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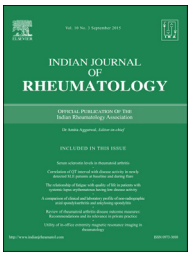

Review Article

Review of rheumatoid arthritis disease outcome measures: Recommendations and its relevance in private practice

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ABSTRACT

The ultimate goal of pharmacological treatment in Rheumatoid Arthritis (RA) is to reach and sustain remission, prevent functional disability and organ damage. Recent improvements and insights in RA treatment such as availability of wider range of disease modifying agents including biological agents have made 'clinical remission' a realistic target for many patients. To optimise RA treatment physicians must monitor the disease activity accurately to adjust treatment according to disease activity levels. In RA, several disease outcomes such as painful and swollen joints, functional impairment and acute phase reactants are recognized as manifestations of underlying disease process. To monitor the disease accurately, an index expressing these outcomes as a single continuous variable is required. The widely used disease outcome measures in clinical trials are the American College of Rheumatology (ACR) recommended indices: DAS28 (ESR or CRP), PAS, PAS-II, RAPID-3, SDAI and CDAI which have different relevance in clinical practice as compared to clinical trials. DAS28 hitherto considered gold standard in measuring RA outcomes in clinical trials may not hold appeal in clinical practice because of complexities associated with its calculations and waiting time due to inclusion of laboratory measurements. In recent times, simpler scores such as RAPID-3 and CDAI are being evaluated in global and Indian studies as a preferred outcome measure in point-of-care clinical setting because of their simplicity and ease of administration especially in a fund-stricken country like India.

1. Introduction

'Remission' as the treatment goal in Rheumatoid Arthritis (RA) is critical for improved clinical outcomes. European League Against Rheumatism (EULAR) task force defines treatment target as 'remission' (especially in early RA) or 'low disease activity' (in established RA) although the target is modified in accordance with co-morbidities and safety considerations.[1] Clinical studies have demonstrated that a 'tight control' of disease activity (treating patients to specified targets with aggressive therapy if necessary) is more effective in achieving

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remission, compared with usual care.[2] EULAR task force now recommends starting therapy with a conventional disease modifying agent ideally combined with glucocorticoids. As per EULAR recommendations (2013 update), patients require frequent monitoring (every 1–3 months), and, in a treat to target approach, patients with no improvement by maximum 3 months of treatment start or who do not attain target by 6 months need therapy adjustment. Such patients benefit from the addition of biological agents in a way similar as if they received them from the beginning.[1] With emerging evidence that treating to target improves clinical outcomes, it is imperative to have disease outcome measures which adequately reflect underlying disease activity so that clinical decisions can be made easily and in a timely manner.

The current article aims to summarize the commonly used disease outcome measures, their applicability in clinical setting especially in a resource constrained developing country like India.

2. Disease outcomes and core set measures in RA

Since RA has a complex underlying pathology, outcome measures will have to measure multiple features such as Disease Activity, Discomfort, Disability and Damage.[3] To promote uniformity in measuring and reporting outcomes in RA, the American College of Rheumatology (ACR), EULAR, and the World Health Organisation/International League Against Rheumatism (WHO/ILAR) have recommended "core" outcomes to be measured in RA. These include: tender joint count (TJC), swollen joint count (SJC), acute phase reactants (APR) [erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)], patient global assessment (PtGA) and provider global assessments (PrGA) of disease activity, patients' assessment of pain and patients' assessment of physical function as well as a radiological changes (for studies of one year or longer).[4,5]

SJC and TJC along with APRs measure disease activity and indicate underlying inflammation. Original ACR joint count included 66/68 joint count and many variables such as tenderness, swelling, limited motion and deformity. The recent modifications include fewer joints (36, 28, 42 joints) and variables such as swelling and tenderness. Joint count is the most specific measure to assess patient's clinical status in RA but include limitations such as poor reproducibility, failure to predict progressive joint damage and functional disability.[6,7] Studies indicate that though TJC and SJC improve to a 20% level over 5–15 years, patients may still experience joint damage, disability and decline in functional status. Therefore, the goal of RA treatment has now shifted to low disease activity or remission rather than a 20% (or even 50%) count improvement.[6]

RA being a disease of the musculoskeletal system results in varied amount of discomfort and disability in the patient. These patient reported outcomes are measured using patient self-report questionnaires such as PtGA and Health Assessment Questionnaire (HAQ). These also help in measuring the overall way in which RA affects the patient at any given point of time. HAQ (and its shorter versions such as Modified HAQ, Multidimensional HAQ, HAQ-II, and Improved HAQ) evaluate patient's difficulty with activities of daily living such as dressing, arising, eating, walking, hygiene, reaching, gripping, and chores.[8] The HAQ also includes 10-cm visual analog scales (VAS) to assess pain and global status assessments. However, patient questionnaires are not as specific as joint counts and may be subject to "gaming" by certain patients to give desired answers.[6]

Natural disease progression in RA leads to progressive joint damage. Standard radiological scores are available such as the one devised by Larsen and Sharp, and modifications by van der Heijde Rau etc. However, radiographic changes are appreciated slowly (at least 6 months to a year). In standard clinical care, rheumatologists seldom have experience in quantitative assessment of radiographs. More so, radiographic damage has little prognostic value for work disability and joint replacement.[6,9]

3. Disease outcome measures in RA: applicability in clinical practice

There is no single standard outcome in RA which can be used as the primary endpoint to assess therapy results in a clinical trial or clinical care setting. Measures which pool assessments of several core set elements into a single, composite index is a better way to assess impact of intervention.[3] Of the 63 currently available disease activity measurement tools, ACR recommends 6: the DAS28 (ESR or CRP), PAS, PAS-II, RAPID-3, SDAI and CDAI.[1] These measures are quick, easy to perform and mostly satisfy the fundamental attributes of outcome measure such as validity, reliability and responsiveness (psychometric properties).[10]

Outcome measures have different applicability in clinical trials as compared to clinical practice. Treatment goal for practitioners is clinical remission or a low disease activity. Categorizing the disease activity as low', 'moderate', 'and high' helps in steering the treatment decisions.[11] Improvement of at least 20% in both TJC and SJC, as well as three of the five additional measures (not including radiograph), known as "ACR 20," is designated as ACR preliminary definition of improvement. Similarly, 'ACR 50' and 'ACR 70' indicate higher thresholds for improvement and minimal disease activity. The composite scores have different cut-off values for defining remission and low disease activity, of which DAS28 scores are widely used. Table 1 describes cut off values for remission and low disease activity for various composite indices. ACR core data set measures 'change' in disease activity, and calculation of ACR 20% response does not allow the measurement of actual disease activity nor enable comparison of a patient's absolute response with that of another one. The EULAR criteria are based on the DAS score, which measures an absolute disease activity and indicates current disease 'state' or severity. DAS is generally considered to have greater utility in determining whether a patient has achieved low disease activity or remission.[2,12,13]

Of the ACR based measures, PAS, PAS-II, and RAPID- 3 are mainly patient reported assessments while CDAI includes

[1] DAS28: Disease Activity Score in 28 joints; PAS: patient activity scale; RAPID: routine assessment patient index data; SDAI: simplified disease activity index; CDAI: clinical disease activity index.