Correlation of Single Time-Point Damage Scores with Observed Progression of Radiographic Damage During the First 6 Years of Rheumatoid Arthritis

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ABSTRACT. ***Objective.*** Aggressive treatment of early rheumatoid arthritis (RA) is recommended to prevent irreversible joint damage. We evaluated the usefulness of single time-point joint radiographs for deciding whether early RA is erosive or nonerosive.

Methods. In an observational study, 179 patients with recent onset of RA symptoms (median 5.1 mo), positive rheumatoid factor, and active polyarthritis had 2 to 8 radiographic observations of hands, wrists, and forefeet during 6 to 60 months of followup. Linear regression lines for all available radiographs were used to determine progression rates of total Sharp score (TSS), erosion score (ES), and joint space narrowing score (JSNS) of each patient.

Results. Using the average of 2 readers' scores, intraclass correlation coefficient was 0.97 and smallest detectable difference was 3.07 for ES, 0.93 and 7.52 for JSNS, and 0.90 and 12.71 for TSS. Mean progression rates per year were 1.20 (ES), 0.67 (JSNS), and 1.85 (TSS). Single time-point radiographs taken within 6 months of symptom onset did not correlate with progression rates (r = 0.01 to 0.07); between 7 and 18 months correlations were weak (r = 0.23 to 0.35), but were better for ES between 19 and 72 months (r = 0.60 to 0.81). Among 53 patients (31%) with no progression of TSS, only 10 of them had zero scores at baseline. Among all 630 radiographs with TSS ≥ 1, 25% were associated with progression rates ≤ 0.

Conclusion. Erosion scores of single radiographic examinations done > 18 months after onset of RA symptoms correlated with progression rates, but earlier radiographs did not sufficiently predict erosive or nonerosive status to guide disease modifying antirheumatic drug treatment decisions. (J Rheumatol 2003;30:705–13)

Key Indexing Terms:
JOINT DAMAGE SCORES EARLY RHEUMATOID ARTHRITIS
PROGRESSION OF JOINT DAMAGE

In addition to prompt suppression of pain and inflammation and improvement of function, prevention of structural damage to joints is an important fundamental goal in the longterm management of rheumatoid arthritis (RA). Evidence that some disease modifying antirheumatic drugs (DMARD) [e.g., methotrexate (MTX), leflunomide, sulfasalazine, corticosteroids] and biological agents [e.g., tumor necrosis factor (TNF) inhibitors, interleukin 1 receptor antagonist] retard the progression of joint damage[1–7] suggests that this goal may be at least partly attainable, and has prompted earlier and more aggressive addition of these interventions to the therapeutic regimen. Indeed, we have suggested that the presence of erosive changes soon after onset is a strong indication for aggressive treatment, and the adequacy of a patient's treatment is at least in part determined by its apparent effect on the progression rate of radiographic damage[8]. However, this additional therapy is associated with additional costs and risks (e.g., MTX hepatic or pulmonary toxicity, dissemination of infections, opportunistic infections, and other rare serious adverse events); also, up to one-third of patients in early RA cohorts may have little or no progression of radiographic damage[8].

Because structural damage to rheumatoid joints is generally considered to be evidence of severe RA, with a poor prognosis for future joint destruction and disability, it is important to be able to accurately determine the presence or absence of radiographic damage in individuals with early RA, and to quantitatively monitor its progression over time. Several validated methods are available to quantitatively score radiographic joint damage, and have been used to document retardation of damage in controlled clinical trials of 6 to 12 months' duration[1-7,9-12]. However, the actual

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scoring of abnormalities often depends on the judgment and interpretation of the reader as to whether an apparent interruption of the subchondral cortical plate is real, or whether a decrease in the distance between the cortices on opposite sides of the joint is real or is due to a slight change in the position of the joint relative to the film and the x-ray beam, a change in exposure of the film, or some other technical factor. Thus the recorded score is an approximation of the true damage and for most patients the "smallest detectable difference" between repeated scoring of the same radiograph[13] is larger than the actual change that has occurred between pairs of radiographs taken at yearly intervals.

Quantile reference curves can be constructed that depict the distribution of radiographic damage scores over time in a population of patients with RA[14]. Similar to pediatric growth curve charts, they suggest that patients could be stratified by their innate rate of progression of joint damage, and that it may be possible to estimate a patient's relative progression quantile by plotting the damage score and disease duration at the time of a single radiographic evaluation on the chart of quantile reference curves.

