Health Assessment Questionnaire Score Is the Best Predictor of 5-Year Quality of Life in Early Rheumatoid Arthritis

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ABSTRACT. ***Objective.*** To evaluate and determine prognostic factors of 5-year quality of life in patients with early rheumatoid arthritis (RA).

Methods. A cohort of 191 patients with RA and disease duration < 1 year was prospectively followed over 5 years. The outcome measure was quality of life as assessed by the Arthritis Impact Measurement Scales 2 (AIMS2). Univariate analysis, then stepwise multiple logistic regression, was used to find independent baseline prognostic variables.

Results. After accounting for death, loss of followup, and missing data, 158 patients (82.72%) were included in the analysis. The mean AIMS2 physical, symptom, psychological, social interaction, and work scores after 5 years were 1.6 (range 0–6.88), 4.0 (0–10), 3.48 (0–9.22), 4.06 (0–8.69), and 1.87 (0–8.13), respectively. The AIMS2 physical component was significantly correlated with Health Assessment Questionnaire (HAQ) score at 5 years. Logistic regression analysis revealed that the baseline values able to predict the 5-year physical, psychological, symptom, social interaction, and work status were, respectively: HAQ score and erythrocyte sedimentation rate (ESR), body mass index (BMI), HAQ; erosion score and sex, HAQ; ESR and anti-perinuclear antibody; matrix metalloproteinase-3 (MMP3) level, joint space narrowing, and tender joint scores; HAQ score and age.

Conclusion. The multidimensional structure of the AIMS2 allowed us to assess the 5-year health-related quality of life in early RA. Using this instrument as an outcome variable, prognostic factors were selected and varied widely depending on the evaluated domain. The baseline HAQ score was the best predictive factor of 4 of the 5 domains of the AIMS2. (First Release Aug 15 2006; J Rheumatol 2006;33:1936–41)

Key Indexing Terms:
RHEUMATOID ARTHRITIS ARTHRITIS IMPACT MEASUREMENT SCALES 2
HEALTH ASSESSMENT QUESTIONNAIRE SCORE QUALITY OF LIFE PROGNOSIS

Rheumatoid arthritis (RA) is the most prevalent chronic arthritis. In many patients, the disease process is severe and results in pain, progressive joint destruction, severe functional disability, deterioration of quality of life, and even death. However, the outcome varies widely. There is heterogeneity of presentation, clinical course, quality of life, and global outcome in the individual patient[1]. Predicting the outcome in RA is thus important for treating patients optimally, with appropriately aggressive therapy at an early stage. Prediction is even more important since new therapies reducing RA progression and joint destruction are now available[2-4].

Several prospective studies[5-15] have identified possible initial individual prognostic factors of RA severity, including clinical disease activity, rheumatoid nodules, systemic manifestations, elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) level, positivity for rheumatoid factor (RF), anti-cyclic citrullinated peptide (CCP) antibodies, HLA-DRB1* genotypes, radiologic evidence of erosions, or poor functional status. These studies were performed with the outcome measures functional disability, joint destruction, and decreased life expectancy, but quality of life has rarely been considered and evaluated despite improvement in quality of life being a major aim of therapeutic strategy[16,17].

A cohort of 191 patients with RA of less than 1 year duration was prospectively followed during 5 years. At 5 years, in addition to functional disability and radiographic evaluation, a disease-specific quality of life questionnaire was administered: the Arthritis Impact Measurement Scales 2 (AIMS2). Its

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multidimensional design allowed assessment of the 5-year health-related quality of life in early RA. Our primary objective was to identify baseline prognostic factors of each domain of the AIMS2 (physical, symptom, psychological, social interaction, and role) in patients with RA at 5 years.

