

Monitoring disease activity in rheumatoid arthritis: an imperative



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‘While existing and imminent new therapies have improved and will continue to improve the situation of patients with rheumatoid arthritis, we will still need further treatment modalities to achieve optimal success in all patients.’

Rheumatoid arthritis (RA) continues to be a disease that leads to progressive joint destruction and disability. Over the last decade, since the introduction of biological therapies in combination with methotrexate, joint destruction and disability have been widely conquered, extra-articular disease has become a rarity, and thus the patients’ fate has significantly improved. Nevertheless, only approximately one in five RA patients achieves remission [1], the state that we would wish to see all our patients reach.

More recently, it has also been shown that treatment decisions based on criteria aimed at attainment of a low disease activity state, as defined by composite disease activity indices, improve outcome in clinical, functional and radiographic terms when compared with unstructured follow-up [2,3]. These data suggest that monitoring disease activity should be part and parcel of the follow-up of RA patients. However, to adhere to such a directive, physicians need to accept this additional workload and patients need to be informed on the necessity of monitoring disease activity on a regular, short-term basis, and even demand it from their doctors. In addition, payers also need to accept the importance of structured patient care and stipulate that such information be obtained. Here, we would like to discuss the evidence behind the importance of regular determination of disease activity in RA and therapeutic decision making on the basis of such information, looking at the perspectives of the three ‘Ps’: the views of the patients, the physicians and the payers.

P1: the physician’s perspective

Evidence is a major driver of physicians’ decision making. There is ample evidence that achieving

a state of remission constitutes the best outcome to be aimed for, and the best way of preventing progression of joint damage [4–6]. Indeed, even in states of low disease activity, joint damage progresses, at least on synthetic DMARDs [4,6]. Moreover, it is likely, mainly for the reason of targeting low disease activity, rather than remission, that joint damage progressed even among the more successfully treated groups in the strategic trials mentioned above [2,3]. Likewise, remission is the best way of reversing disability completely if joint damage is minimal [7]. The observation that physical disability did not fully reverse in recent strategic trials, despite the fact that the majority of the patients were in the early stages of their disease [2,3], reflects the concept that even a state of low disease activity is associated with significant functional impairment [5,7–9]. While therapy with TNF-inhibitors appears to partly dissociate the known links between disease activity and joint damage [10,11], remission is the only state where joint destruction will not accrue irrespective of the type of therapy [4].

But what is low disease activity, and what is remission? A state of low disease activity or remission can not just be judged arbitrarily. Rather, established criteria for these states should be used and their achievement ought to be monitored throughout the course of RA by evaluation of disease activity using respective indices. These require following joint counts and other variables routinely every 3–6 months. Treatment decisions can then be made based on these results. The dynamic approach to therapeutic changes is particularly justified, since recent data have revealed that, on a group level, patients who do not achieve low disease activity within 3–6 months from the start of any type of treatment, including biological agents, will not further improve in the longer term [12].

While physicians may not always like this additional work, they will benefit from it by having patients who are more satisfied (see P2 section) and payers who may be willing to provide the funds for good care (see P3 section). Moreover, if assessing disease activity in all their patients, rheumatologists will soon know the

overall success of their therapeutic performance. Indeed, it would be particularly important to introduce quality measures into patient care more widely. This can be most easily done by using computer-assisted databases [13], which allow the assessment of one's own results in treating a disease such as RA compared with that of others or with general predefined, standard indicators.

In our clinics, we primarily use the clinical disease activity index (CDAI) for rapid decision making. This score simply summarizes tender and swollen joints on the basis of a 28-joint count and evaluator and patient global assessments (on a 10-cm scale), providing a measure – a 'thermometer' ranging between 0 and 76 [14,15]. In particular, the CDAI, as well as its sibling, the simplified disease activity index (SDAI), which additionally comprises C-reactive protein (CRP) in mg/dl [14], appear to be performing particularly well when compared with the rheumatologist's valuation of improvement or the decision to change DMARD therapy [16,17]. Moreover, when dealing with remission, which is today's most important therapeutic aim, these two scores provide the more stringent definitions when compared with others [1,5,18,19].