Given the relative imprecision of radiographic scoring, how accurately can radiographic progression be estimated from the scores of a single time-point radiograph? To evaluate this question, we determined the correlations between single time-point radiograph scores and observed radiographic progression rates in 179 patients with early rheumatoid factor (RF) positive RA (median symptom duration at entry 5.1 mo), who had 710 radiographic evaluations of hands/wrists and forefeet during the first 6 years after the onset of RA symptoms.

MATERIALS AND METHODS

Patients. Patients who met diagnostic criteria for RA[15] and were within 12 months of symptom onset but had not yet been treated with a DMARD were entered in this longterm observational study if RF was positive (titer ≥ 1:80 or ≥ 40 IU) and the patient had ≥ 6 swollen joints and ≥ 9 tender joints. Patients were entered between January 1, 1993, and August 29, 2000, by 41 rheumatologists from 29 practices in the Western Region of the United States and Mexico. Four practices are in university medical centers; the remainder are community practices. Arthritis assessments were scheduled at entry, at 6, 12, and 24 months, and yearly thereafter and included clinical, radiographic, laboratory, and genetic assessments[16-18].

Patients entered the observational study as they became available. At the time of this analysis, study entry (baseline) data were available for 277 patients, 6 month data for 237, 1 year for 222, 2 year for 197, 3 year for 154, 4 year for 131, and 5 year data for 99 patients. The average duration of followup was 3.8 years. Patients could be treated with one or more DMARD at any time after the baseline evaluation. The following DMARD were initiated at the time of the baseline evaluation: MTX by 48% of patients; hydroxychloroquine (HCQ) 19%; sulfasalazine (SSZ) 10%; MTX and HCQ 7%; stepdown bridge (MTX + HCQ + prednisone) 6%; injectable gold 3%; and no DMARD (NSAID and/or prednisone only) 7%. By the sixth month, all patients except one had started DMARD. Changes were made as clinically indicated: at 6, 12 and 24 months MTX use ranged from 64% to 68% of patients, HCQ 32% to 37%, and SSZ 13% to 16%. Between 53% and 58% of patients were taking prednisone at the various assessment points, although some patients stopped prednisone and others started it. Nonsteroidal antiinflammatory drugs (NSAID) were used or changed as clinically indicated. Cumulative patient-years of DMARD use, singly or in combination, were MTX 488 years, antimalarial drug 257 years, SSZ 98 years, intramuscular gold 11 years, azathioprine 14 years, and others 24 years.

Standard posteroanterior radiographs that included both hands and wrists and anteroposterior radiographs that included both forefeet were obtained at entry, 6 months, and yearly in the rheumatologists' offices or by the radiology facility usually used by them. Joint radiographs were available for 232 patients at entry, 151 at 6 months, 129 at 1 year, 104 at 2 years, 66 at 3 years, 48 at 4 years, and 25 at 5 years. These included paired sequential radiographs from 179 patients who had a total of 710 radiographic examinations. The 179 patients had an average disease duration at entry of 5.5 ± 3.0 months, 3.97 ± 1.6 radiographic examinations during 31 ± 18 months of followup (ranges 2 weeks to 11.9 months disease duration, 2 to 8 radiographs, and 6 to 60 months of followup). Two evaluations were available for 36 patients; 143 patients had joint radiographs at more than 2 time points.

