Poor and Good Health Outcomes in Rheumatoid Arthritis: The Role of Comorbidity

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ABSTRACT. ***Objective.*** To assess the predictive value of selected sociodemographic characteristics, rheumatoid arthritis (RA)-specific clinical factors, and comorbidity with respect to patient-reported health outcomes, i.e., pain, disability, and health-related quality of life, among patients with RA.

Methods. Data were collected between 1997 and 2002 among 882 patients with RA of varying disease duration using questionnaires and clinical examinations. Health outcomes were evaluated over 5 years as a function of disease duration by means of random intercept linear regression. Then we selected the 10% of patients with the poorest and best health outcomes during the 5 years of followup compared to others with equal disease duration. Separate multivariate logistic regression analyses were conducted to identify factors associated with poor and good outcomes.

Results. Sociodemographic characteristics seemed to be less important in the prediction of health outcomes. After RA-specific clinical factors, comorbidity appeared to be a major predictive factor for health outcomes. In particular, psychological comorbidity, i.e., depressive symptomatology, was a consistent predictive factor with respect to all health outcomes.

Conclusion. Assessment of comorbidity needs to be incorporated into the management of RA in order to prevent poor outcomes and to adapt therapies to the specific situation of individual patients. Periodic routine screening for and monitoring of somatic and psychological comorbidity should be included in clinical practice. (First Release July 1 2006; J Rheumatol 2006;33:1488–95)

Key Indexing Terms:
COMORBIDITY HEALTH OUTCOMES RHEUMATOID ARTHRITIS

Patients with rheumatoid arthritis (RA) generally have to face physical as well as psychosocial health problems. However, these problems may vary considerably between and within patients. For instance, substantial inter- and intra-individual variability in the course of disability has been recognized[1]. In clinical practice, both clinicians and patients need information on prognosis to guide and direct their management strategies[2]. The prognostic process in RA has widely been studied with respect to different outcomes, e.g., radiographic damage, (work) disability, and mortality[3-25]. Reported prognostic factors encompass sociodemographic characteristics of the patient and RA-specific clinical characteristics. Although varying and sometimes inconsistent results have been reported, factors frequently associated with poor prognosis were older age, female sex, low socioeconomic status, high disease activity, and rheumatoid factor (RF) positivity.

In today's clinical practice, RA-specific clinical factors in particular are incorporated and measured to predict and monitor the disease course, and to adapt treatment to the specific situation of individual patients. The effect of comorbidity on health outcomes in RA has gained increasing attention[26-28].

In this study we elaborate on the role of comorbidity in predicting health outcomes in relation to sociodemographic and RA-specific clinical factors. We investigated the predictive value of sociodemographic factors, RA-specific clinical factors, and comorbidity in patients with RA with respect to relatively poor and good (longterm) health outcomes. We defined health outcomes in terms of self-reported RA-related pain, disability, and health-related quality of life (HRQOL) because we wanted to focus on the burden of RA from the patient's perspective. Our results could guide clinical practice

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in order to achieve the best possible outcomes for individual patients.

MATERIALS AND METHODS

Subjects and procedure. In 1997, we started with a longitudinal study on health and HRQOL among patients with RA. Patients (n = 1200), registered at an outpatient center for rheumatology and rehabilitation in Amsterdam or at one of its affiliated outpatient clinics, were randomly selected from strata of disease duration in order to cover the heterogeneity of RA within the selected group. Inclusion criteria were: having RA according to the 1987 revised American College of Rheumatology criteria[29], being older than 16 years of age, and having sufficient command of the Dutch language to complete the questionnaire. The medical ethical committee approved the study design. Selected patients were asked to participate and to sign a letter of informed consent. The followup period was 5 years (1997–2002).

Data collection and response. Data were collected in 1997, 1998, 1999, and 2002 by means of a self-administered postal questionnaire. In 1997 and 1999 respondents to questionnaires were invited for an additional clinical assessment of a 28-joint count[30] and the erythrocyte sedimentation rate. In 1997, 882 (net response 74%) returned the questionnaire. In 1998, 755 patients (87% of eligible respondents; n eligible = 863) took part in the questionnaire survey. In 1999, 683 patients (81% of respondents; n = 841) returned the questionnaire. In 2002, 529 patients (73% of remaining eligible respondents; n = 720) participated in the followup. The flow of patients is illustrated in Table 1.

