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RECENT-ONSET RHEUMATOID ARTHRITIS: A 1-YEAR OBSERVATIONAL STUDY OF CORRELATIONS BETWEEN HEALTH-RELATED QUALITY OF LIFE AND CLINICAL/LABORATORY DATA

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Objective: **To analyse correlations within and between clinical/laboratory assessments and health-related quality of life variables for recent-onset rheumatoid arthritis at the time of diagnosis and 12 months later.**

Methods: **A total of 297 patients with recent-onset (≤12 months) rheumatoid arthritis were included at diagnosis and followed up for 12 months. Clinical/laboratory assessment was performed by erythrocyte sedimentation rate, C-reactive protein, 28-joint count of tender/swollen joints, physician's global assessment, grip force, grip ability, functional impairment and walking speed. The self-reported health-related quality of life included symptoms (pain, morning stiffness), patients estimated general health, Health Assessment Questionnaire and SF-36.**

Results: **All tested variables improved within 6 months of diagnosis and then remained stable but still affected at the 12-month follow-up. Multivariate correlations between clinical/laboratory variables and health-related quality of life were weak. At inclusion, clinical/laboratory assessments explained 18% of health-related quality of life at the same time-point and predicted 7% of the variation in health-related quality of life after 12 months.**

Conclusion: **The time-course followed similar patterns for most variables, but only a small part of the variation in health-related quality of life was explained or predicted by the clinical/laboratory variables. This implies that health-related quality of life adds important information to clinical/laboratory assessments in clinical practice and should be considered in goal setting together with clinical/laboratory assessment in order to optimize healthcare and outcome.**

Key words: outcome, early rheumatoid arthritis, health-related quality of life, HAQ, SF-36, grip force, walking speed.

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INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune chronic inflammatory disease, which often leads to irreversible joint damage and disability (1). A variety of outcome measures have been used to evaluate disease activity and quality of life in patients with RA (2, 3). The Outcome Measures for Arthritis Clinical Trials (OMERACT) have recommended 5 domains to be included in outcome measures in RA for use in longitudinal observational studies, i.e. health status, disease process, damage, mortality and toxicity/adverse reactions (4). Work disability and costs were also recognized as important. Measures suggested by OMERACT to assess the disease process are, for instance, joint counts regarding tenderness and swelling, global assessment of disease severity, and circulating levels of acute phase reactants. The health status domain was proposed to include questionnaires representing disease-specific and generic quality of life instruments as well as instruments regarding pain, fatigue, physical and psychosocial function. Such questionnaires are intended to evaluate the impact on the patients' health-related quality of life (HRQL) adding information to traditional clinical and laboratory measures of joint disease (5). Hence, the term HRQL is a complex concept, which refers to patients' experiences of illness such as pain, fatigue and disability as well as broader aspects of emotional and social wellbeing (6). In clinical practice HRQL questionnaires can quantify the impact of RA and direct the physician's attention to items that are important to the patient (7). Without information about the correlations between the numerous assessment variables it is difficult to select the most relevant instruments to be followed clinically in order to perform appropriate individual intervention strategies.

Previous studies have described the course of early RA with respect to the disease process and different aspects of health (8–11) as well as the correlation between the disease process and self-estimated HRQL (12–15). The commonly used disease specific Health Assessment Questionnaire (HAQ) and the physical function scale of the generic HRQL instrument Short Form 36 (SF-36) were significantly associated with disease activity and severity in a study group of RA patients with a median duration of 11 years (13). HAQ has also been found to correlate with the physical and social function scales of SF-36 in

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a group of patients with 6 years duration of RA (15). Other scales of SF-36, e.g. physical and emotional roles, showed no association with disease activity measures, indicating that the different scales of SF-36 as intended reflect different aspects (15). In early RA changes in SF-36 and HAQ scores were more strongly related to the patients' pain assessments and the physician's global assessment than to changes in joint swelling and joint tenderness (16). Based on patients with RA of 10 years' duration it was concluded that the level of disability according to HAQ and the physical function scale of SF-36 were not proportional to clinical or laboratory signs of inflammation, and that factors such as educational background, and psychological aspects may affect the disablement outcome (14).

