleukin-1 antagonist anakinra. Traditional and biologic DMARDs have helped many patients to manage their disease.

The introduction of biologic therapies and their medical benefits, coupled with a trend toward earlier and more aggressive treatment strategies, has resulted in major clinical progress in patients with moderate-to-severe RA that rarely have been seen previously. However, despite the proven efficacy of available biologic therapies in improving clinical, radiographic, and HRQoL outcomes, not all patients respond equally to the same therapy. Therefore, having an effective strategy for monitoring treatment response is essential to achieving the long-term disease management goals of each patient.

The need to identify those patients who continue to have active disease despite therapy has resulted in the de-
The development of various assessment tools to monitor clinical response and patient-reported HRQoL outcomes in real-world settings. In this article, we discuss optimal disease management founded on a multidisciplinary approach and provide an overview of select key measures for assessing patient response. Our objective is to discuss methods based on our experience in the clinical practice setting and offer our perspectives and practical advice as rheumatology HCPs to improve patient assessment and care.

**Monitoring Response to Therapy**

Routine monitoring of response to therapy is critical in understanding whether a current treatment regimen is appropriate, or if a change or modification in therapy would be helpful. The methods used to monitor response may vary depending on how well the patient is responding to therapy. Patients at either end of the response spectrum, that is, patients who are in remission or who are not responding to therapy are easy to detect; however, it is the group of patients in the middle, those who have demonstrated a partial or moderate response to treatment, for whom measuring tools are particularly helpful in influencing treatment decisions. It is this group to whom the HCP team, the rheumatologist in particular, needs to pay extra attention in terms of monitoring, to determine whether clinical outcomes can be further improved.

Currently, most rheumatologists in the United States (U.S.) do not regularly use quantitative measures in routine clinical practice, with the exception of laboratory tests; they rely, instead, on subjective observations. However, it is clear that there is significant potential for improving patient outcomes if modification of therapy is driven by the routine use of objective measures. For example, the Tight Control of Rheumatoid Arthritis (TICORA) study has shown that close monitoring of patients using quantifiable measures results in significantly better patient outcomes than subjective monitoring by physicians. The use of a tight control regimen is also supported by results from other clinical trials, including the Behandel Strategieen (BeSt) study, the Finnish Rheumatoid Arthritis Combination Therapy (FinRACo) study, and the Computer Assisted Management for Early Rheumatoid Arthritis (CAMERA) study.

Given time constraints in the clinic, the HCP team may be limited to the use of only a few assessment tools. Therefore, assessment tools should be chosen carefully to ensure that patients are monitored as comprehensively and consistently as possible at each visit. There is no single standardized test to determine an adequate or inadequate response. Historically, rheumatologists gathered information on a patient’s disease status by performing a variety of tests, such as joint counts, laboratory tests, grip strength, walk time, and patient-reported outcomes. Similarly, assessment tools, such as the American College of Rheumatology (ACR) response criteria and the Disease Activity Score (DAS) and its derivatives, are indices of different measures that have been pooled to generate single summary scores. Both the ACR and DAS response criteria are validated and widely accepted for use in clinical trials; however, their use in clinical care has been limited.

The ACR response criteria were designed specifically for use in clinical research to assess changes in the signs and symptoms of RA at the group level. For example, in clinical trials, the ACR criteria are used to determine the proportion of patients that has achieved a percentage improvement in response (ACR response rates); unlike the DAS28 criteria, this tool does not determine the actual degree of disease activity, because it does not take the patient’s disease activity at baseline into consideration. As ACR response rates evaluate group improvements, they are not considered to be appropriate for determining disease activity and clinical response for individual patients in routine practice.

The DAS28 is derived from the original DAS, which evaluates disease activity at a given time point. The DAS28 is a validated clinical index of multiple measures, including a formal 28-joint count, an acute phase reactant measure [erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)], and a patient global assessment of disease activity. While some clinicians use the DAS28 to monitor disease activity, others find it impractical for everyday use, owing to the complicated scoring system and the requirement for a formal joint count as well as a laboratory evaluation of a blood test.

