Clinical assessment of disease activity in rheumatoid arthritis: evaluation of a functional test

A A KALLA,¹ T J v W KOTZE,² O L MEYERS,¹ AND N D PARKYN³

From the ¹Department of Medicine, Rheumatic Diseases Unit, UCT; the ²Department of Medical Biostatistics, MRC, South Africa; and the ³Department of Information Technology, University of Cape Town

SUMMARY A cross sectional analysis of the correlation between clinical, laboratory, and radiological markers of disease activity in 98 patients with classical rheumatoid arthritis (RA) is reported. The median age was 38 years, the median age at onset of disease 29 years, and the median duration of disease seven years. The Keitel function test (KFT) showed good correlation with the Ritchie articular index (RAI) ($p < 0.0001$; $r = 0.5$) and the disability questionnaire (DQ) ($p < 0.0001$; $r = 0.6$). The RAI and DQ correlated weakly with laboratory variables, while the KFT showed significant correlation with the erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and plasma viscosity (PV) ($p < 0.001$; $r = 0.4$; 0.3 ; 0.4). Only the KFT showed significant correlations with bone mass measurements ($p < 0.01$; $r = -0.3$; -0.4), and the Larsen index at the right wrist ($p < 0.0001$; $r = 0.4$). Consensus analysis suggested that the KFT is a useful single clinical test of disease activity in RA. The hand functional index (HFI), a component of the KFT, showed significant correlation with the total KFT ($r = 0.9$). Prospective drug trials are needed to establish the value of the HFI in the monitoring of patients with RA.

Key words: rheumatoid activity monitoring, hand functional index, Keitel function test.

The assessment of disease activity in rheumatoid arthritis (RA) is complicated by the overlap of process and outcome measurements.¹ Since the systemic index of Lansbury (LSI) was published² there have been many reports about its use, but hardly any comparisons with later indices. Numerous statistical approaches have been recommended in the interpretation of research.^{3–5} A 'weighted' articular index has recently been recommended for clinical use.⁶ A recent study introduces the concept of consensus analysis in evaluating changes in the natural history of the disease, comparing a number of laboratory markers.⁷ These reports outline the need for an all-encompassing clinical test of disease activity in RA.

Functional assessment is not a standard component of composite indices.⁸ The Steinbrocker classification of 1948 (American Rheumatism Association (ARA)) has been the standard reference of functional assessment in drug trials.⁹ The Keitel function test (KFT)¹⁰ has been shown to have a high coefficient of generalisability in RA,¹¹ but it has not

been studied as a marker of disease activity. It has been found to be a more reproducible method of clinical assessment than the Ritchie articular index (RAI),¹² which is often a component of protocols evaluating drug treatment.¹³

Several attempts have been made to relate radiological changes to laboratory and clinical variables.^{14 15} The consensus seems to be that 'remission inducing' drugs improve clinical and laboratory variables¹⁶ but do not seem to influence radiological progression.¹⁴ Several reasons may explain this lack of correlation. The most obvious is that these variables are measuring different pathogenetic processes.

Against this background, a cross sectional study was undertaken to evaluate the correlation of measures of functional ability with clinical, laboratory, and radiological assessments of rheumatoid arthritis. Consensus analysis was used to find the most suitable functional test which would convey information regarding all these important changes of the disease.

Materials and methods

The protocol was approved by the research and

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Correspondence to Dr A A Kalla, PO Box 195, Tokai 7966, Republic of South Africa.

ethics committee at the University of Cape Town. It was completed over a 12 month period. The study was confined to a premenopausal, young group of subjects who were independently ambulant, as age,¹⁷ menopause,¹⁸ and physical activity¹⁹ have a significant effect on early radiological changes (osteoporosis), while laboratory changes (erythrocyte sedimentation rate (ESR)) are influenced by age.²⁰

Ambulant patients with definite or classical RA²¹ under 50 years of age, who were attending the arthritis clinics of the rheumatic diseases unit at the University of Cape Town, were selected for study. A protocol was designed to record demographic data, menopausal status, duration of disease, criteria for classification of disease, work capacity, and family history of arthritis. Age at onset was taken as the time of first onset of symptoms of the disease. Patients were evaluated once only.

