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Original Article

Carpal Tunnel Syndrome in Patients with Psoriatic Arthritis: Ultrasonography and Magnetic Resonance Imaging Findings

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Objective: The aim of the present study is to assess carpal tunnel syndrome's (CTS's) ultrasonography (US) and magnetic resonance imaging (MRI) findings in patients with psoriatic arthritis (PsA) and compare them with healthy controls.

Methods: Thirty-nine PsA and twenty-eight healthy volunteers were examined in this study. Demographic and clinical features were recorded. CTS-6, a diagnostic algorithm, was used to estimate the probability of CTS. Electrodiagnostic study (EDS) was applied to all wrists included in the report, where the diagnosis of CTS was made by EDS. The cross-sectional area (CSA) of the median nerve was measured at pisiform bone level by US and MRI.

Results: Regarding to the demographic characteristics, no statistically significant difference was found between the groups. Twelve of 39 (30.76%) PsA patients had CTS, whereas CTS was not detected in the control group (p=0.001). US and MRI showed increased median nerve CSA in PsA patients compared to healthy controls (p=0.005, p<0.001; respectively). Also, US and MRI showed increased median nerve CSA in CTS patients compared to others (p=0.002, p<0.001; respectively). The Pearson correlation coefficient between MRI and US measurements of the CSA was 0.85 (p<0.001).

Conclusion: CTS frequency in PsA patients is found higher than healthy controls. The relationship between CTS diagnosed by EDS and CSA measured by both US and MRI was observed in PsA patients.

Keywords: Psoriatic arthritis, Carpal tunnel syndrome, Ultrasonography, Magnetic resonance imaging

INTRODUCTION

Carpal tunnel syndrome (CTS) is a type of entrapment neuropathy, caused by compression of the median nerve in the carpal tunnel at the wrist as stated in [1]. It accounts for about 90% of all entrapment neuropathies [1]. Electrodiagnostic studies (EDSs) are generally used to diagnose CTS and determine severity. But it is well known that EDS has some limitations. There are factors can limit EDS. Firstly, it is not comfortable both patients and physicians, it may require interventional procedures, secondly need patient cooperation, provide limited information on the etiology of CTS and time consuming, lastly it cannot be used in some patient groups such as patients with dermatological contraindications [2-4]. Recent years, magnetic resonance imaging (MRI) and ultrasonography (US) have facilitated to diagnosis of CTS. In [5-8], the authors found that median nerve cross-sectional area (CSA) measured by US or MRI is associated with CTS. However, there are some studies with conflicting results regarding the median nerve CSA in patients with rheumatic diseases [9-13]. Psoriatic arthritis (PsA) occurs in up

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to 30% of people with psoriasis and can have serious debilitating effects on the peripheral joints, tendon insertions and spine [14]. More recent study of Kaya Subaşı et al. [15], confirm that CTS was detected 15.4% in PsA patients with hand involvement as a result of electrophysiological evaluation.

In this report, we have considered to assess US and MRI findings in all PsA patients, literature review reveals that there is no study to assess US and MRI findings in all PsA patients. This gives us enough motivation for present report, where we aimed to assess CTS's US and MRI findings in patients with PsA and compare them healthy controls.

MATERIALS AND METHODS

This study was considered by physical medicine and rehabilitation (PMR) department of medicine faculty. Selcuk University Medical Faculty Hospital ethics committee proved this study (Decision number: 2019/10) and written approval was taken from all participants. At the beginning of the study, G-Power analysis was performed, from this, the minimum subject number was found to be 26 in each group, which would be necessary to detect a difference at the 5% level (0.05) with an 80% chance (0.2). PsA patients according to the Classification criteria for Psoriatic Arthritis criteria who consecutively applied to the PMR outpatient clinic for PsA follow-up and healthy volunteers who applied to the PMR outpatient clinic enrolled in the study. Patients were excluded from the study if they had history of conditions associated with an increased incidence of CTS except PsA (pregnancy, hypothyroidism, diabetes mellitus, or severe systemic diseases); history or clinical/electrophyscologic finding of radiculopathy, polyneuropathy or any nervous system diseases; history of fractures, severe trauma or surgical interventions involving the wrist; bifid median nerve on wrist imaging and under the age of 18 years, over the age of 65 years. There was no history of rheumatic disease in the healthy volunteer group.

