
Health-related quality of life in patients with rheumatoid arthritis and in patients with ankylosing spondylitis

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ABSTRACT

In this review the influence of rheumatoid arthritis (RA) and ankylosing spondylitis (AS) on a wide range of health-related quality of life (HRQoL) domains will be described. The domains most frequently studied are pain, functional disability, fatigue and mental problems. In addition, age and socio-economic aspects such as employment and economic status as well as education affect patient-reported HRQoL.

Although many studies have assessed the impact on HRQoL of a single disease state, either RA or AS, few studies have focused on a direct comparison between those both diagnostic groups. In general, patients with RA and AS report significant decrements in HRQoL in comparison with the general population. It has been shown that the magnitude of the impairment is similar among both patients group.

Introduction

There is a growing interest in describing and assessing quality of life (QoL), particularly in chronic disabling conditions. Health status describes the impact of illness on a person's ability to participate in life. While health and functional situation are predominantly related to the physical condition, the term "quality of life" includes the wishes, expectations and emotional responses of the individual related to his/her health. Gill and Feinstein suggest that QoL rather than being a description of a patient's health status is a reflection of the way in which patients perceive and react to their health status (1). QoL encompasses the concept of health-related QoL (HRQoL) which describes extend to which one's usual or expected physical, emotional and social well-being are affected by a medical condition and its treatment (2). It is important to notice that the concept of HRQoL differ from that of functional status although these two constructs may highly correlate

for patients (3). Thus, HRQoL can be thought of as the overall impact of the illness and its treatment on patients, and their response to these impacts.

HRQoL is not a single parameter but rather a collection of different health concepts that together paint a picture how a disease affects a patient in daily life. Although there is general agreement that HRQoL is multidimensional, there is no formal consensus on the domains that should be included. The domains most frequently studied are physical, social, psychological, and occupational well-being items. Thus, most prevalent QoL concerns in rheumatologic diseases included pain, functional disability, fatigue and mental problems. In addition, age and socio-economic factors such as employment and economic status as well as education affect patient-reported HRQoL. Consequently, there is a need to explore the burden of rheumatoid arthritis (RA) and ankylosing spondylitis (AS) focusing on a wide range of health dimensions.

Measurement of QoL

Two basic approaches to measure QoL are available: generic instruments that provide a summary of QoL applicable to all people (healthy and any disease), and specific instruments that focus on problems associated with single disease states (2). Commonly used generic health status instruments are the Medical Outcomes Study 36-Item Short Form (SF-36), EuroQoL (EQ-5D), Health Assessment Questionnaire (HAQ) and Health Assessment Questionnaire for the spondyloarthropathies (HAQ-S) (4-7). As a specific QoL instrument in patients with RA, the RAQoL can be used (8). The Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire is the best studied disease-specific measure available to assess HRQoL in AS patients (9). Both specific questionnaires have proven validity and sensitivity for assessment of changes in QoL and are

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based on the needs-based model (9, 10). In this model, QoL is defined as the extent to which individuals are able to meet their needs. By concentrating on needs, items are more likely to be relevant to all patients regardless of age, gender or employment status.

An important advance in HRQoL research is the concept of “minimum clinically important difference” (MCID), defined as the smallest difference in score on an HRQoL instrument that patients perceive as beneficial and that would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management. Differences in scores smaller than the MCID are considered unimportant, regardless of whether statistical significance is reached (11). Values for MCID in domain and SF-36 summary scores have been derived in RA and AS based on correlations with patients-reported improvements in global disease activity (12, 13).

The challenge in HRQoL measurement is its multidimensional nature, which takes into account not only how a person functions physically, mentally and socially, but also incorporates an evaluative component that assesses a person’s satisfaction with his or her current health status. Health status instruments can be used to monitor outcomes in clinical practice, to assess the impact of different diseases on HRQoL, for individual decision making processes and as an end point in clinical trials. HRQoL assessments are particularly important in the absence of a cure for RA and AS and to provide evidence that therapy really makes people feel better.

HRQoL in patients with RA

RA is traditionally considered to be a disease with a major impact on all aspects of HRQoL and may result in significant disability, morbidity and early mortality if untreated or inadequately treated. Almost all patients report about pain and functional disability during the course of their disease considerably influencing their HRQoL. In a cross-sectional survey from Norway it has been demonstrated that pain is the area in which almost 70% of the patients with RA most desired an improvement (14).

