Initial Management of Rheumatoid Arthritis

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KEYWORDS

• Rheumatoid arthritis • Disease-modifying antirheumatic drug
• DMARD

Key Points

- Half of patients who have rheumatoid arthritis (RA) which is diagnosed and treated early by a rheumatologist with the goal of remission or low disease activity can expect to achieve remission while taking their disease-modifying antirheumatic drugs.
- Recently, the recognized benefits of very early therapy of RA highlighted the need to make the diagnosis of RA as early as possible.
- Therapeutic goals and the ability to measure them are critically important in treating any disease.

The prognosis for the patient with newly diagnosed rheumatoid arthritis (RA) has dramatically changed over the last two decades. If a patient is diagnosed and treated early by a rheumatologist with the goal of remission or low disease activity, half of patients can expect to achieve remission while taking their disease-modifying antirheumatic drugs (DMARDs). Strong evidence exists that early diagnosis and aggressive treatment alter the natural history of RA. Clearly, prevention of permanent structural damage to joints, including both erosions and joint-space narrowing as measured on radiographs, but also the prevention of deformities that can occur without erosions, is a strong rationale for early RA treatment.[1,2] Structural damage, when it reaches a critical level, is associated with functional impairment. Although there is evidence in some cases that erosions may heal (at least radiographically), joint-space narrowing and subluxations are permanent.[3–6] A meta-analysis of 12 studies demonstrated significant reduction of radiographic progression in subjects treated early when compared with the subjects treated later. An average delay of 9 months in starting DMARDs significantly

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Rheum Dis Clin N Am 38 (2012) 311–325
doi:10.1016/j.rdc.2012.05.003 **rheumatic.theclinics.com**
0889-857X/12/$ – see front matter

increased radiographic progression. Subjects with more aggressive erosive disease benefited the most from early therapy.[7] However, it is important to note that most patients who have RA fall into the category of poor prognosis by virtue of erosions at baseline, or rheumatoid factor (RF) or cyclic citrullinated peptide (CCP) positivity, and clearly need early intervention.

Some investigators have suggested that there is a window of opportunity in early disease during which therapy is somehow particularly effective. Much data, some referenced above, clearly show that the earlier physicians treat, the better patients do. Most large trials in early disease show a strong correlation of disease duration to outcomes.[8–10] No one can argue that earlier is better, but the window of opportunity concept can be, and sometimes is, carried too far. It should not be assumed that this window somehow closes and then patients do not benefit from therapy. Excellent data demonstrate that in the face of active disease, patients benefit from appropriate DMARD treatment regardless of disease duration.[11–17] It remains debatable whether early therapy can reset the radiographic progression rate of patients for years to come. The Finnish Rheumatoid Arthritis Combination Therapy (FIN-RACo) and the Combination Therapy in Patients with Early Rheumatoid Arthritis (COBRA) trials (see later discussion), among others, suggest this may be true. It is important to keep in mind the many limitations of the open long-term observational nature of these results and how aggressively subjects from these trials were treated to target.

Long-term results (5-year and 11-year) of the FIN-RACo trial suggest that effect of early aggressive intervention on radiologic progression is longlasting.[18–20] In this study, subjects were randomized into two groups. From the start, one group received a combination of DMARDs, including methotrexate (MTX), sulfasalazine (SSZ) and hydroxychloroquine (HCQ), and the other group received SSZ as monotherapy. The first group had prednisolone as part of their regimen; in the second group it was used as needed. After the initial 2 years, the drug regimen became unrestricted and, therefore, similar. At 5 and 11 years, radiologic progression in the SSZ-alone group was significantly higher than in the group treated with the combination of DMARDs. Similar results were demonstrated in the COBRA trial.[21–23] In this trial, 155 subjects were randomized to COBRA therapy (SSZ 2 g/day, MTX 7.5 mg/week, prednisolone starting at 60 mg/day and tapered to 7.5 mg by the seventh week) or SSZ (2 g/day) monotherapy. At 28 weeks, prednisolone was tapered and withdrawn and, after 40 weeks, MTX was stopped. After this, treatment in both groups became unrestricted. Analysis at 5 and 11 years showed a significantly higher rate of radiologic progression in the SSZ group. Both the COBRA and FIN-RACo studies support the hypothesis that aggressive therapy in the early phase of RA results in long-term radiologic benefit that may translate into better functional outcome.

How soon is soon enough? There really is no answer to this question. Treatment within the first 3 months of onset is a goal. A study of a cohort of subjects with early RA with disease duration less than 12 months, treated with tight-control protocol, showed that a major predictor of an American College of Rheumatology (ACR) clinical remission at 12 months is the duration of disease at the time of initiation of treatment. Very early RA was defined as disease with symptoms of less than 12 weeks. Multivariate analysis demonstrated that the only independent predictor of erosives at 12 months was an increase in duration of disease at the time of initiation of treatment (odds ratio [OR] 2.4; CI 1.1–5.6).[24]

EARLY DIAGNOSIS (CLASSIFICATION) OF RA

Recently, the recognized benefits of very early therapy of RA highlighted the need to make the diagnosis of RA as early as possible. With this goal in mind, the ACR and