

## Presence of Fibromyalgia in Patients with Takayasu's Arteritis

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### Abstract

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**Objective** Data regarding the frequency of fibromyalgia (FM) in patients with Takayasu's arteritis (TAK) have not been previously reported. We aimed to investigate the frequency of FM in TAK, defined according to the new 2010 ACR Preliminary Diagnostic Criteria for Fibromyalgia. The association between the ACR-1990 and 2010 FM criteria and the effects of patient-reported outcomes (PROs) on FM were also analyzed.

**Methods** We studied 55 patients (age: 42,30±12,37 years, F/M: 49/6) with TAK and 40 age- and sex-matched controls (age: 41±10.84 years, F/M: 31/9). All patients were examined for FM tender points by two observers and asked to complete the ACR 2010 FM questionnaire for FM. The SF-36, the Health Assessment Questionnaire (HAQ) and hospital anxiety and depression scales (HADS) were used to assess the quality of life. Thirty patients were reevaluated six months later.

**Results** Seven (12.7%) patients with TAK and four patients with HC (10%) fulfilled the 2010 FM criteria ( $p=0.682$ ), while three (5.4%) TAK patients and no controls (0%) met the 1990 criteria ( $p=0.133$ ). FM was found at a significantly higher rate in the active patients than in the inactive patients according to the ACR-2010 FM criteria ( $p=0.006$ ). The SF-36 physical component scores were significantly lower ( $p=0.003$ ) and the HAQ scores were significantly higher in the TAK ( $p=0.006$ ) patients than in the controls.

**Conclusion** The frequency of FM is similar between the general population and patients with TAK. However, the incidence of FM is significantly higher in active patients. The new FM criteria subscales (WPI, SSS) are significantly correlated with scales such as the SF-36, anxiety and depression scales and HAQ in TAK patients, suggesting that, in a minority of patients with FM and TAK, PROs may be affected by the presence of FM.

**Key words:** Takayasu arteritis, fibromyalgia, ACR FM criteria, disease activity

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### Introduction

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Takayasu's arteritis (TAK) is a rare, chronic, large-vessel vasculitis that predominately affects the aorta, its major branches and the pulmonary arteries (1). Various signs and symptoms, such as constitutional features (fever, malaise, anorexia and weight loss), extremity pain, claudication, light-headedness, bruits, absent or diminished pulses and loss of blood pressure, may be present according to the degree of vessel involvement and the level of inflamma-

tion (1, 2).

Fibromyalgia (FM) is a frequently observed form of non-articular rheumatism associated with chronic generalized musculoskeletal pain, fatigue and sleep disturbances that affect the patient's quality of life. Although FM is observed in approximately 3-4% of the general population, patients with inflammatory diseases have a much higher frequency of the condition [17-60% (3)]. To our knowledge, no data have been reported regarding the frequency of FM in TAK patients, and, contrary to that observed in other inflammatory disorders, in our anecdotal experience, the incidence of FM

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**Table 1. The Presence of Fibromyalgia according to the Clinical Activity**

Presence of Fibromyalgia	Clinical Activity		Healthy Controls	p value*
	Active	Inactive		
ACR-2010 FM Criteria (%)	28.5(n:6)	2.9(n:1)	10(n:4)	0.006
1990 FM Criteria (%)	4.7(n:1)	5.8(n:2)	0	0.86

\* p value for comparison between active and inactive patients regarding fibromyalgia

therefore does not appear to increase in patients with TAK.

In this study, we aimed to investigate the frequency of FM in patients with TAK, defined according to the new 2010 ACR Preliminary Diagnostic Criteria for Fibromyalgia. The correlation between the ACR-1990 and 2010 FM criteria and the effects of patient-reported outcomes (PROs), such as the Health Assessment Questionnaire (HAQ), Short-Form 36-item survey (SF-36) and hospital anxiety and depression scales (HADS), on FM were also analyzed.

## Materials and Methods

This study included 55 patients (age: 42,30±12,37 years, F/M: 49/6) with TAK and 40 age- and sex-matched control subjects (age: 41±10.84 years, F/M: 31/9). All patients with TAK fulfilled the criteria of the American College of Rheumatology [ACR (4)]. According to the angiographic classification, 43.6% of the study group patients had type I disease, 50.9% had type V disease, 1.8% had type IV disease and 3.6% had type IIb disease. Fifty patients (90.9%) were receiving oral methylprednisolone therapy. As additional immunosuppression, 33 (60%) patients were receiving azathioprine, 18 (32.7%) patients were receiving methotrexate, three (5.4%) patients were receiving leflunomide and one (1.8%) patient was receiving infliximab therapy. The TAK patients were evaluated using the physician's global assessment (PGA: active/inactive) in terms of clinical activity. All patients were examined for FM tender points by two observers (kappa: 0.648) and asked to complete the new ACR 2010 FM questionnaire for FM (5).

