



Does Carpal Tunnel Syndrome Affect Disease Activity in Patients with Fibromyalgia?

Karpal Tünel Sendromu Fibromiyaljili Hastalarda Hastalık Aktivitesini ve Yaşam Kalitesini Etkiler mi?

Ali Can Karakuyu¹, Damla Cankurtaran², Şükran Güzel², Ebru Umay²

¹Söke State Hospital, Physical Medicine and Rehabilitation Clinic, Aydın, Turkey

²University of Health Sciences, Ankara Diskapi Yıldırım Beyazıt Education and Research Hospital, Physical Medicine and Rehabilitation Clinic, Ankara, Turkey

ABSTRACT

Aim: A high prevalence of carpal tunnel syndrome (CTS) in patients with fibromyalgia has been reported and this seems to affect patients' quality of life. This study aimed to investigate whether there is any relationship between disease activity and quality of life (QoL) in fibromyalgia patients with CTS and electrophysiological and ultrasonographic measurement values.

Material and Method: The cross-sectional study included 102 fibromyalgia patients with CTS symptoms and 102 healthy control subjects. Tender Points Count, Pain Location Inventory, and Symptom Impact Questionnaire were recorded for the FM group. Overall disease impact was assessed with the Fibromyalgia Impact Questionnaire and quality of life with the Nottingham Health Profile. The median nerves of all participants were evaluated electrophysiologically and ultrasonographically. The electrophysiological and ultrasonographic measurements were compared between the groups, then the electrophysiological and ultrasonographic measurements of the fibromyalgia patients were compared with disease activity and QoL.

Results: Compared to the control group and the fibromyalgia group with no CTS determined electrophysiologically, the distal median nerve was found to be enlarged in the fibromyalgia group on ultrasonography ($p=0.001$). The distal median nerve area was determined as a factor with an effect on QoL and disease severity ($p=0.037$, $p=0.041$).

Conclusion: Fibromyalgia patients with CTS symptoms but electrophysiologically normal results can be evaluated with US. CTS severity affects quality of life and disease severity in fibromyalgia. These results, which have been previously shown electrophysiologically, are now supported by US. Further studies are required to confirm these results.

Keywords: Fibromyalgia, quality of life, carpal tunnel syndrome, electrophysiology, ultrasonography

ÖZ

Amaç: Fibromiyalji ve karpal tünel sendromu birlikteliği sık görülmektedir ve bu durumun hastaların yaşam kalitesini etkilediği düşünülmektedir. Bu çalışmada, karpal tünel sendromu olan fibromiyalji tanılı hastalarda elektrofizyolojik ve ultrasonografik ölçüm değerleri ile hastalık aktivitesi ve yaşam kalitesi arasındaki ilişkinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya karpal tünel sendromu semptomları olan 102 fibromiyalji hastası ve 102 sağlıklı kontrol katıldı. Fibromiyalji grubu için hassas nokta sayımı, ağrı yeri envanteri ve semptom etki anketi kaydedildi. Hastalık aktivitesi Fibromiyalji Etki Anketi ile, yaşam kalitesi ise Nottingham Sağlık Profili ile değerlendirildi. Tüm katılımcıların median sinirleri elektrofizyolojik ve ultrasonografik olarak değerlendirildi. Gruplar arasında elektrofizyolojik ve ultrasonografik ölçümler karşılaştırıldı, ardından fibromiyalji hastalarının elektrofizyolojik ve ultrasonografik ölçümleri hastalık aktivitesi ve yaşam kalitesi ile karşılaştırıldı.

Bulgular: Elektrofizyolojik olarak karpal tünel sendromu saptanmayan fibromiyalji grubu ve kontrol grubu hastaları karşılaştırıldığında, ultrasonografide fibromiyalji grubunda distal median sinir alanının genişlemiş olduğu görüldü ($p=0.001$). Ayrıca distal median sinir alanı, yaşam kalitesi ve hastalık şiddetini etkileyen bir faktör olarak belirlendi ($p=0.037$, $p=0.041$).

