

Positive treatment response improves the health-related quality of life of patients with early rheumatoid arthritis

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ABSTRACT

Objective. To examine treatment induced changes in health-related quality of life (HR-QoL) in patients with early rheumatoid arthritis (RA).

Methods. Changes in HR-QoL were assessed by the Nottingham Health Profile (NHP) instrument in 62 consecutive working age patients with recent onset RA with duration of symptoms of less than two years and naïve with regard to disease-modifying antirheumatic drugs (DMARDs) and glucocorticoids. Treatment-response was assessed by the criteria of the European League against Rheumatism (EULAR; 28-joint score; DAS28) at 6 months.

Results. NHP mean scores for pain ($p=0.029$) and emotional reaction ($p=0.035$) at baseline were related to EULAR response at 6 months, i.e. non-responders had the poorest baseline HR-QoL scores. When the patients were grouped according to EULAR response at 6 months there was a statistically significant mean linear change to better HR-QoL in NHP energy ($p=0.0023$), pain ($p<0.001$) and mobility ($p=0.0085$) from baseline to 6 months from the lowest to highest treatment-response level.

Conclusion. Our results show that good treatment-response as measured by the EULAR response criteria translates into improved HR-QoL dimensions for energy, pain and mobility.

Introduction

Health-related quality of life (HR-QoL) as a patient-reported outcome in rheumatoid arthritis (RA) has become an important tool in the clinical evaluation of patients' preferences and perceptions of their health. During the last 10 years the active use of disease-modifying anti-rheumatic (DMARD) and biological drugs has notably improved the course of RA and also function and quality of life (QoL) (2). In fact, due to chronic nature of RA, the major focus of treatment should be to improve the HR-QoL desired by patients (1).

Declined physical capacity and reduced ability to work, but also need for additional help and support from family and friends become apparent in RA patients life from the very beginning of

the disease (3). High levels of self-perceived distress, especially associated with disturbed mood have been found in many areas of functioning in early RA even at the lowest levels of functional disability (4).

The HR-QoL information in early RA has been gathered mainly by using the physical function scale of the Health Assessment Questionnaire (HAQ) (5, 6). HAQ is not an ideal instrument and debate continues how to best measure patient-reported outcomes in RA (6). Multidimensional generic HR-QoL instruments measure in addition to physical functioning also psychological and social domains of health (1). The 36-item short-form health survey (SF36) (7) and the Nottingham Health Profile (NHP) (8) instruments capture also aspects of fatigue, which has been reported by patients to worsen their perceived health (9). Therefore, fatigue has been suggested by the OMERACT group to be incorporated in patient assessment (9). As would be expected, the patients with early RA show poorer HR-QoL than the general population by the SF36 instrument (10). In early RA the negative impact is especially seen in the dimensions for pain, physical functioning and vitality and to a lesser extent in emotional well-being and social isolation (10). Similarly, in the NHP instrument, the dimensions for pain, mobility and energy show poor HR-QoL scores in early RA (11-13).

The purpose of the present study was to examine the changes in HR-QoL in early RA patients. In particular, we focused on whether the cases would show differences according to their EULAR response (14) at six months.

Patients and methods

This study was performed in Jyväskylä Central Hospital which is the only rheumatology clinic in a district serving a population of 250000 (in 1995). The design was approved by the ethics committee of Jyväskylä Central Hospital.

Patients

Sixty-two consecutive working age patients out of the total of seventy with recent onset RA according to the 1987 American College of Rheumatology

Competing interests: none declared.

Table I. Demographics and baseline disease characteristics of 62 early RA patients categorized into three response groups according to EULAR (DAS28) response criteria at six months.

