Quality of Life and Economic Burden of Illness in Very Early Arthritis. A Population Based Study in Southern Sweden

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ABSTRACT. ***Objective.*** To measure health related quality of life (HRQOL) in patients with very early arthritis in a population based study in southern Sweden, and to compare HRQOL at baseline between the different diagnostic groups. Further, we investigated whether HRQOL at baseline correlated with the costs the patients incurred during the study.

Methods. Seventy-one adult patients with arthritis of less than 3 months' duration were referred from primary health care centers to rheumatologists. HRQOL was measured with the Arthritis Impact Measurement Scales (AIMS) and EuroQol at baseline. A comparison of HRQOL measures at baseline and the costs the patients incurred during the study was conducted in 56 of the patients.

Results. Twenty-seven (38%) patients had reactive arthritis (ReA), 17 (24%) undifferentiated arthritis, 15 (21%) rheumatoid arthritis (RA), 4 (6%) psoriatic arthritis, and the rest (11%) other diagnoses. Statistically significant differences were found between the 4 patient groups concerning the AIMS subscales of dexterity, household activity, activities of daily living (ADL) and pain, the patients with RA being most severely affected. There were no statistically significant differences between the 4 diagnosis groups concerning the EuroQol utility and EuroQol visual analog scale (VAS) scores. Of the AIMS subscales, the mobility, physical activity, household activity, ADL, and pain subscales correlated significantly with the incurred costs. Also the EuroQol utility scores and EuroQol VAS scores correlated significantly with the costs. Only the AIMS household activity subscale predicted the costs in the regression analysis.

Conclusion. Patients with RA had significantly worse scores in the AIMS dexterity, household activities, ADL, and pain subscales compared to patients with other arthritides very early in the disease. The EuroQol generic quality of life instrument was less sensitive in detecting differences between patients with early arthritis than the disease-specific AIMS instrument. There was a correlation between the costs and the EuroQol utility scores and EuroQol VAS scores during the very first months of the disease, as well as with costs and the AIMS subscales of mobility, physical activity, household activity, ADL, and pain. (J Rheumatol 2004;31:1717–22)

Key Indexing Terms:
HEALTH RELATED QUALITY OF LIFE ARTHRITIS IMPACT MEASUREMENT SCALES
EUROQOL RHEUMATOID ARTHRITIS REACTIVE ARTHRITIS

The major treatment goals in rheumatoid arthritis (RA) are suppression of disease activity, improving health outcome, and improving pain, functional disability and other health related indicators of quality of life. Traditional measures of disease activity in rheumatic diseases often fail to estimate the impact of the disease on the individual. Perceptions of patients' health and need for care and treatment differ between patients and health professionals[1]. Disease-specific instruments to measure health related quality of life (HRQOL) are often necessary to detect treatment effects, while generic instruments are designed to capture different aspects of health irrespective of disease[2].

Only a few studies have utilized the generic quality of life instrument EuroQol to assess HRQOL in RA, and none to our knowledge in early RA, reactive arthritis (ReA), or undifferentiated arthritis. The EuroQol (EQ–5D) is a 2-part generic HRQOL questionnaire[3]. It is simple and readily applicable, reliable and validated in RA, and has been tested in several countries including Sweden[4-6]. The Arthritis Impact Measurement Scales (AIMS) is a self-administered health status scale questionnaire that covers the physical, social, and emotional well-being of patients with rheumatic

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diseases[7,8]. The only previous study where AIMS has been used to measure HRQOL in patients with early RA (< 1 year) showed that patients with early-onset and established RA experienced comparable clinical and health status effects[9]. The few previous studies assessing costs in RA with a duration of less than one year report a correlation of the costs to Health Assessment Questionnaire (HAQ) results, positive rheumatoid factor, functional disability, lower age, shorter disease duration, and comorbidities[10-14].