Sonuç: Karpal tünel sendromu semptomları olan ancak elektrofizyolojik bulguları normal olan fibromiyalji hastaları ultrasonografi ile değerlendirilebilir. Karpal tünel sendromu şiddeti, fibromiyaljide yaşam kalitesini ve hastalık şiddetini etkilemektedir. Daha önce elektrofizyolojik olarak gösterilen sonuçlar ultrason bulguları ile desteklenebilir. Bu sonuçları doğrulamak için daha fazla çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: Fibromiyalji, yaşam kalitesi, karpal tünel sendromu, elektrofizyoloji, ultrasonografi

Corresponding Author: Şükran Güzel

Address: University of Health Sciences, Ankara Diskapi Yıldırım Beyazıt Education and Research Hospital, Physical Medicine and Rehabilitation Clinic, Ankara, TURKEY

E-mail: sukranguzel@windowslive.com

Başvuru Tarihi/Received: 31.10.2022

Kabul Tarihi/Accepted: 15.11.2022





INTRODUCTION

Fibromyalgia (FM) is a rheumatic disease of the soft tissues, the etiology of which is not exactly known. It is characterized by widespread musculoskeletal pain and tender points, sleep disturbance, morning stiffness, fatigue, irritable bowel syndrome, complaints of paresthesia, pain and a subjective sense of swelling in the hands, as well as frequent psychological distress (1). Paresthesia and sensory alterations are seen in 80% of patients diagnosed with FM (2). Although the mechanism of this symptom in FM is not exactly known, paresthesia is thought to be a result of abnormal sensory perception occurring due to central sensitization (3).

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy and has been reported to affect one in ten people (4). It is caused by compression of the median nerve inside the carpal tunnel in the wrist region as it passes through the carpal tunnel leading to changes in the endoneurial blood flow, oedema formation, and ultimately ischemia and nerve injury (5). CTS is generally characterised by sensory abnormalities including neuropathic pain symptoms such as paresthesia and dysesthesia, numbness, tingling and hyperalgesia (6).

Electrodiagnostic testing is currently considered the gold standard for confirmation of a clinical diagnosis of CTS, but nerve conduction studies (NCS) remain normal in 15% of patients with characteristic clinical features of CTS (7).

Ultrasonography (US) has been shown to be a useful diagnostic tool in CTS (8), with reports in literature showing that the median nerve cross-sectional area (CSA) in the wrist is strongly associated with clinical and electrophysiological severity (9).

There are some studies on the co-existence of these two diseases, which have similar symptoms and affect the same age and gender group, but these studies have only evaluated CTS electrophysiologically (10,11).

The first aim of this study was the evaluation of the median nerve with electrophysiological and ultrasonographic measurement methods in patients with FM with complaints of paresthesia and weakness in the hands and investigate the relationship between these measurement results and disease activity and quality of life. The other aim of this study was to compare electrophysiological and ultrasonographic measurements in FM patients with no CTS and in control group with no CTS.

MATERIAL AND METHOD

Participants

The cross-sectional study included 102 patients attending our outpatient clinic with complaints of

CTS such as paresthesia and weakness in the hands between 2019 and 2020, who were diagnosed with FM according to the American College of Rheumatology (ACR) 2013 diagnostic criteria (12), and 102 age- and gender, body mass index (BMI), and education status-matched healthy control subjects with convenience sampling method.

The voluntary participants in the control group were selected from staff and the relatives and/or caregivers of the patients without any musculoskeletal symptoms or signs. Patients <18 years and >65 years of age and with a history of inflammatory, autoimmune, endocrine, severe renal disease, central nervous system disease were excluded from the study. Patients with a history of trauma, surgery, ganglion cyst, tenosynovitis, tendinitis, peripheral nerve damage or radiculopathy and patients treated with drugs for FM and vitamin deficiency were also excluded. Pregnant and nursing women were not included in the study.

The study protocol was approved by the Local Ethics Committee (Date: 07.01.2019 No:58/23) and all procedures were performed in compliance with the Helsinki Declaration. The protocol was explained to all the study participants, and informed consent was obtained at the beginning of the study.

Demographic characteristics

Age, gender, dominant hand, BMI and education status of both the FM group and the control group were recorded. Education status was classified in 5 groups as illiterate, literate, 5 years education, 8 years education, 11 years education, and more than 11 years education.

Clinical parameters

Symptomatic hand, comorbid diseases, duration of disease, Tender Points Count (TPC), Pain Location Inventory (PLI), and Symptom Impact Questionnaire (SIQR) were recorded for the FM group. Overall disease impact was assessed with the Fibromyalgia Impact Questionnaire (FIQ) and quality of life with the Nottingham Health Profile (NHP).