Disease activity was assessed clinically in several ways, by a single observer (AAK): (a) pain was recorded by the patient on a 10 cm visual analogue scale²²; (b) the patient similarly graded the severity of the disease on a 10 cm visual analogue scale; (c) duration of early morning stiffness²³ was graded on a scale of 0–5, where 0=less than 45 minutes, 1=45 min–2 hours, 2=2–3 hours, 3=3–4 hours, 4=4–5 hours, and 5=5 hours or more; (d) hours to onset of fatigue²³ were graded on a scale of 1–4, where 1=less than 2 hours, 2=2–4 hours, 3=4–6 hours, 4=6 hours or more, (e) the presence or absence of night pain²³ was recorded; (f) warm and swollen joints were individually counted; (g) the response to pain on pressure was recorded for the RAI¹²; (h) the mobility score²⁴ was determined by a disability questionnaire (DQ), scaling the ease with which 24 activities of daily living could be carried out; (i) the KFT,¹⁰ based on the observed performance of 24 tasks, was graded according to degree of performance by the patient; (j) global assessment of disease activity was based on the physician's clinical findings and classed as nil, mild, moderate, and severe; (k) the LSI² was calculated using the grip strength, duration of early morning stiffness and hours to onset of fatigue. The articular index and use of aspirin were not included in deriving the modified index. Grip strength was measured with the Mannefeldt manometer (mmHg).

The KFT was arbitrarily divided, according to the major joints tested, into three groups of joints representing hands and wrists, shoulders, and lower limbs respectively. The hand and wrist component of the test, conveniently named the hand functional index (HFI), is shown in Appendix A.

Several laboratory measures of disease activity were simultaneously tested. The Westergren ESR (mm/h), C reactive protein (CRP) (g/l) (rocket

electrophoresis), and plasma viscosity (PV) (centipoise) (capillary viscometer) were recorded for comparison with the above clinical markers. The modified LSI was calculated as described. Radiological evaluation was performed on both hands radiographed at a tube distance of 100 cm; exposure and development times were standardised for this study. Bone mass was calculated using a digitiser for measurement of inner and outer diameters at the midshafts of six metacarpals. The methods of Barnett and Nordin,²⁵ Dequeker,²⁶ Exton-Smith *et al.*,²⁷ and Horsman and Simpson²⁸ were used in the calculation. The percentage cortical area and six metacarpal hand score were selected as the measures of bone mass as these are considered to be the most precise.^{26–28} The carpometacarpal ratio was calculated by the method of Trentham and Masi.²⁹ The right wrist was then graded for severity according to the modified index of Larsen *et al.*³⁰ All radiological evaluations were performed by a single observer (AAK).

STATISTICAL METHODS

The data were recorded and checked on the IBM personal computer. These were then transcribed to the mainframe computer at the Biostatistics Institute (MRC), which was used for all the statistical calculations. The SAS package^{31–32} and BMDP statistics software³³ were used for all the analyses. Spearman rank correlations were calculated for the various clinical, laboratory, and radiological variables. The results of the ordinal (continuous) variables only are reported as these are probably the most reliable. The respective correlations were cross-tabulated (correlation matrix), which provided easy visualisation of the rank correlation coefficient (*r*) as well as the probability that the correlation was equal to zero (*p* value). The consensus value was the arithmetic average of the ranks of all tests other than the test under scrutiny. Consensus analysis was performed for the modified LSI, ESR, PV, and Larsen index at the right wrist.

Results

The study group consisted of 98 patients (28 male, 70 female), median age 38.1 years (range 18–50), and with a median duration of disease of seven years (range six months–28 years). The ESR (range 1–150 mm/h) was raised in 63%, the CRP (range 0–11 g/l) was raised in 60%, and the PV (range 1.39–3.03 cP) was raised in 80% of the patients at the time of study.

