Patient Questionnaires and Formal Education Level as Prospective Predictors of Mortality Over 10 Years in 97% of 1416 Patients with Rheumatoid Arthritis from 15 United States Private Practices

THEODORE PINCUS, JULIE KEYSOR, TUULIKKI SOKKA, ESWAR KRISHNAN, and LEIGH F. CALLAHAN

ABSTRACT. ***Objective.*** To prospectively analyze patient questionnaire scores concerning functional disability as well as formal education level as potential predictors of premature mortality over 10 years in 1416 patients with rheumatoid arthritis (RA) from 15 private practice rheumatology settings in 11 diverse cities in the United States.

Methods. At baseline in 1985 and periodically over 10 years, patients completed mailed self-report multidimensional health assessment questionnaires (MDHAQ) that included functional disability scores, formal education level, and other demographic and clinical data. Vital status was determined 10 years after baseline. Potential predictors of 10 year mortality were analyzed using descriptive statistics and Cox proportional hazards models.

Results. Vital status was accounted for in 1378 patients, 97.3% of the cohort. The standard mortality ratio was 1.6, similar to most reported series of patients with RA, as 401 patients died versus 251 expected over 10 years. Evidence of "dose-response" relations was seen for age, formal education level, functional disability scores, and helplessness scores as predictors of mortality. In Cox proportional hazards models, age, sex, formal education level, functional disability, and helplessness scores remained significant independent predictors of 10 year mortality.

Conclusion. Functional disability and low formal education level are significant predictors of premature mortality in people with RA under care in US private practice settings, as in most reported cohorts of patients with RA. This study shows that it is possible to account for more than 95% of patients over 10 years using mailed questionnaires to monitor patient status. (J Rheumatol 2004; 31:229–34)

Key Indexing Terms:
RHEUMATOID ARTHRITIS MORTALITY QUESTIONNAIRES
FUNCTIONAL DISABILITY EDUCATION LEVEL

A retrospective study of a cohort of 75 patients with rheumatoid arthritis (RA) in 1982, 9 years after an extensive baseline evaluation in 1973, indicated 5 unexpected observations concerning longterm outcomes[1-3]: (a) people with RA had significant morbidity as well as premature mortality compared to the general population[4]; (b) premature mortality was predicted by more severe disease 9 years earlier, not drug toxicity, suggesting that under-treatment rather than over-treatment was a primary problem in most patients[5-7]; (c) the most effective predictor of premature mortality was a patient questionnaire concerning functional disability, rather than a laboratory test or radiograph[8]; (d) a second independent predictor of premature mortality was formal education level, representing socioeconomic status and patient-determined variables[9]; and (e) the terms disease modifying antirheumatic drugs (DMARD)[10] or remission-inducing drugs[11] were not applicable to most patients at that time, as data from short term randomized controlled clinical trials over 3 years or less were not necessarily applicable to longterm outcomes[12].

These studies were retrospective, hypothesis-generating studies, as have been most reports of other cohorts that have confirmed these observations[13-18]. Few studies have prospectively examined in a hypothesis-testing study whether patient questionnaire data and formal education are significant independent predictors of mortality in RA.

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Furthermore, patient questionnaire data and formal education level are not collected in usual rheumatology care, in contrast to extensive laboratory and radiographic data of considerably lesser value in prognosis and monitoring of patients with RA. One explanation may be that no studies have documented prospectively the generalizability of patient questionnaire data and formal education as prognostic markers for mortality over long periods in patients seen in private practice settings.

We prospectively monitored 1416 patients from the private practices of 15 rheumatologists in 8 states over 10 years from 1985 to 1995 according to patient self-report questionnaires[19–24]. In this report, we present evidence that functional disability according to a patient questionnaire and formal education level are prospective significant predictors of premature mortality over 10 years in these patients with RA.

MATERIALS AND METHODS

Patients. A cohort of 1416 persons diagnosed as having RA by their rheumatologists was assembled in late 1984 from 15 private practice rheumatology settings in 11 cities: Menlo Park, Palo Alto, and Santa Cruz, CA; Vero Beach and Palm Beach, FL; Boise, ID; Minneapolis, MN; Philadelphia, PA; Memphis and Nashville, TN; and Washington, DC. The patients completed a baseline mailed self-report questionnaire in January 1985[21,22], and periodically from 1985 to 1995. A formal review of American Rheumatism Association (ARA) criteria for RA[25] was not available. Further details concerning this cohort have been presented[19-22].