All available radiographs were scored by 2 experienced readers for erosions (scale 0 to 5) and joint space narrowing (scale 0 to 4); total score is the sum of the erosion and joint space narrowing scores. After a brief "training" session in which the readers discussed the scoring scale and reviewed a small group of radiographs to be sure they agreed on the features to be scored, the radiographs were independently scored using the method described by Sharp, *et al*[9,10] to score 17 joints of each hand and wrist for erosions and 16 for joint space narrowing, and 6 joints in each forefoot for erosions and joint space narrowing. Maximum possible scores for hands/wrists are: erosions 170, joint space narrowing 128, total score 298; for feet: erosions 60, joint space narrowing 48, total score 108; for both hands/wrists and feet: erosions 230, joint space narrowing 176, total score 406. Radiographs were read in patient sets, blinded and randomized for sequence. The independent scores of readers 1 and 2 for each radiograph were averaged and this average was used for the analysis. A score of 0.5 (one reader scores 1, the other scores 0) was classified as zero in the categorical analyses. To measure reliability of the readers, intraclass correlation coefficient (ICC) was calculated[19]. This measures the repeatability of the scores by the readers and is widely used in the medical field. Sclerosis or healing of erosions was not evaluated. Because the time interval between pairs of radiographs varied among patients, radiographic progression between observations was determined by dividing the difference between the scores of each pair of radiographs by the months elapsed between them; the progression rate was expressed as change in (total, erosion, or joint space narrowing) score per month; this was annualized when necessary to express progression rate per year. For each patient with 2 or more radiographic observations, the slope of the least-squares linear regression line was calculated to estimate the annualized progression rates of ES, JSNS, and TSS. The smallest detectable difference (SDD) is a statistical method that is based on the 95% limits of agreement[13,20] and assumes that progression scores smaller than the SDD cannot be distinguished from measurement error. The mathematical definition of SDD is the interval defined by 2*SD, where SD is the standard deviation of the average difference between paired scores of the same radiographs[13]. Correlations were calculated using the Spearman method.

RESULTS

Clinical characteristics. Baseline demographics and clinical and laboratory measures of disease activity, initial DMARD, and RA course during followup are summarized in Table 1.

Quantile plots. Figure 1 plots the ES, JSNS, and TSS of all 710 radiographic evaluations of the 179 patients according to the duration of RA symptoms at the time of each radiographic evaluation. The quantile lines divide the populations of scores into fifths and approximate the structural damage strata of this cohort of patients with early RA.

Table 1. Study variables for patients with paired sequential joint radiographs.

Variable	Mean ± SD	No. of Subjects
Baseline Demographics		
Age, yrs	51.55 ± 12.85	179
Sex, % female	76.54	179
Duration of RA (months since the onset of persistent symptoms of RA)	5.52 ± 3.00	179
Baseline Clinical		
Grip strength, mm Hg	143.82 ± 73.83	170
Tender joint count, 0–68	24.02 ± 13.16	176
Swollen joint count, 0–66	20.56 ± 11.17	176
HAQ Disability Index, 0–3	1.22 ± 0.73	168
Physician global, 0–100	50.46 ± 20.55	175
Patient global, 0–100	61.56 ± 24.76	130
Patient global, 0–3	1.28 ± 0.73	164
Pain, VAS, 0–100	60.16 ± 26.68	130
Pain, from HAQ, 0–3	1.56 ± 0.73	167
Disease Activity Score	4.64 ± 1.14	167
Nodules, %	15.91	176
Other extraarticular manifestations, %	11.43	175
Total Sharp score	5.95 ± 7.71	171
Erosion score ≥ 1, %	44.13	171
Prednisone use, %	54.66	161
Baseline Laboratory		
Hemoglobin, g/dl	13.19 ± 1.31	155
Hematocrit, %	39.40 ± 3.67	151
Platelets, × 1000	335.69 ± 109.02	154
CRP, mg/dl	2.71 ± 3.52	178
ESR, mm/h	40.34 ± 23.94	175
Viscosity, mPa.s	1.83 ± 0.20	178
ANA, IU/ml	29.50 ± 69.41	170
Albumin, g/dl	3.99 ± 0.43	125
C3, mg/dl	146.86 ± 30.95	76
C4, mg/dl	34.61 ± 10.95	76
Rheumatoid factor, IU/ml	393.25 ± 516.61	175
Epitope +, %	53.67	177
Initial DMARD		
MTX, %	48.0	
HCQ, %	19.0	
MTX + HCQ, %	7.3	
SSZ, %	9.5	
Step-down bridge, %	6.1	
Gold, %	2.8	
None or other, %	7.3	
RA course during 2 yr follow-up		
ACR 20% responders, (% n/N)	54.19	97/179
ACR 50% responders, (% n/N)	30.72	55/179
New extraarticular manifestations, %	17.44	172
New nodules, %	23.84	172
Sharp Score progression rate/yr	1.85 ± 4.69	179
First-year change in HAQ	–0.48 ± 0.65	144

HAQ: Health Assessment Questionnaire, VAS: visual analog scale.