There is limited information available about the correlation between the professionals' clinical assessments of disease and function and the patients' self-reported HRQL. Further studies are needed to analyse to what extent traditional clinical and laboratory disease markers correlate with HRQL in early RA, and whether there are clinical and laboratory variables that can be used to indicate HRQL. Such information may be helpful to guide the decision on individually tailored multi-professional interventions in early RA. Thus, the present study was carried out with the aim of describing and comparing the course of early RA for a period 1 year from diagnosis regarding clinical and laboratory assessments vs self-reported HRQL aspects of health. Within this aim we also investigated how well these 2 groups of variables could be used at the time of diagnosis to predict the situation 12 months later.

PATIENTS AND METHODS

Swedish TIRA project

In 1996 a prospective study, the "Swedish TIRA" (Swedish acronym for "early intervention in rheumatoid arthritis"), was started (17) in a collaboration between 10 rheumatology units in south-east Sweden. Standardized monitoring was carried out in collaboration with rheumatologists, occupational therapists, physiotherapists and social workers and follow-up was carried out at the time of inclusion (M0) and after 3, 6 (M6), 12 (M12), 18 months, and then once a year. A total of 320 patients with RA were included between January 1996 and March 1998. The first signs of arthritis (joint swelling) were observed at least 6 weeks, but not more than 1 year, before inclusion. All patients fulfilled at least 4 of 7 criteria for RA as defined by the 1987 revised American College of Rheumatology (ACR) classification criteria (18) *or* suffered from morning stiffness (60 minutes or more as judged by the patients), and symmetrical arthritis, and arthritis in small joints (fingers/hands/wrists/feet/toes). Two hundred and fifteen (67%) were women and 105 (33%) men. At the time from inclusion to the 12-month follow-up, 23 patients (13 women and 10 men) dropped out.

Study group

All 297 patients remaining in the TIRA study at the 12-month follow-up constituted the study group; 202 (68%) women (mean age 55 years at inclusion, SD 15 years) and 95 (32%) men (mean age 58 years, SD 15 years). The mean age was significantly higher in men ($p = 0.02$). The median number of ACR criteria was 5 (range 6) with no difference between women and men. Latex-agglutinating rheumatoid factor (RF) was present in sera from 178 patients (60%; 61% in women and 57% in men) at inclusion. At inclusion, co-morbidity was reported for 97 patients (33%). Of these, 63% reported 1 and 22% reported 2 co-morbidities. Cardiovascular disease was the most frequently reported co-morbidity (42%) among the 97 patients, followed by asthma (10%). During the study period the multi-professional team examined patients and interventions were offered when considered adequate. Ongoing medication was registered at all follow-ups. At the time of inclusion 72% of the patients were taking non-steroidal anti-inflammatory drugs (NSAIDs), 20% were taking oral corticosteroids and 2% were taking disease-modifying anti-rheumatic drugs (DMARDs). At inclusion 47% were prescribed DMARDs. At the 12-month follow-up 59% of the patients were taking NSAIDs, 35% oral corticosteroids and 70% DMARDs.

All participants gave written informed consent to participate and the local ethics committees approved the study protocol.

Clinical and laboratory assessments

Erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) were used as laboratory markers of inflammation. A 28-joint count of swollen and tender joints was used (19) and the physician's global assessment of disease activity (PGA) was estimated on a 5-degree scale (0–4) where 0 corresponds to no activity and 4 represents high activity (20). Grip force in the right hand was tested using a digital electronic device ("Grippit", Detektor AB, Göteborg, Sweden) (21). The average grip force value (N) during 10 seconds was recorded. The "Grip Ability Test" (GAT) was performed as described by Dellhag & Bjelle (22) with a score ranging from 10 at the best to 276 at the worst. Functional impairment in hand (0–16), upper limb (0–12) and lower limb (0–16) were assessed by "Signals of Functional Impairment" (SOFI) in which the score 0 represents "can perform" (23). "Walking speed" was defined as the time (seconds) it took to walk 20 m as fast as possible indoors, if necessary the patients used their own assistive devices.

Patient reported variables – HRQL

The patients estimated the duration of morning stiffness (minutes), and graded the average pain intensity during the past week on a 0–100 mm visual analogue scale (VAS; 0 representing no pain and 100 maximal pain). The average well-being during the last week was also rated by the patients on a VAS-scale (0 representing "the best possible" and 100 "the worst possible well-being"). Disability was reported at the time of inclusion and at the 12-month follow-up by the Swedish version of the Health Assessment Questionnaire (HAQ) (24). By the standard Swedish version of Short Form-36 (SF-36) generic aspects of health were reported (25). The 8 scales in SF-36 consist of 4 physical scales ("physical function", "role physical", "bodily pain" and "vitality") and 4 mental scales ("general health", "social function", "role emotional" and "mental health"). Each scale is scored from 0 to 100, where 100 corresponds to full health (26). The SF-36 results at inclusion (M0) and at the 12-month follow-up (M12) were also expressed as the difference (in standard deviations; SD) between the present group and a Swedish reference population (27).

