

CONCISE REPORTS

Early referral, diagnosis, and treatment of rheumatoid arthritis: evidence for changing medical practice

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Abstract

Objectives—To study the delay in starting disease modifying anti-rheumatic drugs (DMARDs) in patients with rheumatoid arthritis (RA), and any changes in medical practice between 1980 and 1997.

Methods—198 consecutive RA patients attending the rheumatology clinics at a teaching hospital, for routine review, had their case sheet reviewed. The dates of symptom onset, general practitioner (GP) referral, first clinic appointment and first use of DMARD were recorded. Data were collected on the erythrocyte sedimentation rate, C reactive protein, rheumatoid factor, and the presence/absence of erosions at the first clinic assessment. Patients were split into four groups according to the date of their first clinic assessment—before 1986, 1987–9, 1990–3, and 1994–7.

Results—There was a sharp drop in the delay between symptom onset and GP referral (before 1986, 21 months; 1987–89, 23 months; 1990–3, 7 months; 1994–7, 4 months, $p < 0.03$), and in the delay between first assessment at the rheumatology clinic and the start of DMARD treatment (before 1986, 32 months; 1987–89, 21 months; 1990–1993, 8 months; 1994–7, 1 month, $p < 0.001$). The number of patients given DMARD treatment within six months of symptom onset increased from 5% (before 1994) to 44% (1994–7). Seventy three per cent of patients waiting more than a year from symptom onset to first clinic appointment already had erosive change, compared with 34% of patients seen within a year.

Conclusions—Patients are being referred earlier in their disease, and DMARDs are prescribed sooner in the disease course. There has been a substantial increase in the proportion of patients treated with a

DMARD within six months of symptom onset.

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The “traditional” pyramid of treatment of rheumatoid arthritis (RA) involved treating patients with non-steroidal anti-inflammatory drugs, before progressing to the use of disease modifying anti-rheumatic drugs (DMARDs) in patients with continuing disease activity. In recent years, this strategy has been rejected, and the early use of DMARDs has been advocated.¹ There is some evidence from a randomised trial, that patients experiencing a delay in receiving DMARD treatment develop more functional disability and radiological progression compared with those patients receiving immediate DMARD treatment.² To identify patients who might benefit from such early intervention, “early synovitis” clinics have been set up. In the past, many patients had already developed established radiological damage at presentation, and it has been hoped that the early identification of RA patients might allow treatment to be started before the development of irreversible joint damage.³ There is evidence from the USA that more patients are being treated with DMARDs,⁴ but there has been no published evidence to confirm that patients are referred and treated significantly earlier in their disease course.

Methods

The study was conducted at a single teaching hospital that provides secondary care for patients with rheumatic diseases. Recruitment was of 198 sequential patients seen in the rheumatology clinics for their routine review, over a six week period. All patients fulfilled the American College of Rheumatology criteria for the diagnosis of RA.⁵ A retrospective case sheet review identified the dates of symptom onset, general practitioner (GP) referral, first clinic appointment, and first use of DMARD. Data were collected on age, sex, erythrocyte sedimentation rate, C reactive protein, rheumatoid factor, and the presence/absence of erosions on hand and foot radiographs at the first clinic assessment. Patients were arbitrarily split into four groups according to the date of their first clinic assessment—before 1986, 1987–9, 1990–3, and 1994–7. Between group comparisons were

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Table 1 Patient details at time of initial clinic visit (medians and interquartile ranges are shown where appropriate)

	Group 1 (pre 1986) (n=36)	Group 2 (1986–1989) (n=36)	Group 3 (1990–1993) (n=52)	Group 4 (1994–1997) (n=74)	Kruskal-Wallis (χ^2)
Age (y)	44 (37–54)	53 (44–63)	53 (42–62)	64 (49–68)	$p < 0.001$
Female (%)	78	86	65	71	(NS)
RF positive (%)	78	86	71	75	(NS)
Erosive (%)	67	54	54	49	(NS $p = 0.4$)
ESR	38 (20–50)	32 (11–46)	29 (19–57)	42 (25–57)	NS
CRP	—	12 (0–39)	20 (0–52)	25 (10–66)	NS