Demographic information, diseases, medications, operation history, cigarette-alcohol uses were questioned in detail and recorded in the patient evaluation form. CTS-6, a diagnostic algorithm based on symptoms and signs of CTS, was used to estimate the probability of CTS [16]. PsA activity was evaluated with disease activity in psoriatic arthritis (DAPSA), a PsA specific disease activity score [17].

Thirty-nine PsA and twenty-eight healthy volunteers were included in this study within 1 year. EDS was applied to all wrists included in the study and the diagnosis of CTS was made by EDS. Three wrists with bifid median from the PsA group were excluded from the statistics. Bilateral ultrasonographic imaging of 1 patient in the control group could not be performed due to the patient's had accident before US examination. Therefore, ultrasonographic measurements of 75 PsA wrist and 54 healthy control wrists were used in the study. In the PsA group, 4 patients did not request MRI, and 3 patients could tolerate a single wrist MRI due to the length of the MRI acquisition time. One patient in the control group was able to tolerate a single wrist MRI due to the long MRI acquisition time. Therefore, MRI measurements of 64 PsA wrist and 55 healthy control wrist were used in the study.

Electrodiagnostic studies

EDSs were performed with UltraPro S100 (Natus Neurology Incorporated, Middleton, WI, USA) device. EDSs were started with median and ulnar nerve motor conduction study and continued with median and ulnar nerve sensory conduction study. All studies conducted under standard room temperature of 25°C. Hand temperature was maintained at 32°C or greater [18]. Electrodiagnostic data were compared with normal reference values and categorized by our laboratory's grading system [19]. The CTS grading scale is as follows: normal (grade 0); very mild (grade 1), sensory nerve conduction velocity slow on palm/wrist measurement; mild (grade 2), sensory nerve conduction velocity slow on palm/wrist and finger/wrist measurement, normal terminal motor latency; moderate (grade 3), in addition to mild severity findings, prolongation of motor distal latency; severe (grade 4), sensory potentials absent but motor response preserved, very severe (grade 5), sensory and motor potentials effectively unrecordable.

Ultrasonography

All US examinations were done by a radiologist with 10 years of experienced in musculoskeletal soft tissue B-mode sonography, who was blinded to the participants' clinical data (M.S.D.). US examinations were performed with a high frequency linear transducer (4~14 MHz; Canon Medical System Corporation, Tustin, CA, USA). Probable causes that could be included in the etiology of CTS were examined. US was performed with the appropriate device while the patient was sitting. In the device, the wrist was kept in supination, neutral deviation and neutral sagittal position. US probe was positioned perpendicular to the long

axis of the forearm. Pisiform bone was used as a reference point for the median nerve cross section in accordance with literature [5]. The measurement was made from the inner border of the hyperechoic ring around the median nerve by using the continuous tracing method (Figure 1) [5]. Each median nerve was examined three times, and the mean value was used in further calculations.

Magnetic resonance imaging

All MRI examinations were performed on a 3-T imaging system (MAGNETOM Skyra; Siemens Healthcare, Erlangen, Germany). The wrist was examined in a pronated position with the arm adducted above the head and fingers extended (superman position). Multi-phased array sixteen channel coil was used for high-resolution wrist imaging. Axial, coronal, sagittal and 3D images were acquired. The sequence parameters of wrist MRI can be seen in Table 1. Magnetic resonance images were obtained including all wrist bones, extensor, flexor tendons, and nerves, from the distal radioulnar joint proximally to the base of the metacarpals distally. The total MRI scan time was approximately 40 minutes.

