

CONCISE REPORT

Comparison between women and men with recent onset rheumatoid arthritis of disease activity and functional ability over two years (the TIRA project)

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Objective: To describe the course of recent onset rheumatoid arthritis (RA) and to compare consequences of the disease in men and women.

Methods: 284 patients with recent onset RA were followed up prospectively for two years from the time of diagnosis. Measures of disease activity (for example, 28 joint disease activity score (DAS28), C reactive protein, morning stiffness, physician's global assessment) and function outcome (for example, range of movement, hand function, walking time) were determined. The patients' self reported assessment of functional capacity (Health Assessment Questionnaire (HAQ)) and grading of wellbeing and pain (visual analogue scale) were registered. Changes over time and differences between men and women were evaluated.

Results: Improvements were seen for all variables within the first three months. Disease activity then remained unchanged. Function variables followed the same pattern during the first year, but then tended to worsen. HAQ scores were similar at baseline, but significantly worse in women than in men at the one and two year follow ups.

Conclusions: Disease activity was well managed and had improved substantially after two years, whereas function seemed slowly to deteriorate. Although disease variables were similar for men and women, functional ability (HAQ) had a less favourable course in women.

The course of rheumatoid arthritis (RA) is unpredictable, but the disease eventually leads to irreversible tissue damage, deterioration of function, progressive work disability, and socioeconomic losses.^{1–5} The most prominent decline in function occurs within the first two years and female sex predicts more severe disease.^{3, 6} During 12 months, van der Heide *et al* found that the disease course could be predicted by baseline values of disability and pain.⁶ It has also been reported that women have a more severe disease than men, including poorer function and more symptoms.⁷

In 1996 a prospective study on recent onset RA ("TIRA") was started with cooperation between 10 rheumatology units (at the hospitals of Eskilstuna, Jönköping, Kalmar, Lindesberg, Linköping, Motala, Norrköping, Oskarshamn, Väster- vik, Örebro) in southeast Sweden. The main goal was to obtain a diagnosis of RA early to enable rapid multiprofessional intervention. Further, the TIRA project aimed at forming a basis for multidisciplinary research. This study is based on the TIRA cohort and was done to describe the clinical course of recent onset RA during two years, and to compare disease consequences in women and men.

SUBJECTS AND METHODS

Subjects

Three hundred and twenty patients with recent onset (6–52 weeks) RA were included in the TIRA project between January 1996 and April 1998. The patients fulfilled four of the seven American College of Rheumatology classification criteria for RA or had morning stiffness of 60 minutes, symmetrical arthritis, and small joint arthritis (fingers/hands/wrists/feet/toes). Other inflammatory rheumatic disease, seronegative psoriasis, serious liver or renal disease were exclusion criteria. The 36 patients (19 women, 17 men) who dropped out during the subsequent two years were slightly older, reported more comorbidity, and rated lower wellbeing at inclusion than those continuing the study. Two hundred and eighty four patients (196 women, 88 men) were followed up in this study. Clinical and laboratory data were collected at inclusion and after 3, 6, 12, 18, and 24 months. At each visit the patient met a rheumatologist as well as a physiotherapist and/or an occupational therapist.

Disease

Tender and swollen joint counts were registered and the average duration of morning stiffness for the past week was estimated by the patient. The physician's global assessment of disease activity (PGA) was scored (0–4), erythrocyte sedimentation rate (ESR) and serum level of C reactive protein (CRP) analysed, and the 28 joint disease activity score (DAS28) calculated at all visits.⁸

Function

A range of movement index ("signs of functional impairment" (SOFI)) was performed, including function assessment of hand, upper and lower limbs.⁹ Walking time, with aids if necessary, was measured by asking the patient to walk 20 m as fast as possible. The Swedish version of the Health Assessment Questionnaire (HAQ) was used.¹⁰ The patients estimated average pain and general health, respectively, by means of a 100 mm visual analogue scale (VAS).

