



## Evaluating the Role of Disease Duration in Fatigue and Quality of Life Among Rheumatoid Arthritis Patients

### Romatooid Artrit Hastalarında Hastalık Süresinin Yorgunluk ve Yaşam Kalitesi Üzerindeki Rolünün Değerlendirilmesi

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#### ABSTRACT

**Objective:** The duration of a disease plays a critical role in understanding its progression and impact on an individual's quality of life and symptom severity. The aim was to investigate the effect of disease duration on fatigue and quality of life in patients with rheumatoid arthritis (RA). **Material and Methods:** The cross-sectional study included ninety-two (female:71, male:21) patients with RA. Clinical and demographic characteristics of patients were recorded. Disease activity (Disease Activity Score in 28 joints with CRP (DAS28-CRP)), fatigue (Bristol Rheumatoid Arthritis Fatigue-Multidimensional Questionnaire (BRAFM-DQ)), and quality of life (Short Form-36 questionnaire (SF-36)) were evaluated in the study. RA patients were categorized into two groups based on the disease duration: duration of the disease <10 years and duration of the disease >10 years. **Results:** Significant differences were found in the pain (p=0.022), general health (p=0.028), and health change (p=0.020) subdomains of SF-36. However, BRAFM-DQ scores and its subdomains showed no significant differences across groups. **Conclusion:** While the duration of RA significantly affects certain aspects of quality of life such as pain and general health, it does not appear to influence fatigue levels. This highlights the persistent and debilitating nature of fatigue in RA patients regardless of disease duration, emphasizing the need for targeted interventions to address this symptom.

**Keywords:** Rheumatoid arthritis, Fatigue, Quality of life, Disease duration

#### ÖZ

**Amaç:** Hastalık süresi, hastalığın ilerleyişini ve hastaların yaşam kalitesi ile semptom şiddeti üzerindeki etkilerini anlamada kritik bir rol oynamaktadır. Bu çalışmanın amacı, romatooid artrit (RA) hastalarında hastalık süresinin yorgunluk ve yaşam kalitesi üzerindeki etkisinin araştırılmasıdır. **Materyal ve Metot:** Enine kesitsel çalışmada, 92 (kadın:71, erkek:21) RA hastası analiz edildi. Hastaların klinik ve demografik özellikleri kaydedildi. Hastalık aktivitesi (Hastalık Aktivite Skoru (DAS28)), yorgunluk (Bristol Romatooid Artrit Yorgunluk-Multidimensional Anketi (BRAFM-DQ-T)) ve yaşam kalitesi (Kısa Form-36 anketi (SF-36)) değerlendirildi. RA hastaları hastalık süresine göre iki gruba ayrıldı: hastalık süresi <10 yıl ve hastalık süresi >10 yıl. **Bulgular:** SF-36 alt alanları olan ağrı (p=0,022), genel sağlık (p=0,028) ve sağlık değişimi (p=0,020) açısından anlamlı farklar bulundu. Ancak, BRAFM-DQ-T skorları ve alt alanları gruplar arasında anlamlı fark göstermedi. **Sonuç:** RA hastalarında hastalık süresi, ağrı ve genel sağlık gibi bazı yaşam kalitesi alanlarını önemli ölçüde etkilerken, yorgunluk seviyelerini etkilemediği bulundu. Bu durum, RA hastalarında yorgunluğun sürekli ve zayıflatıcı doğasını vurgulamakta ve bu semptomu ele alacak hedefe yönelik müdahalelerin gerekliliğini ortaya koymaktadır.

**Anahtar Kelimeler:** Romatooid artrit, Yorgunluk, Yaşam kalitesi, Hastalık süresi

## INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic disorder that predominantly affects small joints, leading to pain, joint destruction, and disability. This autoimmune disease can also involve extra-articular manifestations such as cardiovascular, pulmonary, and gastrointestinal complications, rheumatoid nodules, and vasculitis (1).