Our aim was to analyze HRQOL in a population-based prospective cohort of patients with very early arthritis using AIMS and EuroQol, and to compare the baseline AIMS and EuroQol scores between the different diagnostic groups. Chronic RA is associated with high indirect and direct costs for patients and society. Therefore, we also analyzed correlations of the baseline AIMS and EuroQol scores with the costs incurred by the patients with early arthritis.

MATERIALS AND METHODS

Study setting. Between May 1999 and May 2000, a prospective population-based incidence study of new referrals was conducted to establish the annual incidence of inflammatory joint diseases[15], infections preceding the arthritides[16], and the costs incurred by patients with very early arthritis[17] in southern Sweden. Briefly, 21 primary health care centers, one private outpatient rheumatology unit, and all units at Växjö Central Hospital and at Ljungby District Hospital where patients with inflammatory joint diseases might present, participated in the study. The physicians in the participating health care centers and clinics referred the patients to either the Rheumatology Department at Växjö Central Hospital or the one private rheumatologist participating in the study. The catchment area for adults (age > 16 yrs) was 132,000 people. The inclusion criteria were a recent-onset new joint inflammation with swelling of at least one joint, age > 16 years, and onset of the joint inflammation between May 1, 1999, and May 1, 2000. There was a time limit of 3 months from the onset of symptoms to inclusion. Patients underwent the same clinical and laboratory examinations at presentation and after one month, 3 months, and 6 months or, if they recovered during the first 6 months, up to recovery. A chest radiograph and radiographs of the joints involved were taken at presentation. The number of tender (53-joint index) and swollen (44-joint index) joints, the Ritchie Articular Index[18], and the patients' visual analog scale (VAS) assessment of pain and global assessment were recorded at each visit. The patients filled in the Swedish versions of EuroQol and AIMS at each visit. The diagnosis at the last clinical assessment in the study was used in the final analysis. All patients with RA fulfilled the 1987 American College of Rheumatology (ACR) classification criteria for RA[19]. Arthritis in association with psoriasis, with a negative test for rheumatoid factor, was defined as psoriatic arthritis (PsA)[20]. Diagnosis of Lyme arthritis was based on a medical history of mono- or oligoarthritis with no alternative explanation and a positive serology for *Borrelia burgdorferi* by enzyme-immunoassay (EIA)[21]. ReA was defined as an inflammatory joint disease either preceded by a history of infection less than 2 months from the onset of joint symptoms and verified by cultures or positive serology, or, in the absence of a history of infection, by cultures or serology alone. Patients with arthritis with a prior genitourinary infection, enteric infection, and infections in the upper respiratory tract and soft tissue were also classified as having ReA. Patients with joint inflammation not fulfilling the above criteria were classified as having undifferentiated arthritis. For RA, the American Rheumatism Association (ARA) 1981 criteria were used for remission[22]. Other patients were considered to be in remission in the absence of swollen and tender joints at the clinical assessment. Clinical evaluation by an experienced rheumatologist during the followup was considered the "gold standard." All patients gave their written informed consent. The study protocol was approved by the regional ethics committee at the University of Lund.

The EuroQol. Part 1 of the EuroQol questionnaire assesses self-reported problems on 5 domains, i.e., mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain is divided into 3 levels of severity: no problem, some problem, and extreme problems. By combining one level from each of the 5 domains, a total of 243 health states are defined. A time-tradeoff procedure in a normal adult population (3395 respondents) in the UK has been used to elicit EuroQol utility weights that vary between 1 and –1, 0 being dead, and 1 being in full health[23]. Some health states attract negative scores, indicating that being in some of these states is from a societal perspective regarded as worse than death. Part 2 of the EuroQol records the subject's self-assessed rating of health on a VAS of 0 to 100, 0 being the worst.