Interventions

Instituted, current, and withdrawn drug use was registered at all visits. After physical examination, the patient was offered drug treatment and multiprofessional intervention when considered necessary. In addition, all patients were given the

Abbreviations: CRP, C reactive protein; DAS28, 28 joint disease activity score; DMARDs, disease modifying antirheumatic drugs; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; NSAIDs, non-steroidal anti-inflammatory drugs; PGA, physician's global assessment of disease activity; RA, rheumatoid arthritis; SOFI, signs of functional impairment; VAS, visual analogue scale

Table 1 Changes between follow ups

	Months 0–3		Months 3–6		Months 6–12		Months 12–18		Months 18–24	
	Mean (SD)	p	Mean (SD)	p	Mean (SD)	p	Mean (SD)	p	Mean (SD)	p
Swollen joints (28)										
Women	-4.5 (6)	0.0001	-0.2 (4)	NS	-0.1 (4)	NS	-0.1 (5)	NS	-0.1 (4)	NS
Men	-5.7 (6)	0.0001	-0.7 (5)	NS	-1.1 (5)	NS	+0.4 (4)	NS	+0.4 (5)	NS
Total	-4.9 (6)	0.0001	-0.4 (5)	NS	-0.4 (4)	NS	+0.1 (4)	NS	0	NS
Tender joints (28)										
Women	-4.6 (7)	0.0001	-0.3 (5)	NS	0	NS	-0.4 (4)	NS	0	NS
Men	-4.5 (7)	0.0001	-0.6 (5)	NS	+1.1 (4)	0.04	+0.1 (5)	NS	+0.3 (5)	NS
Total	-4.6 (7)	0.0001	-0.4 (5)	NS	-0.4 (5)	NS	-0.1 (4)	NS	+0.1 (4)	NS
CRP (mg/l)										
Women	-13.7 (25)	0.0001	-0.1 (16)	NS	+1.4 (19)	NS	-1.2 (16)	NS	+0.6 (17)	NS
Men	-11.4 (28)	0.0001	-0.7 (21)	NS	-2.3 (17)	NS	+0.1 (19)	NS	-0.7 (22)	NS
Total	-13 (26)	0.0001	-0.3 (18)	NS	+0.3 (18)	NS	-0.8 (17)	NS	0	NS
ESR (mm/1st h)										
Women	-12.6 (21)	0.0001	0	NS	+0.1 (16)	NS	+0.4 (17)	NS	-1.4 (14)	NS
Men	-8.6 (20)	0.0001	-3.4 (18)	NS	-1.1 (12)	NS	+1.3 (15)	NS	+0.9 (12)	NS
Total	-13 (26)	0.0001	-0.3 (18)	NS	+0.3 (18)	NS	-0.8 (17)	NS	0	NS
Morning stiffness (min)										
Women	-58 (82)	0.0001	+7.4 (59)	NS	+5.5 (69)	NS	-8.2 (58)	0.05	+4.1 (59)	NS
Men	-33 (74)	0.0001	-7.1 (70)	NS	-3.6 (61)	NS	-5.3 (55)	NS	+7.5 (59)	NS
Total	-50.6 (81)	0.0001	+2.7 (63)	NS	+2.6 (66)	NS	-7.3 (57)	0.05	+5 (59)	NS
PGA (0–1–2–3–4)										
Women	-0.6 (1)	0.0001	-0.1 (1)	NS	-0.1 (1)	NS	-0.1 (1)	NS	0	NS
Men	-0.7 (1)	0.0001	-0.2 (1)	0.03	-0.2 (1)	0.005	+0.2 (1)	0.04	0	NS
Total	-0.6 (1)	0.0001	-0.11 (0.8)	0.03	-0.1 (0.9)	0.04	0	NS	0	NS
SOFI hand (0–16)										
Women	-0.6 (2)	0.0001	-0.1 (2)	NS	+0.2 (2)	NS	-0.1 (2)	NS	+0.2 (2)	NS
Men	-0.8 (2)	0.004	+0.1 (2)	NS	-0.4 (2)	NS	+0.5 (2)	0.02	0	NS
Total	-0.7 (2)	0.0001	0	NS	0	NS	+0.1 (2)	NS	+0.1 (2)	NS
SOFI upper (0–12)										
Women	-0.1 (1)	NS	0	NS	+0.1 (1)	NS	-0.1 (1)	NS	+0.1 (1)	NS
Men	-0.1 (2)	NS	-0.1 (2)	NS	0	NS	+0.1 (1)	NS	0	NS
Total	-0.1 (1)	NS	0	NS	+0.1 (1)	NS	0	NS	+0.1 (1)	NS
SOFI lower (0–16)										
Women	-0.7 (2)	0.0001	0	NS	+0.3 (2)	0.02	-0.1 (2)	NS	+0.3 (2)	NS
Men	-0.6 (2)	0.002	+0.3 (1)	NS	0	NS	+0.1 (2)	NS	-0.3 (2)	NS
Total	-0.6 (2)	0.0001	+0.1 (2)	NS	+0.2 (2)	NS	-0.1 (2)	NS	+0.1 (2)	NS
Walking time (s)										
Women	-1.3 (4)	0.0001	+0.2 (3)	NS	+0.3 (3)	NS	-0.1 (2)	NS	+0.3 (2)	NS
Men	-1.3 (4)	0.005	+0.2 (2)	NS	0	NS	+0.4 (2)	NS	+2.2 (14)	NS
Total	-1.3 (4)	0.0001	+0.2 (3)	NS	+0.2 (3)	NS	+0.1 (2)	NS	+0.9 (8)	NS
Pain (mm VAS)										
Women	-10.6 (30)	0.0001	0	NS	+3.8 (25)	0.05	-3.1 (25)	NS	-0.6 (25)	NS
Men	-15 (31)	0.0001	+0.5 (26)	NS	+0.1 (30)	NS	+0.1 (26)	NS	+1.5 (25)	NS
Total	-12 (30)	0.0001	+0.2 (26)	NS	+2.6 (27)	NS	-2.1 (25)	NS	0	NS
Wellbeing (mm VAS)										
Women	-8.8 (31)	0.0001	+0.8 (26)	NS	+2.4 (27)	NS	-2.2 (26)	NS	+0.4 (25)	NS
Men	-3.8 (36)	NS	+2.6 (27)	NS	+0.3 (25)	NS	-1.6 (25)	NS	+3.4 (26)	NS
Total	-7.2 (33)	0.0001	-0.3 (26)	NS	+1.8 (26)	NS	-2 (26)	NS	+1.3 (25)	NS

