Radiographic Damage in Rheumatoid Arthritis Correlates with Functional Disability But Not Direct Medical Costs

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ABSTRACT. ***Objective.*** Few longitudinal data exist on the relationship between radiographic damage and self-reported functional disability and direct medical costs in rheumatoid arthritis (RA). We assessed these relationships.

Methods. One hundred thirty patients with RA (at time of the first available radiograph, mean age 56.6 yrs, 16.9% male, mean disease duration 16.8 yrs) were followed for up to 13.4 years. Semiannually, they reported on functional disability (0 = no difficulty, 3 = unable to do), global severity (0 = very well, 100 = very poor), pain (0 = no pain, 3 = severe pain), and health services utilization through completion of the Stanford Health Assessment Questionnaire (HAQ). Concurrent hand radiographs were scored for erosions and joint space narrowing using the Genant method and a single score summing both erosions and joint space narrowing for both hands was calculated (0 = no damage, 200 = maximum damage). The univariate association of functional disability, global severity, pain, or direct medical costs with concurrent radiographic damage was assessed through Spearman correlations and hierarchical regression models. The hierarchical models permit exploitation of the between-patient and within-patient variation present in our longitudinal data.

Results. At the time of the first available radiograph, mean (SD) levels of functional disability, global severity, and pain were 1.3 (0.7), 39.4 (21.0), and 1.1 (0.7), respectively. At entry into the study, the average radiograph score was 49.7 and upon leaving the study it was 66.9. Patients were followed an average of 6.7 years, with radiograph scores increasing at an average rate of 2.5 units/yr. The Spearman correlation [95% confidence interval (CI)] between average per-patient radiograph score and average per-patient HAQ disability index, average per-patient global severity, average per-patient pain score, and average per-patient direct medical costs was, respectively, 0.42 (0.26, 0.55), 0.23 (0.06, 0.39), 0.20 (0.03, 0.36), and 0.06 (–0.11, 0.23). The mean slope (95% CI) for disability on radiograph score was 0.0186 (0.0132, 0.0226), for severity on radiographs 0.1889 (0.1295, 0.2498), and for pain on radiographs 0.0057 (0.0027, 0.0084). As an example, over 10 years, a 25 unit (i.e., 50%) increase in radiograph scores would, on average, be associated with a 0.46 unit (i.e., 35%) increase in disability, a 4.72 unit (12%) increase in global severity score, and a 0.14 unit (13%) increase in pain, all expressed on the HAQ scales. There was little association between radiograph score and direct medical costs.

Conclusion. A clinically meaningful association exists between radiographic damage and self-reported functional disability, suggesting that interventions that slow radiographic progression may improve the patient's health status. Such a relationship was not observed between radiographic damage and direct medical costs. (J Rheumatol 2001;28:2416–24)

Key Indexing Terms:
RHEUMATOID ARTHRITIS — GENANT RADIOGRAPH SCORES — DISABILITY INDEX
HIERARCHICAL MODELLING — DIRECT MEDICAL COSTS — HEALTH STATUS

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Outcome in rheumatoid arthritis (RA) is a multidimensional construct, expressed through clinical and laboratory variables, radiographic evidence of structural damage, patient self-reported health status, and mortality. Recently, direct and indirect medical costs, representing health resource utilization and lost productivity, respectively, have also been incorporated in studies characterizing the burden of RA. Numerous studies have assessed predictors of radiographic progression, which is often regarded as the gold standard of outcome. However, few longitudinal data exist on the relationship between radiographic damage and other outcome dimensions such as self-perceived health status and medical costs. We describe these relationships and explore demographic variables that may influence these relationships.

MATERIALS AND METHODS

Patients. The cost analysis of this RA database has been described[1,2]. The original study[1] included a total of 1063 patients from Saskatchewan and Montreal, the Saskatchewan patients contributing economic and health status data between 1981 and 1994 inclusively and the Montreal patients between 1989 and 1992. (It should be noted that in the original studies, only data from the years 1983 to 1994 were included.) Over the course of the study interval, new patients could be recruited at any stage of disease duration and continuing patients could withdraw at any time. Therefore, patients potentially contributed information over differing time periods and at different lengths of disease duration. We focus on the Saskatchewan patients who had at least 2 hand radiographs at least 5 years apart and health status and economic data concurrent with radiographs (i.e., within one year preceding or following).

Methods. Patients reported semiannually on functional disability, global severity, and level of pain through a mailed questionnaire. Functional disability was assessed through the Stanford Health Assessment Questionnaire[3], scored from 0 (no difficulty) to 3 (unable to do); and global severity [0 (very well) to 100 (very poor)] and level of pain [0 (no pain) to 3 (severe pain)] were assessed via visual analog scales. Patients were also queried on health resource utilization over the preceding 6 months that could potentially be related to RA. Health resources included outpatient visits to physicians and physical and occupational therapy, laboratory/radiological tests, prescribed and nonprescribed medications, emergency room visits, outpatient surgeries, and stays in acute and nonacute care facilities.