Table 1 shows the ARA classification of functional disability⁹ as well as the UK functional classification.³⁴ In the same table the range for the total Keitel score

and DQ in the respective ARA and UK classes is also shown. It can be seen that there is a wide range of difficulty with activities of daily living, which are not detected in the narrow ARA or UK classification of disability.

The Spearman rank correlation matrix (Table 2) shows the correlation coefficient (r) in the upper triangular matrix and the p value in the lower triangular matrix. The table shows that all the functional tests correlate significantly with the RAI ($p<0.0001$).

Table 3 examines the possible clinical usefulness of the three tests in evaluating disease activity. The DQ and KFT seem to differ in the way in which they relate to these other clinical tests of inflammation, particularly with respect to changes such as warmth or swelling of a joint, early morning stiffness, and hours to onset of fatigue. The LSI (a composite index of disease activity including ESR) correlated impressively ($p<0.0001$) with the three clinical tests (RAI, DQ, KFT) ($r=0.6$; 0.6 ; 0.5 respectively). When the ARA and UK functional classifications were compared with the same clinical variables as above, significant correlations were seen with all the tests.

Table 1 American Rheumatism Association (ARA) and UK functional classification of activities of daily living in 98 subjects with RA*

Functional classification	n	Range of KFT†	Other tests (DQ)†
ARA: 1	22	5-40	0-51
2	76	13-86	6-135
UK: 1	16	5-40	0-51
2	34	6-64	0-99
3	48	18-86	6-135

*The more recent test of global disability (DQ) is shown for comparison.

†KFT=Keitel function test; DQ=disability questionnaire.

Table 2 Correlation matrix showing relation between Ritchie articular index (RAI), disability questionnaire (DQ), and Keitel function test (KFT)*

	RAI	DQ	KFT	ARA	UK
RAI		0.6	0.5	0.5	0.6
DQ	0.0001		0.6	0.6	0.7
KFT	0.0001	0.0001		0.6	0.6
ARA	0.0001	0.0001	0.0001		0.9
UK	0.0001	0.0001	0.0001	0.0001	

*The correlation coefficient (r) is shown in the upper and the p value in the lower triangular matrix (Spearman). Also shown are the comparisons with the older functional classifications (ARA, UK).

Table 3 Comparison of relations of Ritchie articular index (RAI), disability questionnaire (DQ), and Keitel function test (KFT) with standard clinical measures of disease activity in RA

	RAI	DQ	KFT	HFI*
SVAS* r	0.3	0.5	0.4	0.2
p	0.01	0.0001	0.0001	0.02
PVAS* r	0.4	0.5	0.2	0.05
p	0.0001	0.0001	0.03	NS
Fatigue r	-0.4	-0.3	-0.3	-0.1
p	0.0001	0.002	0.01	NS
EMS* r	0.4	0.4	0.3	0.3
p	0.0001	0.0001	0.003	0.008
Physician r	0.5	0.3	0.4	0.5
p	0.0001	0.01	0.0002	0.0001
Warm r	0.3	0.2	0.3	0.34
p	0.01	NS	0.003	0.0004
Swollen r	0.3	0.2	0.4	0.5
p	0.001	NS	0.0001	0.0001
LSI* r	0.6	0.6	0.5	0.4
p	0.0001	0.0001	0.0001	0.0001

*HFI=hand functional index; SVAS=severity of disease on a visual analogue scale; PVAS=pain on a visual analogue scale; EMS=early morning stiffness; LSI=Lansbury's systemic index.

Table 4 shows the relations between the RAI, DQ, KFT, and the three standard laboratory markers of disease activity. The RAI correlated significantly with the ESR ($p<0.05$), but not with the CRP or PV. The DQ correlated significantly with the ESR ($p<0.01$) and PV ($p<0.005$), but not with the CRP. The KFT, on the other hand, correlated significantly with all three laboratory tests ($p<0.0001$; $p<0.002$; $p<0.0002$). The HFI also correlated with all three laboratory tests of disease activity in RA.