MATERIALS AND METHODS

All consecutive outpatients fulfilling American College of Rheumatology criteria for RA of less than 1 year duration from 4 French centers (Montpellier, Paris-Cochin, Toulouse, Tours)[18] and who agreed to be enrolled in a 5-year prospective study were included. They were referred from primary care physicians for the purpose of this study and had never been treated with disease modifying antirheumatic drugs (DMARD). After inclusion, they were all treated with DMARD (methotrexate or sulfasalazine or both), which could be modified during the study according to efficacy and side effects. All patients signed an informed consent form. The study was approved by the ethical review board in Montpellier.

Clinical and biological assessment. The following evaluation data were collected at baseline: age, sex, body mass index (BMI), disease duration, morning stiffness, pain (measured on a visual analog scale), number of swollen and tender joints, disease activity score (DAS), presence or absence of nodules and extraarticular manifestations, Health Assessment Questionnaire (HAQ) score, ESR, CRP level, MMP-3 level, antinuclear antibodies (immunofluorescence technique), IgA and IgM RF (anti-human Fc IgG-ELISA), anti-CCP antibodies (ELISA), antiperinuclear antibodies (immunofluorescence on buccal epithelial cells), anti-RA-33 antibodies (immunoblotting), anti-HSP90 antibodies (ELISA), anticalpastatin antibodies (ELISA; Heidelberg, Germany), and YKL-40 level (radioimmunoassay; Metra Biosystems, San Diego, CA, USA). HLA-DRB1* genotyping was performed as described[11]. Each patient was followed up by the same investigator 6 months after inclusion and once yearly for 5 years.

Radiographic measurement and functional assessment. Hand, wrist, and foot radiographs were obtained at baseline and at 3 and 5 years. They were evaluated by Sharp score modified by van der Heijde, as described[18]. Radiologic evidence of progression was therefore defined by a change of at least 4.1, 4.9, and 7.2 in the erosion, narrowing, and total damage scores, respectively[18]. Functional disability was assessed by the HAQ[19] at baseline and at 5 years.

Quality of life assessment. The 5-year quality of life outcome was assessed by the French version of the AIMS2[20,21]. The AIMS2 is a self-report health status questionnaire with 57 items organized in 12 dimensions: mobility level, walking and bending, hand and finger function, arm function, self-care, household tasks, arthritis pain, work, social activities, support from family and friends, level of tension, and mood. Each dimension includes 4 or 5 items with 5 alternatives on a response scale. These 12 dimensions are aggregated into 5 components or domains — physical, symptom (pain), psychological (affect), social interaction, and role (work) — rated on a scale of 0 (good health) to 10 (poor health status). Finally, a score for each component giving the health profiles of the patient is obtained.

Statistical analysis. Statistical analysis was performed with BMDP statistical software[18]. Different outcome variables were dichotomized into qualitative variables: HAQ score ≤ 1 or HAQ score > 1, radiological scores lower or higher than the median value, absence or presence of radiologic evidence of progression, and quality of life. Quality of life is difficult to measure subjectively, to ascertain cutoff levels and to have clinical meaning. There is no consensus regarding the clinically relevant changes in this kind of quality of life instrument. Cutoff values for each component of the questionnaire that discriminate between severe and mild quality of life were defined as the median of each component. A bivariate analysis of the relationship between all baseline values and each component of the AIMS2 was undertaken by use of the Chi-square test, with Yates's correction when appropriate, or Fisher's exact test. Continuous variables were transformed into categorical variables, with the median value used as cutoff point. A stepwise multiple logistic regression model was used to determine independent prognostic variables. The prognostic variables included in the multivariate model were selected by use of bivariate analysis ($p \leq 0.15$).

RESULTS

Patient characteristics (Table 1). One hundred ninety-one patients (140 women, 51 men) were enrolled in this study. The mean age at diagnosis was 50.5 ± 14.7 years and the mean disease duration at inclusion was 3.6 ± 2.6 months. One hundred thirty-nine patients (80.8%) were positive for IgM or IgA RF (> 20 IU/ml and > 7 U/ml, respectively) at baseline, and 86 (47%) had at least one RA-associated DRB1*04 allele (DRB1*0401, 0404, 0405, 0408). During the 5-year followup, a mean of 1.95 DMARD (range 1–5) were prescribed (methotrexate, 175; sulfasalazine, 147; allochrysine, 41; hydroxychloroquine, 25; D-penicillamine, 14; cyclosporine, 1; anti-tumor necrosis factor-α, 5).

