Predictors of outcome at two years in patients with rheumatoid arthritis[1]

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Summary: The prognostic value of clinical and laboratory measures in 72 patients with rheumatoid arthritis (RA), seen initially within 18 months of disease onset, in predicting function outcome after a further two years was assessed. Limitation of wrist extension was associated with a slow disease onset, a high articular index and a high latex titre. A reduction in global functional capacity, as measured by the Stanford Health Assessment Questionnaire, was associated with a high initial articular index and a high latex titre. Neither outcome was associated with the initial level of acute phase reactants nor with patient or physician's initial assessment of disease activity. It is concluded, first, that factors predicting early disability outcome in RA are not identical to those associated with continuing disease activity; and secondly, that patients' and physicians' judgment of disease activity at diagnosis do not carry any prognostic value for functional outcome two years later.

Introduction

Previously reported studies on the prognostic value of clinical and laboratory variables in patients with rheumatoid arthritis (RA) have tended to use measures of disease activity, for example joint tenderness, early morning stiffness or RA latex titre, as part of the assessment of disease outcome (Jacoby *et al.* 1973, Fleming *et al.* 1976a,b, Masi *et al.* 1976).

The presence of deformity and level of function are probably of more relevance to the patient, but established function measures such as Steinbocker's Functional Capacity (Steinbocker *et al.* 1949) are probably too crude to be of value in a prospective study. The Stanford Health Assessment Questionnaire (HAQ) (Fries *et al.* 1980), which has been validated for use in RA patients in the United Kingdom (Kirwan & Reeback 1983), provides a potentially more useful tool in this respect.

We have therefore investigated the prognostic value of standard clinical and laboratory measures in patients with early RA in predicting early deformity and disability.

Methods

Patients: Patients were recruited from three rheumatology departments. Those with classical or definite RA (Ropes *et al.* 1958) as judged by one observer (JR), who were within 18 months of first onset of symptoms and aged over 18, were eligible for entry. Seventy-six patients were entered, of whom 72 have been followed up for at least 2 years. There were 24 males and 48 females, with an overall median age of 51 (range 22 to 71) and a mean duration of symptoms of 11 months (range 3 to 18).

Baseline measures: All clinical measurements were carried out by a single observer (JR). The mode of disease onset (days, weeks or months), the patient's and physician's assessment of disease activity (nil, mild, moderate or severe) were recorded together with the duration of early morning stiffness (EMS) and a Ritchie articular index (AI) (Ritchie *et al.* 1968). Blood

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Table 1. *Wrist extension by mode of onset*

Wrist extension (degrees)	Disease onset		
	Days	Weeks	Months
Below 70 (n = 17)	3	1	13
Above 70 (n = 55)	18	17	20
Total	21	18	33

χ^2 trend 1df = 5.48, $P = 0.019$

was taken for erythrocyte sedimentation rate (ESR) (Westergren) and C-reactive protein (CRP) (Rocket Assay) and serum was also assayed for latex titre.

Outcome measures: Limitation of wrist extension was measured in preference to grip strength as being a more objective outcome. It is also aimed to compare the radiological changes in the carpus to the limitation recorded. Extension was measured both by goniometer and by eye. The nature of the measurement is such that accuracy by either method is difficult to achieve and thus a more valid approach was to divide patients into one of two groups: those with and without one wrist with under 70 degrees of extension. This classification done by eye was highly repeatable and was validated by goniometer. The HAQ score was calculated from the degree of self-reported difficulty for eight different groups of activities. Each activity was scored from 0 (no problem) to 3 (unable to do), though the use of an aid or appliance automatically gives a score of 2 for that activity. The score for each group was the highest of its constituent questions. The mean score from the eight groups of activities is calculated giving a value between 0.00 and 3.00.

Analysis: The relationships of limitation of wrist extension to mode of onset, patient and physician assessment of disease activity, EMS and latex titre were assessed with the χ^2 test for trend. The mean ESR, CRP and AI, which were continuous variables with a near Gaussian distribution, were compared in the two wrist extension groups using Student's *t* test and the 95% confidence interval calculated. The HAQ scores also showed a Gaussian distribution and the strength of any association with AI, CRP and ESR estimated from Pearson's correlation coefficient. The relationship of HAQ to the non-continuous baseline variables was analysed using the F test for trend. All analyses were carried out using the statistical packages SPSS (Nie *et al.* 1975) and BMDP (Dixon & Brown 1979).