In 1997, 735 patients (83% of the 882 respondents) also completed the clinical examination, and in 1999, 529 patients (77% of the 683 respondents) underwent a clinical examination. A group of patients did not participate in the clinical examinations, whereas they responded to the questionnaire. In 1997 and 1999, 147 of 882 patients (17%) and 154 of 683 patients (23%), respectively, were not examined. In 1997, no differences were observed regarding sex, but nonparticipants in the clinical examination were significantly older ($p < 0.05$) and reported worse levels of disability ($p \leq 0.01$) and worse mental health ($p < 0.05$) than participants in the clinical examination. In 1999, no differences were observed regarding sex and disability, but again nonparticipants in the clinical examination were significantly older ($p < 0.05$) and they reported significantly worse levels of mental health ($p \leq 0.01$) than participants in the clinical examination.

Information about RF positivity was retrieved from the patients' files.

Health outcomes

RA-related pain. The degree of RA-related pain was measured with a 100 mm visual analog scale (VAS pain), ranging from 0 (no RA-related pain) to 100 (RA-related pain as bad as it could be). The VAS is considered to be the most robust quantitative measure for pain[31].

Table 1. Response to the study.

	Year of Investigation			
	1997	1998	1999	2002
Selected patients, no	1200	882	863	811†
Died, no.	0	15	15	87
Moved to an unknown address, no.	14	4	7	4
Eligible, no.	1186	863	841	720
Response to questionnaire, no.	882	755	683	529
Overall response rate*, %	74	87	81	73
Response to clinical examination, no.	735	NA	529	NA

* The overall response rate was calculated based on the response to the questionnaire. † 30 patients had withdrawn after the initial followup in 1999. NA: not assessed.

Disability. Disease impact in terms of disability was assessed with the validated Dutch capacities of daily life questionnaire (VDF)[32]. The VDF, similar to the Health Assessment Questionnaire (HAQ), consists of 20 items measuring the degree of difficulty a patient has in performing activities of daily living (ADL) in 8 areas (dressing and grooming, arising, eating, walking, hygiene, gripping, reaching, and other activities). Responses to each item can range from 0 (no difficulty) to 3 (unable to do). The score is not influenced by the use of aids needed for certain ADL. The scores of each item were averaged to create an overall mean score (range 0–3, higher scores indicating more disability).

Health-related quality of life. HRQOL was assessed with a validated Dutch version of the RAND-36[33]. The RAND-36 is a validated, self-administered, internationally used questionnaire measuring health status with respect to 8 dimensions: physical functioning (PF), social functioning (SF), role limitations caused by physical health problems (RP), role limitations caused by emotional health problems (RE), pain (Pain), mental health (MH), vitality (VIT), and general health perception (GH). Additionally, one single item assesses changes in perceived health during the last 12 months (Change). Because only minimal differences in final subscale scores of the RAND-36 and the Medical Outcomes Study Short Form-36 Health Survey (SF-36) have been reported[34], we computed physical (PCS) and mental (MCS) component summary scales according to the manual for SF-36 health summary scales[35], using Dutch SF-36 population means, standard deviations, and factor score coefficients[36,37]. Higher scores indicate better health status.

Predictive factors

Sociodemographic factors. The variables included were age, sex, marital status [single; together (= married or cohabiting); divorced or widowed], having paid work (yes/no), and socioeconomic status (SES) as indicated by education level. We divided SES into 3 groups: low SES, including patients with no education or primary school level; medium SES, including patients with secondary school level; and high SES, including patients with college or university level.

RA-specific clinical factors. Variables included were disease activity and RF positivity (yes/no). Disease activity was assessed by means of the modified Disease Activity Score (DAS28), including separate 28-joint counts for tenderness and for swelling, without the VAS for "general health assessment"[38].