ICC and SDD. ICC when the same radiographs were scored twice ranged from 0.69 to 0.84 for readers 1 and 2 (Table 2). When the average scores of the first readings for the 2 readers were compared with the average scores of their second readings, ICC were 0.97 for ES, 0.93 for JSNS, and 0.90 for TSS.

The smallest detectable difference between 2 independent readings of the same radiograph by reader 1, reader 2, or the average of readers 1 and 2 are shown in Table 2. The SDD are smaller for the average of the 2 readers than for either alone.

Progression rates. Individual progression rates were calculated by determining the slope of the best fitting linear regression line using the scores of all available radiographs for each subject. Figure 2 plots examples of serial TSS of patients with negative, zero, moderate, and high progression rates. Table 3 shows the mean, SD, median, and range of ES, JSNS, and TSS progression rates per year. Fifty-three (30.6%) patients had ≤ 0 progression for TSS, 48 (28%) for ES, and 78 (45%) for JSNS during a median disease interval of 24 (range 6–60) months.

Effects of DMARD treatment. There were no significant differences in radiographic progression rates between patients initially treated with the various DMARD described in Materials and Methods, nor with regimens that included MTX compared with the non-MTX regimens. There was no statistically significant correlation between the baseline radiographic scores and the selection of initial DMARD. Therefore, no corrections have been made for treatment effects.

Correlation of single time-point radiographic scores with calculated progression rates. Table 4 shows the relationship between single radiographic evaluations done between 0 and 6 months, 7–18, 19–30, 31–42, and 43–72 months after onset of RA symptoms and the progression rates calculated from all available radiographs of each subject. The scores of radiographs taken within 6 months of disease onset had little relationship to progression of structural damage during the next 5 years. Spearman correlations of single time-point radiograph scores with progression rates improved with increased disease duration and were better for ES than for JSNS. The proportion of radiographs with no evidence of damage (total Sharp score 0) decreased as RA duration increased (Table 5), and the proportion of these negative radiographs that were associated with progression rates ≤ 0 increased from 41% for radiographs taken between 0 and 6 months of RA, to 93% for radiographs taken between 19 and 72 months of RA. On the other hand, among those with TSS ≥ 1, between 18% and 28% (25% of 630 films) were associated with progression rates ≤ 0, and this proportion changed little through 72 months of disease duration. Fifty-three patients had TSS progression rates ≤ 0, but only 10 (18.8%) had scores of zero on their baseline radiographs; for 48 with erosion progression rates ≤ 0, 31 (65%) had baseline ES of 0, and for 78 with joint space narrowing progression ≤ 0, 26 (33%) had baseline JSNS of 0 (Table 6).

When one examines the scores of individual radiographs (Tables 6 and 7), the score on the baseline radiograph has little relationship to the probability of subsequent radio-