Characteristic	EULAR (DAS28) response group at 6 months			p-value
	Non-responders (n=14)	Moderate responders (n=14)	Good responders (n=34)	
Demographic				
Female, n. (%)	7 (50)	10 (71)	21 (62)	0.51
Age, year, mean (SD)	51 (10)	51 (8)	48 (11)	0.41
Duration of symptoms (months), median (IQR)	5 (3.7)	6 (4.10)	6 (3.8)	0.28
Measures of arthritis activity				
Erythrocyte sedimentation rate (mm/hr), median (IQR)	21 (6.28)	26 (10.51)	18 (14.34)	0.11
Number of swollen joints, mean (SD)	6.7 (5.5)	8.9 (6.3)	6.0 (5.2)	0.25
Number of tender joints, mean (SD)	6.1 (4.6)	11.2 (6.9)	6.5 (5.0)	0.016
Pain (VAS), mm, mean (SD)	37 (22)	52 (24)	39 (23)	0.13
Patient's global assessment (VAS), mm, mean (SD)	36 (20)	50 (18)	41 (26)	0.30
DAS28, mean (SD)	4.23 (1.20)	5.41 (1.31)	4.61 (0.95)	0.019
Functional capacity				
HAQ, mean (SD)	0.70 (0.52)	0.88 (0.55)	0.60 (0.55)	0.27
Radiographic				
Larsen's score, median (IQR)	0 (0.1)	0 (0.2)	0 (0.1)	0.48

Table II. Baseline scores for different NHP dimensions of 62 early RA patients categorized into three response groups at six months after diagnosis according to EULAR (DAS28) response criteria.

Dimension	EULAR (DAS28) response group at 6 months			p-value
	Non-responders Mean(SD)	Moderate responders Mean (SD)	Good responders Mean (SD)	
Energy score	33 (44)	36 (36)	20 (33)	0.32
Pain score	43 (30)	39 (28)	23 (20)	0.029
Sleep score	46 (38)	40 (33)	21 (35)	0.076
Emotional reaction score	29 (27)	15 (16)	13 (17)	0.035
Social isolation score	6 (11)	4 (7)	2 (8)	0.34
Mobility score	18 (19)	20 (13)	8 (11)	0.015

criteria (15) were studied from Jan. 1995 to Dec. 1996. The duration of symptoms was <24 months at inclusion, and the patients had not previously been treated with DMARDs or with glucocorticoids. After initial assessment, prompt treatment with DMARDs (sulfasalazine as the first drug with few exceptions) was instituted in all patients. Nineteen patients were prescribed low-dose prednisolone (2.5-7.5 mg/day). Eight patients were lost to follow-up: the diagnosis of 3 subjects changed (spondylarthrosis, psoriatic arthritis, and long-standing RA), one fell ill with cancer, one drowned, one was involved in an accident and suffered from neurological symptoms and two did not sign-up. The patients were managed by a multi-disciplinary team to inform and moti-

vate them to self-management and adherence to therapy. The patients were also encouraged to liberally contact the staff of the rheumatology unit by phone. The average stay in the rheumatology unit was 5 days after which the patients were regularly checked at the outpatient unit.

Health-related quality of life

The HR-QoL of the patients was evaluated at baseline and at six months using the first section of the validated Finnish version of the self-report NHP (8, 16). The NHP is a generic measure of subjectively experienced distress and contains 38 statements in six dimensions: physical mobility (8 items), pain (8 items), sleep (5 items), energy (3 items), social isolation (5 items) and

emotional reactions (9 items) (12). The respondent is required to answer "yes" or "no" to each statement depending on whether he or she is currently bothered by problems in the area. The responses are weighted empirically in terms of their perceived severity (8, 17). Each dimension is scored from 0 (no problems or absence of limitations) to 100 (all problems listed are present) (8).

Disease activity and treatment response

For the assessment of disease activity and response to treatment the 28-joint-based Disease Activity Score (DAS28) (18) and the EULAR response criteria (14) were used. The DAS 28 is a composite index including tender and swollen joint counts, patient's self-reported global status on a 0-100mm visual analogue scale (VAS) and erythrocyte sedimentation rate. The EULAR response criteria are categorized as follows: a decrease in the DAS 28 by >1.2 in combination with an end-point DAS 28 <3.2 is defined as a good response, and no response means a decrease in the DAS 28 of <0.6 regardless of end-score or 0.6-1.2 resulting in a DAS 28 of >5.1. Any other changes in scores are regarded as moderate responses.