Table 2. *Wrist extension by initial assessment of disease activity by patient and physician*

Wrist extension (degrees)	Patient assessment				Physician assessment			
	Nil	Mild	Moderate	Severe	Nil	Mild	Moderate	Severe
Below 70 (n = 17)	0	3	10	4	0	6	9	2
Above 70 (n = 55)	0	24	25	6	2	30	21	2
Total	0	27	35	10	2	36	30	4

χ^2 trend 1df* = 3.61 (NS)
*ignoring 'Nil' group

χ^2 trend 1df** = 3.47 (NS)
**collapsing 'Nil' and 'Mild' groups to single category

Table 3. *Wrist extension by initial latex titre*

Wrist extension (degrees)	Latex titre			
	1/40	1/80	1/160	1/320
Below 70 (n = 17)	5	2	3	7
Above 70 (n = 55)	33	6	7	9
Total	38	8	10	16

χ^2 trend ldf = 6.06, P = 0.014

Table 4. *Wrist extension and acute phase reactants*

Wrist extension (degrees)	ESR		CRP	
	mean	s.e.	mean	s.e.
Below 70 (n = 17)	47.8	10.2	34.5	6.9
Above 70 (n = 55)	35.5	3.9	27.5	5.8
Difference	14.3	NS	7.0	NS
95% confidence interval	−7.1	+35.7	−10.7	+24.7

Results

There were 17 patients with at least one wrist with limited extension compared to 55 with no such limitation. The former were more likely to be associated with a slow disease onset (Table 1) but not with initial assessment of disease activity by either patient or physician (Table 2). The mean initial AI in the limited wrist group was 9.5 (s.e. 1.0) which was higher than in the normal wrist group: 6.4 (s.e. 0.4). This difference was highly significant ($P < 0.01$) with a 95% confidence interval of 1.0 to 5.2. There was no difference between the groups in EMS (χ^2 trend 0.95, NS). The laboratory data show an increased likelihood of limited wrist extension with increasing latex titre (Table 3). The ESR and CRP were higher, though not significantly so, in the limited wrist group (Table 4). The 95% confidence intervals, however, were wide (Table 4).

The mean HAQ score was 0.72 (s.d. 0.67, range 0–1.88), confirming the overall good preservation of function in the majority of patients at this stage. The HAQ score, however, was not related to mode of disease onset, duration of EMS, and neither patient's nor physician's assessment of disease activity (Table 5). The initial latex titre had a weak but significant association to subsequent HAQ (Table 6). There was also a weak but statistically significant association between HAQ score and AI ($r = +0.38$, $P < 0.05$) but no association with either ESR ($r = +0.11$, NS) or CRP ($r = +0.17$, NS). The weak association with AI persisted after allowing for the weak effects of ESR and CRP in a stepwise multiple regression ($r = +0.35$, $P < 0.05$).

Table 5. *HAQ score by baseline clinical variables*

Variable	Category	(n)	Mean HAQ (s.d.)	F test for linearity
Mode of onset	Days	(21)	0.72 (0.55)	F = 0.08 (NS)
	Weeks	(18)	0.68 (0.56)	
	Months	(33)	0.75 (0.65)	
Duration of EMS (min)	15	(12)	0.86 (0.57)	F = 0.34 (NS)
	15–60	(27)	0.61 (0.62)	
	90–120	(14)	0.92 (0.69)	
	120	(19)	0.63 (0.59)	
Physician initial assessment disease activity	Nil	(2)	10.7 (0.26)	F = 2.39 (NS)
	Mild	(36)	0.50 (0.48)	
	Moderate	(30)	0.89 (0.61)	
	Severe	(4)	1.24 (0.79)	
Patient initial assessment disease activity	Nil	(0)	—	F = 2.53 (NS)
	Mild	(27)	0.52 (0.52)	
	Moderate	(35)	0.85 (0.61)	
	Severe	(10)	0.76 (0.62)	

Table 6. HAQ score by initial latex titre

Latex titre	No.	Mean HAQ	(s.d.)
1/40	38	0.68	(0.57)
1/80	8	0.69	(0.63)
1/160	10	0.74	(0.59)
1/320	16	0.81	(0.64)

$F = 2.98$, $P < 0.05$

Discussion

The outcomes were measured in this study approximately three years after disease onset and thus these data cannot be extended to longer-term outcome, though the study is continuing.

Both articular index and latex titre at diagnosis were prognostic both for later wrist deformity and functional impairment, although in the case of articular index the effects, though statistically significant, were weak and of limited clinical significance. Neither the patient's nor physician's judgment of disease activity at diagnosis is predictive for these outcomes, but in the latter instance may reflect a judgment policy which might be alterable in the light of the results from this study (Kirwan *et al.* 1983).

It seems possible that a larger study might have produced a significant predictive effect for ESR or CRP, but the wide inter-individual variation for both is such as to make individual prediction in a clinical situation unlikely to be of value. Others have previously reported that those baseline clinical and laboratory measures, which were of little prognostic use in the present study in predicting functional outcome, are nevertheless associated with future disease activity (Jacoby *et al.* 1973, Fleming *et al.* 1976a,b, Masi *et al.* 1976). Thus it is possible that there is a dichotomy in the early stages of RA and that many of the features signifying continuing disease activity may not relate to early functional outcome.

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