opportunity to participate in an educational programme carried out by the multiprofessional team.

About 2.3% of items were missing during the period, on average, with no difference between men and women.

Statistics

Differences between groups were tested by Student's *t* test for paired and unpaired samples. Proportions in subgroups were tested with Fisher's exact test. All statistical tests were two tailed. For all tests $p < 0.05$ was considered to be significant. All statistical calculations were performed using the statistical package SPSS version 9.0 for Windows.

Ethical considerations

All patients gave written informed consent to participate. The study was approved by the local ethics committees associated with the participating hospitals.

RESULTS

Comorbidity was reported for 33% of the patients, with no difference between men and women.

In the total study group, highly significant improvements were seen after three months in all variables except for upper limb function (table 1). At the 6 and 12 months' follow up only the PGA had improved further, and after one year, morning stiffness had improved. Morning stiffness had improved further at the 18 month follow up. HAQ improved significantly from baseline to 12 months ($p < 0.0001$), but not later on (fig 1B).

Differences between women and men

On average the men were older than the women ($p < 0.02$). At baseline, disease and function characteristics were similar. However, men had a worse swollen joint count (mean (SD) 10.8 (6) v 9.1 (6), $p < 0.03$), hand function (SOFI 3.4 (2.9) v 2.4 (2.6), $p < 0.005$), and upper limb function (SOFI 1.8 (2.0) v 0.9 (1.5), $p < 0.0001$) than women. Significant improvements were seen in both groups within the first three months (table 1). In men, the PGA improved further between the 3, 6, and 12 month follow up. Women, on the contrary, reported increasing pain and decreasing function in the lower limbs. Between months 12 and 18, morning stiffness decreased for women,