MRI allows visualization of soft tissue, articular and entheseal lesions, and provides a unique picture of the disease process that cannot be gained using other imaging modalities and also MRI also accepted as the reference standard for peripheral nerve measurement. The wrist MRI images of the participants were evaluated in terms of triangular fibrocartilage complex lesions, tendon pathologies, ligament lesions, bone lesions, osteochondral lesions, synovial diseases, ganglion, and other tumoral lesions and nerve diseases. Then the median nerve CSA was measured. The measurements were performed on the 3D-T2 image; however, when difficulties were encountered while delineating the structure, the T1 image was of help. Median nerve CSA was measured in axial section at the pisiform bone level using the continuous trace method (Figure 2). The MRI measurements were performed within 2 weeks of the US to ensure no interval

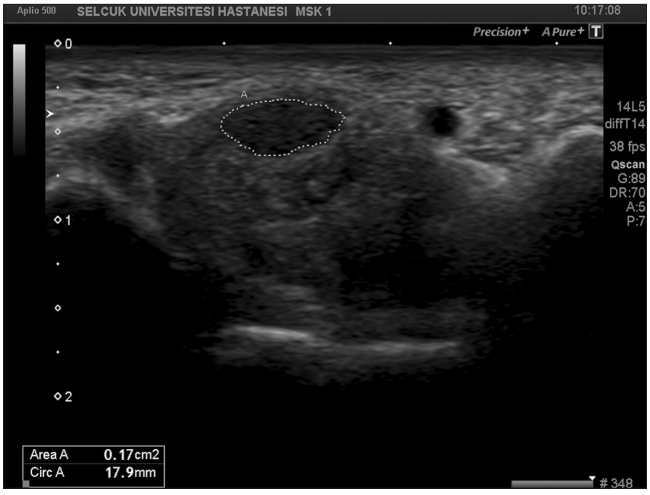

Figure 1. An example of the measurement of the cross-sectional area of median nerve on ultrasonography.

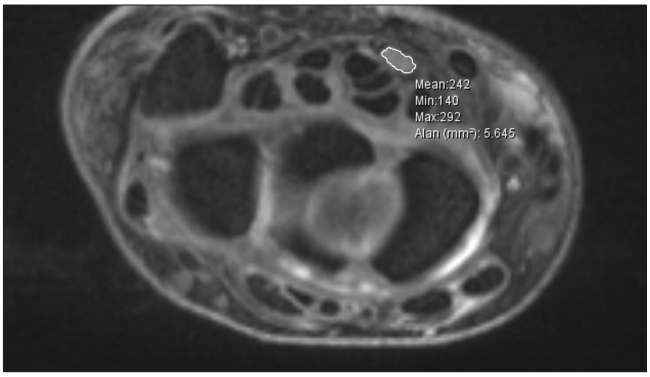

Figure 2. An example of the measurement of the cross-sectional area of median nerve on axial T2-weighted magnetic resonance imaging.

Table 1. The sequence parameters of wrist magnetic resonance imaging

Sequence	FOV (mm)	Matrix/NEX	ST-IP (mm)	TR (ms)	TE (ms)	FA	ETL	Bandwidth (Hz/pixel)
Axial PD TSE FS	10~12	256×256/1	3–0.3	3,200	43	-	43	15.0
Axial T2 TSE	10	256×256/2	3–0.3	3,500	80	-	22	23.0
Coronal T1 SE	10~12	256×256/1	3–0.3	510	10	-	218	18.3
Coronal PD TSE FS	10~12	256×256/1	3–0.3	2,000	35	-	46	15.0
Coronal T2 2D GRE	10~12	240×256/1	0.5–0.5	17	5.6	25	-	19.5
Sagittal PD TSE FS	10~12	256×256/1	3–0.3	3,200	40	-	37	15.0

FOV: field of view, NEX: number of excitation, ST: slice thickness, IP: interslice gap, TR: time of repetition, TE: time of echo, FA: flip angle, ETL: echo-train length, PD: proton-density, TSE: turbo spin-echo, FS: fat-suppressed, SE: spin echo, GRE: gradient recalled echo.

change in nerve CSA. The physician (E.A.T.) who measured the parameters was blinded to the US measurements and EDS. Measurements were made after all participants were included in the study with Picture Archiving and Communication System.

Statistical analysis

The statistical analysis was performed with well-known Statistical Package for the Social Science Program 22.0 (IBM Corp., Armonk, NY, USA). p-values lower than 0.05 were accepted as statistically significant. Descriptive statistics were computed. Comparisons of the mean values of age, height, weight, body mass index (BMI), frequency of CTS, median nerve CSA were performed with t tests; comparison of sex, smoking and dominant hand were performed with the chi-square test between the groups. Receiver operating characteristic (ROC) analysis were used to calculate the cut-off values. The correlation between US and MRI measurements was analyzed with the Pearson correlation test. The correlation between the median nerve CSA and body weight, BMI were analyzed with the Pearson correlation test. The relationship between body weight and median nerve CSA was demonstrated by multiple linear regression analysis.