Direct medical cost assessment. Costs were assessed from a societal perspective. To translate health resource utilization into direct medical costs, costs were assigned to each unit of service according to a previously applied methodology[1]. Canadian national cost estimates were used. The cost of physician services was based on the physician/provincial government negotiated fee schedule. The cost for outpatient laboratory/radiological services, including both technical and professional components, was based on fully allocated hospital costs and a government reimbursement schedule. Estimates of prescription and nonprescription medication costs were calculated based on patient self-report of medication dosage and therapy duration. Costs represented the product of the weighted average cost per milligram, total daily dose, and therapy duration. All prescription data were obtained from Intercontinental Medical Statistics.

Hospital costs were estimated according to the Canadian Institute for Health Information. Based on the patients' reports of their hospital stays, discharge summaries were obtained, and the hospital stays were then classified into Case Mixed Groups and a weight was assigned based on intensity of resource use. Inpatient physician charges were also included in the cost estimates. Outpatient surgeries were costed in a similar manner. Nonacute care facilities included rehabilitation, extended care, and nursing homes, and costs were based on Statistics Canada data on average per diem cost[4,5].

Total direct costs were then estimated by multiplying the unit cost of each service and the number of units of each service and summing the multiplicands. All costs refer to annual costs and were expressed in 1994 Canadian dollars.

Radiographic assessment. All radiographs were read by a single reader (HKG), blinded to the patient self-perceived health status and economic costs. Radiographs were scored for erosions and joint space narrowing according to the Genant method[6,7]. Erosions were scored according to an 8 point scale, with 0.5 unit increments, 0 representing normal, 3.5 representing severe. Fourteen regions were scored in each hand, yielding a maximum score of 49 per hand. Joint space narrowing was scored according to a 9 point scale, with 0.5 unit increments, 0 representing normal, 4.0 representing ankylosed. Thirteen regions were scored in each hand, yielding a maximum score of 52 per hand. The scores for erosions and joint space narrowing were each summed across hands and then normalized to a 0 to 100 scale, and then both scores were summed to yield a maximum total of 200. Postoperative and unreadable joints were treated in one of 2 ways: (1) if a previous radiograph score was available for that joint, it was assigned that value, or (2) if a previous radiograph score was not available, the mean score of the other joints of the hand was imputed. It should be noted that < 2% of the radiographs were treated in that fashion.

Statistical analysis. Descriptive statistics on demographics, disease characteristics, health status, direct medical costs, and radiograph scores are presented. To calculate the mean of each of these variables over a given time interval, the mean of all observations of an individual patient over the interval of interest was first calculated, and then the means were averaged across patients. The median refers to the 50th percentile of patient means.

The univariate association of radiograph scores and disease duration was assessed through a regression model that accounted for within-patient correlations. Spearman correlations between average per-person radiograph score and average per-patient health status measure or average per-patient direct medical costs were also calculated. Spearman correlations over consecutive time intervals were also calculated by correlating the average per-patient radiograph score and average per-patient health status measure or average per-patient direct costs observed in each interval of interest.

To further explore the relationship between radiograph scores and self-perceived health status or direct medical costs, concurrent radiograph scores and HAQ disability index (DI), global severity, or pain scores, or direct costs were first plotted for each patient. Given that the relationship between radiograph scores and health status (either HAQ DI, global severity, or pain) or costs differed across patients, Bayesian hierarchical modelling[8] was done to model the within- and between-patient variations. The advantage of such modelling is that it enables the magnitude of the relationship between radiograph score and health status or costs to be estimated for each subject and subsequently summarized across all patients. Thus, it recognizes individual variations, while still allowing overall conclusions to be drawn.

The full hierarchical model can be described in 3 stages:

1. A separate linear regression model was created within each patient to examine the relationship between self-perceived functional status or costs and radiograph scores. This results in a set of individual specific slopes, where each slope represents the amount of change in health status or costs for each unit change in radiograph score for that patient.
2. The ensemble of slopes, one from each patient, was then used to estimate the population distribution of this relationship (i.e., of slopes) across patients. We assumed that the slopes are normally distributed across subjects.
3. The subject to subject variation in slopes was then explained by regressing the slopes on a variety of patient covariates, i.e., age, sex, disease duration, marital status, and education level. Model selection was made on the basis of Bayesian information criteria.

We used noninformative prior distributions, so that the final estimates are almost completely determined by the data. The results of these regressions are first summarized as a series of probability densities for the slopes of HAQ DI, global severity, pain, or direct costs on radiograph scores. The effect of various covariates on these relationships is then also expressed as a series of probability densities; for example, a density is created that describes the slope of HAQ DI on radiograph score at ages 46 and 72 years. For the regression models, the outcome of total direct medical costs was logarithmically transformed so that the models would have normally distributed errors. Further, for the health resources of emergency room, outpatient surgery, and acute and nonacute health care stays, where the majority of patients did not incur any costs, a logistic rather than a linear regression model was created for each patient in step 1 to assess the relationship between radiograph score and probability of incurring any of these costs.