Among the myriad of symptoms, fatigue is one of the most debilitating, affecting more than 70% of RA patients. The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) have recognized fatigue as a critically important outcome for patients with RA and have recommended that fatigue be systematically reported in all clinical trials involving RA patients (2). Based on pieces of evidence, this fatigue is often described as pervasive, overwhelming, and debilitating, significantly impacting daily activities and overall quality of life (QoL) (3). The multifaceted nature of fatigue in RA patients is influenced by several factors. Persistent joint pain and stiffness exacerbate the sensation of fatigue, while the psychological burden of managing a chronic disease further compounds it (4, 5). Additionally, the inflammation and immune dysregulation inherent in RA demand substantial energy from the body, intensifying fatigue. Furthermore, medications used to manage RA, such as disease-modifying antirheumatic drugs, may also contribute to fatigue (6, 7).

RA's impact extends beyond the physical symptoms, affecting patients' emotional and social well-being (8). The condition can lead to feelings of isolation, depression, and anxiety, which further deteriorate QoL (8, 9). The profound effects of RA on individuals extend to their families, friends, and caregivers, influencing relationships, work productivity, and daily activities. Addressing these challenges requires a comprehensive approach that encompasses both the physical and emotional aspects of the disease (10). A study has shown that early diagnosis and intervention can significantly improve the quality of life for patients with RA. Medical treatments combined with lifestyle modifications, such as exercise, stress management, and a healthy diet, are crucial in managing symptoms and improving well-being (11).

The primary objective of this study is to assess the impact of disease duration on fatigue and quality of life in RA patients. The null hypothesis of the study was that the duration of the disease does not affect fatigue and quality of life in patients with rheumatoid arthritis. The alternative hypothesis of the study was that the duration of the disease does affect fatigue and quality of life in patients with rheumatoid arthritis. By examining the relationship between how long patients have been living with RA and the severity of their fatigue and quality of life, the study aims to provide a deeper understanding of the disease's progression and its broader implications for patient health and well-being. Understanding the relationship between disease duration and these critical aspects can provide insights into better management strategies for RA patients. Additionally, by analyzing how the length of time a patient has RA influences their experience of fatigue and overall QoL, this study seeks to identify potential areas for intervention that may improve patient outcomes.

## MATERIAL and METHOD

### Study Design

The cross-sectional study received approval from the Bingöl University Ethics Committee (dated:16/04/2024, no:24/9), in accordance with the principles outlined in the Helsinki Declaration. The study was carried out at the Clinic of Rheumatology, Ankara Etlik City Hospital. Before beginning this study, all patients signed an informed consent form.

### Patients

The inclusion criteria comprised the following: 1) Patients aged between 18 and 70 years who met the 2010 ACR/EULAR criteria for RA (12); 2) using a regular medication regimen for RA; 3) stable general health condition for the previous 6 months (having no significant illnesses or laboratory abnormalities that require hospitalization or major treatment modifications).

Patients who had a history of malignancies, cognitive deficits, receiving antipsychotic treatment, pregnancy, alcohol dependence, fibromyalgia syndrome, other rheumatic diseases besides RA, neurological diseases such as stroke, multiple sclerosis, and illiterate patients were excluded. Patients with RA who met the inclusion criteria were selected using a probability simple random sampling method.

The post-hoc power analysis was performed with G\*Power 3.1.2.1 software (version 3.1.9.2, Franz Faul, University of Kiel, Kiel, Germany). Ninety-two included patients were found to provide a power of 0.824, based on a Type 1 error rate ( $\alpha=0.05$ ), effect size of 0.55 (considered a medium effect with  $d\geq 0.5$ ), and a one-tailed hypothesis. Therefore, the present sample size was deemed to be sufficiently powered.

RA patients were categorized into two groups based on the disease duration: duration of the disease  $<10$  years and duration of the disease  $>10$  years.