Statistical analyses

All statistics were performed using the statistical packages SPSS for Windows (version 10.0) or SIMCA-P (version 10.0). For variables under investigation mean values and 1 standard deviation (1 SD) are generally reported. In all statistical analysis $p < 0.05$ was regarded as significant. Wilcoxon's signed ranks tests were used to evaluate differences in repeated measures of disease activity and HRQL (patient-reported variables). The normal test was used to test differences between the study group and a reference population with regard to SF-36 (28).

Principal component analysis (PCA). PCA can be viewed as a multivariate correlation analysis, which was performed using SIMCA-P, to analyse the relationships between variables at the time of inclusion and the 12-month follow-up, and to detect whether a number of variables reflect a smaller number of underlying components (29). Principal components with Eigenvalues >2.00 were considered as non-trivial components. A component consists of a vector of numerical values between -1 and 1, referred to as *loadings*. The loading expresses the degree of correlation between the item and the component. A loading is obtained for each measurement variable included in the PCA model. Variables that have high loadings (with positive or negative sign) upon the same component are inter-correlated. We have considered loadings ≥ 0.25 in absolute numbers (i.e. irrespective of sign) to be high and therefore of interest. Items with high loadings (ignoring the sign) are considered to be of large or moderate importance for the component

Table I. *Mean values (M), and standard deviations (SD) for the total group (*n = *297) at inclusion (M0), 6-months (M6) and 12-month (M12) follow-ups, and statistical comparison of changes between M0 and M6, and M6 and M12. The mean response rate for the total of variables was 96%, ranging between 88% and 100%. NS denotes not significant*

	Follow-up			Statistical comparison	
	M0	M6	M12	*p*-value	
Variables	Mean (SD)	Mean (SD)	Mean (SD)	M0 vs M6	M6 vs M12
Clinical/laboratory					
ESR (mm)	35 (23)	24 (20)	23 (21)	<0.001	NS
CRP (mg/l)	29 (28)	16 (20)	16 (21)	<0.001	NS
Swollen joints (1–28)	10 (6)	4 (5)	4 (5)	<0.001	NS
Tender joints (1–28)	9 (7)	4 (5)	4 (5)	<0.001	NS
PGA (0–4)	2 (1)	1 (1)	1 (1)	<0.001	0.034
Grip force (Newton)	113 (89)	144 (99)	146 (98)	<0.001	NS
GAT (0–276)	27 (17)	23 (16)	22 (16)	<0.001	NS
SOFI hand (0–16)	2.8 (2.7)	2.0 (2.3)	2.0 (2.3)	0.047	NS
SOFI upper limb (0–12)	1.2 (1.8)	1.0 (1.6)	1.1 (1.7)	<0.0001	NS
SOFI lower limb (0–16)	2.2 (2.2)	1.6 (1.8)	1.8 (2.2)	<0.001	NS
Walking speed (seconds)	14 (6)	13 (5)	13 (6)	<0.001	0.024
Patient-reported variables HRQL					
Morning stiffness (min)	109 (71)	63 (64)	63 (69)	<0.001	NS
Pain (VAS mm)	47 (25)	36 (26)	39 (27)	<0.001	NS
Well-being (VAS mm)	43 (25)	35 (25)	37 (25)	<0.001	NS
HAQ (0–3)	0.9 (0.6)	–	0.6 (0.6)	–	–
Physical function (0–100)	50 (25)	62 (24)	62 (23)	<0.001	NS
Role physical (0–100)	23 (37)	47 (43)	45 (43)	<0.001	NS
Bodily pain (0–100)	36 (19)	53 (23)	52 (23)	<0.001	NS
General health (0–100)	53 (19)	54 (20)	53 (19)	NS	NS
Vitality (0–100)	42 (21)	55 (23)	55 (24)	<0.001	NS
Social function (0–100)	71 (24)	83 (21)	81 (21)	<0.001	NS
Role emotional (0–100)	49 (45)	69 (41)	71 (39)	<0.001	NS
Mental health (0–100)	66 (19)	77 (17)	76 (19)	<0.001	NS

ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; PGA = physician's global assessment of disease activity; GAT = Grip Ability Test; SOFI = Signals of Functional Impairment; HRQL = health-related quality of life; VAS = visual analogue scale; HAQ = Health Assessment Questionnaire.

under consideration. A cross-validation method, which keeps part of the data out from the model development to assess the predictive power of the model, was used to test the significance of the components.