The need for assessment tools that are practical in clinical care, in terms of simplicity in administration and applicability at the individual patient level, has led to the design of several validated measures of clinical efficacy and HRQoL. Here, we will provide an overview of some of these assessment tools, including insights into their utility and practicality in the clinical setting.

**Practical Aspects**

Evidence from different studies clearly indicate that physician-assessed subjective measures alone are not sufficient to justify maintaining or modifying a patient’s treatment regimen, and treatment decisions that are based on quantitative assessments also lead to improved patient outcomes, as described above. When choosing an assessment tool for use in clinical practice, several factors influence this decision-making process, including the validity of the measure in RA, ease of use, and the relevance of the assessment for the individual patient.

**Validity**

Strength of validity is one of the most important factors in deciding which assessment tool to use. It is important to be sure that the assessment tool accurately measures and is sensitive to changes in RA disease activity. As patients differ in their disease activity level and duration, it is crucial that the tools used to monitor patients’ responses are capable of detecting changes in patients with mild or severe disease.
activity and early or long-standing RA. Healthcare practitioners should consider that it is unlikely that any one assessment tool will be able to accurately capture disease activity across all patient populations. As such, it is still important to supplement the use of assessment tools with other measures as appropriate to the patient, among them: levels of acute phase reactants, annual radiographs for suitable candidates, and record of duration of morning stiffness and pain.

**Ease of Use**
The ease of use of a tool, in terms of both administration and scoring, is important, especially in a busy clinic. A variety of assessment tools are available for use to monitor patient response. Some tools include only patient-reported outcomes, while others require more extensive input, such as laboratory evaluations or formal joint counts. Choosing the right assessment tool that complements the clinic is critical, as only regular use will aid in the close monitoring of a patient’s response to treatment.

**Relevance to the Individual Patient**
Each patient is unique and different patients will value different aspects of their health; therefore, it is impossible to quantitatively assess all aspects of health in patients who enter the clinic. This is one reason why communication between the HCP team and the patient is so important for improving patient outcomes. Issues that are important to the individual patient should be considered as part of the routine care. Patients with RA often suffer from problems that may not be examined as part of the average questionnaire. For example, the physical symptoms of RA, especially fatigue and joint pain, negatively impact body image and lead to complications related to social, sexual, and psychological well-being in many patients. While the rheumatologist’s main focus is controlling the signs and symptoms of RA and preventing joint damage, the nurse often assumes a prominent role in examining the secondary and tertiary outcomes of RA, such as pain, loss of autonomy, physical dependence on others, depression, and sexual dysfunction. For example, the nurse may discuss with the patient the side effects that some medications can have on sexual ability, such as reduced libido. Maintaining a trusting relationship between the nurse and the patient helps to facilitate discussion of these issues, which are not always incorporated into a routine office visit. This important relationship is a crucial part of the nursing role in monitoring disease, as such patient-reported outcomes as pain and depressive symptoms have been shown to be highly predictive of disability.

**Patient-Oriented Management**
Simply listening to a patient’s concerns can reveal a great deal about their health status. Changing the patients’ perception of their illness through support and education can help to improve their overall HRQoL. For many patients, being able to track their own therapeutic changes in terms of their “score” will also motivate them to continue their therapy and healthcare regimen. By closely monitoring response to treatment and by maintaining trusting relationships with patients, the HCP team can make a difference not only to the patient’s disease outcome but also to their overall QoL.