The QoL was evaluated using a validated Turkish translation of the SF-36 (6). The physical and mental component summary scores (PCS, MCS) were calculated based on eight separate subscales of the SF-36 (7). The scores varied from 0 to 100, with higher scores indicating a better quality of life.

There is no validated tool for the functional assessment of large vessel vasculitides (8). We used the health assessment questionnaire, which was primarily developed to evaluate rheumatoid arthritis but is recommended for use in patients with other rheumatic disorders (9). The hospital anxiety and depression scale was used to assess the mental status, (HADS-A, HADS-D) with scores of 8-10 indicating possible, scores of 11-14 indicating probable and scores of 15-21 indicating extreme cases of depression and anxiety. The presence of anxiety and depression was accepted over a score of 8 (10). Thirty patients were reevaluated six months

later. The study was performed according to the Declaration of Helsinki, and all subjects provided their informed consent before participation.

The statistical analyses were performed using the Statistical Package for the Social Sciences 17.0 (SPSS, Chicago, IL, USA) software program. The results were expressed as the mean and standard deviation or median (minimum-maximum) according to the distribution of the data. The independent-samples t-test and chi-square test were used to compare the data. The Spearman correlation test was used to analyze the correlations.

## Results

The mean disease duration was 4.68 (0.1-26) years, the mean ESR (mm/h) was 28.07 (2-91) and the mean CRP level (mg/L) was 8.17 (0-56) in the study group. Seven (12.7%) patients with TAK and four (10%) patients with HC met the ACR-2010 FM criteria, while only three (5.4%) TAK patients and no controls (0%) met the 1990 criteria. No significant differences regarding the frequency of FM were observed according to either the ACR-2010 (p=0.682) or 1990 FM (p=0.133) criteria between the TAK and HC patients. No differences were observed with respect to the two subscales of the 2010 criteria, the Widespread Pain Index (WPI) or the Symptom Severity Scale (SSS) scale between the groups (Table 1).

Twenty-one patients (38.1%) were clinically active. FM was observed significantly more frequently in the active patients (6/21 (28.5%) vs. 1/34 (2.9%)) than in the inactive patients (p=0.006). Although there was also a difference between the active TAK patients and the HC patients, it did not reach a significant level (p=0.063). However, the incidence of FM was similar between the active and inactive patients according to the 1990 criteria (1/21 (4.7%) vs. 2/34 (5.8%) (p=0.86)) (Table 1).

The SF-36 physical component scores (PCSs) were significantly lower (p=0.003) and the HAQ scores were significantly higher in the patients with TAK (p=0.006) than in the patients with HC (Table 2). Comparing the patients with and without FM, all items of the SF-36 were significantly lower in the patients with FM. No differences were observed in the HADS-A, HADS-D or SF-36 Mental Component Score (MCS) between the TAK patients and the controls (Table 2). The rates of anxiety and depression were similar between the patients with TAK and the controls (anxiety: 23.6% vs. 25%, depression: 29% vs. 15%, respectively). However, the

**Table 2. Results of the Patient-reported Outcomes in the TAK Patients and Controls**

	Takayasu's arteritis (n=55)	Healthy controls (n=40)	p values
Symptom Severity Scale	4.2 (0-13)	4.05 (0-8)	0.978
Widespread Pain Index	2.96 (0-16)	2.67 (0-15)	0.957
HADS-A	6.44±5.15	5.95±4.39	0.631
HADS-D	5.09±5	3.80±3.33	0.168
HAQ	0.36 (0-2.35)	0.13 (0-0.8)	<b>0.006</b>
PCS	42.76±11.88	49.4±8.46	<b>0.003</b>
MCS	45.21±11.22	46.7±10.63	0.513

HADS: Hospital anxiety and depression scale- Anxiety and Depression, HAQ: Health Assessment Questionnaire  
PCS:Physical Component Score , MCS:Mental Component Score

presence of FM was significantly correlated with the presence of anxiety ( $r=0.333$ ,  $p=0.001$ ) and depression ( $r=0.347$ ,  $p=0.001$ ).

