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Evaluation of Quality of Life Scales According to Disease Activity in Rheumatoid Arthritis

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ABSTRACT

Objective: In addition to disease activity, quality of life (QoL) of patients with rheumatoid arthritis (RA) is also related to variables like pain, fatigue, depression, anxiety, and sleep quality. We aimed to evaluate the association among disease activity and QoL scales in RA.

Methods: In this cross-sectional study, 92 consecutive RA patients who applied to Ankara City Hospital Rheumatology outpatient clinic in January-December 2020 were included. Demographic, clinical features and laboratory data were recorded. DAS28 for disease activity and pain-visual analogue score(VAS) and fatigue-VAS, hospital anxiety-depression(HAD), Pittsburgh Sleep Quality Index(PSQI), and Nottingham Health Profile(NHP) forms for QoL assessment were filled by one-on-one interviews. Patients were grouped to disease activity as: "Low-DAS28 group" and "High-DAS28 group".

Results: In comparison with DAS28, pain-VAS, and fatigue-VAS, and some NHP scores (such as the total score and pain, physical activity, and fatigue subgroup scores) were significantly higher in the High-DAS28 group than the Low-DAS28 group. However, no difference was found in HAD scores. The sleep disorder subgroup score was higher in the High-DAS28 group but total and other subgroups of the PSQI were similar. Overall DAS28 correlated with NHP total score (0.427, $p<0.001$), pain-VAS (0.731, $p<0.001$) and fatigue-VAS (0.505, $p<0.001$).

Conclusion: To improve the quality of life in rheumatoid arthritis patients is one of the main objectives of treatment. High disease activity seems to be more affecting the patients in terms of pain-VAS, fatigue-VAS, NHP total scores and NHP-pain, NHP physical activity subgroups than other quality of life scales in patients with rheumatoid arthritis.

Keywords: Rheumatoid arthritis, disease activity, quality of life, visual analogue score, sleep quality

Romatoid Artrit Yaşam Kalitesi Ölçeklerinin Hastalık Aktivitesine Göre Değerlendirilmesi

ÖZET

Amaç: Romatoid artrit (RA) hastalarında yaşam kalitesini (QoL) hastalık aktivitesi dışında ağrı, yorgunluk, depresyon, anksiyete ve uyku kalitesi de etkiler. Bu çalışmada RA hastalık aktivitesi ile QoL ölçekleri arasındaki ilişkiyi değerlendirmeyi amaçladık.

Yöntemler: Bu kesitsel çalışmaya, Ocak-Aralık 2020 tarihleri arasında Ankara Şehir Hastanesi Romatoloji polikliniğine başvuran, ardışık 92 RA hastası dahil edildi. Hastaların demografik verileri, klinik özellikleri ve laboratuvar sonuçları kaydedildi. Hastalık aktivitesini değerlendirmek için DAS28, QoL değerlendirmek için ise ağrı-görsel analog skoru (VAS), yorgunluk-VAS, hastane anksiyete depresyonu(HAD), Pittsburgh Uyku Kalitesi İndeksi (PSQI) ve Nottingham Sağlık Profili (NHP) ölçekleri birebir hasta vizitinde doldurulmuştur. RA hastaları hastalık aktvitesine göre "Düşük-DAS28 grubu" ve "Yüksek-DAS28" olarak olarak gruplandırıldı.

Sonuçlar: Düşük-DAS28 ve Yüksek-DAS-28 gruplarının karşılaştırılmasında, ağrı-VAS, yorgunluk-VAS ve bazı NHP skorları (toplam skor ve ağrı, fiziksel aktivite ve yorgunluk alt grup skorları), Yüksek-DAS28 grubunda istatiksel anlamlı olarak daha yüksekti. Ancak HAD skorları her 2 grupta benzerdi. PSQI uyku bozukluğu altgrup skoru Yüksek-DAS28 grubunda daha yüksekti fakat PSQI total skor ve diğer alt grup skorları skorları her 2 grupta benzerdi. Toplam DAS28 skoru ile NHP toplam (0.427, $p<0,001$), ağrı-VAS (0,731, $p<0,001$) ve yorgunluk-VAS (0.505, $p<0,001$) skorları birbiri ile koreleydi.

Tartışma: Romatoid artritli hastalarda yaşam kalitesini iyileştirmek tedavinin temel amaçlarından biridir. Romatoid artrit hastalarında yüksek hastalık aktivitesinin ağrı-VAS, yorgunluk-VAS, NHP toplam skor ile NHP-ağrı ve NHP fiziksel aktivite alt grup skorları üzerine etkisi diğer QoL ölçekleri ve alt gruplarından daha fazladır.