Comorbidity. Somatic as well as psychological comorbidity were assessed. Somatic comorbidity was assessed by a self-report list, adapted from the Health Interview Survey of Statistics Netherlands[39], comprising a broad range of chronic conditions: lung diseases, cardiovascular diseases, diabetes mellitus, gastrointestinal diseases, cancer, kidney diseases, chronic infections, diseases of the gall bladder and liver, chronic back complaints, skin diseases, diseases of the thyroid gland, and neurological diseases. Respondents were asked whether they had had any of these conditions in the previous 12 months. Somatic comorbidity was used as a continuous variable and assessed as the count of the numbers of comorbid conditions.

With respect to psychological comorbidity, we focused on depressive symptoms. Depression is common in patients with RA[40,41] and mood disorders, particularly depression, can be considered among the most frequent indicators of psychiatric morbidity[42]. Depressive symptoms were assessed with a Dutch version of the Center for Epidemiological Study Depression Scale (CES-D)[43]. Scores range from 0 to 60, higher scores indicating more depressive symptomatology.

Statistical analyses. All analyses were carried out using SPSS statistical software v. 11.5.2 for Windows (SPSS Inc., Chicago, IL, USA) and SAS v. 8.02 (SAS Inc., Cary, NC, USA). Results were considered statistically significant when p values were < 0.05.

In the first step of our analyses, we evaluated RA-related pain, disability, and HRQOL (i.e., PCS and MCS) over 5 years as a function of disease duration (as a categorical variable), by means of the mixed-effect modeling procedure ProcMixed of SAS, using random intercept linear regression models. We included all available measurements of the dependent variables to get the best overall picture of individual patients over time instead of depending on a

single measurement. The great advantage of the ProcMixed procedure is that cases are not rejected from analyses because of missing data. We decided to use disease duration groups of relatively short duration, especially in early RA, in order to allow for patients changing from one disease duration group to another during followup. We defined the following disease duration groups: < 1, 1–2, 2–3, 3–5, 5–7, 7–10, 10–15, 15–20, and > 20 years. Based on the Bayesian linear unbiased predictions from these random intercept models, we identified patients who differed extremely from other patients with equal disease duration for each of the selected health outcomes during followup separately, either showing much poorer outcomes (10% poorest = poor outcomes) or much better outcomes (10% best = good outcomes). Thus we identified poorest and best patients during followup from all stages of the disease.

In the second step we compared patients with best and poorest outcomes with respect to sociodemographic and clinical factors, and comorbidity by means of univariate analyses (i.e., Student t tests and chi-square tests) in order to determine whether the patient profiles we obtained were different. With respect to sex, marital status, SES, paid work, and RF positivity we used data from 1997. With respect to age, disease activity, and comorbidity, we computed mean values of all available measurements. Disease activity and comorbidity were not assessed at 5-year followup, i.e., in 2002.

In the third step of our analyses, we conducted separate multivariate logistic regression analyses for both poor and good outcomes (either 10% poorest or 10% best outcomes) on each of the outcome variables to specifically identify sociodemographic and RA-specific clinical factors, and comorbidity predictive for poor and/or good outcomes, i.e., we aimed to determine a predictive profile. In these multivariate analyses we identified predicting variables for poor or good outcomes, respectively, (dependent variables) by including all patients with available data; e.g., with respect to good predictive profiles the 10% best outcome patients were contrasted with the other 90% of patients from the sample (including the 10% worst cases). In case predicting variables were assessed more than once and might show fluctuations during followup, i.e., age, disease activity, and comorbidity, mean values from the available measurements were computed. We did this because the overall outcome was expected to be influenced by the average of a predicting variable during followup, rather than the value of a predicting variable at one particular moment. In addition, the use of mean predictors seems to be more appropriate, since the majority of patients were not followed from the beginning of the disease. Therefore, using solely baseline data of potentially changing predictor variables (e.g., disease activity) probably would have led to more bias than using mean values.

The effect sizes of these variables were expressed as odds ratios (OR) of the logistic regression model, with 95% confidence intervals (95% CI). OR were adjusted for all other variables in the model. To avoid rejection of subjects because of missing data with respect to disease activity, we used the missing indicator method[44] for this variable.