### Data Collection

Sociodemographic characteristics, including age, body mass index, smoking history, smoking exposure, marital status, occupation, were obtained. The duration of disease was also recorded. Disease activity of the participants was assessed with Disease Activity Score-28- C-reactive protein (DAS-28-CRP) (13). All participants were questioned to complete the Short Form- 36 (SF-36) questionnaire for quality of life (14) and the Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional Questionnaire (BRAFMQ) for fatigue (15).

### The Disease Activity

A rheumatologist evaluated the disease activity of patients with RA by utilizing the DAS-28-CRP (13). The DAS28-CRP score is calculated by considering the number of tender joints, number of swollen joints, CRP levels, and the global evaluation score. The DAS28 CRP score was categorised as follows: 0-2.6 for remission, 2.6-3.2 (including 3.2) for low disease activity, 3.2-5.1 (including 5.1) for moderate disease activity and above 5.1 for high disease activity (13).

### The Quality of Life

The SF-36 is a widely used generic health-related quality of life questionnaire designed to evaluate various aspects of well-being. It encompasses eight subscales, each focusing on different domains (16, 17). Higher scores reflect to a higher quality of life on each subscale, which is scored from 0 to 100 (14). A validity and reliability study was conducted on the scale in Turkish (17).

### The Fatigue

The BRAFMQ is a tool utilized to assess the impact of fatigue among patients with RA across various dimensions (15, 18). Comprising a total of 20 items, the BRAFMQ encompasses four subdomains: physical fatigue, fatigue in activities of daily living, cognitive fatigue, and emotional fatigue. All items except the first 3 items are asked to be answered according to a 4-point Likert system (0: not at all, 1: a little, 2: quite a bit and 3: very much). The first 3 items are scored as follows: item-1 is between 0-10, item-2 is between 0-7, and item-3 is between 0-2. The questionnaire evaluates the last seven days. Higher scores indicating elevated levels of fatigue (15, 18). Turkish translation and psychometric properties of the BRAFMQ was performed by Sari et al. (15).

### Statistical Analysis

Statistical Package for the Social Science (SPSS, version 22.0) software was utilized to analyze the data. Visual and analytical tests (Kolmogorov-Smirnov test) were used to test the normality of data. The data are showed as number (percentage) for categorical data, mean (standard deviation) for continuous variables with a normal distribution, and median (interquartile range) for variables without a normal distribution. The sociodemographic and clinical characteristics of the groups (duration of the disease  $<10$  years versus duration of the disease  $>10$  years) were compared with the

independent sample t test or Mann-Whitney U test for parametric data and Fisher's exact test or Pearson chi-square test for categoric data. The Independent Samples t-test was performed to compare the BRAF-MDQ and its subdomains results between the groups. For all statistical significance, a p-value of less than 0.05 was used.

## RESULTS

A total of ninety-two individuals with RA (71 female, 21 male; mean age: 55 (12.8); mean BMI: 28.1 (5.7) kg/m<sup>2</sup>) were included in the current study. The mean DAS28-CRP score of patients was 3.1 (0.7) and the median duration of the disease was 7 (3-13.5) years. Most patients were housewives (n=54, 58.7%) and non-smokers (n=67, 72.8%). The groups were similar in terms of clinical and demographic characteristics (p>0.05). The demographic and clinical characteristics of the patients are indicated in Table 1.

In comparing the SF-36 results based on the duration of the disease, a significant difference was found between the groups regarding pain (p=0.022), general health (p=0.028), and health change (p=0.020). The comparison of the SF-36 results based on the duration of the disease is indicated in Table 2.

The BRAF-MDQ (p=0.475) and its subdomains, including physical (p=0.738), living (p=0.091), cognitive (p=0.400), and emotional fatigue (p=0.270), were similar between the groups. The comparison of the BRAF-MDQ and its subdomains based on disease duration is illustrated in Figure 1.