Partial least squares. Partial least squares or projection to latent structures (PLS) (29), SIMCA-P, was used to investigate the relationships between variables representing the clinical assessment and the self-estimated HRQL-variables at the time of inclusion and at the 12-month follow-up. PLS was also used to investigate in what extent variables representing the clinical assessment at the time of inclusion predicted the HRQL-variables at the 12-month follow-up. The variable influence on projection (VIP) variable gives information about the relevance of each X-variable and each Y-variable pooled over all dimensions and VIP >1.0 is significant. Components with Eigenvalues ≥ 2.00 were considered as non-trivial components. Multiple linear regression (MLR) could have been an alternative method for the prediction, but it assumes that the regressors (X-variables) are mathematically independent and only one Y-variable at a time can be predicted. If multi-colinearity (high correlations) occurs among the X-variables the calculated regression coefficients become unstable and their interpretability breaks down.

Outliers were identified using the 2 methods available in SIMCA-P; (i) score plots in combination with Hotelling's T^2 (identifies strong outliers) and (ii) distance to model in X-space (identifies moderate outliers).

RESULTS

Drop-outs

There were no statistically significant differences between the drop-outs ($n = 23$) and the study group ($n = 297$) concerning the majority of the variables (listed in Table I) except for walking speed, which was significantly lower ($p = 0.007$) in the drop-outs (20 ± 13 seconds) compared with the study group (14 ± 12 seconds).

Clinical and laboratory assessments

At the time of inclusion (M0), the clinical and laboratory assessments revealed moderate disease activity and disability, which had improved significantly at the 6-month follow-up (M6) in most variables (Table I). Thereafter the majority of the variables remained stable but still affected, except for PGA and walking speed, which showed small but significant improvements from M6 to M12. When comparing the 12-month follow-up with inclusion, most variables improved significantly, although still affected, except for SOFI upper limb, which did not change (data not shown).

Patient reported variables – HRQL

At M0 the patients reported moderate morning stiffness, pain and affected well-being, which had improved significantly at M6 and then remained stable but affected during the rest of the study period (Table I). The moderate disability, reported by the patients at the time of inclusion, had decreased at M12 according to HAQ. The generic instrument SF-36 showed that the patients were affected at the time of inclusion. Most scales had improved

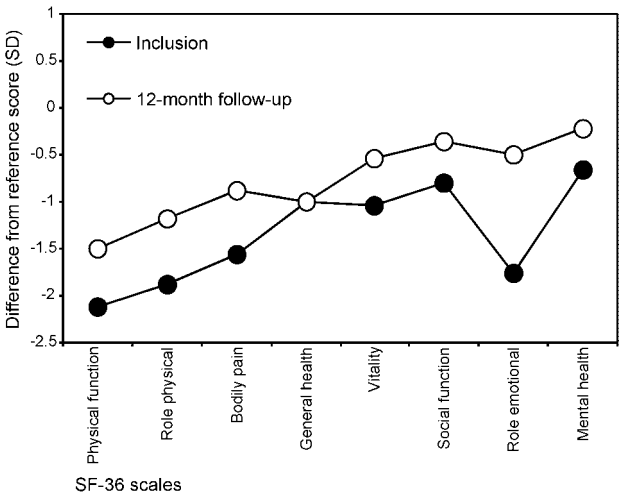

Fig. 1. Differences (in standard deviations; SD) between the mean SF-36 scores in the study group at inclusion and 12-month follow-up compared with values for a Swedish reference population.

significantly at M6 compared with M0 and remained stable but still lowered during the rest of the study period. The exception in SF-36 was general health scale, which was affected but stable during the whole study period.

At both M0 and at M12 the study group had significantly lower values of the SF-36 scales compared with a Swedish reference population (Fig. 1). At M0, the differences in SF-36 were most pronounced with regard to "physical function", "role physical", "role emotional" and "bodily pain", whereas "mental health", "social function" "general health" and "vitality" were closer to references (Fig. 1). The differences related to the Swedish reference group were less pronounced at M12 apart from the scale "general health".