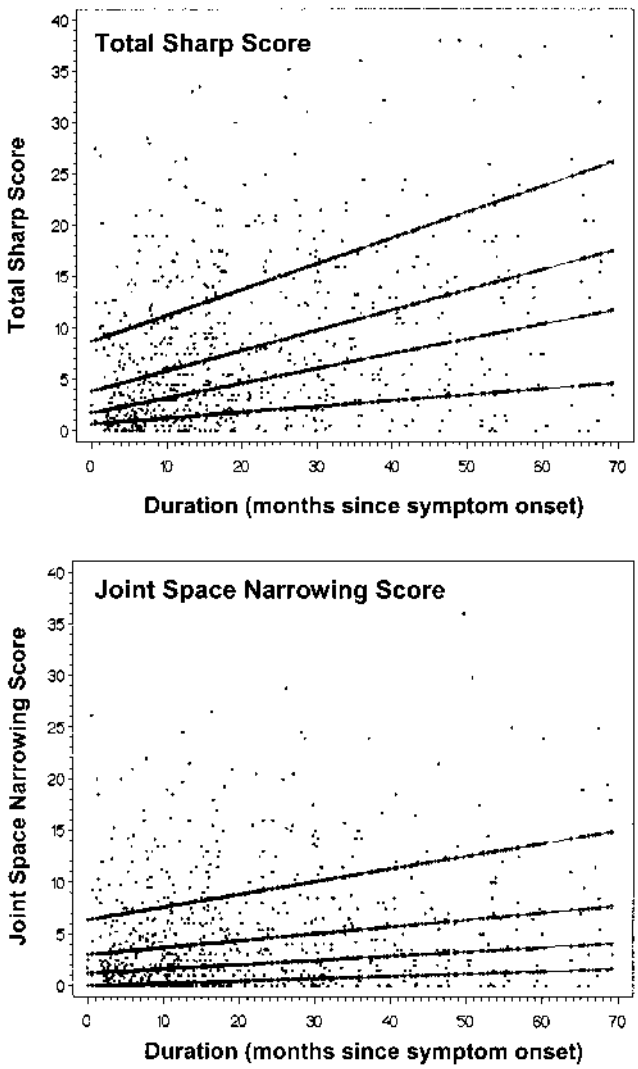

Figure 1. Quantile plots of total Sharp scores, erosion scores, and joint space narrowing scores for 710 radiographic observations of 179 patients during the first 6 years of RF positive RA. Each dot represents the score of a single observation at the indicated time after onset of RA symptoms. Quantile lines separate the entire population of observations into equal fifths, i.e., the lines indicate the 20th, 40th, 60th, and 80th percentiles, and approximate the structural damage strata for this patient cohort.

graphic progression. Beyond 12 months of RA, only a few radiographs with TSS of zero are associated with progression rates > 0, and more than 75% with TSS ≥ 2 are associated with positive progression rates.

DISCUSSION

We assume that the progression rate of structural joint damage, determined from multiple radiographic examinations over time, approximates truth when attempting to estimate the aggressiveness of a patient's RA. Of course, the aggressiveness of structural damage is a function of many factors that may confound one another, e.g., the innate disease severity (reflected in RF, genetic markers and acute phase reactant values, tender and swollen joint counts, physical function and constitutional symptoms) may be moderated by effective drug therapy. Our patients had minimal exposure to drug therapy prior to their baseline radiographs, but subsequent DMARD treatment was determined by their physicians, as appropriate. Thus, as in the usual practice situation, the progression of structural damage in these patients is an amalgam of endogenous patient related characteristics and exogenous treatment related factors that cannot be readily separated. This does not negate the assumption that patients with structural damage (erosions) have stronger evidence for aggressive disease than those without structural damage and deserve aggressive therapy. We did not address the relative merits of various aggressive therapies. Instead, we call attention to the difficulty in deciding whether a patient's RA has been "erosive" or not.

Our findings illustrate the difficulty in differentiating minimally erosive from nonerosive disease early in RA. One is not surprised that many patients with no structural damage visible on radiographs within the first 6 months of RA symptoms later develop joint damage, but 29% of 147 patients who had total Sharp scores ≥ 1 on the initial radiograph, suggesting the presence of joint damage, subsequently had zero or negative progression rates. Indeed, similar to other reports[8], about one-third of this early RA

Table 2. Intraclass correlation coefficients (ICC) and smallest detectable difference (SDD).

	ICC* (No. of radiographs)			SDD		
	Reader 1	Reader 2	Average** of 1 and 2	Reader 1	Reader 2	Average of 1 and 2
Erosion score	0.82 (324)	0.84 (320)	0.97 (320)	5.88	6.57	3.07
Joint space narrowing score	0.73 (273)	0.71 (268)	0.93 (268)	10.08	13.62	7.52
Total Sharp score	0.75 (324)	0.69 (320)	0.90 (320)	14.76	19.52	12.71

* ICC, comparing first and second readings of the same radiographs.
** Average score, 1st reading = (1st reading score by reader 1 + 1st reading score by reader 2)/2
Average score, 2nd reading = (2nd reading score by reader 1 + 2nd reading score by reader 2)/2