**Table 1:** Demographic and Clinical Characteristic of Patients

	RA (All patients) (n=92)	Duration of the disease <10 years (n=54)	Duration of the disease >10 years (n=38)	p value
Age (year), mean (SD)	55 (12.8)	52.9 (13.1)	57.9 (12)	0.064*
Gender, n (%)				
Female	71 (77.2)	39 (72.2)	32 (84.2)	0.214 <sup>a</sup>
Male	21 (22.8)	15 (27.8)	6 (15.8)	
BMI (kg/m <sup>2</sup> ), mean (SD)	28.1 (5.7)	28.1 (5.2)	28.1 (6.4)	0.999*
DAS28, mean (SD)	3.1 (0.7)	3.1 (0.6)	3.2 (0.8)	0.432*
Disease duration (year), median (IQR)	7 (3-13.5)	4 (2-6)	15 (10-20)	<0.001 <sup>b</sup>
History of smoking, n (%)				0.396 <sup>c</sup>
None	67 (72.8)	40 (74.1)	27 (71.1)	
Active	8 (8.7)	6 (11.1)	2 (5.3)	
Ex-smoker	17 (18.5)	8 (14.8)	9 (23.7)	
Smoking exposure, packet*year, median (IQR)	16 (12-40)	15 (12-20)	35 (10-40)	0.458 <sup>b</sup>
Existing of comorbidity, n (%)	50 (54.3)	28 (51.9)	22 (57.9)	0.672 <sup>a</sup>
Education level, n (%)				0.659 <sup>c</sup>
Primary School	42 (45.7)	25 (46.3)	17 (44.7)	
Middle School	7 (7.6)	3 (5.6)	4 (10.5)	
High School	22 (23.9)	15 (27.8)	7 (18.4)	
University	18 (19.6)	10 (18.5)	8 (21.1)	
Master's degree	3 (3.3)	1 (1.9)	2 (5.3)	
Marital status, n (%)				0.161 <sup>c</sup>
Married	68 (73.9)	43 (79.6)	25 (65.8)	
Single	6 (6.5)	4 (7.4)	2 (5.3)	
Divorced	18 (19.6)	7 (13)	11 (28.9)	
Occupation, n (%)				0.065 <sup>c</sup>
Housewife	54 (58.7)	31 (57.4)	23 (60.5)	
Student	2 (2.2)	2 (3.7)	0 (0)	
Active worker	13 (14.1)	11 (20.4)	2 (5.3)	
Retired	23 (25)	10 (18.5)	13 (34.2)	

SD: Standard Deviation; IQR: Interquartile range; DAS28: The Disease Activity Score-28