Relationships between HRQL and clinical/laboratory variables at inclusion

A PCA was made in order to understand the relationships on a general level between the 2 sets of variables (i.e. clinical/laboratory and HRQL). One significant component explaining 28% of the variation was identified and the important variables (i.e. absolute loadings $\geq$0.25) of this component belonged to HRQL assessments, i.e. the scales of SF-36 and HAQ (Table II, first column). In other words, no or only a weak relationship existed between the 2 sets of variables and the variation between patients was more prominent for the HRQL variables because they and not the clinical/laboratory variables loaded markedly upon the first and only significant component.

In order to determine the most important variables among the HRQL variables, a PCA was made based upon these variables alone, which confirmed the pattern seen in Table II, i.e. HAQ, SF-36 (all scales), and pain (VAS) had significant importance (and without marked differences in loadings) while morning stiffness and well-being were less important (data not shown).

The variables associated with the greatest variations between patients in the clinical/laboratory set of variables were the 3 SOFI variables (loadings: 0.42–0.46), grip force (loading: −0.38), GAT (loading 0.36), and walking speed (loading: 0.29) according to a PCA ($R^2 = 0.28$) (data not shown).

As can be expected from the PCA results (Table II) at M0 only weak relationships ($R^2 = 0.18$) existed between the HRQL and clinical/laboratory variables according to a PLS analysis that regressed the HRQL variables using the clinical/laboratory variables as X – variables (Table III). Grip force, walking speed, SOFI lower and PGA were the significant regressors (Table III).

A regression in the opposite direction determined which HRQL variables that were significantly linked to the clinical/laboratory set of variables; HAQ (VIP = 1.51), physical function of SF-36 (VIP = 1.51) and social function of SF-36 (VIP = 1.03) were then significant regressors ($R^2 = 0.16$) (data not shown).

Relationships between HRQL and clinical/laboratory variables at M12

A PCA at M12 based on all variables identified 2 significant components ($R^{2(\text{cumulated})} = 0.43$) (Table II, 3rd and 4th column). Five of the scales of SF-36, pain and well-being together with PGA (i.e. a clinical variable) loaded significantly upon the first

Table II. *The significant components and the loadings from principal component analysis (PCA) at inclusion (M0) and the 12-month follow-up (M12) of clinical/laboratory variables and health-related quality of life (HRQL). R^2 is given for each component in the bottom row. The loadings with absolute values $\geq$0.25 are given in bold*

Variables	M0 p[1]	M12 p[1]	p[2]
Clinical/laboratory			
ESR (mm)	0.12	0.19	**0.30**
CRP (mg/l)	0.13	0.17	**0.34**
Swollen joints (1–28)	0.12	0.18	**0.40**
Tender joints (1–28)	0.13	0.17	0.14
PGA (0–4)	0.20	**0.26**	**0.26**
Grip force (Newton)	−0.22	−0.20	−0.05
GAT (0–276)	0.15	0.13	0.12
SOFI hand (0–16)	0.16	0.11	**0.32**
SOFI upper limb (0–12)	0.13	0.10	0.22
SOFI lower limb (0–16)	0.21	0.18	0.20
Walking speed (seconds)	0.04	−0.03	0.03
Patient-reported variables/HRQL			
Morning stiffness (minutes)	0.14	0.19	0.16
Pain (VAS mm)	0.23	**0.28**	−0.13
Well-being (VAS mm)	0.12	**0.26**	−0.18
HAQ (0–3)	**0.31**	−0.03	−0.01
Physical function (0–100)	**−0.30**	**−0.26**	−0.01
Role physical (0–100)	**−0.26**	**−0.27**	0.10
Bodily pain (0–100)	**−0.29**	**−0.29**	0.14
General health (0–100)	**−0.26**	**−0.25**	0.18
Vitality (0–100)	**−0.29**	**−0.28**	0.22
Social function (0–100)	**−0.26**	−0.23	0.20
Role emotional (0–100)	−0.22	−0.21	0.19
Mental health (0–100)	−0.24	−0.21	**0.29**
R^2	0.28*	0.32*	0.11*

*denotes significant component.
ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; PGA = physician's global assessment of disease activity; GAT = Grip Ability Test; SOFI = Signals of Functional Impairment; VAS = visual analogue scale; HAQ = Health Assessment Questionnaire; p[1] = component 1, p[2] = component 2.

