

From DAS 28 to SAS 1

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Introduction

The main goal of therapy in patients with rheumatoid arthritis (RA) is to achieve remission which is defined as no active joint inflammation and no erosive or functional deterioration (1-4). Thus, in order to monitor disease progression and assess the effects of therapies in RA, rheumatologists need to be able to measure disease activity and damage. This has become much more important with the advent of therapies which make remission a realistic target. Most treatment decisions are guided by clinically obvious synovitis, but we cannot rely on this to distinguish between low disease activity and remission. Various measurement tools have been developed, but none of them is perfect. DAS 28 is a widely accepted tool to measure disease activity and it can be regarded as the gold standard for this kind of assessment. However, clinical remission, as defined by the DAS 28 criterion, is achieved in a minority of patients and even in this subset residual disease activity can be detected in the dominant wrist by ultrasound (US) with synovial hypertrophy in 73% of subjects and power Doppler (PD) signal in 43% (5-7). Furthermore, in a different subset of patients, the achievement of true remission may go unrecognised if the standard applied is the attainment of a DAS-28 score of <2.6 since this may be elevated by factors other than disease activity (8). In such cases there is a risk of inappropriate escalation of treatment. In both these instances US provides a more accurate measure of true remission. An ideal tool should be affordable, readily accessible, non invasive, quick to administer, quantifiable, reproducible, sensitive to change and acceptable to patients. US has many of these characteristics but there is, as yet, no practical US based disease activity scoring system, which can be easily applied

to routine clinical practice. Such an instrument must be quick and easy to perform on suitable US equipment by clinicians with different levels of expertise. Various groups have proposed different joint sets for disease monitoring ranging from a 78 joint set to a 6 joint set (9-13). Even a 6-joint set is challenging in daily clinical practice.

Hypothesis

At present, there is no practical way to scan all potentially affected joints. Accepting that US provides a better assessment of remission than clinical examination or DAS score, then the question is how many sites do we need to monitor by US in order to be able to make appropriate treatment decisions. We argue that meaningful clinical information on disease activity and the achievement of remission may be available from serial monitoring of a single joint, which would act as a representative window to explore disease activity. This approach would overcome the most common objection to the use of US in assessment of disease activity, which is that it is too time consuming to integrate into busy clinical practice. US assessment of a single joint would take no longer than a DAS 28 score. We suggest that the metacarpophalangeal (MCP) joint with the most florid synovitis on initial US screening should be selected as the sentinel joint. In the event that several joints have similar US levels of synovitis the second MCP on the dominant hand, if involved, should be preferred. The skills required to obtain reproducible images from a single joint would be easily learned.

Testing the hypothesis

The idea of monitoring disease activity in RA using US of a single joint is similar to using single simple tests to monitor complex pathologies in other diseases – transfer factor in interstitial

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lung disease, for example. If we set remission as our therapeutic aim in RA then it makes no difference whether there is active disease in one or several joints. While disease activity remains anywhere we have still not achieved our target. It would only be necessary to monitor a larger set of joints if there was evidence to suggest that the sentinel joint might respond differently to treatment compared to all other potentially affected joints. Clinical evidence does not support this concern.

The assessment of a single joint allows a careful assessment of US remission defined as the absence of intrasynovial PD activity. Only when this has been achieved in the sentinel joint will an assessment of other joints be required. If another active joint is detected, this becomes the reference sentinel for further therapy adjustment and monitoring. The application of the Sonographic Activity Score (SAS) requires US equipment capable of detecting low levels of PD activity at a frequency of at least 9 MHz. This is available in most modern US machines.

Single joint monitoring provides an astonishing amount of information on the state of synovitis. Even a 1-minute view of a single joint has a remarkable impact on clinical decision-making process. The old statement that a picture is worth a thousand experiments is particularly appropriate to define the potential of US in the assessment of remission in RA patients. Pictorial evidence can no longer be excluded from the panel of tools that each rheumatologist should use in daily clinical activity.

Although any joint may play the role of sentinel joint, MCP joints should be regarded as the potential best candidates because they provide the best acoustic windows for a careful assessment of joint cavity. Moreover, MCP joints are among the most frequent early targets of the disease. Finally, at the MCP joint all the basic features of chronic synovitis including fluid collection and synovial hypertrophy are readily demonstrated. In selecting the most appropriate sentinel joint we should take account of the fact that MCP joint involvement is an invariable feature of RA. When choosing among the MCP joints we

considered whether it would be better to choose the second MCP joint on the dominant hand as it is the most frequently affected joint but would instead suggest using the most active joint on initial US assessment of the second to fifth MCP joints of both hands. In the event that several joints share equal maximal disease activity then the second MCP joint on the dominant hand should be preferred. This preference is guided by the fact that the second MCP joint is the most vulnerable of the MCP joints to structural damage.

Discussion

Serial US assessments of a single joint to the point of remission should be regarded as an effective and efficient strategy for guiding treatment decisions in RA. Compared to the DAS 28, this approach has the potential to be more objective, more reproducible, more sensitive to change (14-21), and no more time consuming. It would also avoid the drawbacks of the DAS 28, which is too heavily influenced by subjective components such as the visual analogue score for well being and the tender joint count. Additionally, the results of the assessments will be immediately available, allowing treatment adjustments in real time.

It remains to be shown how indicative of overall remission the achievement of SAS1=0 in the sentinel joint is. In practice the lack of this evidence does not undermine our hypothesis. There are two possibilities to consider. Firstly, there is the possibility that the achievement of remission in the sentinel joint is indeed indicative of overall remission. In this case, SAS monitoring has provided a very efficient means of titrating treatment to the desired endpoint. Secondly, there is the possibility that the sentinel joint achieves remission, but there is still disease activity elsewhere. Here too, nothing will have been lost by concentrating on a single joint as treatment will have been titrated based on disease activity present in at least the sentinel joint at all time points prior to the achievement of sentinel joint remission. At that point, further titrations can be guided by another sentinel joint chosen from among the

MCPs and wrists. If no joints amongst this candidate set show evidence of disease activity (SAS1=0) then the search should be extended to other sites such as the metatarsophalangeal joints.

The willingness to escalate therapy in response to low levels of US detected disease activity requires an aggressive approach and an acceptance of remission as a realistic goal in patients with RA. This approach is fast becoming the expected standard of care in RA and is fully justified by evidence showing that even patients with DAS-28 defined remission may suffer continuing structural damage (5, 6). In these patients the presence of PD activity within a joint, (SAS1=1), is evidence of continuing synovitis which, over time, is associated with the risk of further damage.

Conclusion

US is superior to clinical examination for the detection of low levels of disease activity in RA and can detect progression of anatomical damage at a level of resolution of 0.1 mm. Its acceptance as a routine clinical tool has been limited by the perceived difficulty of acquiring the skills needed and then applying them in busy clinical practice. We propose a quick and simple US measure of disease activity, SAS on one joint, using easily acquired technical skills, which can be readily applied to routine clinical care. Studies are needed to compare this approach to other, more onerous US scoring systems and validate it against existing tools used to titrate treatment and assess disease activity.

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