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EVALUATION OF CARPAL TUNNEL SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS BY NEUROMUSCULAR ULTRASOUND AND ELECTROPHYSIOLOGIACAL STUDIES

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ORIGINAL ARTICLE

Evaluation of Carpal Tunnel Syndrome in Patients With Rheumatoid Arthritis by Neuromuscular Ultrasound and Electrophysiological Studies

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Abstract

Introduction: **Rheumatoid neuropathy of the median nerve (MN) is the most common nerve entrapment neuropathy. Diagnosis of carpal tunnel syndrome (CTS) in rheumatoid arthritis (RA) is often dependent on electrophysiological evaluation. However, direct visualization of the nerves is possible with exact localization of the site of disease with neuromuscular ultrasound (U/S).**

Aim: **To evaluate CTS in patients with RA by neuromuscular U/S and electrophysiological studies.**

Patients and methods: **Thirty RA patients were included and were compared with 30 normal individuals as the control group.**

Results: **The current study showed significantly higher cross-sectional area of the MN at the level of tunnel inlet (mm^2), at the level of tunnel (mm^2), and cross-sectional area at the level of tunnel outlet in the RA group as compared with controls ($P = 0.002$, $P < 0.001$, and $P = 0.009$, respectively). There were anatomical anomalies such as the ganglion cyst in five (8.3%) patients, while three (5.0%) patients had a bifid MN and two (3.3%) patients had a persistent median artery among the RA group. CTS in RA patients was diagnosed in 12 (20%) patients by nerve conduction studies, while using U/S, CTS was diagnosed in 16 (26.7%) patients.**

Conclusion: **U/S imaging was found to be a valuable tool in diagnosing CTS even in those with normal nerve conduction studies. U/S can demonstrate the etiology of CTS in RA as a ganglion cyst, bifid MN, and persistent median artery.**

Keywords: Carpal tunnel, Electrophysiological study, Neuromuscular ultrasound, Rheumatoid arthritis

1. Introduction

Carpal tunnel syndrome (CTS) is the commonest extra-articular neurologic manifestation of rheumatoid arthritis (RA).[1] This syndrome involves a set of signs and symptoms, which are caused by many pathologic mechanisms contributing to median nerve (MN) compression. Earlier studies have shown that CTS among RA cases is primarily linked to inflammations of tendons, joints, and the MN,[2] and its diagnosis generally depends on history, physical examination, and nerve conduction studies (NCSs).[3]

Though electrodiagnostic testing is the gold standard for CTS diagnosis, about one-quarter of cases with clinical CTS have no abnormalities in NCSs. Recently, neuromuscular ultrasound (NMUS) has been widely used for diagnosing CTS (sensitivity and specificity are 77.6 and 86.8%, respectively) as it can show carpal tunnel anatomy and morphologic alterations.[4] So, we aimed to evaluate CTS in RA cases by NMUS and NCS.

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2. Patients and methods

Ethical approval and consent statement was Approved by Faculty Council in 2022.

Thirty Egyptian RA patients, diagnosed according to the EULAR/ACR 2010 criteria, of age over 18 years, presenting with neurological manifestations, positive Phalen, and/or Tinel test were included in the study. Patients with hand/wrist trauma, surgery, congenital, or posttraumatic deformity of the hands, fractures, upper limb edema, neurologic disease with peripheral neuropathy (e.g. Guillain-Barre syndrome), systemic disease other than RA, and pregnancy were not included. Thirty normal age-matched and sex-matched individuals were selected as controls.

Each patient was subjected to history taking, and clinical assessment including musculoskeletal and neurologic examination, including disease activity score 28.

Disease activity by disease activity score 28[5]: laboratory tests including CBC, RF, ESR, CRP, and fasting and 2 h postprandial blood glucose were conducted for all participants. All participants were examined with commercially available neuromuscular US equipment using 8–12 MHz linear phased array transducer (APLIO400 Model, Toshiba US machine, California, USA). Bilateral motor conduction studies of the MN and its main branches, and bilateral sensory conduction studies of the MN and its main branches, and bilateral F-responses of the MN were conducted using the Neuropack MEP-9400A/K EMG/EP measuring system was used to perform the electrophysiological studies of this work. The MEP-9400 system software operates on Microsoft Windows.