The SSS was significantly correlated with the HAQ ( $r=0.394$ ,  $p=0.001$ ), HADS-A ( $r=0.573$ ,  $p=0.001$ ), HADS-D ( $r=0.479$ ,  $p=0.001$ ), PCS ( $r=-0.557$ ,  $p=0.001$ ) and MCS ( $r=-0.536$ ,  $p=0.001$ ). The WPI was significantly correlated with the HAQ ( $r=0.674$ ,  $p=0.001$ ), HADS-A ( $r=0.538$ ,  $p=0.001$ ), HADS-D ( $r=0.541$ ,  $p=0.001$ ), PCS ( $r=-0.634$ ,  $p=0.001$ ) and MCS ( $r=-0.358$ ,  $p=0.001$ ).

Six (20%) patients with TAK met the ACR-2010 FM criteria, whereas none of TAK patients met the 1990 FM criteria at the six-month assessment. During the follow-up period, no significant differences between the baseline and six month values were observed in the HAQ, anxiety and depression scale, PCS or MCS scores.

## Discussion

We herein reported the first study to investigate the incidence of fibromyalgia in patients with TAK. In this study, we observed that the presence of fibromyalgia was not increased in the patients with TAK compared to that observed in the healthy controls. No differences were observed in the two subscales of the 2010 criteria or the WPI and SSS scales between the groups. However, the WPI and SSS were significantly correlated with the QoL instruments, such as the HADS, HAQ and Physical and Mental components of the SF-36. These results suggest that, as the new ACR-2010 FM criteria are based on the patient's report instead of the physician's assessment, they are associated with other QoL instruments.

Among other inflammatory rheumatological disorders, FM is present in 23.6% of patients with granulomatosis with polyangiitis [GPA (11)], 13-17% of patients with rheumatoid arthritis (12, 13) and 8.2-67% of patients with systemic lupus erythematosus [SLE (14)] when investigated using the 1990 FM criteria. The presence of fibromyalgia is not corre-

lated with the clinical activity of GPA (10) or SLE (13). However, an association with a higher disease activity score-28 is observed in patients with RA (11, 15). Similarly, we found a higher incidence of FM in the active TAK patients in our study. This finding may reflect the fact that ongoing inflammatory processes contribute to the development of FM in a subset of TAK patients.

Impaired SF-36 scores in TAK patients have been previously demonstrated in two studies (16, 17). In another study of our group, we observed that all items of the SF-36 were impaired in the patients with TAK, with lower scores in the active patients (18). We also observed significantly lower physical component SF-36 scores and all SF-36 subscales in the TAK patients in this study. The FM subscales were significantly correlated with the physical and mental components of the SF-36.

Higher levels of depression and anxiety have also been previously reported in patients with primary systemic vasculitis (10, 19). In a previous study, the HADS-A scale was found to be significantly higher in TAK patients, whereas the HADS-D scale was similar to that observed in the controls (18). Anxiety and depression are closely related with FM, with the prevalence of depression ranging between 20% and 80% and the prevalence of anxiety ranging between 13% and 71% (20, 21). In our study, the presence of FM was also significantly correlated with anxiety and depression.

Currently, there is no specific measurement of the functional ability in patients with primary systemic vasculitides (SV). The HAQ has been previously used for this purpose and observed to be impaired in patients with primary SV (19). Yılmaz et al. also found significantly higher HAQ scores in patients with TAK (18), similar to our results.

A major limitation of our study is the small sample size. However, with the exception of the subset of patients with active disease, no associations with FM were observed, and a larger sample size would possibly not have changed our results. In addition, our follow-up was limited to six months,

and the associations of FM with the disease activity and PROs may be better elucidated with a longer follow-up.

In conclusion, the frequency of FM is similar between the general population and patients with TAK. However, the presence of FM is associated with the disease activity. Although other PROs did not differ from those observed in the patients with HC (except the PCS of the SF-36 and HAQ), the new FM criteria subscales of the WPI and SSS were significantly correlated with scales such as the SF-36, anxiety and depression scale and HAQ in the TAK patients, thereby suggesting that, in a minority of patients with FM and TAK, PROs may be affected by the presence of FM.

**The authors state that they have no Conflict of Interest (COI).**

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