Table 5 shows the correlation of RAI, DQ, and KFT with radiological markers. The RAI and DQ did not show a significant relation with any of the radiological markers used in this study. Although

Table 4 Comparison of relations of Ritchie articular index (RAI), disability questionnaire (DQ), and Keitel function test (KFT) with laboratory markers of disease activity and severity in RA

	RAI	DQ	KFT	HFI*
ESR* r	0.2	0.3	0.4	0.4
p	0.02	0.01	0.0001	0.0003
CRP* r	0.2	0.1	0.3	0.3
p	NS	NS	0.002	0.01
PV* r	0.1	0.3	0.4	0.4
p	NS	0.005	0.0002	0.0003

*HFI=hand functional index; ESR=erythrocyte sedimentation rate; CRP=C reactive protein; PV=plasma viscosity.

the carpometacarpal ratio did not correlate significantly with any of the clinical tests ($p>0.05$), the KFT was the only test which approached significance ($p<0.08$). The KFT was also the only test which showed a significant correlation with metacarpal bone mass and the Larsen index at the right wrist. In addition, the HFI showed more significant correlations with the above radiological markers than did the RAI or DQ.

The component Keitel scores correlated significantly with the total score ($p<0.0001$) (Table 6). The variation in the HFI explained the largest proportion of the variation in the total score ($r=0.873$). In this group of subjects the HFI was able to predict over 75% of the variation in the total KFT (r^2).

Consensus analysis showed that the three clinical tests (RAI, DQ, KFT) ranked comparably against the LSI. The RAI was the weakest test in the ranking against the ESR, PV, and Larsen index at the right wrist. The KFT superseded the consensus value in each ranking process. The results of the comparison of RAI and KFT with the respective consensus is depicted in the histograms in Fig. 1.

Table 5 Comparison of the relations of Ritchie articular index (RAI), disability questionnaire (DQ), and Keitel function test (KFT) with metacarpal bone mass (CA%, M6HS),* carpometacarpal ratio (CMR), and the Larsen index at the right wrist

		RAI	DQ	KFT	HFI*
CA%	r	-0.1	-0.04	-0.3	-0.2
	p	NS	NS	0.002	0.05
M6HS	r	-0.1	-0.1	-0.4	-0.2
	p	NS	NS	0.0006	0.02
CMR	r	0.1	0.01	-0.2	-0.1
	p	NS	NS	0.08	NS
Larsen's index	r	0.1	0.1	-0.4	0.3
	p	NS	NS	0.0001	0.002

*CA%=percentage cortical area; M6HS=six metacarpal hand score; HFI=hand functional index.

Table 6 Relation between the Keitel components and the total Keitel function test (KFT) in the patients with RA*

	HFI†	Shoulder	Lower limb	KFT
HFI		0.5	0.4	0.9
Shoulder	0.0001		0.4	0.7
Lower limb	0.0001	0.0001		0.7
KFT	0.0001	0.0001	0.0001	

*The correlation coefficient (r) is shown in the upper and the p value in the lower triangular matrix.

†HFI=hand functional index.

Fig. 1 Histograms showing the results of consensus analysis. The figure compares the relationship between the KFT and RAI and the respective consensus ranking derived from the RAI, KFT, DQ, and HFI. The tests were ranked with respect to the modified LSI, ESR, PV, and Larsen index at the right wrist. (KFT=Keitel function test; RAI=Ritchie articular index; DQ=disability questionnaire; HFI=hand functional index; LSI=Lansbury systemic index; ESR=erythrocyte sedimentation rate; PV=plasma viscosity.)

Discussion

It has been pointed out by several authors that metacarpal bone mass is lost at a disproportionate rate in some individuals over the age of 50 years.^{17 25 26} The ESR is known to rise with age, which is one reason why the PV is recommended as a more objective marker of inflammatory activity.^{35 36} It has also been shown that functional disability is greater in patients with longer duration of arthritis.^{19 37} For all these reasons it was considered essential to exclude patients over the age of 50 years and those who were severely incapacitated. In this way the significance of correlations between variables need not be clouded by the confounding effects of age and physical activity on laboratory and radiological variables.