Patient questionnaire. The patients completed what has become known as a multi-dimensional health assessment questionnaire (MDHAQ)[24] that includes demographic data including age, formal education level, sex, race, marital status, year of onset of RA, and scales to assess functional disability, pain, and helplessness. Functional disability was assessed according to a modified HAQ (MHAQ)[23,26,27] that includes 8 activities of daily living (ADL) and was reported as scored 1-4, but has been modified to be scored 0-3, similar to the HAQ[28], from which the MHAQ and MDHAQ were derived: 0 = without any difficulty, 1 = with some difficulty; 2 = with much difficulty, and 3 = unable to do, analogous to American Rheumatism Association (ARA) Functional Class[29]. Helplessness was assessed according to the 5-item Rheumatology Attitudes Index (RAI), derived from the 15-item Arthritis Helplessness Index[30-32]. Pain was assessed according to a 10 cm pain visual analog scale, with 0 indicating no pain and 10 indicating the highest degree of pain[28,33]. All data were collected using mailed patient questionnaires; no information was collected concerning physical examination, radiographs, and laboratory tests.

Strategies to maintain cohort. It was recognized in studies of the cohort analyzed between 1973 and 1988 in which all 75 patients were accounted for after 9[1] and 15 years[3], that mortality would have been substantially underestimated without identification of the final 20% of patients in this earlier cohort[1,3,34]. Therefore, several strategies were incorporated to maintain contact with members of the patient cohort: (1) all questionnaires were fewer than 16 pages, generally 12 pages, and could be completed within one hour; (2) if a questionnaire was not returned within one month, a second questionnaire was mailed to each patient; (3) if the second mailed questionnaire was not returned within one month, a telephone call was made to the patient that included verification of vital status and an abbreviated "telephone questionnaire" that included the 8 activities of daily living, level of pain, and global status; (4) the patient who responded only through the telephone query was invited to be contacted only by telephone in future replications, because he or she was unable or unwilling to complete a mailed questionnaire; about 20% of patients elected this option; and (5) if the patient could not be reached by telephone, the office of the referring rheumatologist was contacted for clues as to the patient's whereabouts; we appreciated the helpfulness of the staff of these rheumatologists to locate these patients.

Statistical methods. The data were analyzed using the Statistical Analysis System (SAS), version 6.12, and the Statistical Package for the Social Sciences (SPSS), Version 11. The standard mortality ratio was computed by comparing the mortality of persons in the cohort to age- and sex-specific expected general US mortality. Baseline measures for patients who died over the 10 year followup period were compared to those in surviving patients; statistical significance of differences was determined using the Student's t test for continuous variables and the chi-square test for dichotomous variables.

Cox Proportional Hazard models were computed for each baseline variable, adjusted for age, sex, education, and duration of disease. A forward conditional multivariable Cox regression model was computed to estimate possible independent contributions of functional disability, pain, and helplessness to predict 10 year mortality, controlling for age, sex, marital status, formal education level, and duration of disease.

RESULTS

Patient cohort. The mean age of the study cohort at baseline was 56.0 years, and mean duration of disease 11.7 years; 77% were women, and 92% were Caucasian, typical for cohorts of patients with RA assembled during the 1980s. The mean level of formal education was 12.5 years (Table 1). At baseline, the mean score for functional disability on the MHAQ (range 0-3) was 0.6; mean visual analog pain scale score (range 0-10) was 3.9; and mean helplessness scale score (range 1-4) was 2.3.

Ten-year mortality. After 10 years of observation, vital status was known concerning 1378 patients or 97.3% of the initial 1416 participants. It was known that 401 of the 1378 patients had died, versus 251 expected according to the age and sex of the patients. The standard mortality ratio (SMR) was 1.6, similar to most reports of higher mortality rates in cohorts of patients with RA[35].

Patients who died over the 10 years had significantly higher age, lower formal education level, and were more likely to be male or non-married (Table 1). No significant differences according to race were seen between those who survived or died (Table 1). Patients who died had significantly higher baseline scores for functional disability, pain, and helplessness (Table 1).

In Cox proportional hazards models (Table 2), variables at baseline that were predictive of a significantly higher risk of mortality over 10 years included high age, male sex, few years of formal education, high functional disability, pain, and helplessness (Table 2), while race and duration of disease in the entire cohort were not significant predictors. Evidence of "dose-response" relations was seen for age, functional disability, helplessness, and formal education level as predictors of mortality (Figure 1). In the multivariable Cox proportional hazards model, age, male sex, formal education level, functional disability, and helplessness were independent predictors of 10 year mortality (Table 3).