By including all available measures from all patients from all measurement times we aimed to minimize selection bias due to loss to followup or missing data.

RESULTS

Study population. A total of 882 patients (response rate 74%) enrolled in 1997 in our study (Table 2); they had a mean disease duration of 8.9 years (SD 9.8, range 0–66.7) and a mean age of 59.8 years (SD 14.8, range 18.5–91.6). The majority were women (71.9%). The impact of RA concerned all domains of HRQOL, as indicated by the scores of the RAND-36.

In 2002, 529 respondents completed the questionnaire. Compared to the rest these 529 patients had been characterized in 1997 by statistically significant better HRQOL (PCS, $p < 0.001$; MCS, $p < 0.05$) and less disability ($p < 0.001$), but not by less RA-related pain ($p = 0.3$). They were younger ($p < 0.001$) and had overall a more favorable SES ($p < 0.001$), but did not differ with respect to gender ($p = 1.0$).

Patient profiles. The 10% "poorest outcomes" patients and the 10% "best outcomes" patients showed different profiles in the univariate analyses with respect to the selected sociodemographic and clinical characteristics and comorbidity (Table 3). Generally, "poorest outcomes patients" were, in comparison to "best outcomes patients," more often women, they were older, had a less favorable SES, had paid work less often, and were less often married/cohabiting. Further, they had a higher disease activity assessment, except with respect to MCS, and they reported more somatic and psychological comorbidity. RF positivity was only elevated with respect to disability among "poorest outcomes patients."

Factors predicting poor outcomes. Sociodemographic factors seemed to be less important than clinical factors (Table 4) in the prediction of poor outcomes. Female sex and older age were risk factors for disability. Medium SES decreased the risk of poor PCS. For paid work and marital status, no statistically significant associations could be detected. RF positivity was a risk factor with respect to disability. Disease activity was a risk factor for pain, disability, and poor PCS; but on the other hand it seemed to decrease the risk of poor MCS. Somatic comorbidity appeared to be a risk factor for pain, disability, and PCS, but not with respect to MCS. Finally, psychological comorbidity consistently increased the risk for poor outcomes with respect to pain, disability, PCS, and MCS.

Factors predicting good outcomes. Here again, sociodemographic factors seemed overall to be less important (Table 5). Older age was a protective factor with respect to RA-related pain. Medium SES hampered good MCS. Disease activity hampered good outcomes with respect to pain, PCS, and disability. Somatic comorbidity hampered good outcome with respect to PCS, but appeared to be associated with good outcome of MCS. Finally, psychological comorbidity hampered good outcomes with respect to pain, disability, PCS, and MCS.

DISCUSSION

In clinical practice clinicians need prognostic information to guide therapy decisions and management strategies, and to counsel or reassure patients; while patients need this information for their coping process and self-management. It has been described that well conducted inception cohort studies, with complete followup and well described objective outcomes, would provide the most reliable and accurate prognostic information[2,25]. Therefore, some limitations of our study should be discussed. We followed patients of various disease duration for 5 years, aiming to cover the heterogeneity of RA. This approach enabled us to study health outcomes broadly, including short-term consequences as well as longterm consequences. Since we compared patients to others with equal disease duration we took into account that outcomes and prognosis are associated with disease duration. Loss to followup might introduce bias into longitudinal studies. In our study, patients who participated in the last year of the followup peri-

Table 2. Characteristics of study population at baseline (n = maximum 882).