The LSI² needs to be modified for use in clinics such as ours, where salicylates are rarely used in the management of RA. Use of a weighted articular index is also complex and time consuming. The RAI¹² has been widely used for its simplicity and was chosen as the articular index for this study. It may be regarded as the 'gold standard' in clinical studies. Thermography is a reproducible technique of measuring activity in RA,³⁸ but it is not generally available for use in a busy practice. The ARA criteria for remission include the absence of fatigue, morning stiffness, and night pain.²³ These variables are relatively subjective, possibly making them

unsuitable as markers of activity in RA, despite their wide clinical application. Also, physicians are known to be inconsistent in their clinical judgment of disease activity,³⁹ and a simple, reproducible, meaningful clinical test is needed. When some of these 'external' tests were used, two thirds (or more) of our patients had active disease.

This seems to be the first comparison of the LSI with other disease activity markers (RAI). Ritchie *et al* showed good reproducibility between three observers,¹² while other workers have been unable to reproduce the test adequately between observers.¹¹ In fact, the RAI was recently modified to improve the interobserver reproducibility.⁴⁰

Although the KFT was developed as a global measure of function in RA,¹⁰ and the DQ as a measure of mobility,²⁴ it appears from Table 3 that these functional tests also measure disease activity. The significant correlation between the above tests (RAI, DQ, KFT) and the LSI suggests that they are all suitable markers of systemic disease. It is important to note that the HFI also correlated significantly with the LSI.

Although both functional tests (DQ, KFT) correlate significantly with the RAI, the tests are not predictive of each other ($r < 0.8$). The significant correlation between the RAI, DQ, and KFT confirms the clinical impression that active disease has a negative effect on functional capabilities. Caution is required in the interpretation of correlations where the dependent variable has a narrow range (ARA, UK functional classifications) as the predictive value (r^2) may need to exceed 50% to be meaningful. The broader ranges of the KFT and DQ suggest that they may be suitable functional tests for comparison with the RAI, which is established as a clinical test of global disease activity in RA. It is interesting that the DQ and KFT not only test function but also give a significant reflection of disease activity. The ARA and UK functional classifications also show significant correlations with the RAI. They explain less of the variation in RAI than might be expected by chance, however.

Our findings of a good correlation between the KFT and RAI are the first such report. Although all three global tests showed good correlation with other clinical markers of disease activity in RA, it is interesting that the DQ did not correlate significantly with warmth or swelling of the joints. Table 3 shows also that the DQ reflected equally the patient's impression of severe disease and pain, while the KFT correlated more closely with the patient's impression of disease severity than pain.

Mielke and Deicher showed the limited significance of laboratory variables in assessing disease activity in RA.⁴¹ The significant correlation between

these clinical tests (RAI, DQ, KFT) and the ESR could be anticipated from the positive correlation with the LSI. The lack of correlation between the RAI and CRP confirms a recent report.⁷ The DQ also showed no significant correlation with the CRP, while the KFT correlated significantly with all three laboratory tests (Table 4). This suggests that the KFT may be a more useful global clinical test of disease activity than the DQ or RAI.

Several workers have commented on the lack of correlation between improvement in clinical and laboratory variables and radiological change in the same patients.^{14 15} Some of the difficulties in assessing disease activity radiologically may be due to the confusion in differentiating 'process' changes from 'outcome' measures.^{1 42}

Capell questioned the type of radiological changes used in evaluating drug responses in RA.⁴³ Scott and Bacon have shown that the erosion in RA is irreversible, except under unusual circumstances.¹⁴ Buckland-Wright, using the technique of microfocal radiography, has shown that early erosions can be scored and monitored for change.⁴⁴ Schorn has shown an increase in the metacarpal index with penicillamine treatment, confirming the sensitivity of bone mass measurement as a suitable end point for monitoring the effects of remission inducing drugs.⁴⁵

Table 5 shows that the RAI and DQ did not correlate significantly with any of the radiological variables recorded in this study. Our finding of an inverse relation between KFT and bone mass confirms the recent observation that bone mass falls with increasing disability, despite adequate ambulation.¹⁹ Although none of the three tests showed a significant correlation with the carpometacarpal ratio, the KFT came closest at the 10% level of confidence. The KFT was also the only test which showed a significant correlation with the Larsen index at the right wrist.