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Table 1. Mean values at baseline of 1378 patients with RA who survived or died over a 10-year period (p value from Student's t test or chi-square test).

	Total n = 1378	Alive n = 977	Dead n = 401	p
Demographic Measures				
Age at baseline*	56.0 (14.1)	52.1 (13.8)	65.3 (9.9)	< 0.0001
% Female	77.0	79.0	73.0	0.007
% Caucasian	92.0	92.0	94.0	0.174
% Married	70.0	72.0	66.0	0.013
Formal education level*	12.5 (3.0)	12.9 (2.9)	11.5 (3.1)	< 0.0001
Clinical Status Measures				
Disease Duration*	11.7 (9.6)	11.3 (9.7)	12.8 (9.5)	0.009
Functional disability*	0.6 (0.6)	0.6 (0.5)	0.8 (0.6)	< 0.0001
Pain*	3.9 (2.8)	3.7 (2.7)	4.6 (2.9)	< 0.0001
Helplessness score*	2.3 (0.5)	2.3 (0.5)	2.5 (0.5)	< 0.0001

* Mean (SD) of continuous variables.

Table 2. Unadjusted and adjusted hazard ratios of demographic, clinical, and self-report questionnaire scores.

	Unadjusted Hazard Ratio (95% CI)	Adjusted Hazard (95% CI)
Demographic variables and duration of disease		
Age at baseline	1.1 (1.1, 1.1)	1.1 (1.1, 1.1)
Male	1.4 (1.1, 1.7)	1.4 (1.1, 1.9)
Not married	1.3 (1.1, 1.6)	1.4 (0.8, 1.4)
Non-white	0.7 (0.5, 1.1)	—
Duration of disease	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)
Years of formal education		
≥ 12	1.0	1.0
9–11	1.7 (1.3, 2.2)	1.0 (0.8, 1.4)
≤ 8	2.5 (1.9, 3.2)	1.3 (1.0, 1.8)
Stratified clinical variables		
Functional disability		
0.0–0.12	1.0	1.0
0.13–0.86	1.2 (0.9, 1.7)	1.0 (0.6, 1.5)
0.87–3.0	2.3 (1.8, 3.0)	1.6 (1.0, 2.7)
Pain		
0.0–3.7	1.0	1.0
3.8–6.8	1.5 (1.1, 1.9)	1.2 (0.9, 1.7)
6.9–10.0	1.7 (1.3, 2.2)	1.3 (0.9, 1.8)
Helplessness score		
1.00–2.00	1.0	1.0
2.01–2.50	1.6 (1.2, 2.1)	1.2 (0.9, 1.7)
2.51–4.00	2.6 (2.0, 3.4)	1.4 (1.0, 2.1)

DISCUSSION

Our study indicates a SMR of 1.6 in 1378 patients with RA from 15 private practices in 11 diverse locales in the US, similar to other reported series of patients with RA with baselines in the 1980s[36]. The data are consistent with findings that RA may be a severe disease in the community[37], and evidence that mortality rates have not changed substantially in cohorts first observed in 1965, 1975, and 1985[38,39]. However, all these patients had been treated initially prior to 1985, when drugs widely used today, particularly methotrexate, were not available, and treatment strategies were much less aggressive. Recent evidence of improved mortality experience in responders to methotrexate[40,41] suggest that mortality rates in RA may be improving.

The data indicate that patient functional status according to a self-report questionnaire and formal education level are significant predictors of 10-year mortality in RA, when studied prospectively in a cohort of 1384 patients with RA from 15 US private practices. Patient functional status scores on a self-report questionnaire have now been documented to provide effective prediction of mortality in RA in 3 databases studied at Vanderbilt University over 5 years or more: a cohort of 75 patients studied from 1973 to 1988[1-3], a cohort of 210 patients studied from 1985 to 1990[42], and the

