Correlation of Fatigue with Clinical Parameters and Quality of Life in Rheumatoid Arthritis

Romatoid Artritte Yorgunluk ile Klinik Parametreler ve Yaşam Kalitesi Arasındaki İlişki

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Abstract

Objective: We aimed to investigate fatigue and its relationship with disease activity, radiological findings and quality of life in patients with rheumatoid arthritis (RA).

Materials and Methods: 41 patients who were diagnosed as RA according to criteria of ACR and 38 healthy controls were enrolled to this study. Patients were asked to record the severity of rest pain (Visual Analog Scale) and duration of morning stiffness. Fatigue was evaluated by the Multidimensional Assessment of Fatigue (MAF) test. Disease activity and quality of life were assessed respectively with DAS-28 and Short Form-36 (SF-36). Radiologic involvement was evaluated according to modified Larsen's grading system.

Results: The mean age of patient and control groups were 50.9±13.4 years and 50±10.1 years, respectively. Two groups were similar with respect age (p=0.744). The median MAF total score was higher in patients with RA (38.5, min-max: 4-50) than in control subjects (22.5, min-max: 0-42) (p<0.001). There were significant correlations between MAF and DAS-28 scores (r=0.478, p=0.004), rest pain (r=0.491, p=0.001), ACR functional scale (r=0.563, p<0.001) and four dimensions of SF36; physical role (r=-0.504, p=0.014), bodily pain (r=-0.416, p=0.048), vitality (r=-0.522, p=0.011), emotional role (r=-0.523, p=0.011).

Conclusion: Fatigue symptom may be quite disabling for patients with rheumatoid arthritis. It is affected by disease activity and pain but not by disease duration and radiologic score. Therefore, it is concluded that fatigue is essentially related with disease activity rather than the chronic inflammatory process in RA.

(Turk J Rheumatol 2010; 25: 63-7)

Key words: Rheumatoid arthritis, disease activity, fatigue, quality of life, radiological involvement

Received: 26.08.2008 **Accepted:** 02.12.2008

Özet

Amaç: Romatoid artritli hastalarda yorgunluğu ve onun hastalık aktivitesi, radyolojik bulgular, yaşam kalitesi ile ilişkisini araştırmayı amaçladık.

Yöntem ve Gereçler: ACR kriterlerine göre 41 RA tanısı konmuş hasta ve 38 sağlıklı kontrol bu çalışmaya dahil edildi. Hastaların sabah tutukluğu süresi ve o anki ağrı (Görsel Analog Skala: VAS; 100 mm) derecesi kaydedildi. Yorgunluk, Multidimensional Assessment of Fatigue (MAF) skalası ile değerlendirildi. Hastalık aktivitesi ve yaşam kalitesi, sırasıyla Hastalık Aktivite Skalası-28 (DAS-28) ve Short Form-36 (SF-36) ile değerlendirildi. Radyolojik tutulum ise modifiye Larsen evrelemesine göre derecelendi.

Bulgular: Hasta ve kontrol grubunun ortalama±SS yaşları sırasıyla, 50.9 (13.4) yıl ve 50 (10.1) yıl idi. Her iki grup arasında anlamlı farklılık yoktu (p=0.744). Ortanca MAF toplam skoru RA'lı hastalarda (38.5, min-max: 4-50) kontrol grubuna oranla (22.5, min-max: 0-42) yüksek bulundu (p<0.001). MAF ile Disease Activity Scale (DAS-28) skoru (r=0.478, p=0.004), istirahat ağrısı (r=0.491, p=0.001), ACR fonksiyonel skala (r=0.494, p=0.001), fiziksel rol (r=-0.504, p=0.014), vücut ağrısı (r=-0.416, p=0.048), vitalite (r=-0.522, p=0.011) ve emosyonel rol (r=-0.523, p=0.011) gibi SF-36'nın dört alt grubu arasında anlamlı ilişki vardı.

Sonuç: Yorgunluk semptomu RA'te belirgin disabiliteye neden olabilmektedir. Hastalık aktivitesi ve ağrıdan etkilenirken hastalık süresi ve radyolojik skordan etkilenmemektedir. Bu semptomun RA'teki kronik enflamatuvar süreçten çok hastalık aktivitesi ile ilişkili olduğu düşünülmektedir.

(Turk J Rheumatol 2010; 25: 63-7)

Anahtar sözcükler: Romatoid artrit, hastalık aktivitesi, yorgunluk, yaşam kalitesi, radyolojik tutulum

Alındığı Tarih: 26.08.2008 **Kabul Tarihi:** 02.12.2008

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doi: 10.5152/tjr.2010.03

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease affecting primarily the joints and causing pain, deformity, joint destruction and disability (1). The impacts of RA include systemic features such as fatigue, weight loss and increased mortality (2).

Fatigue is a common and quite important symptom in patients with RA (3-6). It's prevalence in RA has been found to be 80-93% (5-8). Although it is so common, it is not investigated in the routine follow-up of RA patients (3-18). Excessive fatigue may lead to a reduction in both the quality and quantity of work output (9). No research has been found in the literature regarding the relationship of fatigue with quality of life and radiologic involvement in patients with rheumatoid arthritis.