3. Results

A nonsignificant difference was reported among the studied groups as regards sex, age, residence, BMI, or handedness. The disease duration 'years' was in the range of 1 and 33 with a mean of 9.60 ± 4.68; disease activity ranged from 2.5 to 7.3 with a mean of 3.68 ± 1.07; 18 (60%). RA cases showed low disease activity, eight (26.7%) cases showed moderate disease activity, and four (13.3%) cases showed high disease activity. In the RA group: Tinel's test was positive in 17 (28.3%) wrists, patients had a positive Phalen's test in 35 (58.3%) wrists, and the reverse Phalen's test was positive in 29 (48.3%) wrists. US findings in the RA patients group are shown in Table 1. There was a significantly higher cross-sectional area (CSA) at the level of tunnel inlet (mm^2), CSA at the level of tunnel (mm^2), CSA at the level of tunnel outlet (mm^2), and inlet/midforearm ratio in RA patients as compared with controls ($P < 0.05$). Also, there was a statistically significantly higher FR at the level of the tunnel inlet (mm^2), FR at the level of tunnel (mm^2), and FR at the level of tunnel outlet (mm^2) in the RA group compared with controls ($P < 0.05$) (Table 2). A significant difference was found among both groups according to latency (ms) and amplitude W (mv) ($P < 0.001$) among motor nerve conduction for MNs. There was a statistically significant higher latency 'ms' in the RA group compared with the control group. Also, there was a highly statistically significant higher amplitude and CV in the control group compared with the RA group, among sensory nerve conduction for MNs ($P < 0.001$ for all) (Table 3). US detected anatomical anomalies such as the ganglion cyst in five (8.3%) wrists, bifid median nerve (BMN) in three (5.0%) wrists, and persistent median artery (PMA) in two (3.3%) RA wrists (Table 4). Table 5 shows that the prevalence of the affected outcome of NCS was 24 (40%) wrists, while the affected outcome of US was 29 (48.3%) wrists among the RA group (Figs. 1 and 2).

Table 1. Ultrasound findings in rheumatoid arthritis patients group.

Radio-carpal joint by ultrasonography	RA group ($N = 60$) [n (%)]
Synovial hypertrophy	39 (65.0)
Effusion	32 (53.3)
Bone erosion	31 (51.7)
Power Doppler	23 (38.3)
Median nerve ultrasound findings	
Intraneural PDSs	12 (20.0)
Altered nerve echogenicity	10 (16.7)
Long scan (compressed)	8 (13.3)
Bifid nerve	2 (3.3)
Ultrasonography findings of flexor tendons	
Tenosynovitis flexor tendons	19 (31.7)
Flexor digitorum superficialis	6 (10.0)
Flexor digitorum profundus	5 (8.3)
Flexor pollicis longus	4 (6.7)
Flexor carpi radialis	4 (6.7)
Power Doppler signals	6 (10.0)
Flexor digitorum superficialis	2 (3.3)
Flexor digitorum profundus	2 (3.3)
Flexor pollicis longus	1 (1.7)
Flexor carpi radialis	1 (1.7)

4. Discussion

The current study aimed to evaluate CTS among RA patients by neuromuscular US and electrophysiological studies. To obtain this aim, 30 RA cases were included and were compared with 30 normal individuals as controls.

In the present study, CTS in RA cases was diagnosed in 24 (40%) wrists by NCS. While using U/S,

Table 2. Comparison between studied groups as regards ultrasonographic findings and transverse scan of the median nerve at different levels.