Joint radiology

Radiographs of hands and feet were scored according to the Larsen method (19).

Functional capacity

For the assessment of functional capacity the Finnish version of the self administered HAQ questionnaire (score 0-3) was used (5, 20)

Statistics

The results were expressed as mean or median, standard deviation (SD) or interquartile range (IQR). The statistical significance between groups was evaluated by analysis of variance (ANOVA), Kruskal-Wallis test (Monte Carlo *p*-value) or chi-square test. The mean changes in the NHP dimensions were compared between groups using a bootstrap-type analysis of covariance with the baseline value as covariable. However, as the NHP variables were skewed,

a bias-corrected bootstrap estimation was used to derive a 95% confidence interval (95%CI) (5000 replications).

Results

The demographic and clinical characteristics of RA patients at baseline grouped according to their EULAR responses at six months are shown in Table I. With the exception of somewhat higher baseline DAS 28 and tender joint count in cases with moderate response the data between the response groups were comparable. At baseline, no NHP dimension showed a correlation with the DAS28 (data not shown).

The non-responders at six months had the poorest HR-QoL mean NHP scores at baseline for pain ($p=0.029$) and emotional reaction ($p=0.035$) (Table II). On the other hand, there was a linear change towards better HR-QoL in NHP energy ($p=0.0023$), pain ($p<0.001$) and mobility ($p=0.0085$) at 6 months from the lowest to highest treatment response level (Fig. 1).

Discussion

Our study assessed changes in HR-QoL during the six months period from the diagnosis in patients with RA who were treated by a multidisciplinary approach including early and continual DMARD strategy. Expectedly, we were able to show that a good treatment response translates in favourable changes in energy, pain and mobility dimensions of the HR-QoL by the NHP instrument. This finding may indicate that pain, energy and mobility reflect disease activity-related problems of RA patients, while sleep, emotional reaction and social isolation dimensions may more tightly associated with illness perception (21). Traditionally, clinicians' decision making has based on process measures in RA such as disease activity and radiological damage in joints. However, multidimensional HR-QoL questionnaires provide relevant and complementary information from patients' perspective that is not provided by biomedical tests (22). Our findings confirm, that the patients' experience complete the process measures and ensures, that clinical decisions are meaningful also from the patients' point of view.