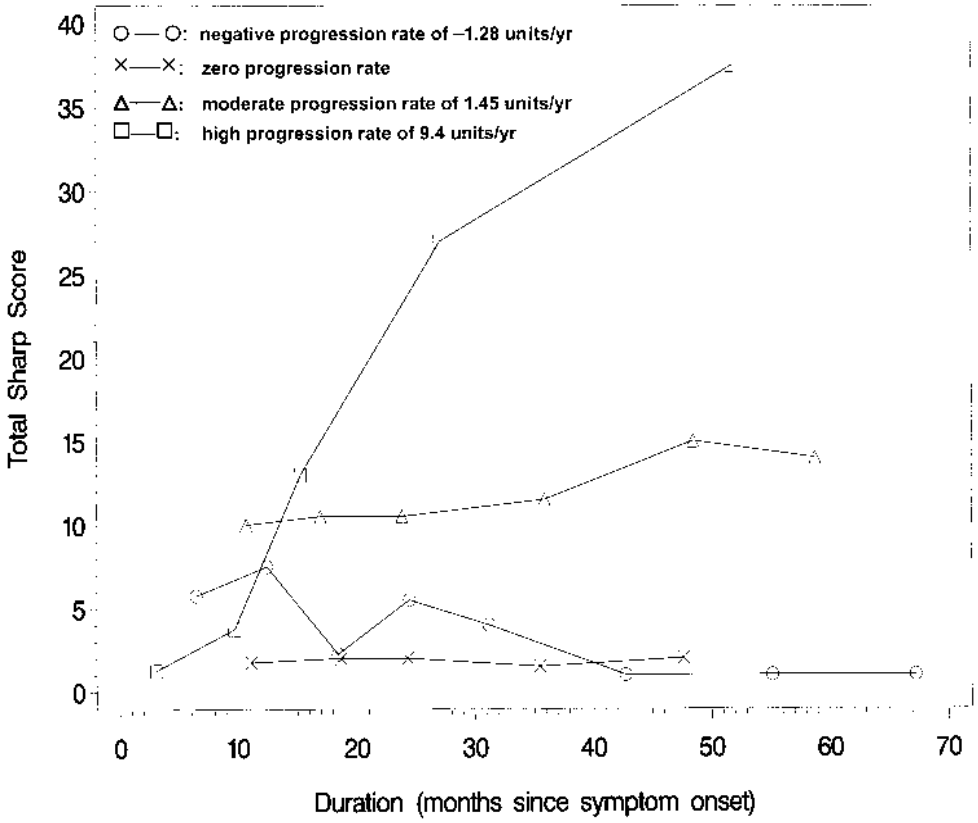

Figure 2. Examples of total Sharp scores of serial radiographs of 4 patients, one with a negative progression rate of minus 1.28 units per year; one with zero progression rate; one with a moderate progression rate of 1.45 units per year; and one with a high progression rate of 9.4 units per year. The progression rate is calculated from the slope of the best fitting linear regression line.

Table 3. Radiographic progression rates (per year); n = 179 patients; interval between first and last radiograph = 6 to 60 months (median 24, mean 31 ± 18).

	Mean	SD	Median	Range	Interquartile Range*
Erosion score	1.203	2.022	0.6	–3.39 to 11	1.814
Joint space narrowing score	0.671	3.347	0.055	–8.01 to 34.5	1.238
Total Sharp score	1.853	4.689	0.906	–7.63 to 45.5	3.100

* Interval between 25th and 75th percentiles.

cohort had no radiographic progression during an average followup of 3 years, despite entry requirements for an aggressive phenotype (RF positive with active polyarticular inflammation) at baseline. The impact of treatment cannot be determined from this analysis; almost all the patients received standard DMARD, but progression of damage during the observed treatment intervals did not differ significantly with different DMARD regimens. Leflunomide and the TNF inhibitors that have little or no lag time before the onset of benefit were used infrequently in this cohort, but MTX, prednisone, and/or SSZ were used by the majority of the patients.

To a considerable extent, the poor correlation of single radiograph damage scores early in RA to subsequent progression is due to uncertainty in scoring minimal changes. The smallest detectable difference for the average of the scores of the 2 readers was smaller than that of the individual readers, supporting the recommendations of Fries, *et al*[21] favoring the use of multiple readers. Nevertheless, the SDD of 12.71 for the TSS was 6.9 times the average TSS progression rate per year for this population, which helps to explain the finding of negative progression rates of structural damage to joints, although healing of previously observed erosions has not been entirely ruled out[22]. The SDD for erosion score (3.07) was smaller than that for JSNS or total score, but was still 2.6 times its mean progression rate per year. Thus, in the early stage of RA, the error term in radiographic scores is often much greater than the observed score, and any projection of progression rate from a single observation covers an extremely wide band.