Characteristic	Available no.	
Disease duration, mean (range; SD)		8.9 (0–66.7; 9.8)
No. patients per disease duration group, yr		
< 1	102	
1–2	165	
2–3	98	
3–5	58	
5–7	62	
7–10	88	
10–15	135	
15–20	71	
> 20	103	
Predictive factors		
Women, no. (%*)	882	634 (71.9)
Age, mean, yrs (range; SD)	882	59.8 (18.5–91.6; 14.8)
SES, no. (%*)	869	
High		123 (14.2)
Medium		526 (60.5)
Low		220 (25.3)
Paid work, no. (%*)	872	180 (20.6)
Marital status, no. (%*)	874	
Together (married/cohabiting)		559 (64.0)
Single		97 (11.1)
Divorced/widowed		218 (24.9)
Rheumatoid factor-positive, no. (%*)	874	547 (62.6)
DAS28, mean (range; SD)	691	3.6 (0.2–7.7; 1.3)
Somatic comorbidity, mean (range; SD)	874	1.1 (0–7; 1.3)
Psychological comorbidity, mean (range; SD)	858	12.3 (0–49; 9.2)
Health outcomes		
VAS pain, mean (range; SD)	837	40.6 (0–100; 28.1)
Disability, mean (range; SD)	876	0.66 (0–2.75; 0.62)
RAND-36, mean (range; SD)		
Physical functioning	862	49.0 (0–100; 27.2)
Social functioning	875	68.8 (0–100; 27.6)
Role physical	832	39.7 (0–100; 42.4)
Role emotional	825	70.8 (0–100; 41.5)
Mental health	855	70.5 (4–100; 19.5)
Vitality	860	53.8 (0–100; 20.6)
Pain	874	54.8 (0–100; 23.1)
General health	849	49.7 (0–100; 20.3)
Change	871	49.1 (0–100; 26.6)
PCS	802	35.8 (9.0–61.7; 10.8)
MCS	802	49.2 (16–72.6; 11.4)

* Valid percentages are shown. PCS: physical component summary scale; MCS: mental component summary scale.

od had better health outcomes at study entry than those patients who did not participate. However, all patients, including those measured only at baseline, were included in defining patients with poorest and best outcomes. Taking these considerations into account, we believe that our results pinpoint suitable risk and protective factors with respect to patient-reported health outcomes, irrespective of disease stage.

This study assessed the predictive value of sociodemographic and RA-specific clinical factors and comorbidity with respect to patient-reported health outcomes, i.e., pain, disability, and HRQOL in terms of PCS and MCS.

Our study revealed the major influence of somatic and psychological comorbidity in predicting health outcomes. Somatic comorbidity was identified as a risk factor for poor outcomes with respect to pain, disability, and PCS. In addition, somatic comorbidity hampered good outcome with respect to PCS. Based on previous findings[27] we would emphasize the need for examining in more detail the differential effects of specific comorbid conditions on disability and HRQOL in RA.

Psychological comorbidity, i.e., depressive symptoms, appeared to be a risk factor for poor outcomes and to hamper good outcomes with respect to all health outcomes under study, i.e., pain, disability, PCS, and MCS. In particular, the effects of depressive symptoms, although statistically highly significant, may not appear at first to be very strong, given the

Table 3. Patient profiles: characteristics of 10% "poorest" (N_{max} = 88) compared to 10% "best" (N_{max} = 88) outcomes patients (univariate comparisons).

	VAS Pain		Disability		PCS		MCS	
	Poorest	Best	Poorest	Best	Poorest	Best	Poorest	Best
Sex, %[a]								
Men	18.2	45.5	14.8	43.2	14.8	45.5	22.7	34.1
Women	81.8	54.5***	85.2	56.8***	85.2	54.5***	77.3	65.9
Age, mean yrs	61.8	63.6	67.7	61.6**	65.1	58.5**	61.7	61.3
SES, %								
High	4.6	18.4	5.9	17.2	12.8	21.8	8.0	21.6
Medium	54.0	59.8	47.1	60.9	50.0	66.7	60.9	58.0
Low	41.4	21.8**	47.1	21.8***	37.2	11.5***	31.0	20.5*
Paid work, %[a]								
No	92.9	73.9	98.8	76.1	94.2	62.5	94.3	78.4
Yes	7.1	26.1***	1.2	23.9***	5.8	37.5***	5.7	21.6**
Marital status, %[a]								
Together	58.6	74.7	50.0	71.6	54.7	75.0	55.2	78.4
Single	14.9	10.3	9.3	12.5	11.6	14.8	12.6	5.7
Divorced/widowed	26.4	14.9	40.7	15.9***	33.7	10.2**	32.2	15.9**
Rheumatoid factor, %[a]								
No	35.2	34.1	26.1	41.4	35.2	39.8	39.1	38.4
Yes	64.8	65.9	73.9	58.6*	64.8	60.2	60.9	61.6
DAS28[b], mean	4.8	2.6***	4.6	2.9***	4.3	2.6***	3.7	3.5
Somatic comorbidity[b], mean	2.0	0.7***	1.9	0.8***	2.0	0.6***	1.8	0.9***
Psychological comorbidity[b], mean	21.0	6.0***	20.6	7.7***	18.7	5.9***	27.4	4.4***