TPC (tender point count) was determined by applying pressure of <4 kg to 18 symmetrical points on both sides of the body. If the participants felt pain, the tender point was considered positive. The total number of tender points was recorded as the TPC score. The maximum score of TPC was 18 (13).

The PLI score was recorded as the number of the pain locations of 28 points (jaw, neck, mid-upper back, front of chest, mid lower back, upper back, lower back, shoulders, arms, hands, wrists, hips, thighs, knees, ankles, feet) over the past 7 days (0-28) (12).

SIQR evaluates the intensity of 10 common symptoms (pain, energy, stiffness, sleep, depression, memory, anxiety, tenderness, balance, sensitivity to loud noises,

bright lights, odors and cold) over the last 7 days. Each symptom is scored between 0-10, and the total score range is 0-100) (13).

FIQ is a self-reported questionnaire which assesses the impact of FM symptoms on the physical and mental health of patients. Physical impairment, number of days feeling good, work missed, ability to do work, pain, fatigue, rest, stiffness, anxiety, and depressive symptoms are measured with the FIQ. Each subscale has a maximum score of 10, and these are added to give the total score, with higher scores indicating a negative impact (0-100) (14).

NHP was used to evaluate the quality of life in patients. NHP is a patient-reported scale, comprising 38 items and 6 subscales: physical mobility (8 questions), pain (8 questions), sleep (5 questions), emotional reactions (9 questions) social isolation (5 questions), and energy level (3 questions). It measures the distress of patients in physical, emotional, and social domains (15).

Electrophysiological evaluation

Both the FM group and control group underwent motor and sensory NCS of the median and ulnar nerves, using Medelec Synergy 10 channel ENMG (Oxford, U.K.) equipment applied by the same observer. The NCS were performed using the technique described by Oh S (16). The upper extremities were placed in a relaxed and comfortable position with the arm extended, palm up. Sensory nerve action potential (SNAP), sensory nerve velocity (Vsens), common nerve action potential (CMAP), distal motor latency (DML), and motor nerve velocity (Vmotor) were measured using supramaximal stimulation and surface electrode adjustment for skin temperature. CTS was diagnosed electrophysiologically if the median sensory velocity recorded from digit 2 was <41.25 m/s, common nerve velocity recorded from the palm was <34 m/s or the median DML measured from the beginning of the stimulus artifact to the onset of the action potential by stimulating the median nerve at the wrist (5 cm proximal to the active recording electrode placed on the abductor pollicis brevis muscle) was >3.6 ms. The severity of CTS was evaluated in three groups as mild, moderate, or severe. Mild CTS was defined as decreased sensory nerve velocity (with or without SNAP below the lower standard limit, no conduction block or mild conduction block, and no thenar electromyography (EMG) abnormalities (if tested). Moderate CTS was defined as abnormal median sensory velocity as above and (relative or absolute) prolongation of the DML, conduction block may be present, and minor thenar EMG abnormalities may be present; Severe CTS was defined as decreased median CMAP and sensory nerve velocity, with either an absent SNAP or mixed NAP, or a low-amplitude or absent thenar CMAP, conduction block may be present, and thenar EMG abnormalities are often present (17).

Ultrasound evaluation

All ultrasound evaluations were performed by the same experienced observer using a high resolution 12 MHz linear probe (GE Logiq P5, General Electric Korea). After all participants were positioned with the arm in extension, forearm in supination and wrist in a supine neutral position, CSA was measured at two different levels using a continuous tracing method along the inner border of the epineurium (18). Proximal CSA of the median nerve was measured at the radiocarpal joint, and the distal CSA of the median nerve was measured at the level of the proximal carpal bones.

Comparisons

Electrophysiological and ultrasonographic evaluations of both extremities were applied to all the subjects in both the FM and control groups by the same physician on the same day. In the FM group, the electrophysiological, and ultrasound results were compared with clinical parameters, disease severity and quality of life.

Statistical analysis

The power of the study was calculated using the G Power 3.1.8 analysis method. The minimum number of participants required for a 15% change in the fibromyalgia impact questionnaire was 98 for each group. (at 80% power level, statistical significance $p < 0.05$). The study was planned with a minimum of 196 participants, 98 patients in each group.