**Emerging Assessment Tools**

**Clinical Efficacy Assessment Tools for Clinical Practice**
The aim of clinical measures, such as radiographs and joint counts, among others, should be to provide a comprehensive view of a patient’s disease activity. In addition, they should be performed regularly and consistently in order to be useful for close monitoring of the patient’s progress. In reality, radiographs often are only performed once yearly at most, and rheumatologists in the U.S. generally do not perform a formal joint count at every visit. More frequent assessment of joint damage can be provided by measuring acute phase reactants. While elevated ESR and CRP levels have been shown to correlate with radiographs, it appears that they do not correlate as well with functional disability and mortality. Moreover, a recent study has shown that questionnaire results for physical function are more highly correlated to severe long-term outcomes, such as disability and premature mortality, than laboratory tests and radiographs. Therefore, assessments of joint function and functional ability should be supplemented with patient-reported outcomes.

Several emerging assessment tools for monitoring clinical response of patients in the clinic are described in Table 1. These clinical assessment tools are indices that measure different aspects of RA and have their own unique advantages, which are listed in the table. Tools such as the Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI) were designed for use in clinical practice. They are both derived from the DAS28 and have high correlations to DAS28 scores. However, both the SDAI and CDAI are simpler to use and easier to calculate than the DAS28. The SDAI and CDAI include 28-joint counts, patient global assessment of disease activity, and physician global assessment of disease activity. Unlike SDAI, CDAI does not require a blood test for evaluation of an acute phase reactant; therefore, complete results can be obtained and used to drive treatment decisions at the same time as the patient’s visit.

The Global Arthritis Score (GAS) is another clinical assessment tool designed for use in routine rheumatology practice. It comprises three measures: pain, modified Health Assessment Questionnaire (HAQ) and a 28-tender joint count. The GAS has been shown to have high correlations with other validated outcome measures, such as the DAS28 and SDAI, in the clinical practice setting. Scoring of the GAS is relatively easy and, because it does not involve evaluation of an acute phase reactant, the score can be calculated and used immediately.
Routine Assessment of Patient Index Data (RAPID) 3 is an index that incorporates three patient-reported measures found on the Multidimensional HAQ (MDHAQ): physical function, pain, and patient estimate of global status. Derived from the HAQ, the MDHAQ is a patient-reported questionnaire that also measures sleep quality, anxiety, depression, and fatigue in a patient-friendly format. The further inclusion of other patient-reported outcomes from the MDHAQ, such as a patient-reported joint count and a physician estimate of global status, make up the RAPID derivatives RAPID4 and RAPID5, respectively. The MDHAQ can be easily completed by a patient in 5 to 10 minutes. Without the requirement of any formal joint counts or laboratory tests, calculation of the RAPID3 score is also simple and quick. In clinical trials, RAPID3 provided similar results to the DAS28 scores and the ACR core data set.
Health-Related Quality of Life Assessment Tools for Clinical Practice

Patient-reported HRQoL outcomes are increasingly seen as important aspects of RA management. One report even has shown that patient-reported outcomes of pain and depression can be more predictive of disability than radiographs in patients with RA. Therefore, it may be useful to incorporate patient-reported HRQoL assessments into the clinical monitoring strategy of HCPs in order to better understand the patient’s condition.

Validated tools measuring patient-reported HRQoL outcomes have been generated for use in the clinic. Evaluation of a patient’s response to therapy via patient-filled questionnaires can help to identify areas within the HRQoL dimensions for which the patient is performing poorly and help the rheumatology team to direct their attention to those areas during treatment. Table 2 describes some of the patient-reported HRQoL assessment tools that can be used in clinical practice.

HRQoL questionnaires come in either generic or disease-specific styles. Generic questionnaires can detect aspects of the disease that are not characteristically evaluated in RA-specific measures and also can be used to compare patient populations across different diseases. While this type of questionnaire can be less responsive to change than disease-specific questionnaires, several have been shown to be valid in assessing HRQoL in patients with RA. RA-specific questionnaires are derived from the experiences of the RA patient and, therefore, are closely related to aspects most impacted by the disease.