The AIMS. The AIMS has been shown to be practical and easily understandable to both the examiner and the patient, and to be simple, reliable, valid, repeatable, and sensitive to change in RA, PsA, and systemic lupus erythematosus (SLE)[8,24-26]. The physical scales correlate with grip strength, joint counts, the Larsen index, morning stiffness, the pain VAS, the erythrocyte sedimentation rate (ESR), and the HAQ[7,27,28]. The AIMS has been validated in several countries including Sweden[29]. The AIMS scales include 9 health status scales: mobility (moving around in the community), physical activity, dexterity (hand function), household activities (routine housework), activities of daily living (ADL: basic self-care tasks), social activity (interaction with family and friends), anxiety, depression, and pain. In addition, questions on the patients' subjective health perception are included. The scales contain 4 to 7 items. The patient responses are summed to obtain scale scores, and the scale scores are indexed to a range of 0 to 10 for comparable analysis. A low value indicates a high health status[7]. The AIMS was revised in 1992 (AIMS2)[30], but the original AIMS was used in this study.

Cost analysis

Direct costs. A previous communication presents the cost analysis of the present patient material in detail[17]. Briefly, both indirect and direct costs were analyzed. Inpatient stays and outpatient visits to Växjö Central Hospital at the departments of medicine, orthopedic surgery, general surgery, infectious diseases, and dermatology were recorded from the onset of symptoms to the last clinical assessment in the study. Visits to general practitioners, physiotherapists, and occupational therapists were also recorded. Costs for standard laboratory safety monitoring associated with treatment with disease modifying antirheumatic drugs (DMARD) were recorded. Only the use of corticosteroids and DMARD was recorded. The costs of diagnostic laboratory analyses were not included, as the patients were enrolled in a study protocol. Costs for aid appliances at home, transportation, nonprescription medication, complementary therapy, assistive devices, and patient time-costs were excluded. The costs of radiographs were included. The costs of comorbidities were not recorded.

Indirect costs. In the Swedish social security system, the employer reimburses the salary for the first 14 days of sick leave. After 14 days of sick leave, the employee is reimbursed by the National Health Insurance Institution. In addition, patients may have private health insurance, but this is not obligatory. The National Health Insurance Institution provided the time period and reimbursement for patients in the study with sick leave for over 2 weeks. Usually the reimbursement is 90% of the salary. The costs for sick leave, i.e., loss of salary, were calculated from this. The costs for the first 2 weeks of sick leave were also included in the analysis. For patients with sick leave of less than 2 weeks, the number of days of sick leave was obtained from patient records, and labor union databases were used to provide information on the mean incomes for the different professions in 2000. Change of work or work loss due to other reasons was not included in the analysis of indirect costs.

Unit costs. Unit costs were obtained from the finance department of Kronoberg County Council. The National Pharmacotherapeutical

Catalogue for the year 2000 was used to obtain drug prices. Discount rate analysis was not used, as the followup was less than one year. A sensitivity analysis was performed. All costs are presented in US dollars [$1 = 8.53 Swedish kronor (SEK), £1 = SEK 13.80, 1 Euro = SEK 8.71 in January 2000].

The results of the cost analysis have been reported in detail[17]. Data for 56 patients were included in the cost analysis. The excluded patients did not differ demographically from those included. Costs were analyzed from the onset of symptoms to the last control in the study. All patients generated costs. The costs per patient in the different patient groups were skewed. The median cost per patient in the entire group was $3362 [interquartile range (IQR) 1359–5044]. The median cost for a patient with RA was $4385 (IQR 1488–8004). For a patient with ReA, the median cost was $4085 (IQR 988–7192). For a patient with undifferentiated arthritis and other arthritis, the median costs were $1482 (IQR 922–4212) and $3361 (IQR 1359–5044), respectively. For the whole patient group, direct costs caused 56% and indirect costs 44% of the total costs.

Statistics. The Normal Score Test for several independent samples was used to calculate the mean values, standard deviations, and p values of the baseline EuroQol and AIMS scores in the 4 diagnosis groups[31]. Spearman's rho test was used to calculate the correlations between the baseline EuroQol and AIMS scores of the entire patient group, irrespective of diagnosis, to the costs incurred by the patients. Median regression analysis was used to model the relationship between costs and predictor variables (AIMS subscales).