Data obtained in the study were analyzed statistically with SPSS vn.25.0 software. Descriptive statistics were presented as mean \pm standard deviation for continuous variables and percentages (%) for nominal variables. The Kolmogorov-Smirnov test was used to assess the conformity of data to normal distribution. In the comparisons between the groups, mean values were compared with the Independent simple t-test for continuous variables. Fisher's Exact test was used to compare categorical values between groups. Correlations between electrophysiological and ultrasound evaluations and clinical parameters were analyzed with the Pearson's correlation test. Then a simple linear regression analysis was applied for statistical significance. (Dependent variable: median nerve distal CSA) (Independent variable; sleep subscale and total scores of SIQR, FIQ, energy, sleep subscales and total score of NHP). Accordingly, the regression equation model was created as $y = mx + b$ ($m = \text{slope}$, $b = \text{intercept}$). m and b values were calculated with the Least squares estimation (19). Values of $p < 0.05$ were considered statistically significant.

RESULTS

The demographic characteristics of the FM and control groups are presented in **Table 1**. All participants in both



the FM (n=102) and control groups (n=102) were female. The mean age of the FM group was 44.50±8.31 years and the mean age of the control group was 46.10±5.65 years. There was no significant difference between the two groups in respect of gender, age, dominant hand, education status and BMI (p>0.05).

Table 1. Comparison of demographic characteristics of FM and control group

Demographic Parameters	FM Group n=102	Control Group n=102	P
Age (years)mean±SD	44.50±8.31	46.10±5.65	0.07**
Dominant hand n (%)			0.74*
Right	97 (95.1)	99 (%97.1)	
Left	5 (4.9)	3 (2.9)	
Education status n (%)			0.22*
Not illiterate	0	3 (2.9)	
Literate	4 (3.9)	8 (7.8)	
5 years education	68 (66.7)	63 (61.8)	
8 years education	10 (9.8)	18 (17.6)	
11 years education	13(12.7)	7 (6.8)	
Over 11years education	7 (6.9)	3 (2.9)	
BMI (kg/cm2)mean±SD	29.11±7.34	27.58±4.61	0.07**

SD:Standard deviation, BMI:body mass index, FM: Fibromyalgia * = Fisher's Exact test, **=Independent simple T test,

The clinical parameters and quality of life scores of the FM group are shown in **Table 2**. In the FM group, all participants complained of paresthesia and weakness in both the right and left hands. Electrophysiological examinations were performed on 204 hands of 102 FM patients and 204 hands of the control group. Normal electrophysiological studies were detected in 93 (45.6%) hands in the FM group. Mild CTS was determined in 77 (37.7%) hands and moderate CTS in 34 (16.7%) hands in the FM group. There was no patient with severe CTS in the FM group according to the electrophysiological studies. Although there were no complaints of paresthesia and weakness in the control group, CTS was detected in 3 hands in the control group. Therefore, the study continued with 201 hands in the control group.

The comparisons of the electrophysiological and ultrasound evaluation results between the groups are shown in **Table 3**. The values of median SNAP, median Vsens, median DML, proximal CSA median, distal CSA median were determined to be significantly different between the two groups (p=0.012, p=0.018, p=0.015, p=0.001, p=0.001, respectively).

The clinical parameters and quality of life showed no significant difference between those without CTS, or with mild CTS and moderate CTS in the FM group (p>0.05) (**Table 4**).

Compared to the healthy control group and FM patients with CTS symptoms but electrophysiologically normal results, the distal CSA on USG was found to be wider in the FM group (p=0.001) (**Table 4**).