RESULTS

The mean age (SD) of the patients with PsA was 45.51 years (10.04 years), and that of the healthy volunteers was 45.46 years (9.15 years) (p=0.984). Twenty-six patients (66.7%) with PsA were female, while twenty (71.4%) healthy volunteers were female (p=0.883). The demographic and clinical features of participants were summarized in Table 2.

In the PsA group, 12 of 39 (30.76%) PsA patients had CTS, whereas CTS was not detected in any of 28 patients in the con-

Table 2. Demographic and clinical features of participants

Demographic and clinical features	Psoriatic arthritis (n=39)	Control group (n=28)	p-value
Age (yr)	45.51±10.04	45.46±9.15	0.984
BMI (kg/m^2)	29.80±6.25	29.05±4.37	0.568
Sex, Female	26 (66.7)	20 (71.4)	0.883
Disease duration (min, max), yr	4 (0.08, 27)		
Smoking habit, smoking	26 (66.7)	19 (67.9)	0.999
Dominant hand, right	37 (94.9)	24 (85.7)	0.227
ESR (min, max), mm/h	15 (3,72)		
CRP (min, max), mg/L	4.13 (1, 44.70)		
Clinical subypes of psoriatic arthritis			
Symmetrical polyarthritis	12 (30.8)		
Asymmetrical oligoarthritis	15 (38.5)		
Predominant DIP joint involvement	1 (2.6)		
Predominant spondyloarthritis	11 (28.2)		
Drug			
NSAID	2 (5.1)		
csDMARD	24 (61.7)		
Biologic DMARD	5 (12.9)		
Biologic DMARD + csDMARD	5 (12.9)		
DAPSA			
Remission	7 (17.9)		
Low	19 (48.7)		
Moderate	7 (17.9)		
High	6 (15.4)		

Values are presented as mean±standard deviation or number (%). BMI: body mass index, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, csDMARD: conventional synthetic disease-modifying anti-rheumatic drug, DAPSA: disease activity in psoriatic arthritis, DIP: distal interphalangeal, DMARD: disease-modifying anti-rheumatic drug, min: minimum, max: maximum, NSAID: non-steroidal anti-inflammatory drug.

trol group (p=0.001). In the PsA group, 17 of 75 (22.67%; 2 very mild [11.8%], 14 mild [82.4%], 1 moderate [5%]) wrists had CTS, while in the control group, none of the 56 wrists had CTS (p<0.001).

From Figure 3, it is clear that US and MRI show bigger median curve CSA for PsA patients compare with healthy control group (p=0.005 for US, p<0.001 for MRI). This is also true for CTS patients, furthermore US and MRI show bigger median curve for any other considered group in this study (p=0.002 for US, p<0.001 for MRI). According to result of EDS, we can divide PsA patients into two group as: PsA patients with normal EDS and PsA patients with CTS, from this, we see that CTS have larger median nerve CSA compared to PsA patients with normal EDS. This result makes statistically significance difference with both US and MRI (p=0.001, p=0.003; respectively).

Bigger CSA of the median nerve was measured in PsA patients which have normal EDS than healthy control group with both US and MRI. This situation creates a statistically significant difference in MRI measurements (p=0.026), but it is not statistically significant in US measurements (p=0.180). Median nerve CSA measured by US and MRI can be seen in detail in Figure 3.

ROC analysis was performed to determine the threshold value of median nerve CSA for CTS diagnosis. For US measurement median nerve CSA >9 mm^2 had CTS with 63.4% specificity and 82.4% sensitivity (p<0.001, AUC [area under the curve]=0.780) and for MRI measurement >10.52 mm^2 had CTS with 68.9% specificity and 81.2% sensitivity (p<0.001, AUC=0.798).

If the results of PsA patients are included in the analysis only; no statistically significant cut-off value was obtained for the ultrasonographic median nerve CSA measurement. Using the ROC curve, the best cut-off point for median nerve CSA for MRI measurement was 9.28 mm^2 with sensitivity and specificity of 93.7% and 43.7% (AUC=0.740, p<0.001) in PsA patients.