RESULTS

One hundred thirty patients had radiographs available on at least 2 occasions at least 5 years apart, with concurrent health status and economic data also available. The mean (SD) interval between radiograph and patient self-report data was 104 (73) days and the median (interquartile range) was 84 (48–156) days. The average time interval between radiographs was 3.3 years. Table 1 presents the demographic and clinical characteristics, health status, and direct medical costs of all Saskatchewan patients for whom radiograph data were available and the patients for whom radiograph data were not available. Patients contributing radiograph data were slightly older with longer disease duration; a greater proportion were female and married. Contributors of radiograph data also had poorer self-perceived health status and higher medical costs, likely due at least in part to their older age. At the time of the first available radiograph, mean (SD) levels of functional disability, global severity, and pain for contributors of radiograph data were, respectively, 1.3 (0.7), 39.4 (21.0), and 1.1 (0.7).

Table 2 presents the mean radiograph and health status scores and annual direct medical costs through consecutive 5 year periods of disease duration. It should be noted that changes in the patients making up the cohort across time may have the effect of minimizing the estimates of actual disease progression experienced by an individual patient.

The 130 patients contributing radiograph data were followed an average of 6.7 years, with average radiograph scores increasing from 49.7 to 66.9 at an average rate of 2.5 units/year. At entry into the study, the average radiograph score was 49.7 and upon leaving the study, it was 66.9. The Spearman correlation [95% confidence interval (CI)] between average per-patient radiograph score and average per-patient HAQ DI, average per-patient global severity score, average per-patient pain score, and average per-patient direct medical costs was, respectively, 0.42 (0.26, 0.55), 0.23 (0.06, 0.39), 0.20 (0.03, 0.36), and 0.06 (–0.11, 0.23). Table 3 shows the Spearman correlation between these variables over consecutive time intervals.

Figure 1 shows the strength of the relationship between HAQ DI and radiograph scores, i.e., the slope, for patients with slope at the 10th, 25th, 50th, 75th, and 90th percentiles. As illustrated in the figure, the relationship between functional status and radiograph scores varied across patients. To examine this relationship, a linear regression model would have been inappropriate as it would not have allowed for this between-patient variation in the association between radiograph scores and self-perceived functional status. The relationship between radiographs and the functional

Table 1. Characteristics of contributors versus noncontributors of radiograph data.

	Patients Providing Radiograph Data, n = 130		Patients Not Providing Radiograph Data, n = 729	
	Mean (SD) or %*	Median (IQR)	Mean (SD) or %*	Median (IQR)
Age, yrs	62.4 (9.9)	63.4 (55.4, 69.9)	61.4 (13.5)	63.2 (52.4, 71.5)
Female	83.1		72.6	
Married	76.9		69.0	
Education level, yrs	10.4 (2.7)	10 (8, 12)	10.8 (3.2)	11 (8, 13)
Employed	27.7		26.9	
Clinical feature				
Disease duration, yrs	22.5 (10.5)	20.4 (14.5, 28.5)	20.9 (10.9)	19.1 (13.3, 26.8)
Questionnaire data				
Disability score, 0–3	1.6 (0.7)	1.6 (1.0, 2.1)	1.4 (0.9)	1.4 (0.6, 2.0)
Global severity, 0–100	45.3 (17.0)	44.8 (35.1, 55.7)	40.7 (21.7)	42.6 (25.0, 54.0)
Pain, 0–3	1.3 (0.5)	1.3 (0.9, 1.6)	1.2 (0.7)	1.2 (0.7, 1.7)
Total direct medical costs				
Annual, 1994 Cdn $	4177 (3934)	2908 (1691, 5154)	3458 (6176)	1612 (871, 2875)

* Values for female, married, and employed are at entry into the RA cohort and are percentages. Other values are mean [standard deviation (SD)]; for each value, a mean was calculated for each patient and then a mean (SD) across patients was calculated. In the calculation of the mean for each patient who provided radiograph data, all observations since entry into the RA cohort were used, not only those values since they contributed a radiograph. For comparison with the noncontributors of radiograph data, where means are calculated based upon all data since entry into the RA cohort, it is appropriate to characterize contributors of radiograph data since they entered the RA cohort, not only upon provision of a radiograph.
IQR: interquartile range.