Table 2. Disease characteristics in FM group

Parameters	FM Group n=102 mean±SD
Disease duration (years)	2.19 ±1.65
Tender Point Count (0-18)	14.79 ±3.45
Pain location inventory	24.99±5.69
Symptom Impacy Questionare (0-10 cm)	
Pain	6.95 ±1.72
Energy	6.39 ±2.07
Stiffness	5.45 ±2.48
Sleep	6.03 ±3.16
Depression	4.80 ±2.96
Memory	5.42 ±2.84
Anxiety	5.38 ±3.19
Tenderness	5.06 ±3.17
Balance	3.35 ±2.94
Enviromental sensivity	6.23±2.69
Total score	28.83 ±12.05
Fibromiyalgia Impact Questionare	59.27 ±15.90
Nottingham Health Profile	
Pain	72.66 ±27.01
Energy	81.10 ±21.15
Sleep	40.69 ±35.36
Physical mobility	34.45 ±19.33
Emotionalreaction	50.16 ±26.83
Social isolation	29.99 ±32.45
Total score	51.33 ±16.07

SD:Standard deviation, FM: Fibromyalgia

Table 3. Comparison of electrophysiologic and ultrasound measurement values between FM and control group

Parameters	FM Group n=204 mean±SD	Control Group n=201 mean±SD	P*
Median SNAP (µV)	44.81±15.51	47.15±11.67	0.012
Median Vsens (m/s)	39.86±5.05	44.27±6.11	0.018
Median CMAP (mV)	10.77±2.84	12.24±2.64	0.012
Median DML (ms)	3.01±0.75	2.55±1.02	0.015
Median Vmotor (m/s)	59.83±6.04	58.68±7.12	0.093
Proximal CSA median (cm2)	0.25±0.26	0.10±0.03	0.001
Distal CSA median (cm2)	0.23±0.27	0.09±0.06	0.001

SD: Standard deviation, µV=mikrovolt, mV=milivolt, cm2:square centimeter, m/s: meter/second, ms: millisecond FM: fibromiyalgi, SNAP: sensory nerve action potential, Vsens: sensorial nerve conduction velocity, CMAP: compound nerve action potential, DML:distal motor latency, Vmotor: motor nerve conduction velocity, CSA: cross section area, p*: Paired simple T test, Bold p values are statistical difference

Table 4: Comparisons between control and FM group with normal electrophysiology (No CTS)

Parameters	FM group (No CTS) n=93 hands mean±SD	Control Group n=201 hands mean±SD	p
Median SNAP(µV)	46.50±12.54	47.15±11.67	0.822*
Median Vsens(m/s)	43.07±6.17	44.27±6.11	0.561*
Median CMAP (mV)	11.60±2.36	12.24±2.64	0.128*
Median DML (ms)	2.64±0.42	2.55±1.02	0.643*
Median Vmotor(m/s)	58.71±4.60	58.68±7.12	0.939*
Proximal CSA median (cm2)	0.11±0.01	0.10±0.03	0.548*
Distal CSA median (cm2)	0.15±0.08	0.09±0.06	0.013*

SD: standard deviation, µV= mikrovolt, mV= milivolt, cm2:square centimeter, m/s: meter/second, ms: millisecond FM:fibromiyalgia, CTS:carpal tunnel syndrome, SNAP: sensory nerve action potential, Vsens: sensorial nerve conduction velocity, CMAP: compound nerve action potential,DML:distal motor latency Vmotor: motor nerve conduction velocity, CSA: cross section area, p*: Paired simple T test, Bold p values are statistical difference

Correlations of the electrophysiological and ultrasound findings with clinical parameters and quality of life in the FM group are shown in **Table 5**. There were no significant correlation between disease characteristics and, electrophysiologic severity and proximal CSA in FM group ($p>0.05$). Positive moderate correlation was detected between distal CSA and sleep subscale and total scores of SIQR, FIQ, energy, sleep subscales and total score of NHP ($p<0.05$).

Table 5: Correlation of electrophysiologic and ultrasound values with disease evaluation parameters in FM Group