[a] Valid percentages are shown. [b] Mean of available measurements. Disability measured with the VDF[32]. Statistically significant differences with respect to tests of the overall distribution are flagged (* $p < 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$). PCS: physical component summary scale; MCS: mental component summary scale.

Table 4. Poor health outcomes over time: predictive value of sociodemographic factors, RA-specific clinical factors, and comorbidity (results of multivariate logistic regression; n_{max} = 882).

	VAS Pain	Disability	PCS	MCS
Hosmer-Lemeshow (p)	0.759	0.902	0.333	0.885
Nagelkerke R^2	0.318	0.329	0.201	0.573
Sex				
Men[a]	1.0	1.0	1.0	1.0
Women	1.3 (0.6–2.5)	**2.2 (1.1–4.5)***	1.9 (1.0–3.8)	0.9 (0.4–2.1)
Age[b]/10	1.0 (0.8–1.2)	**1.3 (1.1–1.6)***	1.2 (1.0–1.5)	0.9 (0.7–1.2)
SES				
High[a]	1.0	1.0	1.0	1.0
Medium	1.9 (0.6–5.9)	0.9 (0.3–2.9)	**0.4 (0.2–1.0)***	0.8 (0.3–2.4)
Low	3.3 (1.0–11.1)	1.8 (0.6–5.4)	0.6 (0.2–1.4)	0.8 (0.2–2.6)
Paid work				
No[a]	1.0	1.0	1.0	1.0
Yes	0.8 (0.3–2.3)	0.2 (0.02–1.4)	0.5 (0.2–1.3)	0.4 (0.1–1.5)
Marital status				
Together[a]	1.0	1.0	1.0	1.0
Single	1.6 (0.7–3.5)	1.3 (0.5–3.3)	1.3 (0.6–2.9)	0.6 (0.2–1.8)
Divorced/widowed	0.6 (0.3–1.1)	1.0 (0.5–1.7)	1.0 (0.6–1.8)	1.2 (0.6–2.6)
Rheumatoid factor				
No[a]	1.0	1.0	1.0	1.0
Yes	1.1 (0.7–1.9)	**2.0 (1.1–3.5)***	1.0 (0.6–1.7)	0.9 (0.5–1.7)
DAS28[b]	**2.1 (1.6–2.8)*****	**1.7 (1.3–2.3)*****	**1.4 (1.1–1.8)****	**0.6 (0.4–0.8)*****
Somatic comorbidity[b]	**1.3 (1.1–1.6)****	**1.2 (1.0–1.5)***	**1.4 (1.1–1.6)*****	1.1 (0.9–1.4)
Psychological comorbidity[b]	**1.1 (1.1–1.1)*****	**1.1 (1.1–1.1)*****	**1.1 (1.0–1.1)*****	**1.3 (1.2–1.4)*****

[a] Reference category. [b] Mean of available measurements. * $p < 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$. PCS: physical component summary scale; MCS: mental component summary scale.

Table 5. Good health outcomes over time: predictive value of sociodemographic factors, RA-specific clinical factors, and comorbidity (results of multivariate logistic regression; $n_{max} = 882$).