Functional and radiological outcome. These data have been described in detail[19]. Briefly, disability as measured by the HAQ was less severe after 3 and 5 years of disease than at baseline. The median HAQ score decreased from 1.25 to 0.37 during this period (mean 1.3 ± 0.7 to 0.6 ± 0.6; $p < 0.001$). Most patients (78.2%) had HAQ scores lower than 1 (mild disability) after 5 years compared with 34.7% at baseline. By contrast, 19.1% had severe disability (HAQ > 2) at baseline compared with 5.8% at 3-year and 4.5% at 5-year followup. Finally, 90% of the patients showed improved disability scores.

By 5-year followup, the total damage, erosion, and joint space narrowing (JSN) scores increased from 3.6 ± 7.7 to 17.9 ± 22.3 ($p < 0.001$), 1.7 ± 4.5 to 6.9 ± 9.5 ($p < 0.001$), and 1.9 ± 3.7 to 11.0 ± 15.4 ($p < 0.001$), respectively. Median total

Table 1. Baseline characteristics of 191 patients with early RA.

Characteristic	Mean ± SD
Female*	140 (73.3)
Age, yrs	50.5 ± 14.7
Disease duration, mo	3.6 ± 2.6
Pain (0–100 mm VAS)	57.5 ± 22.00
Morning stiffness, min	84.9 ± 79.4
Ritchie index	17.5 ± 8.5
Tender joints, no.	21.7 ± 10.5
Swollen joints, no.	9.0 ± 5.9
HAQ	1.3 ± 0.7
Nodules*	11 (5.7)
ESR, mm/h	40.2 ± 28.5
CRP, mg/l	34.1 ± 43.2
IgM or IgA RF-positive*	139 (80.8)
Antiperinuclear antibody, %	49.9
Anti-CCP antibody, %	58.9
DAS	4.1 ± 0.8
HLA-DRB1*04†*	86 (47)
HLA-DRB1*01*	54 (29.5)
Sharp score at baseline	3.6 ± 7.7
No. of DMARD/patient	1.7

* n (%) of patients. † RA associated DRB1*04 genes: 0401, 0404, 0405, 0408.

Sharp scores were 1.0 at baseline, 4.0 at 3 years, and 10.0 at 5 years. At 3- and 5-year followup, significant radiographic evidence of progression was observed in 71 (41.3%) and 87 (55.8%) patients in terms of total damage score, in 55 (31.8%) and 75 (48.1%) in erosion score, and in 46 (26.6%) and 62 (39.7%) in JSN score.

5-year quality of life. Thirty patients (11.52%) were lost to followup (6 patients died, 2 refused further followup, 22 moved out of the area). The 5-year AIMS2 scores were missing for 3 additional patients. Data for 158 patients were available at 5 years. The baseline data of the 33 patients that were not available for the 5-year analysis did not differ from those of the whole cohort. The 5-year AIMS2 physical, pain, psychological, social, and work scores are reported in Table 2. A significant correlation (r = 0.70) was obtained between the 5-year HAQ score and the 5-year AIMS2 physical domain, but not between these variables and 5-year radiographic progression.

Predictive factors of 5-year quality of life. According to bivariate analysis, the 5-year physical domain was associated with baseline HAQ score, DAS, CRP level, Ritchie index, pain, BMI, tender joint count, morning stiffness, and ESR, but stepwise multiple logistic regression revealed only HAQ score and ESR as independent variables (Table 3).

The 5-year symptom (pain) domain was associated with HAQ score, DAS, ESR, IgA RF, pain, morning stiffness, and CRP level. The variables able to predict the 5-year symptom domain by logistic regression analysis were HAQ score, ESR, and IgA RF (Table 3).