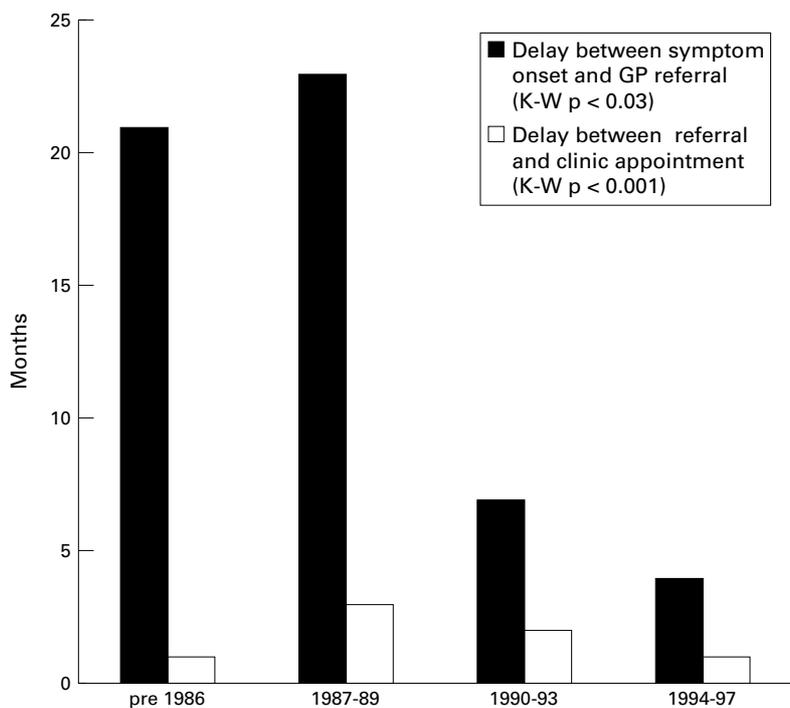


Figure 1 Median delay from symptom onset to GP referral, and from referral to clinic appointment.

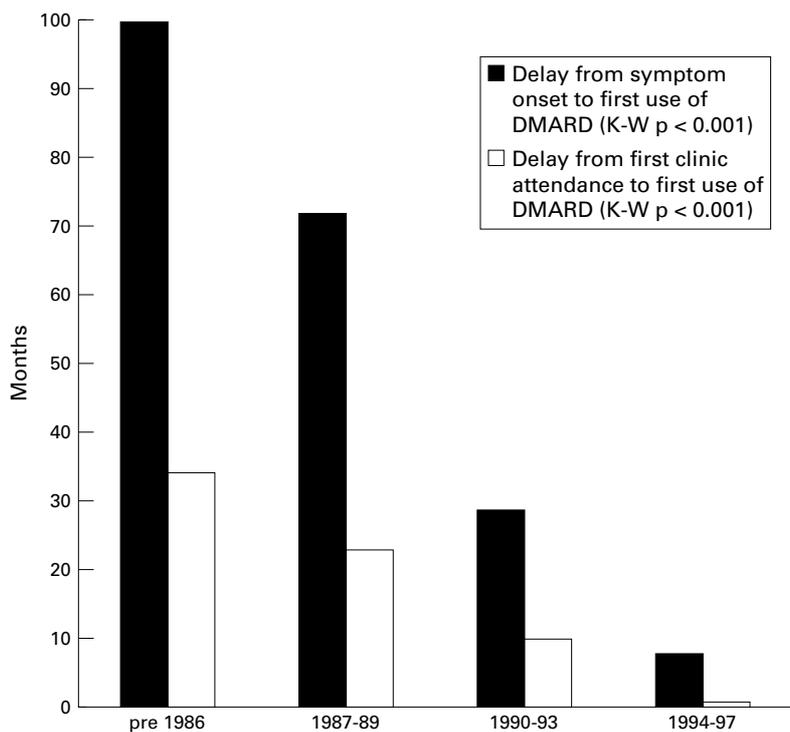


Figure 2 Median delay from (1) symptom onset, and (2) first attendance at clinic, to the first use of DMARD treatment.

analysed using Kruskal-Wallis and χ^2 tests where appropriate. All statistical tests were performed using a SPSS v7.5.1 for Windows (1996).