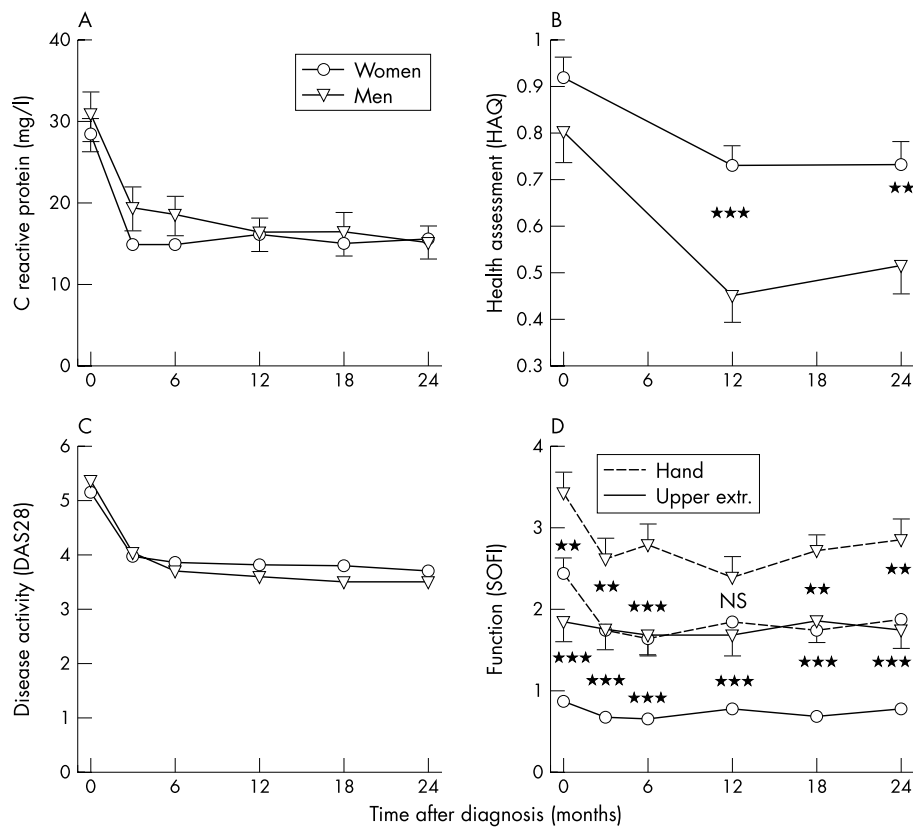


Figure 1 Variation in (A) CRP level, (B) HAQ score, (C) DAS28, and (D) hand/upper limb function (SOFI) over time in women and men. Bars represent SEM. *** $p < 0.001$, ** $p < 0.01$.