Pain increased slightly with the duration of RA (0.03 units on visual analog scale (VAS) per year (95% CI 0.02–0.03)), while anti-tumour necrosis factor (TNF)- α blocker therapy improved pain by 0.53 to 0.70 units on VAS (15). Progressive deterioration in physical function is reported in longitudinal series of RA patients prior to the introduction of the new disease-modifying antirheumatic drugs (DMARDs). Scott *et al.* demonstrated average increases of 0.033 per year in HAQ scores (16). Women with RA have been reported to have more functional disability than men (17).

Fatigue has been consistently mentioned as an important outcome by patients with RA, but it is seldom included in routine clinical assessments. Clinically important levels of fatigue are present in 40–80% in RA patients (18). From the patient’s perspective, fatigue has consequences on all aspects of QoL and is seen as important because fatigue affects other outcomes like work or social activity. Fatigue has been identified as the consequence of disease that differentiates best on a series of QoL aspects such as disability and well-being (19). Nevertheless, overlap of depression presenting with symptoms of fatigue may additionally influence HRQoL. Depressive symptoms are frequent in RA and may occur with at least mild severity in up to 42% of RA patients (20).

Although the physical domain might be most affected, the significant effect of RA on the mental health should not be underestimated. RA patients above the age of 40 years had worse overall scores for mental component summary (MCS) score of the SF-36. Comparison with the general population revealed a reduction of -0.27 for mental health measured by standardized difference scores (s-scores), indicating a low to moderate disease effect for mental health (21). However, patient’s psychological state needs to be assessed as a variable, independent of physical impairment.

An improvement in clinical response criteria is well known in patients with active RA when treating with DMARDs and biologics. Meanwhile, meaningful impact on HRQoL parameters have been demonstrated in randomized controlled trials with DMARDs and

especially with biologics as well. Normally, improvement in QoL parameters is accompanied by improvement in physical function.

Persistent active disease may lead to reduced productivity and increased rates of work disability resulting in a worse quality of life. Patients with RA are at risk of work disability from the very start of their symptoms. Prospective cohorts show that 20–30% of patients with RA become permanently work disabled during the first 2–3 years of the disease (22). Work disability appeared to be 4–15 times higher than in the general population (23). Females with RA had a fourfold increased risk of work disability compared to men (24).

HRQoL in patients with AS

AS the main entity of the spondyloarthritis (SpA), is a chronic condition with a variable disease course (25). Since AS usually starts in early adulthood, the average duration of disease is longer compared to RA. Consequently, the impact of AS on HRQoL of patients can be important. The burden of illness of AS is less well defined than for RA, but there is an increasing awareness that the impact of AS on HRQoL is comparable to that in RA.

Patients with AS report significantly impaired health on all scales of the SF-36 compared with the general population. The most prevalent HRQoL concerns include stiffness, pain, fatigue and sleep problems (26). Functional disability is the main contributor to the burden associated with AS. Compared with patients with other medical conditions, patients with AS have the lowest scores in the physical domains (27). Ward has indicated that longer disease duration and increasing age are associated with decreased functioning, whereas performing back exercises and having a greater degree of social support improves functioning (28). In this prospective longitudinal study the HAQ-S increased over a median of 5 years at an average rate of 0.0168 units per year. In a study from Norway, women with AS reported worse physical functioning, more physical limitations, and a greater reduction in vitality measured by SF-36 than men (29). However, the

crude effect of the disease is greater in men as shown by standard difference scores of SF-36 between AS group and general population (30).

Pain is considerable influencing HRQoL in AS patients. 83% of the patients report about any problems with pain, for one third of them it is very important (26). Again, women were 2 to 3 times more likely than men to have greater pain. Patients with AS reported significantly more back pain than the global pain in patients with RA (44 versus 25 mm on VAS pain), but pain is comparable in the peripheral joints for the two groups (31).

Fatigue has been described as a major symptom in AS, with up to 65% of the patients reporting (32). Van Tubergen *et al.* showed that scores on the BASDAI fatigue question were significantly associated with scores on several dimensions of the SF-36 and with the ASQoL, suggesting that HRQoL is influenced by the degree of fatigue (33).