The KFT is an unacceptably time consuming test and not suitable for a busy clinic. When the test was subdivided into three component parts it was shown that in these subjects global involvement was common. The results showed that the total KFT could be adequately predicted by a test of hand function (HFI) alone ($r = 0.873$; $p < 0.0001$). This is a tremendous saving on the time taken to complete the full KFT, and is less than the time taken to perform the RAI or DQ. The preceding tables showed that the HFI correlated significantly with several clinical, laboratory, and radiological changes in RA. In a busy clinic time is often a limiting factor. The RAI can be performed within five to seven minutes,¹² whereas the KFT requires about 12 minutes.¹⁰ The HFI is performed in less than one

minute! It is, therefore, very suitable for clinical use, particularly as it correlates significantly with other disease activity markers.

When consensus analysis⁶ was used the KFT fulfilled several of the requirements for a clinical test of disease activity in RA: (a) it was conveniently divided into component parts which show strong correlations with the total test score; (b) of the three main clinical tests studied, it showed correlation with semiobjective tests such as the ESR, CRP, and PV; (c) it correlated also with bone mass measurements and the Larsen index at the right wrist, suggesting that osteoporosis may be a significant end point in the radiological evaluation of the effects of remission inducing drugs in the treatment of RA, as suggested by Schorn *et al.*⁴⁵

Fries regards disability as an essential dimension in the measurement of outcome.⁴²⁻⁴⁶ Our findings suggest that the KFT is also a process variable. The sensitivity to change needs to be validated in prospective studies (analogous to earlier evaluations of change in RAI, ESR, CRP, and radiological abnormalities of RA) in drug trials. The first such study with auranofin was able to show significant improvement in KFT as one measure of outcome.⁴⁷ Further studies are needed to establish the full potential of the HFI as a measure of outcome in RA.

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Appendix A: Hand functional index (HFI)

Test Items	Grading		Criteria
	Right	Left	
1. Tip of thumb touches hypothenar of 5th finger	0	0	Test performed fully and with no delay
	1	1	Test performed fully but with effort or delay, or both
	2	2	Tip of thumb touches proximal phalanx 3 and 4
2. Bending of 2nd finger	3	3	Neither realised
	0	0	Clutched normally
	1	1	Cannot be bent fully; tip reaches palm
...3rd....4th....5th fingers	2	2	Fingertip does not reach palm
			As above
6. Forearm held horizontal, palmar surfaces pressed together point upward	1	1	Test performed fully and no delay
	2	2	Test performed fully with effort or delay, or both
	3	3	Volar and dorsal flexion of wrist 45°

7. Forearm held horizontal, dorsal surfaces pressed together point downward	1	1	Fully; no delay
	2	2	Fully; with effort or delay, or both
	3	3	Palmar and ventral flexion of wrist 45°
8. Both backs of hands simultaneously on the table; elbows held rectangularly; ulnar margin of hand lifted	0	0	Performed fully
	1	1	Backs of hands on table; margin cannot lift
	2	2	Backs of hands not full on table
9. Radial margins of hands simultaneously placed on table; thumb points downward before table edge; planes of hands not inclined inward; no lateral bending of trunk	0	0	Performed fully
	1	1	Planes of hands perpendicular; cannot be inclined inward
	2	2	Planes of hands not vertical