\*Independent sample t test

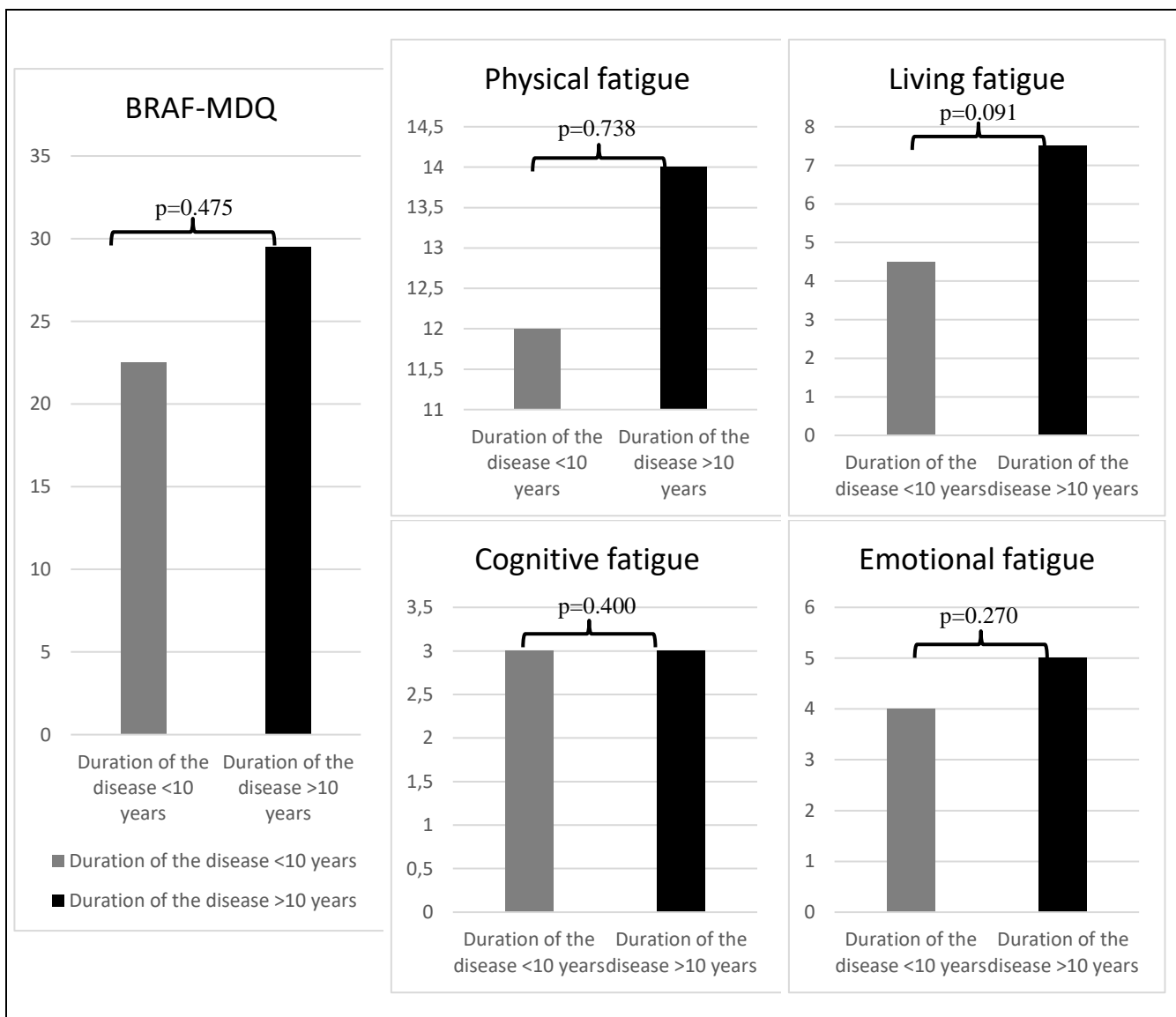
<sup>a</sup> Fisher's exact test<sup>b</sup> Mann-Whitney U test<sup>c</sup> Pearson chi-square test

**Table 2:** The Comparison of The SF-36 Results Based on The Duration of The Disease

	Duration of the disease <10 years (n=54)	Duration of the disease >10 years (n=38)	p value*
	Median (IQR)	Median (IQR)	
Physical function	50 (15-75)	35 (10-55)	0.050
Role limitations due to physical health	37.5 (0-100)	0 (0-75)	0.106
Role limitations due to emotional problems	33.3 (0-100)	0 (0-100)	0.737
Energy/fatigue	50 (30-60)	32.5 (15-55)	0.056
Emotional well-being	60 (48-76)	56 (40-80)	0.469
Social function	62.5 (37.5-87.5)	50 (37.5-87.5)	0.766
Pain	67.5 (32.5-90)	43.7 (20-77.5)	<b>0.022</b>
General health	55 (35-70)	45 (25-55)	<b>0.028</b>
Health change	75 (25-75)	50 (25-75)	<b>0.020</b>

IQR: Interquartile range.

\*Mann-Whitney U test

**Figure 1:** The Comparison of The BRAF-MDQ and Its Subdomains Based on The Duration of The Disease



## DISCUSSION and CONCLUSION

The results of the current study offer significant insights into the influence of disease duration on fatigue and QoL in patients with RA. Our findings highlight several significant differences in the experiences of patients with shorter versus longer disease duration, particularly in terms of pain, general health, and perceived health changes.