Anahtar Kelimeler: Görsel analog skoru, hastalık aktivitesi, romatoid artrit, uyku kalitesi, yaşam kalitesi

Rheumatoid arthritis (RA) is a multisystemic, inflammatory chronic articular disease whose extra-articular organ involvements may be seen on disease course. RA prevalence is 0.5-1%(1), more in women than men (2). Chronic inflammation in RA also causes morbidities in addition to disease activity, and all of these affect quality of life. In the course of RA, disease activity may progress with remissions and exacerbations. Although there are many different assessment scales, disease activity is frequently evaluated with The Disease Activity Score-28 (DAS28) score in the studies (3). DAS28 is very useful for both RA disease activity assessment and follow-up.

As in all chronic diseases, it is important to assess the quality of life in RA. Pain, fatigue, anxiety, depression and deterioration in sleep quality are among the causes affecting the quality of life in RA. Although there are diverse methods, quality of life may be evaluated with both general and specific scale in RA disease. For this purpose, pain-Visual Analogue Scale (VAS), fatigue-VAS (4), Hospital Anxiety and Depression (HAD) Scale (5), Nottingham Health Profile (NHP) (6, 7), and Pittsburgh Sleep Quality Index (PSQI) (8) scales are frequently used to evaluate quality of life in patients with RA. The number of tender-swollen joints and elevated acute phase markers may also be associated with all these quality of life scales (9, 10).

In this study, we have evaluated the association among disease activity and quality of life scales in RA patients.

MATERIALS AND METHODS

A total of 92 consecutive RA patients who applied to the Ankara City Hospital rheumatology outpatients clinic between January-December 2020 were included into our cross-sectional study. Diagnoses of patients with RA met the 2010 American College of Rheumatology classification criteria (11). Patients under the age of 18, with mental illness and pregnancy were excluded. The patients were interviewed face to face, their anamnesis was taken, and physical examinations were performed. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies which were assessed in routine outpatient clinic visits were recorded. Disease activity of RA was scored with the DAS28 score. DAS28 score is defined as remission for ≤2.6, low disease activity for 2.6-3.2, moderate disease activity for 3.2- 5.1, and high disease activity for ≥5.1 . Patients with DAS28 score in remission or low disease activity were grouped as "Low DAS28 group" and those with moderate and/or high disease activity were grouped as "High DAS28 group".

Pain-VAS, fatigue-VAS, HAD, NHP, and PSQI scales were administered to the patients to assess their quality of life. Pain-VAS and fatigue-VAS scores between 0-10 were marked on standard scales by the patients. The HAD anxiety scale was used to measure anxiety levels, and scores of ≥11 and above were considered significant in terms of the presence of anxiety. The HAD depression scale was used to measure depression levels, and scores of ≥8 and above were considered significant. Scores of 5 and above in PSQI were considered significant for poor sleep quality. In the NHP, evaluation was made with a maximum of 100 points in each subgroup in 6 subgroup inquiries. A high score meant that the patients' quality of life was poor. The presence of anxiety and depression was evaluated both as a percentage and a score, separately. Both the total score and the subgroup scores were compared in the NHP and PSQI scales (Table 2). The study was approved by the ethics committee of Ankara City Hospital (30.01.2020-E-kurul-E1-19-205).

Statistical analysis was performed using Statistical Product and Service Solutions 24.0 (IBM Corp., Armonk, NY, USA). The conformity of the variables to the normal distribution was examined with histogram, probability graphs and Shapiro-Wilk test. The $\chi 2$ test was used to compare categorical variables. The categorical variables were defined as percentages, the continuous datas as mean±standard deviation (SD) or median with interquartile range (IQR). Mann-Whitney U or Student t test was used to compare continuous variables. While investigating the associations between non-normally distributed and/or ordinal variables, the correlation coefficients and their significance were calculated using the Spearman test. A p value of below 0.05 was considered statistically significant.

RESULTS

A total of 92 RA patients included in this study, 68 (74%) were female and the mean age was 57.9±13.4 years. Of the 14% patients were smokers and 69% had at least one comorbidity. The mean±SD DAS28 score was 3.3±1.4, the median Pain-VAS score was 4 (IQR:5), and the fatigue-VAS score was 5 (IQR:8).

When the patients were compared according to DAS-28 scores, 48% (n=44) were in the Low-DAS28 group and 52% (n=48) were in the High-DAS28 group. In Table-1, the general and laboratory findings of all RA patients and

both groups are given, separately. Age, female gender, body mass index, frequency of patients with at least one comorbidity and smoking were higher in the High-DAS28 group than in the Low-DAS28 group. In both groups, the frequency of RA patients for more than 5 years was around 80%, and there was no difference between RF and CCP positivity (Table 1).