The aim of this study was to determine the severity of fatigue in RA and its relationship with disease activity, quality of life, clinical, radiological and functional parameters.

Materials and Methods

Patients

Forty-one patients who were diagnosed as RA according to the criteria of American College of Rheumatology (ACR) (19) and 38 healthy subjects were included in this study. Patients with malignancy, fibromyalgia syndrome, other systemic inflammatory rheumatic diseases and psychiatric disorders were excluded.

Demographic data and treatment history were recorded in all cases. A 100 mm visual analogue scale (VAS) was used to determine the pain intensity at rest and during activity. Duration of morning stiffness (minute), presence of night pain and disease duration (month) were noted. Disease activity score (DAS) for 28-joint counts and its constituent components 28 tender joint count, 28 swollen joint count, patient's global assessment were recorded (20).

The Multidimensional Assessment of Fatigue (MAF) scale contains 16 items and measures five dimensions of fatigue: namely, severity, distress, impact on activities of daily living and timing. Each 100 mm VAS was changed to a 10-point numerical rating scale. Scores ranged from 0 (no fatigue) to 50 (severe fatigue) (5).

Radiographs of the hand and foot were assessed by the same physician (YT). 44 joints were evaluated: 10 metacarpophalangeal, 10 metatarsophalangeal, 18 proximal interphalangeal, 4 interphalangeal of the thumbs, 2 wrist and 2 ankle joints. Each joint was graded on a 0-5 point scale (0, normal condition; 1, slight abnormality; 2, definite abnormality; 3, marked abnormality; 4, severe abnormality; 5, mutilating abnormality) according to Larsen (21).

Laboratory investigation included erythrocyte sedimentation rate (ESR) (using the standard Westergren method), serum C-reactive protein (CRP) (using the nephelometer assay), total blood count and rheumatoid factor measurements.

Functional status of RA patients was evaluated according to the ACR functional classification. According to this stage 1: patient can function normally, stage 2: patient can work and perform his or her daily activities with minor limitations, stage 3: patient can take care of him or herself but has major limitations, stage 4: patient is totally dependent (19).

The Medical Outcomes Study Short Form 36 (SF-36) was used to assess health-related quality of life. The SF-36 is a widely applied generic instrument for measuring health status, and consists of 8 domains: physical functioning, social functioning, physical role, emotional role, mental health, vitality, bodily pain, and general health perception. Scores range from 0 (worst) to 100 (best) with higher scores indicating better health status (22, 23).

Statistical Analysis

Statistical analyses were performed by using the software Statistical Package Sciences (SPSS) for Windows version 11.0. For the discrepancies among the groups, Mann-Whitney U test and student's t test were used. Spearman's correlation coefficient was used to assess relationship between fatigue and clinical parameters. Significance level was 0.05.

Results

The mean age of patient and control groups were 50.9±13.4 years and 50±10.1 years, respectively. Two groups were similar with respect to age (p=0.744). The median MAF total score was higher in patients with RA (38.5, min-max: 4-50) than in control subjects (22.5, min-max: 0-42) (p<0.001). The demographic and clinical characteristics of patients and control subjects are shown in Table 1. Components of MAF (degree, severity, distress, impact and timing) are shown in Table 2.

There were significant correlations between MAF and DAS-28 scores (r=0.478, p=0.004), rest pain (r=0.491, p= 0.001) and ACR functional scale (r=0.494, p=0.001). There was a significant negative correlation between MAF and four dimensions of SF36; physical role (r= -0.504, p=0.014), bodily pain (r=-0.416, p=0.048), vitality (r=-0.522, p=0.011), and emotional role (r=-0.523, p=0.011). No significant relationship was found between MAF and disease duration, morning stiffness, Larsen score, ESR, CRP and hemoglobin levels (p>0.05) (Table 3).

Discussion

Fatigue, has been reported as an important symptom in RA and appears to be multifactorial and multidimensional (3-6). Currently, MAF is used to determine various characteristics of the fatigue symptom in RA patients.

Table 1. Comparison of demographic and clinical parameters between groups

	Patient Group (n= 41)	Control Group (n= 38)	p
Age [year]	50.9±13.4	50±10.1	0.744
Sex (F/M)	36/5	35/3	0.713**
BMI [kg/m^2]	28.5±4.2	27.3±4.5	0.222
MAF [median, min-max]	38.5 (4-50)	22.5 (0-42)	<0.001*
Disease duration [month]	124.9±101.3		
Morning stiffness [minute]	80.9±75.1		
Rest pain [VAS, median, min-max]	50 (0-100)		
DAS-28 [median, min-max]	6.1 (2.5-8.1)		
ACR-functional score [median, min-max]	2 (1-3)		
Radiographic evaluation			
Larsen hand	30.1±10.7		
Larsen foot	12.2±2.8		
Laboratory tests			
Hemoglobin (gm/dl)	12±1.5		
ESR (mm/h)	42.6±25.1		
CRP (ng/mL)	16.4±24.3		