Numerous studies in the literature have demonstrated that QoL is significantly lower in RA patients compared to the healthy population (8, 9, 19). Consistent with previous studies, our findings revealed that patients in both groups exhibited lower scores in the SF-36 subgroups. A meta-analysis indicates that RA significantly impairs QoL, with pooled scores from the SF-36 showing that physical domains are more adversely affected than mental health domains. This suggests that RA has a more substantial impact on physical QoL compared to mental well-being (19). Furthermore, several studies have emphasized the association between disease duration and SF-36 subgroups (20, 21). Kiebles et al. demonstrated a significant positive relationship between disease duration and overall emotional well-being, as well as role limitations due to emotional problems, indicating that patients with a longer duration of symptoms may exhibit a greater level of acceptance of their condition compared to those with recent onset disease (20). In contrast, Barlow et al. found no statistically significant differences in QoL between patients with short disease duration ( $\leq 1$  year) and those with longer disease duration ( $\geq 10$  years) (22). However, the current study indicated that QoL, specifically regarding pain, general health, and health change, decreased in the group with a long disease duration ( $>10$  years). There are varying results regarding the relationship between disease duration and QoL in RA patients in the literature. While this relationship has not yet been conclusively demonstrated in an RA population, studies on other inflammatory conditions have found a significant correlation between disease duration and increased disease acceptance. Therefore, when evaluating disease duration and other symptoms in RA patients, assessing their level of disease acceptance is important.

It was anticipated that longer disease duration, resulting in joint erosions and prolonged suffering, would correlate with higher fatigue levels. Two cross-sectional studies found a significant relationship between longer disease duration and fatigue (23, 24). Belza et al. proposed that fatigue is primarily influenced by disease- and sex-related factors, such as disease duration, functional status, and sleep quality (23). In contrast, one cross-sectional study (25) and two longitudinal studies (26, 27) did not find an association between disease duration and fatigue. Similarly, a systematic review indicated that RA patients experience significant fatigue in the early and later stages of the disease (28). Similarly, disease duration was not found to influence fatigue levels in our study. Notably, our findings indicate fatigue levels are significantly high from the onset of the disease and do not vary with disease duration. Consistent with these studies, our study did not identify any difference in fatigue levels between patient groups with a disease duration of less than 10 years and those with more than 10 years. RA patients experience significant fatigue both in the early and later stages of the disease. The possible mechanisms underlying these parameters remain unclear, indicating the need for further studies to elucidate the relationship between disease duration and fatigue.

The present study has some limitations. Firstly, patients were not compared based on disease activity. Secondly, we did not consider the patients' economic and socio-cultural levels in the study. Thirdly, patients were not asked about exercise habits or physical activity levels that could directly impact fatigue. Additionally, while disease acceptance may influence patients' perceptions of fatigue and quality of life, our study did not examine this aspect, representing another limitation. Fatigue affects patients from the onset of the disease; therefore, future research should investigate the underlying mechanisms of persistent fatigue in RA and identify targeted interventions to decrease this debilitating symptom. Understanding the interplay between disease duration, inflammation, and fatigue can lead to more effective treatments and support for RA patients. Additionally, longitudinal

studies that track changes in fatigue and QoL over time in response to different treatment regimens would provide deeper insights into managing RA more effectively.

This study highlights that while disease duration in RA significantly affects pain, general health, and health change, its impact on fatigue is not clear-cut. Comprehensive care strategies that address immediate and long-term health challenges are essential for improving the quality of life for RA patients.

**Acknowledgment:** Thank you to all our patients who completed the study.

**Declaration of Ethical Code:** In this study, we undertake that all the rules required to be followed within the scope of the "Higher Education Institutions Scientific Research and Publication Ethics Directive" are complied with, and that none of the actions stated under the heading "Actions Against Scientific Research and Publication Ethics" are not carried out.

The study received approval from the Bingöl University Ethics Committee (dated:16/04/2024, no:24/9), in accordance with the principles outlined in the Helsinki Declaration. Before beginning this study, all patients signed an informed consent form.

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