By using multiple logistic regression analysis, we found that body weight has a statistically significant effect on median nerve CSA measured by US (p<0.001, r=0.197) and MRI (p<0.001, r=0.213). There was no statistically significant relationship between median nerve CSA and age, height, DAPSA score, PsA duration, C-reactive protein.

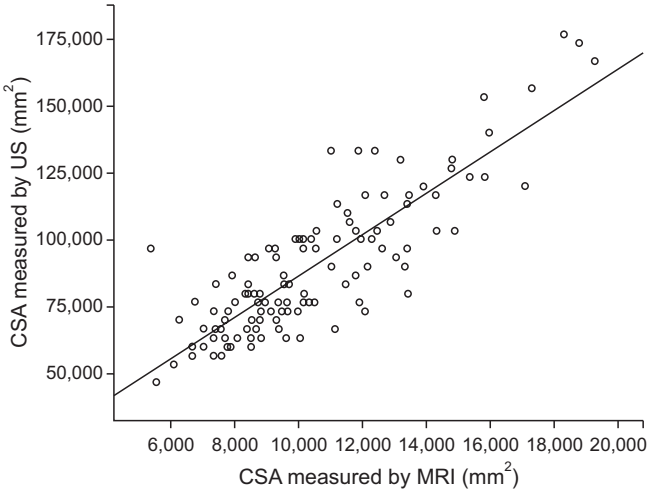

Figure 4. US versus MRI CSA. Trend-line demonstrates correlation of 0.85. US: ultrasonography, MRI: magnetic resonance imaging, CSA: cross-sectional area.

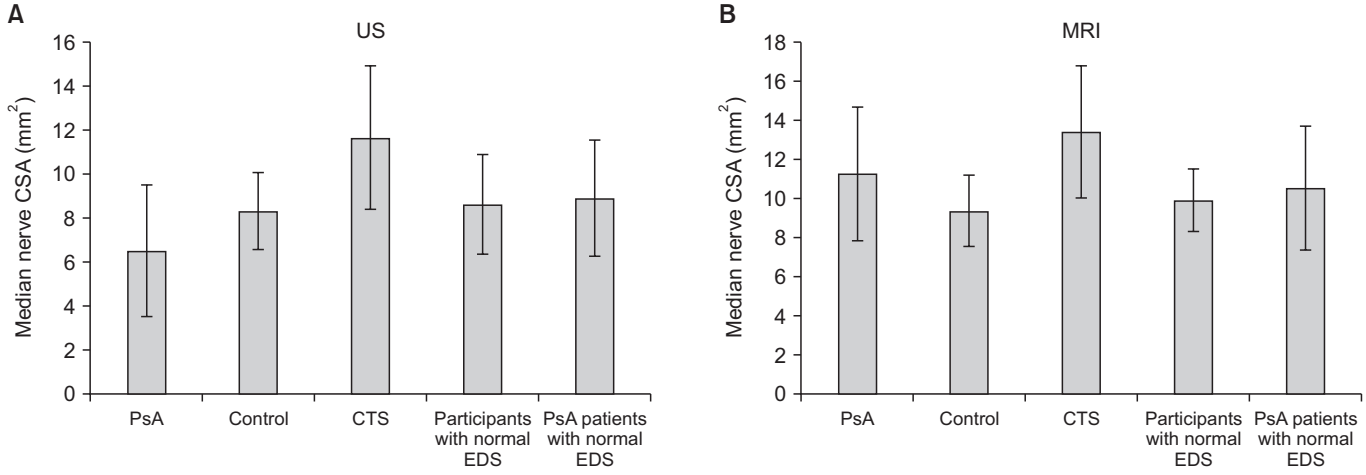

Figure 3. Mean median nerve cross-sectional areas with error bars (standard deviation) for ultrasonography (US) (A) and for magnetic resonance imaging (MRI) (B). CSA: cross-sectional areas, PsA: psoriatic arthritis, EDS: electrodiagnostic study, CTS: carpal tunnel syndrome.

The Pearson correlation coefficient between MRI and US measurements of the CSA of the median nerve was 0.85 (p<0.001), demonstrating strong correlation (Figure 4).