The comparison of the groups in terms of the quality of life scales was shown in Table 2. In this assessment, the median pain-VAS and fatigue-VAS scores were higher in the High-DAS28 group than in the Low-DAS28 group. While anxiety and depression were found to be 10.9% and 15.2%, respectively, in the entire RA group; there was no difference between the groups in terms of the presence of HAD-anxiety, HAD-depression and their total scores. In the NSP scoring, which is another scale in which we evaluate the quality of life, the median total score was higher in the High-DAS28 group than the Low-DAS28 group. In the NHP subgroup analysis, NHP-pain, NHP-physical activity and NHP-fatigue scores were statistically higher in the High-DAS28 group. In the PSQI scoring, in which we evaluated the sleep quality, we found that the sleep quality index was poor in 34.8% of all patients. No statistically significant difference was found in terms of PSQI subgroups when the patients with RA were compared according to their DAS-28 levels, except for the median PSQI-sleep disorder (Table 2).

Overall DAS28 disease activity correlated, in the expected directions, with NHP total score (Spearman's rho = 0.427, $p < 0.001$), pain-VAS (0.731, $p < 0.001$) and fatigue-VAS (0.505, $p < 0.001$). However, there was no correlation between the disease activity and PSQI total score, HAD-anxiety and HAD-depression.

DISCUSSION

In this study, we evaluated the associations with disease activity in RA patients and the quality of life parameters such as sleep quality, quality of life, pain, fatigue, anxiety, and depression. As expected, we found that increased disease activity had a negative impact on pain-VAS, fatigue-VAS scores. In addition to these, the NHP-pain, NHP physical activity was higher in the High DAS28 group. However, there was no relationship between disease activity and PSQI total score, and most PSQI subgroups except for the sleep disorder subgroup.

Table 1. Demographic, clinical and laboratory characteristics of the rheumatoid arthritis patients between the Low DAS28 and High DAS28 groups

	All patients n=92	Low DAS28 Group n=44	High DAS28 Group n=48	P
Age, year (mean ± SD)	57.9±13.4	55.3±13.9	61.8±12.7	**0.020**
Female, n (%)	68 (73.9)	26 (59.1)	42 (87.5)	**0.002**
Smoking, n (%)	13 (14.1)	11 (25.0)	2 (4.2)	**0.004**
Married, n (%)	83 (90.2)	39 (88.6)	44 (91.7)	0.625
Body mass index, kg/m^2 (mean ± SD)	28.1± 4.8	27.1±4.3	29.3±5.1	**0.027**
Rheumatoid arthritis disease duration > 5 years	73 (79.3)	35 (79.5)	38 (79.2)	0.964
Lives with his/her family, n (%)	88 (95.7)	42 (95.5)	46 (95.8)	0.929
Education level≤ Primary education,n (%)	67 (72.8)	30 (68.2)	37 (77.1)	0.093
At least one comorbid disease, n (%)	63 (68.5)	22 (50.0)	41 (85.4)	**<0.0001**
RF positivity, n (%)	61 (73.5)	29 (72.5)	32 (74.4)	0.843
Anti-CCP positivity, n (%)	45 (54.2)	19 (47.5)	26 (60.5)	0.236
CRP, mg/dL, median (IQR)	6 (10)	6 (6.5)	7 (10.0)	0.170
ESR, mm/h, median (IQR)	20 (15)	17 (19)	23 (17)	**0.009**
Pain-VAS, median (IQR)	4 (5)	0 (3)	5 (4)	**<0.0001**
Fatigue-VAS, median (IQR)	5 (8)	2 (5.3)	5 (5)	**<0.0001**
Precision joint count, median (IQR)	2 (4)	1.5 (2)	4 (6)	**<0.0001**
Number of swollen joints, median (IQR)	0 (0)	0 (0)	0 (0)	0.058

DAS28; Disease activity score-28, RF; Rheumatoid factor, anti-CCP; anti-cyclic citrullinated peptide, CRP; C-reactive protein, ESR; Erythrocyte sedimentation rate, VAS; Visual Analog Scale

Table 2. Comparisons of pain, fatigue VAS, HAD anxiety and depression, NHP and PSQI scores of the rheumatoid arthritis patients between the Low DAS28 and High DAS28 groups