Thus, physicians are confronted with several very important challenges: to follow patients thoroughly using established disease activity scores; to aim at remission and adapt therapy if at least a state of low disease activity is not achieved upon appropriate therapy within 3–6 months; and to inform their patients on the importance of attaining remission and the risks they bear in the presence of continuing disease activity, even if pain is well controlled.

P2: the patient's perspective

Patients want to feel well. Unless informed accordingly, they do not care whether they have swollen joints or high levels of acute-phase reactants or high global disease activity in their physicians' view – they wish to have no pain and to be able to function well [20]. On the other hand, it is interesting that a state of symptoms that is acceptable to patients does not relate proportionally to the baseline disease activity state, but rather appears to constitute the attainment of a particular level of (moderate) disease activity [21] – a certain status. However, even patients' judgement of major improvement is afflicted with significant residual disease activity. Unfortunately, as stated above, any degree of residual disease activity,

moderate or even low, will lead to accrual of joint damage over time and, consequently, to the development of irreversible disability.

Patients generally tend to look at their state 'today' and, at best, with a glimpse at 'tomorrow', but not at their potential fate in the long term. Therefore, they need to be made aware of the consequences of today's disease activity, especially given that these consequences may be very severe and occur in the years to come, not in the short term. It is often difficult for patients to understand that treatment needs to be adapted even if they feel well. In other words, it is often difficult to accept that a little bit of residual swelling or raised CRP may need attention with more intensive treatment, even if everything is well otherwise.

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Of equal importance, patient compliance to our therapeutic recommendations needs to be secured. This requires rheumatologists and their RA patients to be aligned with respect to the treatment aims and the paths leading to their achievement. To allow patients to understand rheumatologists' thinking, they have to be informed on the scores that we apply. Patients with hypertension know of the importance of achieving a normal blood pressure, patients on anticoagulant therapy know about the range of International Normalized Ratio that they need to attain in order to successfully prevent the complications of their underlying disease, patients with diabetes know their HbA1c, blood glucose levels and so on. The simplicity of the CDAI now allows patients with RA to understand the score's composition and calculation, as well as the states aimed for, as defined by the respective cutpoints, as if it were a blood pressure or an INR value. We provide our patients with a credit-card-sized card on which the CDAI values obtained at each clinic visit are entered, so the patients know the evolution of their disease *vis-à-vis* the therapeutic aim.

P3: the payer's perspective

Let us assume an idealized payer: a payer who wants to reimburse the most effective therapy for a given patient with a given disease (we say most effective, not most expensive); a payer who cares about the long-term risk of the disease as much

as about the long-term risk of its treatment; a payer who wishes to prevent unnecessary expenses; and a payer who wishes to optimize outcomes for the patients by providing benchmarks of therapeutic success and asking physicians for quality indicators on the patients that they treat.

This payer should likewise be informed on the current state-of-art – that remission is the goal and the state that prevents bad outcome most effectively. This payer would not only urge rheumatologists to aim for the best outcome for the patient, but would provide them with the respective funds for the regular, proper assessment of RA patients. Insisting that therapy be switched if a treatment regimen did not lead to low disease activity within 3–6 months (unless it constitutes the ‘last resort’) would be part of a strategy that prevents continuing expenses for insufficient therapies and, at the same time, may lead to better outcomes for the patient. Ultimately, this will mean a better quality of life for patients with RA, preservation or resurrection of their employment status and reduction of long-term societal costs.

Further developments are needed

While existing and imminent new therapies have improved and will continue to improve the situation of patients with RA, we will still need further treatment modalities to achieve optimal success in all patients. As long as the causes of

RA are unknown, targeting molecules involved in the pathogenesis will cover the needs of an increasing number of patients. There will be a need to study the effects of various therapies in patients with residual low disease activity, for which current targeted therapies are not licensed. The other open question relates to defining strategies for patients who have achieved desired states, such as remission: shall successful treatments be continued indefinitely? Shall they be reduced but partly continued? Shall they be discontinued? All of these questions will require new studies. Likewise, we will have to find markers allowing for the prediction of outcome, so therapies can be tailored to the need of an individual patient.

Thus, while much has been achieved, there are still many open questions requiring resolution. The prospects of gaining these additional pieces of information are excellent.

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