Parameters	Electrophysiologic severity		Proximal CSA		Distal CSA	
	r	P*	r	P*	r	P*
Disease duration (years)	0.102	0.697	0.361	0.339	0.190	0.555
Tender Point Count (0-18)	0.136	0.377	0.244	0.527	0.424	0.215
Pain location inventory	0.227	0.381	0.277	0.471	0.239	0.352
FIQ	0.231	0.889	0.488	0.220	0.515	0.045
Nottingham Health Profile						
Pain	0.088	0.745	0.335	0.417	0.369	0.176
Energy	0.031	0.910	0.494	0.214	0.513	0.041
Sleep	0.266	0.320	0.272	0.328	0.692	0.047
Physical mobility	0.470	0.066	0.511	0.195	0.147	0.600
Emotional reaction	0.031	0.910	0.494	0.214	0.204	0.466
Social isolation	0.055	0.839	0.825	0.094	0.429	0.110
Total score	0.070	0.795	0.633	0.049	0.154	0.044
SIQ (0-10 cm)						
Pain	0.112	0.668	0.293	0.445	0.369	0.159
Energy	0.458	0.064	0.146	0.708	0.128	0.636
Stiffness	0.165	0.526	0.322	0.399	0.387	0.138
Sleep	0.124	0.636	0.074	0.785	0.658	0.048
Depression	0.361	0.236	0.191	0.622	0.162	0.550
Memory	0.090	0.730	0.169	0.664	0.230	0.391
Anxiety	0.057	0.828	0.166	0.669	0.109	0.688
Tenderness	0.406	0.106	0.400	0.287	0.390	0.136
Balance	0.254	0.326	0.390	0.327	0.400	0.125
Environmental sensitivity	0.059	0.823	0.271	0.480	0.124	0.647
Total score	0.637	0.124	0.399	0.287	0.442	0.046

FM: Fibromyalgia, FIQ: Fibromyalgia Impact Questionnaire, SIQ: Symptom Impacy Questionnaire; r: correlation coefficient, *: Pearson's correlation test

According to the regression analyses, an increase in the SIQR total score and high disease severity were factors effective on increasing distal CSA ($p=0.037$, $p=0.041$). (**Table 6**)

Table 6: Simple Linear Regression Analysis between Median Nerve distal CSA and sleep

	R2	B	SE	95%CI (lower-upper) for B	p
Sleep (SIQR)	0.186	1.714	0.569	0.584-2.843	0.037
Total SIQR score	0.067	0.860	0.367	0.072-1.647	0.058
FIQ	0.189	2.561	0.836	0.901-4.220	0.041
Energy (NHP)	0.263	0.923	0.337	0.506-1.461	0.052
Sleep (NHP)	0.074	0.402	0.157	0.063-0.742	0.124
Total NHP score	0.021	0.337	0.379	0.482-1.157	0.190

CSA: cross section area, SIQ: Symptom Impacy Questionnaire, FIQ: Fibromyalgia Impact Questionnaire, NHP: Nottingham Health Profile, R2: R squared, B: unstandardized regression coefficient, SE: coefficients standard error, CI: confidence interval.

DISCUSSION

This study was designed to evaluate the median nerve with electrophysiological and ultrasonographic measurement methods in FM patients with complaints of CTS symptoms and to investigate if these results had an effect on disease activity and quality of life.

No matter how much contradictory data have been published in recent years, there are increasing numbers of studies reporting a correlation between FM and CTS. Some studies have supported the idea that the rate of CTS is higher in patients with FM compared with that in the normal population (20).

However, Sarmer et al reported CTS at the rate of 10% in FM patients and 4% in control subjects, and the difference did not reach statistically significant levels (21). In another study, electrodiagnostic findings of CTS were detected in 24% of FM subjects and in %29 of the control group (22). Silva et al. studied CTS with ultrasonography only in 41 FM patients and 42 healthy control subjects and found no statistically significant difference between the groups, and concluded that it would be difficult to clinically distinguish FM patients with CTS from those without it (23). The high prevalence of CTS in the fibromyalgia population is thought to be associated with the common underlying mechanisms. Currently, there is no study explaining the mechanisms of why CTS is frequently seen in patients with fibromyalgia. CTS is an associated condition that represents the peripheral nociceptive mechanisms in fibromyalgia. Although the dominant mechanism in fibromyalgia is thought to be central sensitization, peripheral nociceptive mechanisms such as peripheral ischemia, microtrauma, and increased nociceptor activity can lead to central pain sensitization (24).

Unlike other studies, in the current study, CTS was evaluated both electrophysiologically and ultrasonographically. The results of this study showed that compared to the healthy control group, the distal CSA measured on USG was significantly larger in patients who had CTS symptoms but were electrophysiologically evaluated as normal.