	VAS Pain	Disability	PCS	MCS
Homer-Lemeshow (p)	0.228	0.402	0.083	0.957
Nagelkerke R^2	0.293	0.134	0.298	0.369
Sex				
Men[a]	1.0	1.0	1.0	1.0
Women	0.9 (0.5–1.4)	0.7 (0.5–1.2)	0.7 (0.4–1.2)	1.2 (0.7–2.2)
Age[b]/10	**1.4 (1.1–1.8)****	1.1 (0.9–1.3)	1.1 (0.9–1.4)	1.1 (0.8–1.3)
SES				
High[a]	1.0	1.0	1.0	1.0
Medium	0.9 (0.5–1.9)	1.0 (0.5–2.0)	1.2 (0.6–2.3)	**0.5 (0.2–0.9)***
Low	1.1 (0.4–2.5)	1.0 (0.4–2.3)	0.7 (0.3–1.7)	0.5 (0.2–1.3)
Paid work				
No[a]	1.0	1.0	1.0	1.0
Yes	1.1 (0.5–2.3)	0.8 (0.4–1.6)	1.3 (0.7–2.6)	0.6 (0.3–1.2)
Marital status				
Together[a]	1.0	1.0	1.0	1.0
Single	1.1 (0.4–2.6)	1.1 (0.5–2.4)	1.7 (0.8–3.6)	0.4 (0.1–1.3)
Divorced/widowed	0.6 (0.3–1.3)	0.8 (0.4–1.5)	0.6 (0.3–1.3)	0.8 (0.4–1.6)
Rheumatoid factor				
No[a]	1.0	1.0	1.0	1.0
Yes	1.5 (0.9–2.5)	0.9 (0.6–1.5)	1.0 (0.6–1.7)	1.0 (0.6–1.6)
DAS28[b]	**0.5 (0.4–0.6)*****	**0.7 (0.6–0.8)****	**0.6 (0.4–0.7)*****	1.2 (1.0–1.6)
Somatic comorbidity[b]	0.9 (0.7–1.1)	0.9 (0.7–1.1)	**0.7 (0.5–0.9)***	**1.3 (1.0–1.7)***
Psychological comorbidity[b]	**0.9 (0.8–0.9)*****	**0.9 (0.9–1.0)*****	**0.9 (0.8–0.9)*****	**0.7 (0.7–0.8)*****

[a] Reference category. [b] Mean of available measurements. * $p < 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$. PCS: physical component summary scale; MCS: mental component summary scale.

listed odds ratios. However, it should be kept in mind that depressive symptoms were measured continuously (on a scale from 0 to 60), meaning that the listed odds ratios were predicted for just 1 point change of depressive symptoms.

In accord with our previous study on the effect of specific comorbid conditions on HRQOL in RA[27], the present study reinforces that assessment of comorbidity should be incorporated routinely into clinical practice in order to achieve the best possible outcomes for individual patients.

The overall effect of sociodemographic factors in relation to RA-specific clinical factors and comorbidity in predicting health outcomes was rather limited. Older age was a risk factor for disability, whereas it appeared to be protective for pain experience. Female sex was identified as a risk factor for disability as well. Although marriage is generally assumed to be beneficial for health, no statistically significantly multivariate associations at all could be detected between marital status and poor or good health outcomes. This lack of association might confirm that not only the marital status but also the quality of the relationship influences the health of individuals, as described previously[45,46]. While low SES is generally considered to be associated with poor health, our results might indicate that lower SES need not by definition be a risk factor for poor health outcomes over time. In a previous study in the same patient population we found that relative differences with respect to disability and depressive symptoms declined between different SES groups over time, as patients with low SES grow worse less quickly than patients with a high SES[47].

With respect to RA-specific clinical factors, we confirmed the relative importance of disease activity in predicting outcome. Overall, clinical factors were risk factors for poor outcomes and hampered good outcome. Rheumatoid factor showed a rather strong association with high disability, measured with the disease-specific VDF, but not with any other outcome.

In conclusion, next to RA-specific clinical factors, comorbidity is a major predictive factor for poor and good health outcomes. Periodic routine screening for and monitoring of somatic and psychological comorbidity should be included in clinical practice in order to achieve the best possible outcomes for individual patients. Comorbidity makes the care of patients with RA even more complex. Our findings support the necessity of close cooperation and good communication between the various healthcare providers, since we cannot expect all patients to coordinate the care they receive and to oversee potential dangers and complications, e.g., drug interference or even contraindications.

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