For the psychological (affect) component, bivariate analysis identified CRP level, BMI, DAS, HAQ score, Ritchie index, erosion score, sex, anticalpastatin antibody, MMP-3 level, tender joint count, total damage score, ESR, and pain. Regression analysis (Table 3) identified as independent variables only BMI, HAQ score, erosion score, and sex.

The 5-year social component was associated with antiperinuclear antibody, MMP-3 level, IgA RF, total damage score, tender joint count, CRP level, JSN score, and morning stiffness by bivariate analysis, but only antiperinuclear antibody, MMP-3 level, JSN score, and tender joint score were independently predictive (Table 3).

For the 5-year work (role) component, the initial associated variables were HAQ score, DAS and age at diagnosis, Ritchie index, and BMI, but the independent variables were HAQ score and age at diagnosis only (Table 3).

According to the Fisher exact test, no correlation was seen for any domain with extraarticular manifestations, IgM RF, anti-CCP antibody, anti-HSP90, and HLA-DRB1* genes.

Table 2. Arthritis Impact Measurement Scales 2 score at 5 years (n = 158).

	Physical Component	Symptom Component	Psychological Component	Social Interaction Component	Role Component (work)
Mean score	1.6	4.0	3.48	4.06	1.87
Range	0–6.88	0–10	0–9.22	0–8.69	0–8.13
Median value	1.21	3.37	4.0	3.87	1.25

Table 3. Prognostic factors for 5 years in the 5 domains of the AIMS2 (stepwise logistic regression).

	Coefficient	SE	OR	95% CI
Physical scale				
HAQ	2.207	0.430	9.09	3.88–21.3
ESR	0.709	0.423	2.03	0.88–4.69
Symptom scale				
HAQ	1.335	0.419	3.80	1.66–8.72
ESR	0.980	0.413	2.66	1.18–6.04
IgA RF	0.902	0.553	2.47	0.82–7.38
Affect scale				
BMI	1.460	0.501	4.31	1.59–11.7
HAQ	1.397	0.494	4.04	1.52–10.8
Erosions	1.064	0.483	2.90	1.11–7.56
Sex	0.947	0.550	2.58	0.86–7.69
Social interaction scale				
APN antibody	1.293	0.469	3.64	1.44–9.24
MMP3	–0.983	0.477	0.374	0.14–0.96
Joint space narrowing	1.075	0.468	2.93	1.16–7.43
Tender joints	0.945	0.481	2.57	0.99–6.69
Role scale				
HAQ	1.905	0.760	6.72	1.45–31
Age	1.557	0.912	4.74	0.76–29.8

RF: rheumatoid factor, APN: antiperinuclear.

Among independent prognostic variables of 5-year quality of life, baseline HAQ score was selected in 4 out of 5 domains (physical, psychological, symptom, and role components) and appeared to be the best predictor of 5-year quality of life.

DISCUSSION

This multiparameter prospective study of 191 patients with early RA provided new information to predict 5-year quality of life in early RA, and highlighted the importance of the baseline HAQ score as an important prognostic factor of RA outcome. The AIMS2, a RA-specific questionnaire, was used to assess the 5-year quality of life.

The patient characteristics were similar (sex ratio, age, biological and clinical measures of disease activity) to other prospective RA cohorts[5-10,13,14,16]. All the patients were DMARD-naive at baseline and then were mainly treated with sulfasalazine, methotrexate, or a combination of these. This prospective study confirmed that most patients with early RA have a fairly good 5-year prognosis for functional outcome despite progressive joint destruction as evaluated by the modified Sharp score[19].

Very few studies have evaluated quality of life of patients with RA with specific questionnaires and during followup. The 5-year quality of life has been evaluated with the AIMS[16] and AIMS2[22-24]. Three-year anxiety and depression findings have also been reported with use of the AIMS[25].