This could be attributed to the common pathophysiology of CTS and FM. In a study by Chinn et al, it was reported that cytokines and chemokines led to the neuroinflammation, which can be described as classic (involving a mechanical nociceptive stimulus) or neurogenic in FM (25). In a study that investigated the immune profile of patients diagnosed with CTS and compared with healthy control subjects, Moalem-Taylor et al found that CTS is associated with an increase in systemic inflammatory modulating cytokines/chemokines, which potentially regulate neuropathic symptoms. In addition, a significant relationship was found between CTS severity and serum levels of inflammatory mediators (26). There may be



another reason for this result. In the literature, it has been shown that electrodiagnostic testing for CTS may be normal in some patients who have typical clinical features of CTS, but sonographic abnormalities (diagnostic of CTS) may be seen in up to 50% of this population. Borriri et al evaluated the differences in sonographic parameters of CTS patients with normal and mildly abnormal NCS. Evaluation was made of 169 wrists (101 patients) with a clinical diagnosis of CTS, and 40 wrists of 20 healthy control subjects. 49 wrists were classified as mild NCS-positive and 38 as NCS-negative based on the laboratory NCS normal values. It was found that 26% of the NCS-negative group had abnormal CSA and the CSA also differed significantly between the two groups (27).

Another study proved that the rate of undiagnosed CTS in women with FM is much higher than that reported in the general population (28). Therefore, it can be recommended that symptomatic patients should be evaluated ultrasonographically in addition to electrophysiologically.

In this study, the majority of patients diagnosed with CTS electrophysiologically were of mild severity, and there were no patients with severe CTS. This could be due to the fact that electrophysiological findings do not have a significant relationship with other parameters. However, low Vsens and CMAP, which are sub-parameters of NCS, are associated with increased CTS severity. These sub-parameters were found to have an effect both on the increase in the pain subscale of quality of life and disease severity.

The median CSA size has been found to be an effective factor on the SIQR total score and high disease severity. In a study by Fahmi et al. electrophysiological evaluation was made of 40 FM patients and 60 healthy control subjects and the frequency of CTS was found to be higher in the FM patients than in the control group. That study also reported a highly statistically significant correlation between the severity of CTS and the FIQ scores of FM patients (29). The correlation between electrophysiological findings and disease severity and pain scores in the current study was similar to these previous results.

To the best of our knowledge, this is the first study to have evaluated FM patients with CTS symptoms with both US and NCS in respect of disease severity and quality of life.

This study had some limitations. First was that only patients with CTS symptoms were included in the patient group and asymptomatic subjects in the control group. Secondly, it is an important deficiency that the occupational status of the participants is not questioned. Because, occupational status is an important factor in the etiology of CTS. Another limitation was that this study did not contain long-term follow-up of FM patients.

CONCLUSION

CTS is more frequent in patients with FM than in the normal population. FM patients with CTS symptoms but electrophysiologically normal results can be evaluated with US. CTS severity affects quality of life and disease severity in fibromyalgia. These results, which have been previously shown electrophysiologically, are now supported by US. Further studies are required to confirm these results.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the University/local human research ethics committee (Date: 07.01.2019, Decision No: 58/23).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Wolfe F, Smythe H, Yunus M, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990;33(2):160-72.
2. Wolfe F, Anderson J, Harkness D, et al. A prospective, longitudinal, multicenter study of service utilization and costs in fibromyalgia. *Arthritis Rheum* 1997;40(9):1560-70.
3. Yunus M. Symptoms and signs of fibromyalgia syndrome: an overview. In: Wallace D and Clauw D, eds. *Fibromyalgia & Other Central Pain Syndromes*. Philadelphia: Lippincott Williams & Wilkins; 2005. p.125-32.
4. Padua L, Coraci D, Erra C, et al. Carpal tunnel syndrome: clinical features, diagnosis, and management. *Lancet Neurol* 2016;15(12):1273-84.
5. Kuwabara S. Carpal tunnel syndrome: demyelination or ischemic conduction block? *Clin Neurophysiol* 2009;120(2):223-4.
6. Wiperman J, Goerl K. Carpal tunnel syndrome: diagnosis and management. *Am Fam Physician* 2016;94(12):993-9.
7. American Association of Electrodiagnostic Medicine, American Academy of Neurology, and American Academy of Physical Medicine and Rehabilitation. Practice parameter for electrodiagnostic studies in carpal tunnel syndrome: summary statement. *Muscle Nerve* 2002;25(6):918-22.
8. Beekman R, Visser LH. Sonography in the diagnosis of carpal tunnel syndrome: a critical review of the literature. *Muscle Nerve* 2003;27(1):26-33.
9. Visser LH, Smidt MH, Lee M. High-resolution sonography versus EMG in the diagnosis of carpal tunnel syndrome. *J Neurol Neurosurg Psychiatry* 2008;79(1):63-7.
10. Nacir B, Genc H, Duyur Cakit B, et al. Evaluation of upper extremity nerve conduction velocities and the relationship between fibromyalgia and carpal tunnel syndrome. *Arch Med Res* 2012;43(5):369-74.