Table III. *Partial least squares regression (PLS) of health-related quality of life (HRQL) variables (Y-variables; see Table II) using the different clinical/laboratory variables as regressors (X-variables). For each variable is given variable influence of projection (VIP) and values >1.0 is considered significant and given in bold. The explained variance (R^2) is shown in the bottom row. Analysis were made at inclusion (M0) and at 12-month follow-up (M12)*

Variables	M0 VIP	M12 VIP
ESR (mm)	0.57	0.92
CRP (mg/l)	0.69	0.91
Swollen joints (1–28)	0.75	**1.02**
Tender joints (1–28)	0.63	**1.02**
PGA (0–4)	**1.10**	**1.32**
Grip force (N)	**1.41**	**1.23**
GAT (0–276)	0.95	0.94
SOFI hand (0–16)	0.93	0.75
SOFI upper limb (0–12)	0.77	0.55
SOFI lower limb (0–16)	**1.32**	0.92
Walking speed (seconds)	**1.40**	**1.19**
R^2	0.18	0.20

ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; PGA = physician's global assessment of disease activity; GAT = Grip Ability Test; SOFI = Signals of Functional Impairment.

component. PGA and pain (VAS) correlated negatively with 5 scales of SF-36: physical function, role physical, bodily pain, general health and vitality. The second component mainly reflected intercorrelations between clinical/laboratory variables (i.e. ESR, CRP, swollen joint count, PGA and SOFI hand).

Only 20% of the variation in HRQL variables was explained by the clinical/laboratory variables (Table III). PGA, grip force, walking speed, tender joint count and swollen joint count were the significant regressors.

The regression in the opposite direction identified physical function of SF-36 (VIP = 1.43), morning stiffness (VIP = 1.37), bodily pain of SF-36 (VIP = 1.08), pain intensity (VIP = 1.03), role physical of SF-36 (VIP = 1.01) and well-being (VIP = 1.01) as the significant variables when regressing the clinical/laboratory set of variables ($R^2 = 0.18$) (data not shown).

Can the variables at M0 predict the situation at M12?

Even though it was possible to predict the HRQL at M12 using the clinical/laboratory variables at inclusion as regressors, only a small part of the variation ($R^2 = 0.07$) was explained. The following variables were of significant importance: walking speed (VIP = 1.62), grip force (VIP = 1.45), GAT (VIP = 1.20) and SOFI lower (VIP = 1.04). A model with somewhat higher R^2 was obtained when the HRQL variables at M0 were used to regress the HRQL variables at M12 ($R^2 = 0.15$). Four scales of SF-36 at M0 had significant importance: vitality (VIP = 1.33), mental health (VIP = 1.29), physical function (VIP = 1.09), and social function (VIP = 1.02) (data not shown).

A significant model ($R^2 = 0.17$) also existed when the clinical/laboratory variables at M0 were used to regress the clinical/laboratory variables at M12; grip force (VIP = 1.49), SOFI upper (VIP = 1.23), SOFI hand (VIP = 1.20) and ESR (VIP = 1.18) were significant regressors (data not shown).

DISCUSSION

In collaboration with general practitioners, arthritis patients with symptom duration of less than 12 months were recruited to the Swedish TIRA cohort during 27 months 1996–98. Multiprofessional intervention and structured follow-up was carried out in all cases, regardless of the degree of disease activity. Although, due to the inclusion criteria, patients with slowly developing disease were excluded, it is reasonable to believe that the Swedish TIRA cohort is a fair approximation of the average Swedish recent-onset RA population and a valuable reference for future prospective cohorts. The main findings of the present study were: (i) that most clinical and laboratory as well as HRQL variables improved within 6 months of diagnosis and then remained stable over the study period; (ii) that only weak correlations existed between clinical/laboratory and HRQL variables; and (iii) that both at inclusion and at the 12-month follow-up, the HRQL variables explained more of the variation between subjects than clinical/laboratory variables did.