References

- Fries J F, Spitz P W, Kraines R G, Holman H R. Measurement of patient outcome in arthritis. *Arthritis Rheum* 1980; **23**: 137-45.
- Lansbury J, Haut D D. Report of a 3-year study on the systemic and articular indexes in RA. *Arthritis Rheum* 1958; **1**: 505-20.
- McGuire R J, Wright V. Statistical approach to indices of disease activity in RA—with reference to a trial of indomethacin. *Ann Rheum Dis* 1971; **30**: 574-80.
- Mallya R K, Mace B E W. The assessment of disease activity in RA using a multivariate analysis. *Rheumatology and Rehabilitation* 1981; **20**: 14-17.
- Bombardier C, Tugwell P. A methodological framework to develop and select indices for clinical trials: statistical judgment approaches. *J Rheumatol* 1982; **9**: 753-7.
- Thompson P W, Silman A J, Kirwan J R, Currey H L. Articular indices of joint inflammation in rheumatoid arthritis. *Arthritis Rheum* 1987; **30**: 618-23.
- Bull B S, Levy W C, Westengard J C, *et al.* Ranking laboratory tests by consensus analysis. *Lancet* 1986; **327**: 80.
- Scott D L, Farr M, Hawkins C F, Wilkinson R, Bold A M. Serum calcium levels in rheumatoid arthritis. *Ann Rheum Dis* 1981; **40**: 580-3.
- Steinbrocker O, Traeger C H, Batterman R C. Therapeutic criteria in rheumatoid arthritis. *JAMA* 1949; **140**: 659-62.
- Keitel W, Hoffman H, Weber G, *et al.* Ermittlung der prozentualen funktionsminderung der Gelenke durch einen Bewegungsfunktions-test in der Rheumatologie. *Deutsche Gesundheitswesen* 1971; **26**: 1901-3.
- Eberl D R, Fasching V, Rahlfs V, *et al.* Repeatability and objectivity of various measurements in rheumatoid arthritis: a comparative study. *Arthritis Rheum* 1976; **19**: 1278-86.
- Ritchie D M, Boyle J A, McInnes J M, *et al.* Clinical study with an articular index for the assessment of joint tenderness in patients with RA. *Q J Med* 1968; **37**: 393-406.
- Rhind V M, Bird H A, Wright V. A comparison of clinical assessments of disease activity in RA. *Ann Rheum Dis* 1980; **39**: 135-7.
- Scott D L, Bacon P A. Joint damage in RA: radiological assessment and the effects of anti-rheumatic drugs. *Rheumatol Int* 1985; **5**: 193-9.
- Scott D L, Grindulis A, Struthers G R, Coulton B L, Pope A J, Bacon P A. Progression of radiological changes in rheumatoid arthritis. *Ann Rheum Dis* 1984; **43**: 8-17.
- Dixon J S, Wright V. Outcome measures and anti-rheumatic drugs: a critical appraisal. *Clin Exp Rheumatol* 1986; **4**: 1-2.
- Avioli L. Age-related changes in bone mass. In: Aitken M, *et al.* *Osteoporosis in clinical practice*. Bristol, London: Wright, 1986: 37-43.