11. Ersoz M. Nerve conduction tests in patients with fibromyalgia: comparison with normal controls. *Rheumatol Int* 2003;23:166-70.
12. Bennett RM, Friend R, Marcus D, et al. Criteria for the diagnosis of fibromyalgia: validation of the modified 2010 preliminary American College of Rheumatology criteria and the development of alternative criteria. *Arthritis Care Res* 2014;66(9):1364-73.
13. Koçyiğit BF, Okyay RA. The relationship between body mass index and pain, disease activity, depression and anxiety in women with fibromyalgia. *PeerJ* 2018;6:e4917.
14. Sarmer S, Ergin S, Yavuzer G. The validity and reliability of the Turkish version of the Fibromyalgia Impact Questionnaire. *Rheumatol Int* 2000;20(1):9-12.
15. Yüksel S, Elhan AH, Gökmen D, et al. Analyzing differential item functioning of the Nottingham health profile by mixed Rasch model. *Turk J Phys Med Rehabil* 2018;64(4):300-7.
16. Oh SJ. *Clinical electromyography: nerve conduction studies*. 3th ed. Philadelphia:Lippincott Williams & Wilkins;2003.
17. Stevens JC. AAEM minimonograph# 26: the electrodiagnosis of carpal tunnel syndrome. *American Association of Electrodiagnostic Medicine. Muscle Nerve* 1997;20(12):1477-86.
18. Ng AWH, Griffith JF, Lee RKL, et al. Ultrasound carpal tunnel syndrome: additional criteria for diagnosis. *Clin Radiol* 2018;73(2):214.e11-214.e18.
19. González-Rodríguez G, Blanco Á, Corral N, et al. Least squares estimation of linear regression models for convex compact random sets. *ADAC 1* 2007;67-81.
20. Ginanneschi F, Filippou G, Adinolfi A, et al. Spasmophilia and entrapment nerve syndrome comorbidities in fibromyalgic patients:a possible neuromuscular pain generator. *Reumatismo* 2018;70(4):251-6.
21. Sarmer S, Yavuzer G, Küçükdeveci A, et al. Prevalence of carpal tunnel syndrome in patients with fibromyalgia. *Rheumatol Int* 2002;22(2):68-70.
22. Caro XJ, Galbraith RG, Winter EF. Evidence of peripheral large nerve involvement in fibromyalgia: a retrospective review of EMG and nerve conduction findings in 55 FM subjects. *Eur J Rheumatol* 2018;5(2):104-10.
23. Silva FJ, Kanegusuku V, Bortoncello R, et al. Carpal tunnel syndrome and fibromyalgia. *Acta Reumatol Port* 2016;41(3):275-6.
24. Crofford LJ. The relationship of fibromyalgia to neuropathic pain syndromes. *J Rheumatol Suppl* 2005;75:41-5.
25. Chinn S, Caldwell W, Gritsenko K. Fibromyalgia pathogenesis and treatment options update. *Curr Pain Headache Rep* 2016;20(4):25.
26. Moalem-Taylor G, Baharuddin B, Bennett B, et al. Immune dysregulation in patients with carpal tunnel syndrome. *Sci Rep* 2017;7(1):8218.
27. Borire AA, Hughes AR, Lueck CJ, et al. Sonographic differences in carpal tunnel syndrome with normal and abnormal nerve conduction studies. *J Clin Neurosci* 2006;34:77-80.
28. Ferry S, Hannaford P, Warskyj M, et al. Carpal tunnel syndrome: a nested case-control study of risk factors in women. *Am J Epidemiol* 2000;151(6):566-74.
29. Fahmi DS, El-Shafey AM. Carpal tunnel syndrome in fibromyalgia patients – A crucial factor for their functional impairment. *Egypt Rheumatol* 2013;35:175-9.