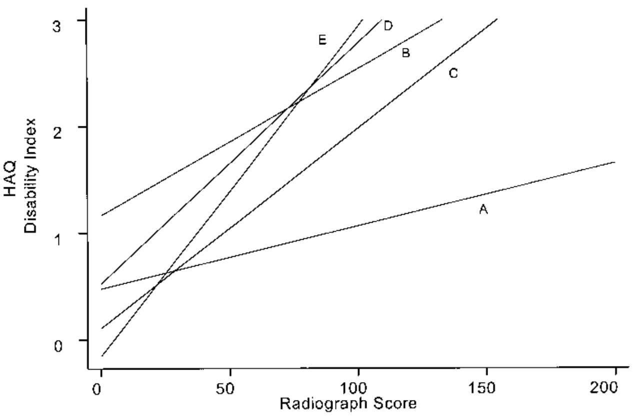

Figure 1. Representative patient slopes of HAQ DI versus radiograph scores. As an illustrative example, a patient having a slope at the 10th percentile means that 90% of patients have a slope of DI versus radiograph score exceeding 0.0059. The y-intercept can vary across patients.
A = 10th percentile slope 0.0059
B = 25th percentile slope (1st quartile) 0.0137
C = 50th percentile slope (median) 0.0187
D = 75th percentile slope (3rd quartile) 0.0225
E = 90th percentile slope 0.0308

outcomes of global severity and pain as well as direct medical costs also varied across patients, motivating the choice of hierarchical modelling, which can accommodate between-patient variation, to describe these relationships.

Figure 2A shows the probability density for the slopes of HAQ DI on radiograph score. The mean slope [95% confidence interval (CI)] was 0.0186 (0.0152, 0.0226) HAQ DI units per unit increase in radiograph score. As an illustrative example, over 10 years, a 25 unit increase in radiograph score, representing a 50% increase over mean score at baseline, would be associated with a 0.46 (i.e., 25×0.0186) unit or 35% increase over baseline disability. The mean (95% CI) for the slope of global severity on radiograph score was 0.1889 (0.1295, 0.2498), for pain on radiograph score 0.0057 (0.0027, 0.0084), for log of total direct costs on radiograph score 0.0013 (–0.0026, 0.0051), and for probability of incurring either outpatient surgery, emergency room, or acute or nonacute care costs was 0.0066 (–0.0012, 0.0146) (Figures 2B–E). Therefore, over 10 years, a 25 unit increase in radiograph score would be associated with a 4.72 unit (i.e., 12%) increase in global severity, a 0.14 unit (13%) increase in pain, a 3% increase in natural direct costs, and 16% increase in probability of incurring either outpatient surgery, emergency room, or acute or nonacute care hospital costs.

While these results convey the average relationships between radiograph scores and the other variables, Figures 2A–E show that there are considerable individual to individual variations in these relationships. In fact, even the direction of the relationship, in terms of whether the slope for an individual patient will be positive or negative, is not certain, even if the overall mean slope in all cases was positive.

Figures 3A–D show the effect of several covariates on the relationship between functional status or costs and radiograph scores. As patients age, the slope between HAQ DI (Figure 3A) or global severity (Figure 3B) and radiographic damage increases. As an example, patients in the 10th percentile of age, i.e., 46 years, have a mean slope of HAQ DI on radiograph score of 0.0148, whereas those in the 90th percentile of age, i.e., 72 years, have a mean slope for this relationship of 0.0225. Patients with more education have a

Table 2. Radiograph scores and health status and direct medical costs over time.

	Disease Duration, yrs													
	0–5		5–10		10–15		15–20		20–25		25–30		30+	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Radiograph score, 0–200	23.7 (18.4)	21.9 (9.2, 31.9)	36.4 (21.4)	37.8 (20.3, 52.0)	50.4 (32.3)	47.1 (26.6, 74.7)	57.8 (36.5)	55.2 (30.3, 77.4)	64.6 (40.4)	70.3 (21.9, 89.6)	68.7 (44.3)	69.5 (32.4, 96.1)	84.2 (40.0)	92.0 (53.0, 107.9)
HAQ DI, 0–3	1.3 (0.5)	1.3 (1.1, 1.7)	1.2 (0.7)	1.3 (0.8, 1.8)	1.3 (0.8)	1.4 (0.7, 1.9)	1.4 (0.8)	1.5 (0.7, 2.1)	1.5 (0.8)	1.4 (0.8, 2.1)	1.5 (0.7)	1.5 (1.2, 2.1)	1.8 (0.6)	1.8 (1.5, 2.4)
Global severity, 0–100	38.2 (15.9)	37.5 (27.0, 49.1)	38.7 (18.2)	40.0 (26.1, 52.4)	42.5 (19.3)	44.9 (28.4, 56.7)	43.0 (17.6)	45.1 (30.0, 53.6)	44.7 (19.9)	43.5 (34.5, 55.0)	44.3 (20.1)	41.3 (30.0, 58.2)	49.6 (20.6)	53.8 (34.3, 63.9)
Pain, 0–3	1.2 (0.5)	1.3 (0.9, 1.6)	1.1 (0.5)	1.2 (0.7, 1.5)	1.2 (0.6)	1.1 (0.8, 1.5)	1.2 (0.6)	1.3 (0.8, 1.7)	1.3 (0.6)	1.4 (0.8, 1.7)	1.3 (0.6)	1.4 (0.9, 1.6)	1.4 (0.6)	1.4 (0.9, 1.8)
Annual direct medical costs, $ 1994 CDN	6078 (6217)	4252 (2164, 7689)	4204 (3659)	2855 (1604, 5310)	4722 (5273)	2675 (1588, 5575)	4661 (9956)	2207 (1029, 4223)	3484 (3590)	2260 (1059, 3911)	4269 (4707)	2078 (1233, 5070)	4062 (3971)	2705 (1676, 4304)
No. of patients	18*		35		57		61		47		34		31	
Mean disease duration, yrs	3.8		7.8		12.5		17.5		22.2		26.9		36.6	

* It should be noted that patients can contribute data to more than one time interval and that a single patient could have several data points over a 5 year interval.
IQR: interquartile range.