Many reports find that baseline radiographic damage scores predict subsequent radiographic progression[23-27], but few studies have had baseline radiographs within our average of 6 months from symptom onset. Since radiographic damage is the consequence of joint inflammation and needs time to develop, reliable radiographic evidence of joint damage lags behind the initial clinical onset of signs and symptoms of inflammation. In our cohort of patients with early seropositive RA, this lag time appears to be about 6 to 18 months. We found that correlations of single radiograph damage scores with progression rates improved as disease duration increased and were quite respectable after 19 months beyond the onset of RA symptoms, with r values of 0.6 to 0.81 for erosion scores. After 19 months, 85% to 90% of radiographs with TSS of zero were associated with ≤ 0 progression rates, suggesting clinical usefulness. However, during the same range of disease durations, 27% of radiographs with TSS ≥ 1 also were associated with no radiographic progression. About 90% of radiographs with scores ≥ 10 taken > 30 months after symptom onset were associated with positive progression rates.

How do the findings of this study inform clinical deci-

Table 4. Correlations between single radiograph scores at various durations of RA and calculated individual progression rates.

RA Duration† at Time of Radiograph, mo	No. of Single Radiographs (Patients)	Correlation Between Single Radiograph Scores and Progression Rate		
		Total Score	Erosion Score	Joint Space Narrowing Score
0–6	106 (104)	0.072	0.072	–0.015
7–18	277 (165)	0.255*	0.347*	0.225*
19–30	130 (121)	0.483*	0.599*	0.364*
31–42	88 (83)	0.589*	0.647*	0.415*
43–72	109 (72)	0.745*	0.810*	0.571*

* $p < 0.001$ Spearman correlation coefficient. † Months since onset of persistent symptoms of RA.

Table 5. Relationship of single time-point radiograph scores to calculated progression rates ≤ zero.

RA Duration† at Time of Radiograph, mo	No. of Single Radiographs (Patients)	Radiographs with Total Sharp Score Zero		Radiographs with Total Sharp Score ≥ 1	
		No. (%)	No. (%) with Progression ≤ 0	No. (%)	No. (%) with Progression ≤ 0
0–6	106 (104)	17 (16.0)	7 (41.2)	89 (84.0)	24 (27.0)
7–18	277 (165)	35 (12.6)	19 (54.3)	242 (87.4)	67 (27.7)
19–30	130 (121)	14 (10.8)	13 (92.9)	116 (89.2)	27 (23.3)
31–42	88 (83)	5 (5.7)	5 (100)	83 (94.3)	16 (19.3)
43–72	109 (72)	9 (8.3)	8 (88.9)	100 (91.7)	25 (25.0)

† Months since onset of persistent symptoms of RA.

Table 6. Relationship of radiographic damage scores at various durations of RA† to calculated progression rates > 0. N = number of patients with score in the indicated range. Total N = 173 patients. Six patients who had the baseline radiograph after the 12th month of RA are not included. For each patient, if multiple radiographs within the time interval, only the first one within the interval is used. Scores of 0.5 are categorized as 0. For each patient, calculated progression rate is the slope of the best-fit linear regression line for all available radiographs.

	Baseline Radiograph (at 0–12 mo)		Radiograph at 13–30 mo of RA		Radiograph at 31–42 mo of RA		Radiograph at 43–72 mo of RA	
	No. Patients	% with Progression > 0	No. Patients	% with Progression > 0	No. Patients	% with Progression > 0	No. Patients	% with Progression > 0
Total Sharp score								
0	26	62	18	17	5	0	6	0
≥ 1	147	71	142	77	78	79	66	77
≥ 2	113	73	129	79	74	78	62	79
≥ 3	97	73	115	79	71	77	59	80
≥ 5	70	69	85	80	58	83	51	84
≥ 10	34	65	49	82	39	87	35	91
≥ 15	12	42	28	82	20	85	24	100
Erosion score								
0	94	67	51	47	18	28	14	7
≥ 1	79	78	109	83	65	91	58	91
≥ 2	48	75	92	85	58	90	55	91
≥ 3	37	78	69	88	51	90	41	93
≥ 5	17	65	42	88	33	91	34	97
≥ 10	2	50	12	75	10	90	18	100
≥ 15	2	50	6	83	5	80	12	100
Joint space narrowing score								
0	51	49	40	28	15	20	15	13
≥ 1	122	57	120	66	68	66	57	67
≥ 2	94	60	102	71	57	65	52	69
≥ 3	77	60	86	69	47	62	44	68
≥ 5	51	61	64	73	34	76	32	78
≥ 10	21	67	28	82	16	88	20	90
≥ 15	6	67	12	83	6	100	8	100