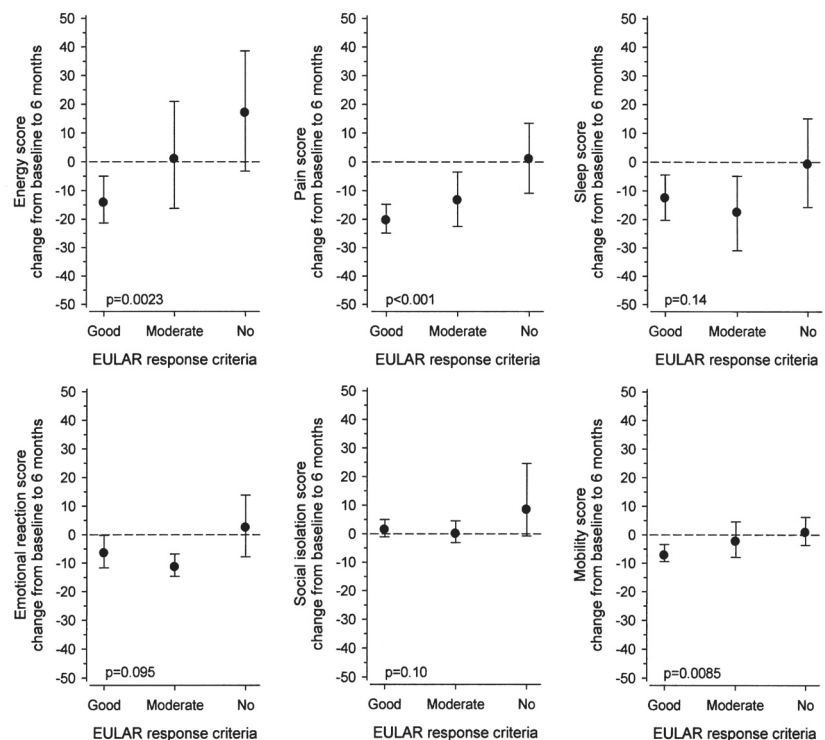


Fig. 1. Mean changes (95% CIs) of different NHP dimensions at six months for 62 patients with early RA classified in three categories according to the EULAR (DAS28) response criteria. 95% confidence interval obtained by bias-corrected bootstrapping (5000 replications). (Decrease means improvement and increase deterioration of the dimensions).

Significant pain relief was achieved in our patients with good and moderate EULAR responses. It has been reported previously that especially relief of pain, but also of fatigue are outcomes desired by RA patients (9, 23). Nature of fatigue has been shown to be multidimensional in RA patients' experience and reduced energy most probably relates to fatigue reported by RA patients (24). Early RA patients suffering from severe fatigue and running out of energy are at risk for poorer QoL profile compared to those having minor fatigue problems (12). Although absence of fatigue is one of the remission criteria in RA (25) the association of fatigue and disease activity has been controversial (26, 27). Recent studies with biological drugs have reported rapid and significant improvement in fatigue in association with clinical improvement (28, 29). It is noteworthy that NHP energy along with NHP pain was the most responsive dimension in our study. Further, only the RA patients who showed good treatment-response reached a significant improvement in

NHP energy dimension. The finding indicates that marked improvement in fatigue in patients with early RA can be obtained by treatment with conventional DMARDs.

We emphasize that in the present study the RA patients, who showed good EULAR response at six months had better baseline HR-QoL in all NHP dimensions than the patients in other response categories, although the clinical characteristics between the groups were comparable. Thus, we may conclude, that other factors than disease activity *per se* impacts on HR-QoL, too. The patients with early RA suffering from high levels of pain and negative mood have been reported to be prone to maladaptive coping and poorer QoL (30). In early RA emotional disturbances rather than disease activity or HAQ disability have accounted most reliably for subjective handicap (4). The non-responders in our study perceived especially high pain and emotional distress. Psychological functioning was not assessed in the study. Therefore, it is not possible to evaluate if the non-

responders suffered for instance more depressive symptoms or poorer coping than the other patients.

The advantage of the prospective study design is that the direction of causality between changes in HR-QoL and disease activity can more reliably be evaluated than in cross-sectional studies. Many HR-QoL instruments have problems with large floor and ceiling effects (the percentage of the sample achieving the best and worst possible scores) (31). In our study remarkable floor effects were seen in all the NHP dimensions. At the baseline the distributions of patients with scores of 0 in different dimensions varied from 19% for pain to 82% for social isolation. It has been suggested that HR-QoL instruments with floor and ceiling effects within the range 1%-15% meet the standards of measurement for individual-patient application (31). Thus, the results in our study evaluating RA patients in group-level cannot necessarily be interpreted for individual patients. Large floor effects at the baseline before health intervention are problematic because improvement cannot be documented in longitudinal monitoring. It is also important to keep in mind when interpreting the present results that the NHP items are dichotomous and thus indicate the extreme points of illness or health. This could mean that a patient with acceptable initial scores fails to improve even if the improvement is obvious.

In conclusion, rheumatoid arthritis places considerable burden on patients' HR-QoL. However, the HR-QoL dimensions for pain, energy and mobility of patients with early RA greatly improved in those patients who showed better treatment-responses assessed by the EULAR criteria, while in the non-responders the changes were minor ones. Therefore, special attention should be paid to those patients with poor treatment-responses to prevent the negative impact of RA on patients' functioning and well-being.

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