RESULTS

Seventy-one patients were included in the study. For 3 patients, the EuroQol VAS score was missing. For 11 patients the EuroQol utility score (part 1) was missing. The patients had either not answered the questions, or the answer was impossible to interpret. Of these 11 patients, 5 had RA, 3 had undifferentiated arthritis, one had Lyme disease, and 2 had ReA. The diagnoses are shown in Table 1. The group designated "other diagnoses" consisted of one patient each with SLE, polymyalgia rheumatica, erosive osteoarthritis with synovitis, mixed connective tissue disease, and ankylosing spondylitis. The clinical characteristics of the 4 groups are shown in Table 2. The EuroQol and the AIMS scores in the 4 diagnosis groups are shown in Table 3. There was a statistically significant difference between the 4 diagnosis groups in the AIMS subgroups of dexterity, household activity, ADL, and pain scores, with RA patients having the worst scores in these scales. For the EuroQol utility and EuroQol VAS scores, there was no statistically significant difference between the 4 diagnosis groups. The scores for the AIMS subscales of depression and anxiety were very similar in the 4 diagnosis groups, and some patients even fulfilled the criteria of probable depression, having scores > 4.0[32]. The mean anxiety scores were somewhat higher than the depression scores in all groups. The EuroQol utility scores correlated with the EuroQol VAS scores (r = 0.66, 95% confidence interval 0.48 to –0.79).

Table 1. Diagnosis and number of patients in each diagnosis group for the study population of 71 patients at 6 months.

Diagnosis	Men	Women	Total (%)
Rheumatoid arthritis	6	9	15 (21)
Reactive arthritis	9	18	27 (38)
Psoriatic arthropathy	2	2	4 (6)
Undifferentiated arthritis	7	10	17 (24)
Sarcoid arthritis	2	0	2 (3)
Lyme arthritis	0	1	1 (1)
Other diagnoses	0	5	5 (7)
Total	26	45	71 (100)

We studied the correlation between the baseline EuroQol and AIMS scores with the costs incurred by patients during the 6-month followup irrespective of diagnosis using the Spearman rho test. Of the AIMS subscales, the subscales for mobility (r = 0.30, 95% CI 0.04 to 0.52), physical activity (r = 0.44, 95% CI 0.20 to 0.63), household activity (r = 0.51, 95% CI 0.29 to 0.68), ADL (r = 0.34, 95% CI 0.08 to 0.55), and pain (r = 0.33, 95% CI 0.07 to 0.55) correlated significantly with the costs incurred. Also, the EuroQol utility scores and EuroQol VAS scores correlated significantly with the costs: r = –0.45 (95% CI –0.64 to –0.21) and r = –0.38 (95% CI –0.59 to –0.13), respectively.

We also studied the relationship between the baseline AIMS subscales and EuroQol scores with the costs incurred by patients using a median regression analysis to see which AIMS subscales predicted costs. Only the baseline AIMS subscale for household activity emerged from the forward stepwise median regression model as an explanatory variable for costs (Table 4).

DISCUSSION

This is the first study to assess health related quality of life in very early RA, ReA, and undifferentiated arthritis. We observed that all arthritis, even relatively mild joint inflammation, has a negative effect on HRQOL early in the disease course. The AIMS scores for pain, anxiety, and depression subscales were high in all patient groups and comparable to earlier studies on RA.

We also observed a significant correlation between the HRQOL and the costs incurred by patients during the first months of disease. We confirmed that the negative influence of RA starts during the first few weeks and months, RA patients having significantly worse scores in the AIMS dexterity, household activity, ADL, and pain subscale scores compared to other groups very early in the disease. The AIMS scores of our RA patients were quite similar to the scores reported previously in RA patients with longer durations of disease[33-37]. Since RA typically affects the small joints of the hands, the impact on dexterity and ADL early in the disease course is logical, and since RA is often more aggressive than, for example, self-remitting ReA, we did not find the AIMS results surprising.