Results

Table 1 shows the details of the study patients. Patients who have attended the clinic longest appear to have presented at a significantly earlier age possibly because older patients have since died or become too infirm to attend. The apparent trend for a higher percentage of patients presenting before 1986 to have erosive

Table 2 Percentage of patients presenting with erosive changes according to delay from symptoms to initial clinic appointment

Delay from symptom onset	0-3 months	4-6 months	6-12 months	>12 months
Number	34	34	24	91
Erosive (%)	35	36	33	73

disease at presentation, is not significant ($p=0.396$), and overall there was no evidence of any significant reduction in disease severity over time.

DELAYS TO RHEUMATOLOGICAL ASSESSMENT

Figure 1 shows the delay from symptoms onset to referral by a GP and time from referral letter to clinic visit. There has been a significant reduction in the delay between the onset of symptoms and GP referral to a specialist rheumatology clinic (before 1986 = 21 months, 1987-89 = 23 months, 1990-3 = 7 months, 1994-7 = 4 months, $p<0.03$). Although there has been significant variation in the median time from GP referral to clinic appointment ($K-W p<0.001$), this is of doubtful clinical significance, as the variation is from one to three months. The rate of seropositivity for rheumatoid factor was similar in patients referred early (that is, < 3 months from symptom onset) compared with those referred later (75% v 80% respectively).

DELAY TO DMARD THERAPY

The percentage of patients exposed to a DMARD in each group was similar ranging from 87% in group 3 to 94% in group 2. Figure 2 shows details of the delays in the use of DMARD treatment, with a sequential fall in the time to starting the first DMARD. The fall is highly significant for both the delay between the onset symptoms and the first prescription of DMARD treatment ($K-W p<0.001$), and the delay between the patient's first rheumatology clinic assessment and DMARD use ($K-W p<0.001$). The median delay to starting a DMARD from the first clinic appointment is one month in the 1994-1997 group, and in this group 44% of patients were prescribed a DMARD within six months of symptom onset, compared with 5% of patients from the other three groups. The most significant factor in the delay to starting a DMARD remains the time from initial symptoms to presentation to a rheumatologist.

RADIOGRAPHIC CHANGES AT PRESENTATION

One hundred and eighty three patients had hand and feet radiographs at their initial visit to the rheumatology clinic. Table 2 shows the percentage of patients with erosive changes at presentation, according to the delay between symptom onset and first clinic visit. There was little difference in the percentage of patients with erosive changes at presentation until the delay to a clinic appointment was greater than one year.

Discussion

The lag time from symptom onset to the start of DMARD treatment can be divided into two components: (1) the length of time between symptom onset and GP referral to a rheumatologist and (2) the delay from first rheumatology clinic attendance to starting a DMARD. Our results demonstrate that over time there has been a change in both GP referral practice and DMARD prescribing favouring early initiation of DMARD treatment.

Over the years, patients have been referred to the rheumatology clinic after a shorter and shorter duration of symptoms. The length of time between symptom onset and GP referral is dependent on two variables—the delay from symptom onset to consultation with a GP and the time taken for the GP to decide that specialist assessment is required. It is possible that patients are seeking help from their GP earlier, but Chan *et al*⁶ concluded that the principal cause of diagnostic delay in RA was because of physician delay, and not patient delay in seeking medical advice. Data regarding symptom duration before GP consultation were not available from the case records studied. Therefore, we cannot exclude the effect of this variable, although it is unlikely to account for the magnitude of change seen.

This change in GP referral practice favouring early specialist management of RA occurred during a time when the medical literature has advocated the use of DMARDs in early RA. Patients previously not considered to require DMARD treatment according to the “pyramid model” may have been managed by their GP alone without specialist paramedical support. From our data it seems that GPs now recognise the need for early referral in RA, although even in those patients referred recently, only 43% had symptoms of less than three months duration at the time of referral. This suggests there is further scope for reductions in the delay to rheumatology referral.