Our results at the time of inclusion concerning clinical and laboratory assessments as well as follow-up data, are in accordance with earlier reports (8, 9, 11). Moreover, a previous report from the Swedish TIRA cohort showed that disease activity and functional ability improves significantly within 3 months of diagnosis and start of intervention (17). Disease activity then remained essentially stable for at least 2 years, whereas function seemed to slowly deteriorate, especially in women (17). Although we have previously reported that men in the Swedish TIRA cohort had a more benign disease course than women (17), PLS regression analyses in the present study do not indicate any significant influence of age or sex concerning the multivariate relations between clinical/laboratory and self-reported variables (unpublished data). Further knowledge regarding sex and/or age differences in HRQL is needed in order to optimize intervention.

In agreement with the findings of Kosinski et al. (16), our results confirm that the time course of all SF-36 scales follow similar patterns except for the scale "general health". The fact that "general health" was reduced but stable during the study period may indicate that this aspect is independent of changes in disease activity and disability, at least during the first year after diagnosis of RA. Other possible explanations are that this aspect of health is unmet by health professionals, that it relates to aspects of life that go beyond the responsibility of health professionals and/or that this scale has relatively low sensitivity as compared with the other scales of SF-36. Like us, Kosinski et al. (16) found that mental health according to SF-36 was relatively close to references. Apart from lower values concerning "role physical" and "bodily pain" in an RA population with a mean duration of 13 years, Husted et al. (30) found SF-36 results comparable to ours at the 12-month follow-up.

HRQL measurements are presumably important to consider for the evaluation of interventional effects, to define outcome, and to define healthcare needs for patients with RA both at the collective and the individual level (2, 3). When possible, it is recommended to supplement generic HRQL instruments with disease-specific ones (31). At present, SF-36 and HAQ are the most used generic and disease specific instruments (6). In this study we found that SF-36 and HAQ results correlated significantly at the time for diagnosis of recent-onset RA, whereas this was not the case at the 12-month follow-up when the average disease activity was lower. However, 12 months after inclusion other HRQL aspects, e.g. pain (VAS) and well-being (VAS), were found to be important. The increasing importance of pain aspects with increasing disease duration was also evident when we investigated which of the patient-reported variables that were strongest linked to the clinical/laboratory variables. Opposite to the situation at inclusion, aspects of pain were significantly linked to the clinical/laboratory variables at the 12-month follow-up, i.e. when the patients had improved according to clinical and laboratory variables. The explanation for these observations is not evident and more research is needed to unravel the mechanisms behind the growing importance of pain despite lower disease activity with increasing disease duration.

We found that the HRQL variables explained most of the variation between subjects both at inclusion (6 scales of SF-36 and HAQ were significant) and at the 12-month follow-up (5 scales of SF-36, pain/VAS and well-being/VAS were significant). These results also indicate weak multivariate correlations between clinical/laboratory and patient-reported (HRQL) variables and that HRQL estimates may offer additional important information. This interpretation was also confirmed in the PLS regressions, where the clinical/laboratory assessments explained only 18–20% of the variation in HRQL between inclusion and the 12-month follow-up. Poor correlation between disease activity measures and disability has also been reported by others (12).

The physician's global assessment of disease activity, grip force and walking speed were stable significant regressors of the patient-reported (HRQL) set of variables at inclusion as well as 12 months later. At inclusion, "SOFI lower limb" also contributed, as did swollen and tender joint counts at the 12-month follow-up. In the prediction perspective walking speed and grip force were the most important clinical/laboratory variables at inclusion when regressing the self-reported HRQL variables at the 12-month follow-up. Taken together, these results indicate that some of the clinical/laboratory variables, grip force, walking speed, and possibly PGA, show stable relationships with the HRQL set of variables, while other clinical/laboratory variables are disease- or duration-dependent. However, these observations must be viewed in the light of the low, but significant, explained variation. Based upon our findings, it is not possible to predict the HRQL situation with any precision, since about 80% of the variation in the HRQL variables were unexplained at the time for diagnosis and 12-month follow-up of early RA. The precision was still lower in a prospective perspective, in view of the fact that only 7% of the variance in the HRQL variables at the 12-month follow-up was explained by the clinical and laboratory variables at inclusion. Escalante & del Rincon (14) reported that the physical function scale of SF-36 and the modified HAQ were explained to 33% by disease factors and to 26% by age, sex, psychological status and depression in a study group with a mean duration of 10 years, which deviate a bit from our results. Furthermore, they concluded that there are relative influences of psychosocial factors (14).

In conclusion our results support earlier reports that HRQL measures are not strongly associated with disease activity (15) and that these measures might provide information, which may prove useful to identify needs for intervention (13).

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