	Low DAS28 Group n=44	High DAS28 Group n=48	p
Pain-VAS, median (IQR)	0 (3)	5 (4)	**<0.0001**
Fatigue-VAS, median (IQR)	2 (5.3)	5 (5)	**<0.0001**
Anxiety, n (%)	3 (6.8)	7 (14.6)	0.232
HAD-Anxiety score, median (IQR)	1.5 (3)	2 (5.7)	0.289
Depression, n (%)	5 (11.4)	9 (18.8)	0.324
HAD-Depression score, median (IQR)	1 (3)	2 (6)	0.196
NHP-Pain score, median (IQR)	0 (87)	100 (96)	**<0.0001**
NHP-Physical activity score, median (IQR)	0 (100)	100 (100)	**<0.0001**
NHP-Fatigue score, median (IQR)	65 (100)	100 (0)	**0.001**
NHP-Sleep score, median (IQR)	0 (0)	0 (0)	0.270
NHP-Social isolation score, median (IQR)	0 (0)	0 (0)	0.296
NHP-Emotional reaction score, median (IQR)	0 (0)	0 (0)	0.093
NHP-Total, median (IQR)	100 (202)	300 (100)	**<0.0001**
PSQI poor sleep quality,n (%)	13 (29.5)	19 (39.6)	0.315
PSQI-Total, median (IQR)	3 (4)	4 (5)	0.158
PSQI-Subjective sleep, median (IQR)	0 (0)	0 (0)	0.810
PSQI-Sleep latency, median (IQR)	1 (2)	1 (2)	0.323
PSQI-Sleep time, median (IQR)	0 (1)	0 (1)	0.818
PSQI-Sleep Efficiency, median (IQR)	0 (0)	0 (1)	0.766
PSQI-Sleep Disorder, median (IQR)	0 (0)	0 (0)	**0.032**
PSQI-Sleeping pill, median (IQR)	0 (0)	0 (1)	0.109
PSQI-Daytime Dysfunction, median (IQR)	0 (2)	0 (2)	0.503

DAS28; Disease activity score 28, VAS; Visual analog scale, HAD; Hospital Anxiety and Depression Scale, NHP; Nottingam Health Profile, PSQI; Pittsburgh Sleep Quality Index

Sleep disturbance could be accompanied to 50-70% of RA patients, and this rate is two-three times higher than in the normal population (12, 13). In fact, the frequency of sleep disturbance was found to be 80% in two studies conducted in Greece and Brazil (14, 15). In our study, sleep disturbance in our RA patients was found to be less than the studies in the literature (34.8%). Differences such as ethnicity, smoking habits, consumption of alcohol, sample size of the study populations, differences in treatment protocols and the kind of scales which evaluate the sleep quality/disturbance may have caused the lower frequency of sleep disorder in our study than literature.

In the literature, mostly, increased disease activity in RA had a negative effect on the sleep quality (14-18). Conversely, some studies found no association between sleep quality and disease activity in RA, like our findings (19, 20). Loppenthin et al. also found that no significant association between disease activity and pain or sleep quality, but mental and physical fatigue was associated with sleep quality in RA patients. Apart from the disease activity, increased proinflammatory cytokines in RA have been found to lead to a decrease in sleep quality, so it was hypothesized that the increased cytokine levels may not be correlated with the DAS28 scores. (21, 22). Another possibility was that sleep quality assessment was not evaluated by objective methods such as polysomnography and multiple sleep latency testing (19). These hypotheses may be valid for our results as to why we could not find a correlation between disease activity and sleep quality.

Pain, fatigue, depression, and sleep quality impairment are known symptoms of RA and they are interrelated factors to each other. (9). For example, pain may affect sleep quality directly or indirectly by increasing depression (10). Loppenthin et al. was found general and mental fatigue were independent markers affecting poor sleep quality in patients with RA. These findings were also associated with the association of depression and fatigue (19). All these factors may lead to deterioration in quality of life in patients with RA (10).

In our study, there was no difference in PSQI total score between RA disease activity and sleep quality. No statistically significant association was found among PSQI subgroups and RA disease activity, except for the PSQI-sleep disorder subgroup. However, we did not think that this difference was clinically significant. In studies involving more patients, the relationship between PSQI total

score and subgroups and RA disease activity should be evaluated.

The main limitations of our study are the lack of a control group due to its cross-sectional design. A limited number of patients was also a major limitation of this study. Another limitation of our study is that no evaluation was made in our group in terms of fibromyalgia, which can be seen frequently in RA patients. The absence of some RA-specific scales, health assessment questionnaire (HAQ) and other QoL assessments was another limitation of our study.

In conclusion, pain-VAS, fatigue-VAS and NHP total score and NHP-pain, NHP physical activity subgroup scores from quality of life scales were higher in patients with high-disease activity RA patients than those RA patients with low-disease activity. PSQI-Sleep quality, anxiety and depression scores were not different according to RA disease activity. Improving the quality of life in RA patients is one of the main goals of treatment. Therefore, while evaluating the success of treatment, besides the disease activity parameter, we should also consider the factors of sleep quality, pain, fatigue, anxiety and depression. According to our findings, disease activity is primarily associated with pain, fatigue, and physical activity. Finally, prospective studies with larger numbers of patients are needed to achieve more valid results.

All authors declare that they have no conflicts of interest.

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