Only the baseline AIMS subscale for household activity emerged from the forward stepwise median regression model as an explanatory variable for costs. This was somewhat surprising, and remains difficult to explain.

We found statistically significant differences in the AIMS

Table 2. The clinical characteristics of the study population at inclusion. "Other" also includes psoriatic arthropathy, sarcoid arthritis, and Lyme disease.

Characteristic	RA, n = 15	ReA, n = 27	Undifferentiated, n = 17	Other, n = 12
Mean age (SD)*, yrs	58 (14)	46 (18)	51 (17)	52 (19)
No. of female patients (%)	9 (60)	18 (67)	10 (59)	8 (67)
Mean ESR (range)	38 (2–90)	31 (2–100)	19 (4–78)	38 (7–100)
Median Ritchie score (range)	4 (0–15)	1.5 (0–8)	1 (0–9)	1.5 (0–6)
Median no. of swollen joints (range)	9 (1–28)	2 (0–14)	1 (0–4)	2 (1–12)
Patients with RF present (%)	4 (27)	1 (4)	3 (18)	2 (17)
No. of patients in remission at 6 mo (%)	5 (33)	20 (74)	8 (47)	4 (33)

* One patient missing. ESR: erythrocyte sedimentation rate, RF: rheumatoid factor.

Table 3. The baseline AIMS and EuroQol values in the patient population in the different diagnosis groups. Data are mean value (range) median. "Other" includes psoriatic arthropathy, sarcoid arthritis, and Lyme disease.

	RA, n = 15	ReA, n = 27	Undifferentiated, n = 17	Other, n = 12	p
EuroQol utility*	0.4 (-0.4 to 0.8) 0.4	0.6 (0.0 to 1.0) 0.7	0.7 (0.3 to 1.0) 0.8	0.6 (0.2 to 0.9) 0.7	0.11
EuroQol VAS**	53 (12 to 90) 50	63 (0 to 90) 60	65 (0 to 95) 70	67 (30 to 92) 80	0.37
AIMS subscales					
Mobility	1.6 (0 to 6.3) 0.6	1.2 (0 to 6.2) 0	0.8 (0 to 6.3) 0	1.1 (0 to 6.3) 0	0.64
Physical activity	5.9 (0 to 10) 8.0	4.8 (0 to 10) 4.0	4.0 (0 to 8) 4.0	4.3 (0 to 10) 4.0	0.48
Dexterity	5.9 (0 to 10) 6.0	2.5 (0 to 10) 1.0	3.2 (0 to 10) 2.0	2.2 (0 to 6) 2.0	0.007
Household activity	1.7 (0 to 7.7) 1.5	0.7 (0 to 3.9) 0	0.6 (0 to 6.2) 0	0.6 (0 to 2.3) 0.8	0.05
Social activity	3.6 (1 to 6.5) 3.3	3.6 (0.5 to 7.5) 3.8	4.2 (2 to 7) 4.5	4.1 (0 to 9) 3.8	0.63
ADL	0.8 (0 to 5) 0	0.05 (0 to 1.3) 0	0 (0) 0	0.1 (0 to 1.3) 0	0.005
Pain	7.2 (4 to 9) 7.5	5.7 (1.5 to 9.5) 6.5	4.5 (1.5 to 6.5) 5.0	5.6 (1.5 to 8.5) 5.5	0.004
Depression	2.0 (0 to 4.3) 1.3	2.0 (0.3 to 5.3) 1.8	2.0 (0.3 to 6.7) 1.5	2.0 (0.7 to 4.3) 1.8	0.96
Anxiety	3.5 (0.3 to 7) 3.7	2.7 (0.3 to 5.3) 2.7	2.9 (1.0 to 7.3) 2.2	3.0 (0 to 7) 3.3	0.64
Health perception	2.9 (0.6 to 5) 3.1	3.6 (0 to 6.9) 3.8	3.0 (0.6 to 6.3) 2.5	3.9 (1.3 to 8.8) 3.4	0.53

* 11 patients missing, ** 3 patients missing. VAS: visual analog scale, ADL: activities of daily living.