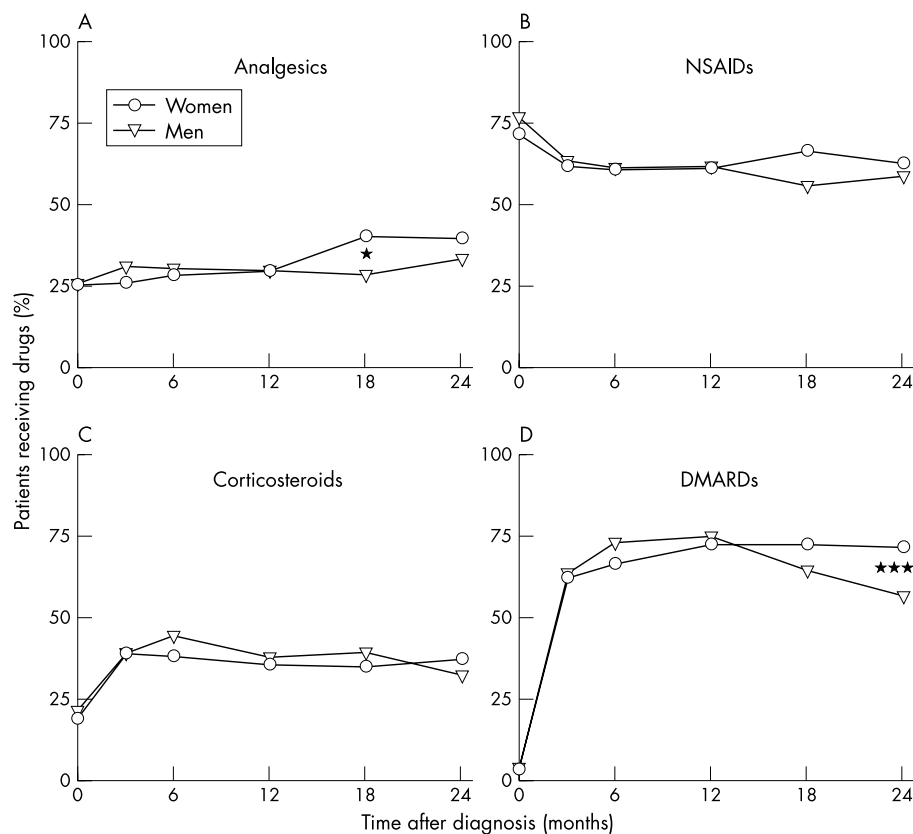


Figure 2 Variation in the percentage of patients receiving drug treatment with (A) analgesics, (B) NSAIDs, (C) corticosteroids, and (D) DMARDs at inclusion and follow up visits. * $p < 0.05$, *** $p < 0.001$.

whereas in men the PGA deteriorated. No significant changes were seen between months 18 and 24.

The changes over time in CRP, DAS28, and HAQ followed the same pattern (fig 1). The mean values for CRP and DAS28 did not differ between men and women at any time. After one year the mean HAQ score was better in men than in women ($p < 0.0001$), and the difference remained at the two year follow up ($p < 0.002$). The differences in hand and upper limb function remained throughout the study (fig 1). At one year's follow up women reported poorer wellbeing than men (means (SD) VAS 39 (25) mm *v* 32 (23) mm, $p < 0.04$).

Figure 2 illustrates drug treatment with analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and disease modifying antirheumatic drugs (DMARDs). At the three month follow up, 62% of the patients took DMARDs with no difference between women and men. At the 24 month visit the corresponding figures were 71% for women and 55% for men ($p < 0.001$). Furthermore, at the 24 month follow up, DMARD drug treatment was discontinued in more men than women ($p = 0.0072$).

DISCUSSION

This study can be regarded as a Swedish reference for baseline data, general interventional strategies, and two year clinical course in recent onset RA during 1996–2000. The most remarkable improvements occurred rapidly and were similar in women and men. All measurements reflecting disease activity improved considerably within three months and then remained stable. The reasons for the rapid improvement are not immediately evident, because we are describing the net effects of a multitude of contributing circumstances. Early institution of DMARDs is one likely explanation. Surprisingly, and somewhat disappointingly, however, despite the intention to institute DMARDs rapidly, only about 60% took such drugs three months after the diagnosis of RA. Notably, fewer men than women were treated with DMARDs after 24 months. The reason for this is not obvious, but men might have had less functional impairment than women, as reflected by the HAQ.

Initial improvement in disease activity and function followed by deterioration after one year has been reported previously.^{11–12} Wiles *et al* found that a 12 month HAQ predicts disability after five years better than baseline HAQ.¹³ In accordance with previous reports,^{13–15} we found no differences between women and men in the HAQ at diagnosis, but it became (and remained) much worse in women after one year. Although the swollen joint count was significantly higher in men at the start of the study, no differences in the DAS28 were found at any time between men and women, which contrasts with the finding of Kuiper *et al*.¹⁴ However, in contrast with men, we found that women reported worsening pain and wellbeing over time.

Measured by the SOFI index, hand and lower limb function showed considerable initial improvements, probably because the baseline scores of the hands/legs were worse than those of the arms (SOFI upper). At all times the results for the functioning of hands and upper limbs were much worse for men than for women, possibly because the men were older. Considerable improvements were seen both in men and women, although the differences between men and women remained.

To conclude, function in recent onset RA seemed to deteriorate slowly, despite the fact that disease activity was well managed and had improved substantially in most patients two

years after diagnosis. Although disease variables were similar for men and women, functional capacity measured with the HAQ had a less favourable course in women, who also had DMARDs more frequently prescribed.

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