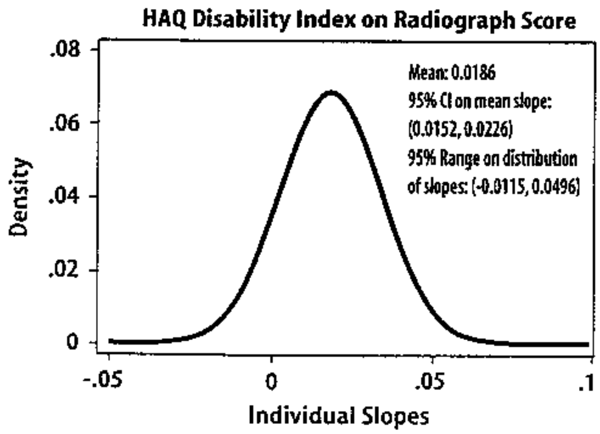

Figure 2a. The probability density for slopes of HAQ disability index on radiographic damage. As an example, over 10 years, a 25 unit increase in radiographic damage would be associated with a 0.46 unit increase in disability.

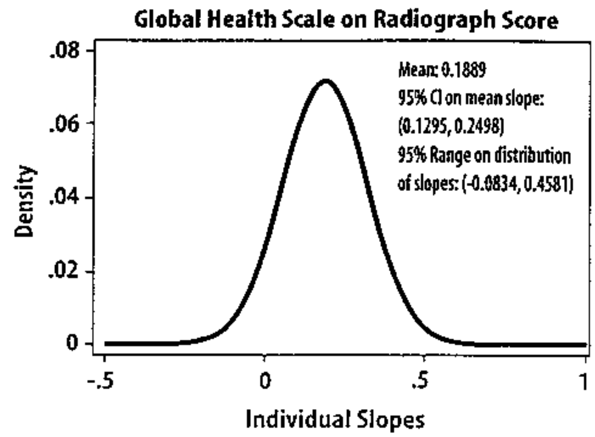

Figure 2b. The probability density for slopes of global well-being on radiographic damage. As an example, over 10 years, a 25 unit increase in radiographic damage would be associated with a 4.72 unit increase in global well-being.

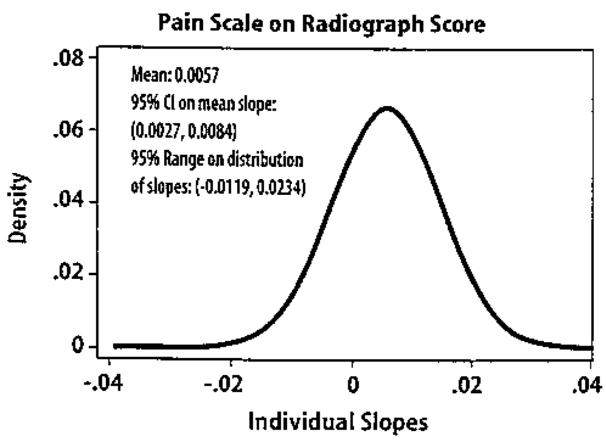

Figure 2c. The probability density for slopes of pain on radiographic damage. As an example, over 10 years, a 25 unit increase in radiographic damage would be associated with a 0.14 unit increase in pain.

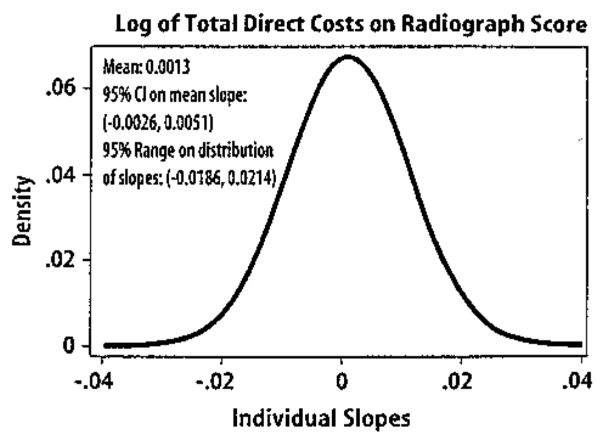

Figure 2d. As an example over 10 years, a 25 unit increase in radiographic damage would be associated with a 3% increase in log of direct costs.