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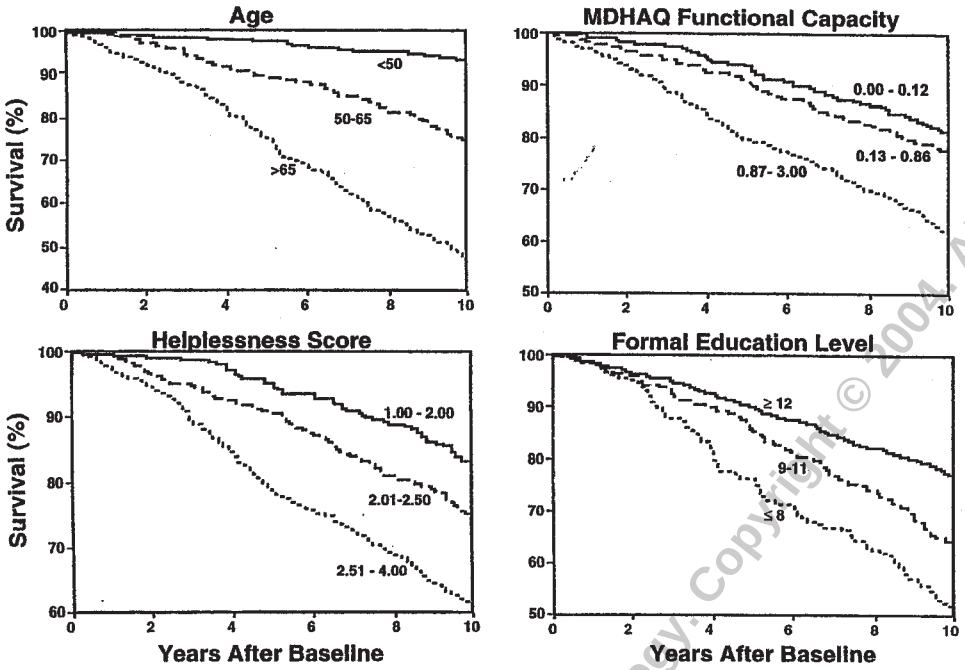

Figure 1. Survival of 1378 patients with RA from 15 US private practices over 10 years according to baseline values.

Table 3. Cox proportional hazards model to analyze predictors of mortality in 1378 patients with RA.

	Hazard Ratio	95% CI		p
		Lower	Upper	
Age	1.08	1.06	1.09	< 0.001
Male	1.41	1.12	1.78	0.004
Formal education level	1.04	1.01	1.08	0.020
Functional disability	1.74	1.43	2.11	< 0.001
Helplessness score	1.43	1.20	1.86	0.008

present cohort of 1416 patients from 15 rheumatology private practices studied from 1985 to 1995[22]. Functional status has also been documented as a predictor of mortality in retrospective and prospective data from other databases[13–18,38].

Functional disability also appears to predict hospitalization and death effectively in AIDS[43], congestive heart failure[44], and elderly patients[45-48]. We have suggested previously that rheumatologists monitor functional disability using a patient questionnaire in routine clinical care[49-51].

Associations of formal education and mortality have also been documented in each of the 3 Vanderbilt cohorts[2,22,42], as well as in other cohorts of patients with RA[17,18]. All patients in this study were identified in private rheumatology practices, supporting a suggestion that associations between education level and mortality are explained only in small part by limited access to medical care on the part of socioeconomically disadvantaged individuals[52], but more likely reflect issues of self-management and social conditions[52]. It has been suggested that formal education is a surrogate for behavioral variables endogenous to the patient, which appear associated with longterm outcomes[9,52,53]. Disparities in health according to socioeconomic status have been widening, rather than narrowing, over the last decade in the US, the Netherlands, and the United Kingdom[52].

Two important limitations are seen in our study. First, no data are available concerning traditional RA measures such as the joint count, radiographs, or laboratory tests. However, considerable evidence indicates that even when these traditional measures are available, patient questionnaire data predict mortality independently, as significantly as any currently available clinical measure[42]. Second, we do not have available data from the US general population that likely would have led to recognition of an even greater risk according to poor functional status. Other studies outside the US have indicated that poor functional status in the general population is a predictor of mortality[54].

Our study documents that it is possible to account for more than 95% of patients monitored over 10 years in the US using mailed patient questionnaires, with aggressive strategies to maintain the cohort. Most people with RA complete a patient questionnaire in the clinic or by mail without complaint, as they recognize that the matters queried, functional status, pain, and global status are generally among their primary concerns[55]. The HAQ[28], Clinical

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HAQ (CLINHAQ)[56], MHAQ[23,26], and MDHAQ[24] can be used to monitor clinical status in usual care of patients with RA in the clinic, as well as in a mailed questionnaire program. These questionnaires can add considerably to rheumatology care and research.

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