Table 4. Median regression models for costs using the AIMS subscales as predictor variables.

	Models			
	Full		Forward Stepwise*	
AIMS Subscales	Coefficient, ß (95% CI†)	p	Coefficient, ß (95% CI†)	p
Mobility	–8.6 (–18.3 to 1.1)	0.081		
Physical activity	3.4 (–1.7 to 8.5)	0.18		
Dexterity	–3.4 (–9.7 to 3.0)	0.29		
Household activity	23.1 (2.3 to 43.9)	0.031	13.6 (7.8 to 19.4)	< 0.001
Social activity	–6.9 (–15.8 to 2.1)	0.13		
ADL	–13.2 (–57.3 to 31.0)	0.55		
Pain	1.3 (–6.8 to 9.3)	0.75		
Depression	3.1 (–18.9 to 25.1)	0.78		
Anxiety	4.5 (–9.6 to 18.6)	0.52		
Health perception	–3.0 (–9.6 to 3.6)	0.37		
Constant	32.3		15.2	

† 95% confidence interval obtained by bootstrapping (1000 replications). * Only variables entered into the model are shown.

pain subscale comparing the different diagnosis groups, but not in the EuroQol scores. This stresses the importance of also using a disease-specific quality of life instrument.

The EuroQol utility scores from our study are comparable to scores reported by Wolfe, *et al*[38], and are higher than the score reported by Hurst, *et al* in one study, 0.29[5], but are comparable to the median EuroQol utility scores in their other study for patients in functional classes I and II, 0.76 and 0.59, respectively[6]. There are several concerns with respect to the performance of EuroQol in RA; for example,

the difficulty in discriminating between functional classes and pain, probably due to the scaling of the individual questions[6,38]. We are aware of the possible bias presented by using utility values for the United Kingdom in Swedish patients.

Our study is the first to show that HRQOL measures also correlate with the costs caused by arthritis early in the course of the disease. In a study of Australian patients with RA with a mean disease duration of 16 years, the factors associated with costs were female sex, pension, private health insurance, general health measured with the Medical Outcome Study Short Form-36 instrument, HAQ, and receiving assistance from family and friends[39]. That HRQOL correlates with costs is logical, since patients feeling ill, and having problems in coping with the disease and disease related factors, often contact the health care system. Because of the small size of the subgroups and the skewedness of the costs, we decided to analyze costs for the entire patient population irrespective of diagnosis.

One strength of our study is the population based approach, where we investigated patients with very early arthritis regardless of disease severity, thus reducing the bias usually found in data from secondary or tertiary care centers that see only the most severely affected patients. However, there are some caveats in this study. First, the study population was heterogeneous and relatively small, and the subgroup analyses must therefore be interpreted with caution; for example the sample size for RA is 15 patients in the costs analysis. Second, the cost analysis and correlations with the HRQOL instruments were performed on 56 patients and not on the entire patient population, and due to this the results must be interpreted with caution. Third, some of the EuroQol data were missing, presenting a bias. Additionally, the AIMS and EuroQol instruments have not been validated for ReA or undifferentiated arthritis, but it might be argued that the early clinical picture of these diseases compares well to early RA. We were not able to assess the influence of income or occupation on costs or HRQOL in this study.

In summary, we report results of analyses of HRQOL in patients with very early RA, ReA, and undifferentiated arthritis using a generic and a disease-specific HRQOL instrument, i.e., the EuroQol and the Arthritis Impact Measurement Scales. We confirmed the negative impact of RA very early in the disease course. The EuroQol was less sensitive than the AIMS in detecting differences in the quality of life between patients with early arthritis. There was a correlation between HRQOL and the costs incurred by patients during the first 6 months of disease.

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