- 18 Van Soesbergen R M, Lips P, van den Ende A, van der Korst J K. Bone metabolism in rheumatoid arthritis compared with postmenopausal osteoporosis. *Ann Rheum Dis* 1986; **45**: 149–55.
- 19 Als O S, Gotfredsen A, Riis B J, Christiansen C. Are disease duration and degree of functional impairment determinants of bone loss in RA? *Ann Rheum Dis* 1985; **44**: 406–11.
- 20 Shearn M A, Kang I Y. Effect of age and sex on erythrocyte sedimentation rate. *J Rheumatol* 1986; **13**: 297–8.
- 21 Ropes M W, Bennett G A, Cobb S, Jacox R, Jessar R A. Revision of diagnostic criteria for rheumatoid arthritis. *Bull Rheum Dis* 1958; **9**: 175–6.
- 22 Huskisson E C. Measurement of pain. *Lancet* 1974; **ii**: 1127–31.
- 23 Pinals R S, Masi A T, Larsen R A. Preliminary criteria for clinical remission in rheumatoid arthritis. *Arthritis Rheum* 1981; **24**: 1308–15.
- 24 Badley E M, Wagstaff S, Wood P H N. Measures of functional ability (disability) in arthritis in relation to range of movement. *Ann Rheum Dis* 1984; **43**: 563–9.
- 25 Barnett E, Nordin B E C. The radiological diagnosis of osteoporosis: a new approach. *Clin Radiol* 1960; **11**: 166–74.
- 26 Dequeker J. Quantitative radiology: radiogrammetry of cortical bone. *Br J Radiol* 1976; **49**: 912–20.
- 27 Exton-Smith A N, Millard P H, Payne P R, Wheeler E F. Method for measuring quantity of bone. *Lancet* 1969; **ii**: 1153–4.
- 28 Horsman A, Simpson M. The measurement of sequential changes in cortical bone geometry. *Br J Radiol* 1975; **48**: 471–6.
- 29 Trentham D E, Masi A T. Carpo-metacarpal ratio: a new quantitative measure of radiological progression of wrist involvement in RA. *Arthritis Rheum* 1976; **19**: 939–44.
- 30 Larsen A, Dale K, Eck M. Radiological evaluation of RA and related conditions by standard reference films. *Acta Radiol [Diagn] (Stockh)* 1977; **18**: 481–91.
- 31 SAS Institute Inc. Cary N C, ed. *SAS user's guide: basics*. Version 5. SAS Institute Inc, 1985: 1–1290.
- 32 SAS Institute Inc. Cary N C, ed. *SAS user's guide: statistics*. Version 5. SAS Institute Inc, 1985: 1–956.
- 33 Dixon W J, Brown M B, Engelman J, *et al.* (eds). *BMDP statistics software*. Berkeley, LA, London: University of California Press, 1985: 1–733.
- 34 Joint committee of the medical research council and Nuffield Foundation on clinical trials of cortisone, ACTH, and other therapeutic measures in chronic rheumatic diseases. A comparison of cortisone and aspirin in the treatment of early cases of rheumatoid arthritis. *Br Med J* 1954; **i**: 1223–7.
- 35 Pickup M E, Dixon J S, Hallett C, Bird H A, Wright V. Plasma viscosity—a new appraisal of its use as an index of disease activity in RA. *Ann Rheum Dis* 1981; **40**: 271–5.
- 36 Wright V, Dixon J S, Bird H A. Therapeutic significance of laboratory results in rheumatic diseases. *Semin Arthritis Rheum* 1985; **15** (suppl 2): 8–13.
- 37 Scott D L, Symmons D P M, Coulton B L, Popert A J. Long-term outcome of treating rheumatoid arthritis: results after 20 years. *Lancet* 1987; **i**: 1108–11.
- 38 Devereaux M D, Parr G R, Page Thomas D P, Hazleman B L. Disease activity indexes in RA: a prospective, comparative study with thermography. *Ann Rheum Dis* 1985; **44**: 434–7.
- 39 Joyce C R B, Hammond K R. Improving clinical judgement. *Br J Rheumatol* 1983; **22** (suppl): 14–17.
- 40 Hart L E, Tugwell P, Buchanan W W, Norman G R, Grace E M, Southwell D. Grading of tenderness as a source of interrater in the Ritchie articular index. *J Rheumatol* 1985; **12**: 716–7.
- 41 Mielke H, Deicher H. Correlation of inflammatory RA disease activity with laboratory parameters. *Scand J Rheumatol* 1985; **14**: 22–4.
- 42 Fries J. F. Toward an understanding of patient outcome measurement. *Arthritis Rheum* 1983; **26**: 697–704.
- 43 Capell H A. Can treatment really influence the radiological progression of RA? *Br J Rheumatol* 1986; **25**: 2–6.
- 44 Buckland-Wright J C. X-Ray assessment of activity in rheumatoid disease. *Br J Rheumatol* 1983; **22**: 3–10.
- 45 Schorn D. Osteoporosis in the rheumatoid hand: effects of treatment with D-penicillamine and oral gold. *S Afr Med J* 1983; **63**: 121–3.
- 46 Fries J F. The assessment of disability: From first to future principles. *Br J Rheumatol* 1983; **22** (suppl): 48–58.
- 47 Bombardier C, Ware J, Russell I J, *et al.* Auranofin therapy and quality of life in patients with rheumatoid arthritis. Results of a multicenter trial. *Am J Med* 1986; **81**: 565–78.