In our study, patients referred early were no more likely to be seropositive for rheumatoid factor, in contrast with the findings of Chan *et al*, who found that patients positive for rheumatoid factor were more likely to be diagnosed early, but that even patients with “typical” presentations had a diagnostic delay of > 2 months after first medical encounter. Studies have shown that rheumatologists are more likely to make timely and correct diagnoses of arthritis compared with primary care physicians.⁷ In view of this GPs should be encouraged to seek early specialist assessment in all cases of inflammatory arthritis in an attempt to decrease the delay to diagnosis and introduction of appropriate treatment. In this hospital, there has been no distinct “early synovitis” clinic, showing that substantial improvements in the speed of diagnostic and therapeutic services can be achieved outwith this setting.

DMARD prescribing practice has also changed over time. Although the percentage of patients that had ever received a DMARD was similar in all four “year groups”, patients presenting after 1990 had DMARD treatment

started significantly earlier than those presenting before 1990. This is particularly evident in the 1994–1997 group, where the median delay to starting a DMARD after first clinic attendance was one month. A further delay exists between the time of referral to the clinic and first clinic appointment. We were able to demonstrate a statistically significant fall in this delay although in clinical terms this was only from a median of three months to one month.

The outcome of these changes is significantly earlier initiation of DMARD treatment. The median delay from symptom onset to initiation of DMARD treatment has fallen from over eight years to eight months, and there has been a striking increase in the number of patients treated with DMARDs within six months of symptom onset (from 5% before 1994, to 44% in 1994–7). How early in the course of RA should DMARD treatment be started? The definitive answer to this question still evades us. The early course of RA is incompletely understood and evidence that aggressive early treatment improves long term outcome is still awaited. From studies of hand bone mass in RA by dual energy x ray absorption scanning, there is evidence of bone loss after six months disease duration.⁸ Other workers have shown that the rate of radiological progression is highest in the first year of disease.^{9,10} Assuming the aim of treatment in early RA is suppression of disease activity before structural damage occurs, we can conclude that DMARD treatment should be started as early as possible in the course of RA.

Radiological erosions were found at presentation in 71% of patients with symptom duration of >12 months before first rheumatology clinic attendance. None of these patients had received DMARD treatment before clinic attendance. Similarly, Van der Heijde *et al*,¹⁰ in a three year prospective radiographic follow up study of 90 patients with early (< 1 year duration) RA, found that 70% showed radiographic damage after three years of study. The authors stated that these patients could be identified at one year of study, and those with little evidence of radiological progression at one year were unlikely to show significant progression over the following two years. This suggests that the pattern of disease progression is established early in RA. Although patients with symptom duration of < 12 months were less likely to be erosive at presentation, surprisingly, we found that patients with <3 months symptom duration were as likely to have radiological erosions at presentation as patients with between 3 and 12 months symptom duration.

This study is not without limitations. In view of its retrospective nature we are reliant on accurate documentation at the time of presentation. We determined symptom duration from the date of onset of first symptoms as recorded in GP letters or first clinic letters and therefore it is approximate. In addition, patients with insidious symptoms find it difficult to recall the date of onset of such symptoms and this becomes more difficult with increasing symptom duration. Recruitment of consecutive patients attending the clinic for routine review

may have resulted in a bias towards more severely affected patients being included in the study population as these patients attend for review more frequently. In addition, selection bias is likely to affect patients who presented in earlier years. As a result of increased mortality, older patients, patients with severe RA and patients with co-morbidity will be under-represented in the earlier groups studied and patients with mild, non-progressive disease are likely to have been discharged from follow up. It has been noted that no excess mortality has been detected in patients seen early in the course of their disease,¹¹ which is evidence that our observed reductions in the time to first referral are not an artefact resulting from a high mortality of such patients, and consequent under-representation in the early “year groups”.

In conclusion, we have demonstrated significant changes in medical practice, with respect to RA, over the past 10–15 years. GPs are referring patients with arthritis earlier for specialist rheumatological care and DMARD treatment is started earlier in the course of RA. Accepting that DMARD treatment should be started at the earliest opportunity, further study should be undertaken to identify ways in which we can further reduce the delay to initiation of DMARD. However, despite this it may

not be possible to treat some patients before the development of irreversible structural damage.

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