Although the physical aspects of health seem to be most severely affected, the disease impact on mental health is considerable. A study by Barlow *et al.* showed that one third of the AS patients reported a high level of depressive symptoms undermining the stereotype of the "typical" AS patient as being less depressed than other people with other forms of arthritis (34). In addition, disease status scores like BASDAI correlates significantly with anxiety and depression (35). The disease impact on HRQoL is considerable especially in those with less education (30). Thus, special attention should be paid to this aspect and educating patients about the disease may play an important role in coping with the disease.

In a variety of studies significant association between HRQoL improvements and clinical response criteria has been shown in patients with active AS receiving TNF- α blockers therapy (27). As expected, the physical component summary (PCS) of the SF-36 has changed more than the MCS due to therapy in these studies.

The improvement of HRQoL during treatment with TNF- α blockers is accompanied by significant improvement in productivity and reduced work-day loss among employed patients with

AS (36). Nevertheless, AS may cause work disability up to 36% primarily depending on disease duration (37). The dependence from disease duration is important to notice since AS evolves slowly and progressively mainly in patients in their 3rd decades. Employment is 11% (OR: 0.82; 95% CI: 0.78-0.87) lower and work disability 15% (OR: 3.10; 95% CI: 2.77-3.42) higher than expected in the general Dutch population (38). Interestingly, while income was not associated with reduced QoL, income loss due to work disability resulted in a worse HRQoL (39).

Comparison

As stated above, pain and impaired mobility as well as fatigue and depression are common features of both RA and AS. A direct comparison of HRQoL between RA and AS has been made in only few studies. According to a Dutch study the impact on several dimensions of SF-36 in patients with RA and AS of working age is comparable (40). In addition, the level of fatigue and the way patients cope with stressors of the disease (measured by the Multidimensional Fatigue Inventory (MFI) and the Coping with Rheumatic Stressors (CORS) instrument) is also similar. In a recent study, patients with RA and chronic arthritides including patients with SpA reported the very same poor HRQoL scores compared to an age-standardized general population (0.810 and 0.815 versus 0.903 on a 0-1 scale) (41).

These findings confirm the conclusion of the German rheumatological database that RA and AS generate similar amounts of disability, pain, and impact on well-being (42). Patients with RA and AS were equally disabled in functions like washing and drying oneself or standing in line. Comparison of pain intensity between age and sex matched groups of patients with RA and AS revealed that for patients younger than 70 years there is little difference between both disease groups or between women and men (severe pain (VAS $\geq$ 7) in female RA and AS patients: 33.8 and 34.2%, and male RA and AS patients: 33.1 and 32.7%). However, for higher age groups there is a marked difference between women and men in both diagnostic groups. This gender difference

is much more striking than the difference between AS and RA (severe pain in female RA and AS patients: 40.8 and 44.6%, and male RA and AS patients: 27.0 and 29.8%).

Treatment is one of the most important factors which can influence the HRQoL of the patients. There is one retrospective meta-analysis on the efficacy of TNF-blockers in RA versus AS. Larger improvements in HRQoL in SpA patients have been attributed to the relatively better efficacy of TNF-blockers in the treatment of SpA (43).

The socio-economic consequences in RA and AS have been compared recently (44). Work loss is one of the most important outcomes of chronic inflammatory rheumatic diseases. In addition, work status is after disease characteristics, the most important determinant influencing HRQoL in patients with RA and AS (40). The lowest standardized employment ratios (SER) of 0.78 (1.0=population) has been calculated in patients with RA compared to patients with AS (0.94) in a study by Mau *et al.* (44). The SER declined significantly with disease duration. In female RA patients the SER is 0.93 (95%CI: 0.90-0.95) after $\leq$ 5 years of disease and declined to 0.56 (95%CI: 0.54-0.59) after $>$ 10 years. No significant difference from the population is found in the SER in AS patients with a disease duration $\leq$ 10 years. In patients with longer-lasting AS, there is a slightly higher chance of employment in AS compared to RA (SER 0.88, 95%CI: 0.83-0.92 for men; SER 0.91, 95%CI: 0.84-0.99 for women).

Conclusion

Patients with RA and AS report significant reduction in HRQoL in comparison with the general population. It has been shown that the magnitude of the impairment is similar among both patients group. The decreases in HRQoL are attributed to various domains, mainly pain, impairment in physical function, fatigue and mental health. These domains and the strategies patients use to cope with disease burden influence socioeconomic factors. Thus, maintenance of physical function is no longer the only treatment goal for RA and AS but also to improve, restore, and preserve HRQoL.

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