No consensus and cutoff limits have been established regarding clinically meaningful changes with this kind of quality of life instrument. Uhlig, *et al*[16] chose 2.0 and 3.0 as cutoff values for the physical and psychological components, respectively, of the AIMS. On the basis of their clinical experience, the same investigators[22] selected levels of health status to be of clinical importance. This level was 4.0 for the physical, social interaction, and affect domains of the AIMS2. A level of 4.0 has also been proposed for the AIMS depression scale[23]. This level is close to the median values obtained for 3 of the 5 domains that we chose as cutoff limits in our study (Table 2). The median values of the physical and role components were lower in our study (1.21 and 1.25, respectively) and seemed to be less affected after 5-year followup than the other domains. Taken together, our 5-year AIMS2 median and mean values are in agreement with the 5-year data reported by Uhlig, *et al*[22] and are slightly lower than those reported by Riemsma, *et al*[24].

A significant correlation was observed at 5 years between disability as measured by the HAQ and the AIMS2 physical domain. A similar observation was reported with both the AIMS and AIMS2[20,26,27], but discrepancies between the 2 health status instruments for physical function have also been noted, with a trend to higher AIMS mean score deterioration over time compared with disability as measured by the HAQ[16]. No correlation was observed at 5 years between radiographic damage and HAQ or AIMS2 scores including physical domain. These data are consistent with previous reports showing a link between radiographic scores and disability but only after 6 to 10 years of disease duration[28,29].

A few reports have evaluated the prognostic factors of quality of life in early RA[16]. Our study is the first to examine predictive factors of the 5-year quality of life in RA with use of the AIMS2 and all components, as a specific outcome questionnaire.

The 5-year AIMS2 physical domain was independently predicted by the baseline HAQ score and ESR. This observation is consistent with that from a previous study, in which we found that 5-year disability measured by the HAQ was also predicted by baseline HAQ score and ESR[19]. Similar results have been reported by Uhlig, *et al*[16], who found that baseline HAQ score and AIMS physical component were associated with 5-year AIMS physical function. These authors, as well as Wolfe and Cathey[30], reported that baseline psychological status was also useful for predicting physical outcome. Unfortunately, since AIMS2 scores were not performed at baseline, it was impossible to evaluate these variables as prognostic factors of the 5-year AIMS2 domains.

Psychological domain at 5 years was also independently predicted by baseline HAQ score in addition to BMI score, sex, and erosion score. By contrast, Uhlig, *et al*[16] found that baseline psychological status was the only independent predictor of psychological health status after 5-year followup, which is in agreement with other reports[31,32]. Hawley and Wolfe[23] found no association between change in disease variables and anxiety or depression.

For the symptom (pain) domain, HAQ score, ESR, and positivity for IgA RF at baseline were prognostic factors in our study. Initial pain[17,33], depression, and social life[32,34] have also been associated with later pain level. The influence of psychosocial factors on pain in patients with RA has been extensively reported[32,35,36].

Baseline HAQ score and age were predictive of 5-year work disability (role domain). HAQ score has already been considered the best predictive factor of work disability[35-37]. Advanced age, number of involved joints, disease activity, initial radiographic evidence of erosion, education level, and strenuous work[38-42] have also been reported to be associated with work outcome. The social interaction component was the only domain for which HAQ score was not independently predictive, but it was predicted by antiperinuclear antibody, MMP-3 level, joint space narrowing, and tender joint scores.

Our study determined that in early RA, baseline HAQ score was the best predictive factor of 5-year quality of life, since it predicted 4 of the 5 AIMS domains at 5-year followup. This information is consistent with previous reports, which demonstrated that baseline HAQ predicted 5-year HAQ disability[19,30,43,44], 5-year AIMS physical status[16], work disability[37,45,46], and mortality[41], but not structural damage[15]. Other baseline predictive factors of some 5-year AIMS2 domains have also been identified, but these interactions look very heterogeneous and weaker than the link with HAQ score. Thus,

regarding the number of analyses performed, some interactions might have been obtained by chance and no conclusion is allowed.

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