† Months since onset of persistent symptoms of RA.

sions about patients with newly diagnosed seropositive RA? The 3 to 5 year outcome was surprisingly good, with no radiographic progression in 31% of these DMARD treated patients. After 18 months of RA symptoms (and an average of 12 months DMARD treatment), single radiograph erosion scores correlated reasonably well with the progression rates determined for the entire available time-span, but radiographs taken during the first 6 months of symptoms did not correlate with subsequent progression rates. If an early window of opportunity occurs during the first 6 to 12 months after symptom onset, during which initiation of aggressive DMARD treatment has a major effect on the subsequent progression of structural damage, the presence or absence of an erosion on the initial joint radiographs cannot be used to decide whether the patient has an aggressive or benign phenotype for structural damage, because half the patients with negative initial radiographs went on to progressive joint damage, and one-quarter of those with positive initial scores did not have progressive joint damage. Only after 43 months of disease did more than 95% of patients with erosion scores ≥ 5 have progressive damage.

We conclude that the most practical approach to the aggressive management of clinically active, RF positive early RA is to treat everyone with a DMARD, even though some of these patients may not develop aggressive joint damage. The damage score on the initial radiograph cannot be used to reliably determine whether to use a stronger DMARD, e.g., MTX, leflunomide or TNF inhibitor, or a less aggressive DMARD such as an antimalarial, sulfasalazine, or minocycline. Radiographs taken more than 18 months into the disease course provide a somewhat better indication of the aggressiveness of structural damage, but the best estimate of progression requires repeated radiographs over multiple time-points. Since essentially all our patients were treated with DMARD, this study cannot be used to estimate the proportion of non-DMARD treated seropositive early RA patients who will remain nonerosive, nor can it be applied to patients with seronegative RA.

APPENDIX

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Table 7. Distribution of scores of individual radiographs at various durations of RA†. Relationship to calculated progression rates > 0. N = number of patients with score in the indicated range. Total N = 173 patients. Six patients who had the baseline radiograph after the 12th month of RA are not included. For each patient, if multiple radiographs within the time interval, only the first one within the interval is used. Scores of 0.5 are categorized as 0. For each patient, calculated progression rate is the slope of the best-fit linear regression line for all available radiographs.

	Baseline Radiograph (at 0–12 mo)		Radiograph at 13–30 mo of RA		Radiograph at 31–42 mo of RA		Radiograph at 43–72 mo of RA	
	No. Patients	% with Progression > 0	No. Patients	% with Progression > 0	No. Patients	% with Progression > 0	No. Patients	% with Progression > 0
Total Sharp scores								
0	26	61.6	18	16.7	5	0.0	6	0.0
1 to < 2	34	64.7	13	61.6	4	100.0	4	50.0
2 to < 3	16	68.7	14	78.6	3	100.0	3	66.7
3 to < 5	27	85.2	30	76.7	13	53.8	8	50.0
5 to < 10	36	72.2	36	77.8	19	73.7	16	68.7
≥ 10	34	64.7	49	81.6	39	87.2	35	91.4
Erosion score								
0	94	67.0	51	47.1	18	27.8	14	7.1
1 to < 2	31	83.9	17	70.6	7	100.0	3	100.0
2 to < 3	11	63.6	23	73.9	7	85.7	14	85.7
3 to < 5	20	90.0	27	88.9	18	88.9	7	71.4
5 to < 10	15	66.7	30	93.3	23	91.3	16	93.7
≥ 10	2	50.0	12	75.0	10	90.0	18	100.0
Joint space narrowing score								
0	51	49.0	40	27.5	15	20.0	15	13.3
1 to < 2	28	46.4	18	38.9	11	72.7	5	40.0
2 to < 3	17	58.8	16	81.2	10	80.0	8	75.0
3 to < 5	26	57.7	22	54.6	13	23.1	12	41.7
5 to < 10	30	56.6	36	66.7	18	66.7	12	58.3
≥ 10	21	66.7	28	82.1	16	87.5	20	90.0

† Months since onset of persistent symptoms of RA.

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