* Mann-Whitney U test; **Fisher's Exact test; F: female, M: male; BMI: Body Mass Index; MAF: Multidimensional Assessment of Fatigue; DAS-28: Disease Activity Score; ACR: American College of Rheumatology; ESR: erythrocyte sedimentation rate; CRP: C reactive protein

Table 2. Scores of the multidimensional assessment of fatigue subgroups in both groups

Subgroups	Patient Group (n= 41)	Control Group (n= 38)	p
Degree (0-10)	7 (1-10)	5 (0-10)	0.006*
Severity (0-10)	7 (1-10)	5 (0-10)	0.001*
Distress (0-10)	7 (1-10)	5 (0-10)	0.001*
Impact on activities of daily living (0-10)	7 (1-10)	5 (0-9)	<0.001*
Timing (0-10)	7.5 (0-10)	5 (0-10)	0.003*

Values are median (range); *Mann-Whitney U Test

Since MAF is short and easy to complete, it can be used in clinical practice for multiple purposes including assessment of baseline reports of fatigue.

In our study, the mean MAF total score was higher in patients with RA than in control subjects. Additionally, sub scores of the MAF were higher in RA patients. Similarly, Belza et al (5) and Mancuso et al. (14) reported that fatigue scores were significantly higher in persons with RA compared to healthy controls.

We found that the total scores of MAF were significantly correlated with the DAS-28 scores which is in accordance with the results obtained by Pollard et al. (9). In contrast to these studies, Huyser et al. (11) did not find a correlation between fatigue and disease activity. A former study however, emphasized that lack of fatigue was a feature of clinical remission in RA (7).

Pain is a major problem experienced by patients with RA and affects mobility and quality of life (24). In concordance with the results of other studies, we demonstrated a significant correlation between fatigue and pain (5, 9, 10, 12-14). Pain is one of the most important symptoms that increase during the active phase of RA (25). We can conclude that increased pain in patients with higher disease activity is accompanied by a more severe fatigue.

A relationship was shown between the MAF and ACR functional scale scores in our study. Several authors have investigated functional status and fatigue and found a significant correlation between them (4,7,10). Studies investigating the relationship between fatigue and quality of life in RA have contradictory results (9,12). Vitality and mental health which are subgroups of SF 36 have been found significantly correlated with fatigue (9). Wolfe et al. (12), did not demonstrate a significant relationship between the MAF scores, vitality and physical function. However in our study, we found a correlation between MAF and four dimensions of SF36.

No significant relationship was found between the MAF scores, disease duration and Larsen scores. Belza et al. (8), have also reported that no significant correlation exists between the severity of fatigue and disease duration. In contrast to these, Riemsma et al. (13), have found a significant relationship between fatigue and disease

Table 3. Correlation between MAF and clinical parameters in patients with rheumatoid arthritis

	MAF r	p
Age (year)	0.087	0.600
BMI (kg/m^2)	0.068	0.758
Morning stiffness (min)	0.147	0.370
Disease duration (month)	0.023	0.889
DAS-28 score	0.478	0.004*
Rest pain (mm)	0.491	0.001*
ACR-functional score	0.494	0.001*
ESR (mm/h)	0.173	0.319
CRP level (mg/L)	0.044	0.804
Hemoglobin level	-0.203	0.235
Larsen Score	-0.049	0.825
SF-36 sub-groups		
Physical function	-0.324	0.131
Physical role	-0.504	0.014*
Bodily pain	-0.416	0.048*
General health	-0.351	0.101
Mental health	-0.189	0.387
Vitality	-0.522	0.011*
Emotional role	-0.523	0.011*

*Spearman's correlation coefficient; BMI: Body Mass Index; MAF: Multidimensional Assessment of Fatigue; DAS-28: Disease Activity Score; ACR: American College of Rheumatology; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; SF-36: Short Form-36

duration. No research has been conducted so far that aims to investigate the relationship of radiologic involvement with fatigue. Radiological findings become more prominent as the disease acquires chronicity (26). Since we did not find any correlation between fatigue and disease duration, it may not be surprising to determine the lack of relationship between the radiologic involvement and fatigue.

In our study, laboratory measurements like ESR, CRP and hemoglobin levels were found to be not related to fatigue. Riemsma et al. (13), found similar results for ESR and hemoglobin levels. Belza et al. (5), have reported that fatigue and CRP are not related. Both CRP and ESR are nonspecific markers of inflammation that correlate with disease activity (27), as well as being sensitive measures of change in response to treatment in clinical trials (28).

Morning stiffness is caused by edema of the synovium and periarticular tissues in inflammatory conditions. It is most pronounced after sleep, due to redistribution of interstitial fluid during sleep (29). There were no correlation between MAF total scores and morning stiffness in our study. In accordance with this finding, Pollard et al. (9), reported no relationship between fatigue and morning stiffness.

In conclusion, fatigue as a major symptom in RA patients, needs to be measured properly with respect to its intensity by appropriate measures, such as MAF. The MAF provides more insight into specific dimensions of fatigue. Fatigue becomes more prominent as disease activity increases which seems to be independent of the disease duration. Quality of life is affected negatively by fatigue in patients with rheumatoid arthritis.

Conflict of Interest

No conflict of interest is declared by authors.

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