The HAQ is a generic, self-administered questionnaire often used in clinical research to assess physical function. Assessments include dressing or grooming, arising, eating, walking, hygiene, reach, grip, and outside activity. The questionnaire takes approximately 5 to 10 minutes for the patient to answer and, typically, can be completed easily in the waiting room. The modification of the HAQ for use in clinical care has led to the development of the MDHAQ, which also measures fatigue, as well as the psychological aspects of sleep, depression, and anxiety. As mentioned earlier, parts of the MDHAQ are used to generate the RAPID scores.

The Medical Outcomes Study Short Form-36 (SF-36) is another generic self-administered questionnaire that measures eight subscales, including physical function, role limitations due to physical problems, general health perceptions, vitality, pain, social function, general mental health, and role limitations due to emotional problems. The SF-36 has been shown to be valid for use in patients with RA, with results correlating well with both patient and physician global assessments and with HAQ scores. Although the questionnaire only takes approximately 5 minutes for the patient to complete, scoring the results, which requires a computer, is considered complex.

The Rheumatoid Arthritis Quality of Life (RAQoL) questionnaire is an RA-specific instrument derived from the experiences of patients with RA. The 30-item questionnaire assesses the extent to which RA impacts the patient’s mood and emotion, social life, hobbies, everyday tasks, personal and social relationships, and physical contact. Studies indicate that the RAQoL is a reliable and valid tool, with results comparable with the DAS28, the Dutch version of the HAQ, and a measurement similar to the SF-36.

For this review, we have summarized several assessment tools that we consider to be practical and convenient for use by rheumatology HCPs in routine clinical practice. This is not an exhaustive list, however, and beyond the tools described here, there are a number of emerging assessments that also may be used to monitor patient response in the clinic.

Conclusions

The clinical outcomes of patients with RA have improved in recent years due to an early and aggressive approach to treatment strategy. Further improvements are possible by utilizing a team approach to monitoring patient response and basing treatment decisions on quantitative assessments. Effective disease management should involve a collaborative approach between the HCPs of the rheumatology team, including the nurse and rheumatologist. Various members of the multidisciplinary team forge unique relationships with patients, enabling them to examine different elements of the disease, including clinical, physical, psychological, social, and economic aspects. The advantage of using a team approach is that a global representation of how well a patient is responding to therapy can be formed.

While clinical assessments are traditionally performed solely by rheumatologists, the assessment tools described in this review may also be performed by highly-trained, well-informed rheumatology nurses. If these assessments are done prior to the rheumatologist entering the examination room, it may allow for more face-to-face contact between the physician and patient. In addition, these measures can be utilized as a method of communication between the infusion nurse and the rheumatologist who refers their patient to an infusion center. The information obtained by the nurse can give additional insight to the rheumatologist, who may see the patient on a less frequent basis.

In determining the right assessment tools for monitoring response, various practical issues may affect the rheumatology team’s choices. We have provided in this discussion an overview of different measures and validated assessment tools for use in routine clinical practice, including those assessing clinical efficacy and patient-centered benefits. Clinical measures such as CDAI, GAS, and RAPID3 allow HCPs to easily and quickly quantify disease activity levels and patient responses to therapy. Other patient-reported HRQoL outcome measures can help to identify issues that the patient is facing and also help to form a more comprehensive understanding of the patient’s progress.
In our clinical practice, we have found the RAPID3 assessment tool to be useful for quantitatively monitoring the patient’s response to therapy. This fast and simple tool supplemented with a close patient–HCP relationship has allowed us to determine whether our patients are responding adequately to therapy.

Currently, many rheumatology HCPs base their treatment decisions on subjective judgment, rather than quantitative measures. Clear evidence from several studies, including the TICORA, BeST, FinRaCo and CAMERA studies, show that treatment decisions that are driven by quantitative monitoring are significantly better than subjective monitoring for improving patient outcomes. Therefore, incorporating quantitative assessment tools in the current management strategy of the rheumatology HCP could vastly improve the outcomes of patients with RA.

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References