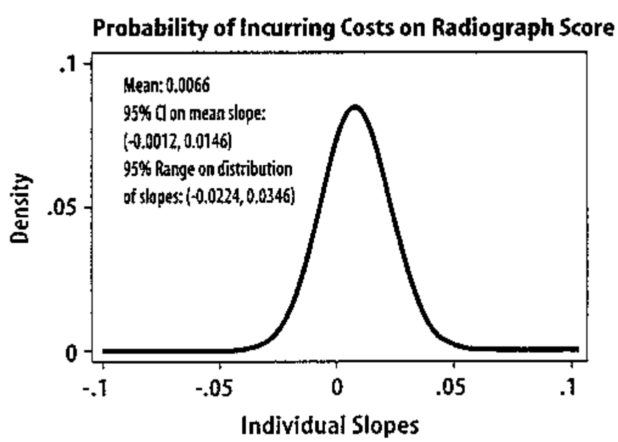

Figure 2e. As an example over 10 years, a 25 unit increase in radiographic damage would be associated with a 16% increase in the probability of incurring these costs and a 25 unit decrease in radiographic damage would be associated with a 16% decrease in the probability of incurring these costs.

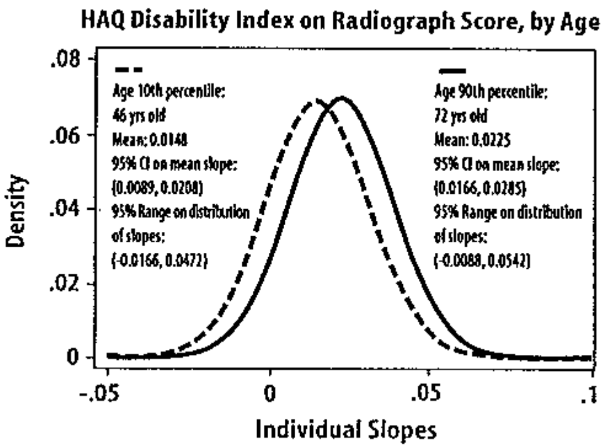

Figure 3a. Effect of age on the distribution of slopes of disability on radiographic damage. As patients age, the slope between disability and radiographic damage increases.

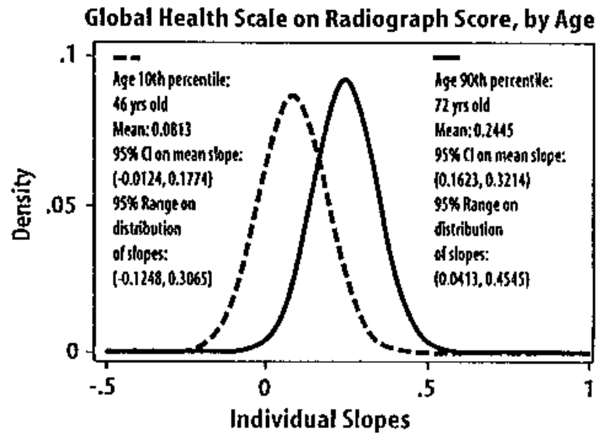

Figure 3b. Effect of age on the distribution of slopes of global well-being on radiographic damage. As patients age, the slope between global well-being and radiographic damage increases.

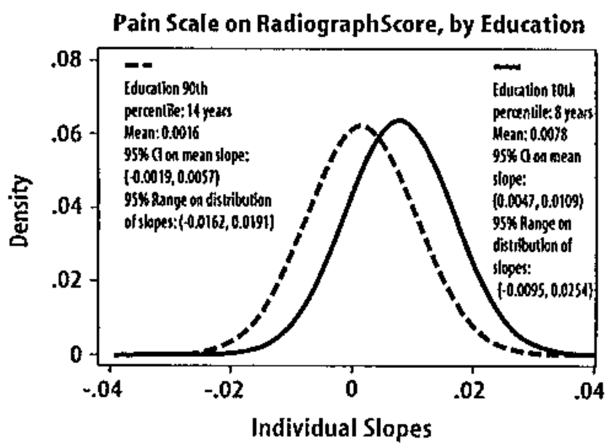

Figure 3c. Effect of education on the distribution of slopes of pain on radiographic damage. Patients with more education have a smaller slope between pain and radiographic damage.

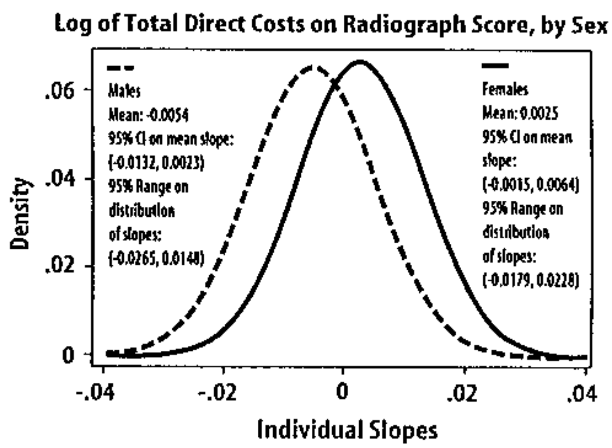

Figure 3d. Effect of gender on the distribution of slopes of total direct medical costs on radiographic damage. Females have a larger slope between costs and radiographic damage.

weaker relationship between pain and radiograph scores (Figure 3C), and women have a stronger relationship between direct medical costs and radiograph scores (Figure 3D).