Based on EDS results, 75 wrists of PsA patients can be divided into two group as wrists with CTS found in EDS (17 wrists) and normal wrists (58 wrists). We found that there is a significant difference between the groups in terms of CTS-6 score (median [min, max]: 8 [0, 18], 0 [0, 21.5], respectively; p=0.009). For PsA patients with CTS; Phalen's test (8 [47.1%] positive vs 11 [19.0%] positive; p=0.028), Tinel's test (8 [47.1%] positive vs. 12 [20.7%] positive; p=0.058), and nocturnal symptoms (10 [58.8%] positive vs. 10 [17.2%] positive, p<0.001) are more positive than CTS free PsA patients. However, we found that there is no significant difference between the groups with regards numbness predominantly or exclusively in the median nerve territory (2 [11.8%] vs. 8 [13.8%], p=0.999) thenar atrophy and/or weakness (3 [17.6%] positive vs. 8 [13.8%] positive; p=0.704) or 2 point discrimination (median [min, max]: 3 mm [1, 4], 2 mm [1, 5], respectively; p=0.491).

We also analyzed CTS of PsA patients (n=12) and compare them with PsA patients without CTS (n=27), we found that DAPSA (median [min, max]: 12.17 [0.57, 67.21], 11.19 [0.41, 77.14], respectively; p=0.799), erythrocyte sedimentation rate (median [min, max]: 17.5 [8, 54], 13 [3, 72], respectively; p=0.499), CRP (median [min, max]: 4.75 [2.02, 22.3], 4.07 [1, 44.7], respectively; p=0.327), which indicate that there is no significant difference between groups with regards to their CTS. Therefore, we conclude that disease activity was not associated with CTS.

DISCUSSION

In this study we assess CTS's US and MRI findings in patients with PsA then compare those healthy controls. CTS was detected at a rate of 30.76% in patients with PsA by using EDS. This is the first study to show an increase in median nerve CSA with the diagnosis of CTS in PsA patients.

CTS is the one of the most common form of entrapment neuropathies and peripheral neuropathies [1,20]. CTS is usually idiopathic but it can be seen more in some disease like diabetes mellitus, hypothyroidism, rheumatologic disorders [21-24]. Also, this is the first study assessing CTS frequency by EDS in all PsA patients. In recently, Kaya Subaşı et al. [15] assess CTS frequency in PsA patients but in this study they only involved PsA patients which have hand involvement. Kaya Subaşı et al. [15] detected CTS in 15.4% of patients with PsA (only patients with hand involvement) by electrophysiologically. This rate is considerably lower than what we found in our study. One of the reasons for this difference may be that Kaya Subaşı et al. [15] calculated the frequency of CTS in PsA patients by using the wrists, not the patients. In addition, in our study, BMI is seen to be higher. An increase in BMI may increase susceptibility to CTS [25].

For CTS diagnose, usually EDS perform [26,27]. But in recent years there are lots of studies that perform US and MRI to diagnose CTS [5-8]. Both US and MRI are comfortable for patients and physicians, provides anatomical imaging and guides in terms of etiology. Also especially US widely use in rheumatology for detection of early inflammatory changes, monitor and confirm treatment [28]. Therefore, if these imaging methods were used, they can provide us information about CTS as well. The most important criteria is the increase of median nerve CSA for both US and MRI. Because, the compression of the median nerve in the carpal tunnel causes edema, proliferation of fibrous tissue in the proximal of the compression zone, swelling of the nerve and increased CSA [29]. Using the continuous trace method around the inner hyperechoic border of the median nerve at the pisiform level is seen as the most precise method for US measurements [30]. Hence, we use this method for both US and MRI for comparing data.

In the studies conducted on normal population, median nerve CSA was found to be bigger in patients with CTS than in patients without CTS, similar to our study [5-8]. However, there are conflicting results in studies on median nerve CSA in rheumatic diseases [9-13,15]. We also mentioned that Hammer et al. [12] studied median nerve CSA by US in 154 rheumatoid arthritis (RA) patients without CTS symptoms. Hummer et al. [12] compare their results with existing literature, they found that CSA of the median nerve is similar to those without rheumatic disease. Limitation of their study, since the half of the study group having a disease duration of less than 1 year; they were not able to use objective diagnosing methods such as EDS, CTS-6. Also in this study, measurement of CSA was measured at distal volar crease level within the hyperechoic boundary of the nerve, unlikely our study. Yagci et al. [10] similarly investigated median nerve CSA in 30 RA patients without CTS symptoms. They used 30 healthy control group in their study. EDS was performed on all participants by them. In this study, unlike Ham-