DISCUSSION

Our study is one of the few to examine the relationship between radiographic damage and self-reported health status; it is the only study to evaluate the relationship between radiographic damage and direct medical costs and to involve patients with mean disease duration at study entry exceeding 16 years. Further, it is the only study to evaluate this relationship through the statistical technique of hierarchical modelling. The differing relationship between radiograph scores and health status across patients and the desire to express the magnitude of this relationship motivated the choice of this approach.

Our models examining the influence of demographic variables on the relationship between radiograph scores and self-perceived health status or costs may have been improved by considering additional independent variables. Several studies have shown that clinical and laboratory markers of disease activity such as number of tender and swollen joints, rheumatoid factor positivity, and erythrocyte sedimentation rate are predictors of both radiographic progression and functional disability[9-27]. Such variables, however, were not measured regularly across all study participants and therefore could not be included in our analysis.

Although several studies assess correlates of radiographic progression and functional disability[10-19], fewer examine the relationship between radiograph score and self-reported health status[20-27]; none examine the relationship

Table 3. Spearman correlations between radiograph scores and concurrent health status or costs over time.

	Disease Duration, yrs						
	0–5	5–10	10–15	15–20	20–25	25–30	30+
Radiograph scores vs HAQ DI	0.15	0.23	0.42	0.54	0.27	0.23	0.22
	(–0.34, 0.58)*	(–0.11, 0.52)	(–0.18, 0.62)	(0.33, 0.70)	(–0.02, 0.51)	(–0.12, 0.53)	(–0.15, 0.53)
Radiograph scores vs global severity	–0.21	0.17	0.20	0.27	0.04	0.06	0.14
	(–0.62, 0.28)	(–0.17, 0.48)	(–0.06, 0.44)	(0.02, 0.49)	(–0.25, 0.32)	(–0.28, 0.39)	(–0.23, 0.47)
Radiograph scores vs pain	–0.17	0.05	0.22	0.20	–0.06	0.07	0.06
	(–0.59, 0.32)	(–0.29, 0.38)	(–0.04, 0.45)	(–0.06, 0.43)	(–0.34, 0.24)	(–0.28, 0.39)	(–0.30, 0.41)
Radiograph scores vs direct costs	0.29	0.37	0.20	0.33	–0.01	0.14	–0.04
	(–0.20, 0.67)	(0.04, 0.62)	(–0.07, 0.44)	(0.08, 0.53)	(–0.29, 0.28)	(–0.21, 0.45)	(–0.39, 0.32)
No. of patients	18**	35	57	61	47	34	31

* 95% CI in parentheses below Spearman correlation. ** It should be noted that patients can contribute data to more than one time interval and that a single patient could have several data points over a 5 year interval.

between radiograph score and medical costs. Wolfe, *et al*[10] described the radiographic progression of 256 patients with RA who were seen within 2 years of disease onset and were followed for up to 19 years. The slope of radiograph score was regressed on the means of the self-reported variables of global severity and pain as well as on the means of several clinical and laboratory measures and demographic features. In these multivariate models, clinical and laboratory variables were predictors of radiographic progression, but self-reported health status variables were not associated. Spearman correlations between radiographic progression and the means of HAQ DI, global severity, and pain were, respectively, 0.212, 0.149, and 0.168. Van Leeuwen, *et al*[11] followed 149 patients with disease duration of < 1 year for 3 years and observed a Spearman correlation between radiographic progression and HAQ DI at 3 years of 0.306.

The studies assessing the relationship between radiograph score and health status generally show clinically meaningful associations and are summarized in Table 4. Drossaers-Bakker, *et al*[20] assessed 132 women with RA at 0, 3, 6, and 12 years of disease duration (Table 4). The Spearman correlation between hand and foot radiograph score and HAQ DI at 0, 3, 6, and 12 years of followup were, respectively, 0.22, 0.29, 0.41, and 0.57. In this same population, the correlation of large joint radiograph score and HAQ DI at 12 years was 0.60 and large and small joint involvement were closely associated[28]. Mottonen, *et al*[21] followed 142 patients with early onset RA for 6 years and reported a Spearman correlation between radiograph score and HAQ DI at study entry of 0.31, increasing to 0.51 by study end. Leirisalo-Repo, *et al*[22] assessed 145 patients with disease onset of < 2 years and followed them for up to 13 years. The Spearman correlation between radiograph score and HAQ DI was calculated annually. It tended to increase over time, ranging from 0.15 at year 1 to 0.75 at year 9. Kaarela, *et al*[23] calculated the Spearman correlation between radiograph score and HAQ DI for 103 patients of 8 years disease duration at 0.68; Pincus, *et al*[24] reported a Spearman correlation

Table 4. Studies evaluating correlation between radiograph scores and functional disability.

Author	No. of Patients	Mean Disease Duration at Time of Assessment, yrs	Spearman Correlation
Drossaers-Bakker, (1999)[20]	132	0	0.22
		3	0.29
		6	0.41
		12	0.57
Mottonen (1998)[21]	142	0	0.31
		6	0.51
Leirisalo-Repo (1999)[22]	145	1*	0.15
		9	0.75
Kaarela (1993)[23]	103	8	0.68
Pincus (1989)[24]	259	12.4	0.31
Hakula (1993)[25]	91	15.3	0.46
Sokka (2000)[26]	141	11.8 (= median)	0.28
Fex (1996)[27]	113	1	0.11
		5	0.006

* The Spearman correlation was assessed annually, but only the lowest and highest are reported here.

for 259 patients of mean disease duration of 12.4 years at 0.31; and Hakula, *et al*[25] reported a Spearman correlation for 91 patients with mean disease duration of 15.3 years at 0.46. Sokka, *et al*[26] found the correlation between radiograph scores and HAQ DI in 141 patients with RA with median disease duration of 11.8 years to be lower than previously reported, at 0.28. Fex, *et al*[27] assessed 113 patients with RA within 2 years of disease onset and followed them annually for 5 years. In contrast to the preceding studies, the Spearman correlation between radiograph score and HAQ DI at study entry and at 5 years was only 0.11 and 0.006, respectively.

We observed that the correlation between radiographic damage and HAQ DI increased with disease duration up to 20 years. However, this correlation would be more appropriately estimated if the composition of the patient cohort was consistent over time. Since most patients did not provide sufficient data to allow inclusion in several observation intervals, the patient cohort changes across time intervals. Patients who are more disabled are likely dropping out, which has the effect of minimizing the disease progression observed for an individual patient. The magnitude of this effect can be estimated by comparing the univariate association of radiograph score and disease duration as predicted by linear regression, i.e., 2.5 units per year, to that observed by following patients over time (Table 2). As observed in Table 2, mean radiograph score progressed from 23.7 to 84.2 over 32.8 years, implying an association between radiograph score and disease duration of 60.5/32.8 = 1.8 units per year.

We report a correlation of 0.42 with a mean disease duration of 20.2 years (i.e., refers to time over which patients contributed radiographs), which is comparable to the 0.51[22] observed at 10 years (data not shown), the 0.57[20] and 0.31 (24) observed at 12 years, and the 0.46 reported at 15 years[25]. It has been suggested[26] that early in the disease, functional ability is more influenced by disease activity as reflected by pain than by radiographic evidence of joint damage. Wolfe has recently reported, in a study involving over 30,000 observations on about 2000 patients with RA, that HAQ DI is more influenced by pain, psychosocial factors, and disease activity than structural damage, although structural damage was not directly assessed in this study[29]. It is possible that if the interval between self-report and radiographs had been even shorter than the mean of 104 days in our study, the correlations between radiograph scores and health status or direct cost data may have been higher. However, our allowable interval of one year makes our estimates of the association between radiographic damage and health status or direct costs conservative and more robust.

Although a positive association between radiographic damage and HAQ DI was observed by ourselves and others, we observed little association between radiographic damage and direct medical costs. In our work on a much larger sample of the RA cohort[2], a positive association was observed between HAQ DI and total direct medical costs, suggesting that perhaps because of the association between HAQ and radiographic damage, radiographic damage would also be correlated with medical costs. However, the association we previously observed between HAQ DI and costs was largely due to the association between HAQ DI and nonacute care hospital stays. Patients in our radiographic study used nonacute care less intensively. As shown in Table 1, although patients participating in the radiographic study were more disabled with higher direct medical costs, these costs were largely due to acute care hospital stays that we reported[2] as less related to functional disability than nonacute care costs. Further, it is thought that later in the disease, the articular involvement is largely irreversible and therefore less aggressive intervention may be offered by the provider. It is also possible that the very disabled patients were unable to visit the provider, thereby using fewer health resources than their less disabled counterparts. Therefore, this lack of association between direct medical costs and radiographic damage is not surprising.

In addition to expressing the relationship between radiographic damage and health status through correlation coefficients, we also assessed this relationship through hierarchical modelling. Unfortunately, the lack of any other studies in the rheumatic diseases examining this relationship using this methodology makes comparison with the published literature impossible.

Our study included only patients having at least 2 hand radiographs over a 5 year interval and concurrent health status and cost data. When compared to patients not fulfilling such criteria, these patients have poorer self-reported health status, likely reflecting inclusion in our study of patients with more severe disease. It is possible that the association between radiographic damage and health status that we observed may differ for patients with radiograph and HAQ scores outside the range of those observed in our study participants.

In conclusion, we have observed that, although there is much individual variation, a clinically important association exists between radiographic damage and self-perceived functional health status. This suggests that interventions that slow radiographic progression may improve the patient's functional status. Overall, there is little association between radiographic damage and total direct medical costs. However, for female patients, there is a stronger relationship. Given the strong association between functional status and radiographic damage, it is anticipated that there will also be an association between indirect costs resulting from lost productivity and radiographic damage. This is the subject of continuing work.

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