mer et al. [12], median nerve CSA was found to be increased at the hamatum, pisiform and radioulnar joint levels in RA patients. The limitation of this study can be seen as small number of patients. In our study, when we compared PsA patients which have normal EDS and healthy control groups which have normal EDS too; US and MRI shows increased CSA of the median nerve in patients with PsA. This situation creates a statistically significant difference in MRI measurements (p=0.026), but it is not statistically significant in US measurements (p=0.180). Our study's limitation is that our CTS population was small in number, too. Larger studies are needed on this situation.

Another study by Hammer et al. [11], 12 patients with rheumatic diseases (RA: n=7; PsA, n=2; ankylosing spondylitis: n=1; Sjogren syndrome: n=1; unspecified polyarthritis: n=1) which have CTS diagnosed EDS compared to 30 RA patient without CTS symptoms and 30 healthy control group. In this study, larger median nerve CSA was observed in 12 CTS patients compared to the other groups. As in Hammer's other study, EDS was not perform to asymptomatic participants in this study [11,12]. CTS group was small in number and heterogeneous and they did not analyze the severity of the symptoms [12]. Besides, they measured CSA at the level of the distal volar crease, within the hyperechoic rim in, which is the difference between their work and ours. The median (range) value in the CTS patients was detected 15.7 mm^2 in their work. This value is quite high compared to other studies [9,15,31]. Hammer et al. [12] consider this situation as most patients with CTS can have severe CTS. In the study of Karadag et al. [9], patients with a CSA of the median nerve above 13 mm^2 were diagnosed CTS, so larger CSA in CTS patients is an expected result. Therefore, we did not compare this study with others.

In a recent study conducted by Kaya Subaşı et al. [15], median nerve CSA was measured by US as 8.52 mm^2 (2.19 mm^2), 8.97 mm^2 (2.41 mm^2), 7.09 mm^2 (1.83 mm^2) in RA, PsA, control groups, respectively, and there was a significant difference compared to the control group. In our study, median nerve CSA was measured as 9.49 mm^2 (3.00 mm^2), 8.30 mm^2 (1.73 mm^2) in PsA, control groups, respectively. In both studies, measurements were made at the level of the pisiform bone and without including the hyperechoic rim. Since CTS was detected with a higher frequency in our study, it can be expected to see larger CSA in the PsA group. The reason for the difference between the control groups may be the higher BMI in our study. In the study by Kaya Subaşı et al. [15], according to electromyoneurography results, 78 wrists with PsA divided into 3 groups as normal, mild and moderate CTS. There was no significant difference between the groups in median nerve CSA. In our study, when PsA patients divided into two groups: PsA patients with normal EDS and PsA patients with CTS; PsA patients with CTS have larger median nerve CSA. This situation makes statistically significant difference (p=0.001). Beside, our results are consistent with other studies in the literature on RA patients and the normal population.

The limitations of our study were that our CTS population may be considered small and most of them are mild. We think that this study will be one of the precursors of CTS studies in PsA patients. Multicenter studies including larger patient groups are needed for the classification of CTS, determination of appropriate cut-off values, diagnosis of CTS without EDS, and detection of CTS patients by imaging methods.

CONCLUSION

CTS frequency in PsA is found higher than healthy control group. The relationship between CTS diagnosis with EDS and CSA measured by both US and MRI was observed in both PsA patients and all participants. Median nerve CSA can be measured in all PsA patients who had wrist MRI or US for any reason. Diagnosis can be supported by US or MRI in patients who cannot undergo EDS or who do not accept EDS. Moreover when using US or MRI in PsA patients, cut-off values obtained from normal people should not be used.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

F.L., I.A.G., and M.S.D. designed the study, E.A.T drafted the manuscript. E.A.T, F.L., I.A.G, M.S.D, E.B.B., H.K. and M.K.K. contributed to the acquisition and analysis of data. All authors validated and reviewed the drafted manuscript. All authors approved the final manuscript.

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