Ultrasonography finding	RA group (*N=60*)	Control group (*N=60*)	*t*-test	*P* value
CSA at the level of tunnel inlet (mm^2)				
Mean ± SD	9.08 ± 2.04	7.79 ± 0.79	3.018	0.002*
Range	6.99–17.54	6.99–8.58		
CSA at the level of the tunnel (mm^2)				
Mean ± SD	10.42 ± 3.31	8.83 ± 0.84	3.867	<0.001**
Range	8.17–20.57	7.98–9.67		
CSA at the level of tunnel outlet (mm^2)				
Mean ± SD	8.99 ± 1.96	7.65 ± 0.69	2.434	0.009*
Range	7.16–15.79	6.96–8.34		
Inlet/midform ratio	4.07–1.61	2.77–1.14	3.682	<0.001**
FR at the level of tunnel inlet (mm^2)				
Mean ± SD	1.24 ± 1.01	0.91 ± 0.08	3.274	<0.001**
Range	0.93–3.24	0.82–0.99		
FR at the level of the tunnel (mm^2)				
Mean ± SD	1.60 ± 1.43	1.03 ± 0.10	3.871	<0.001**
Range	1.03–3.56	0.93–1.13		
FR at the level of tunnel outlet (mm^2)				
Mean ± SD	1.21 ± 1.13	0.84 ± 0.10	2.841	0.004*
Range	0.77–3.62	0.74–0.95		

Data are expressed as mean ± SD. *P value 0.002; **P value <0.001.
CSA, cross-sectional area, using t independent sample t-test for mean ± SD.

Table 3. Comparison between both groups as regards motor and sensory nerve conduction for median nerves.

Median nerves	RA group (N = 60)	Control group (N = 60)	Test value	*P* value
Motor nerve conduction				
Latency (ms)				
Mean ± SD	3.19 ± 0.50	3.23 ± 0.69	−0.363	0.717
Range	2–4.2	2–4		
Amplitude W (mv)				
Mean ± SD	10.36 ± 2.26	13.33 ± 1.50	−8.472	<0.001**
Range	6–15	10–15		
NCV (m/s)				
Mean ± SD	55.65 ± 5.14	56.30 ± 4.27	−0.753	0.453
Range	43–66	45–65		
Sensory nerve conduction				
Latency (ms)				
Mean ± SD	3.60 ± 0.97	2.92 ± 0.56	4.681	<0.001**
Range	1–5	2–4		
Amplitude (mv)				
Mean ± SD	16.53 ± 8.78	23.18 ± 6.13	−4.809	<0.001**
Range	4–42	11–35		
NCV (m/s)				
Mean ± SD	50.97 ± 9.85	65.73 ± 6.45	−9.713	<0.001**
Range	34–65	55–75		

Data are expressed as mean ± SD. **P value <0.001.
NCV, nerve conduction velocity, using t independent sample t-test for mean ± SD.

Table 4. Other findings for the ultrasound among the rheumatoid arthritis group.

Other findings	US [*n* (%)]
Ganglion cyst	5 (8.3)
Bifid median nerve	3 (5.0)
Persistent median artery	2 (3.3)

Total = 60 lateral nerves.
US, ultrasound.

CTS was diagnosed in 29 (48.3%) wrists. In line with our findings, Smerilli et al.[2] reported a clinical diagnosis of CTS using U/S in 23 wrists out of 114 RA wrists. In addition, Karadag et al.[6] using U/S, reported CTS in 30 (15%) of 200 wrists of RA patients. A higher prevalence of CTS was reported in the Mahmoud et al.[7] study, using combined U/S and electrophysiological assessment. CTS was

Table 5. Prevalence of carpal tunnel syndrome among rheumatoid arthritis cases according to nerve conduction study and ultrasound.

Prevalence	RA group ($N = 60$) [n (%)]
Outcome of NCS	
Normal	36 (60.0)
Affected	24 (40.0)
Outcome of US	
Normal	31 (51.7)
Affected	29 (48.3)

Total = 60 lateral nerves.
NCS, nerve conduction study; RA, rheumatoid arthritis; US, ultrasound.

diagnosed in 71 (95.9%) out of 74 wrists by NCS. This discrepancy could be explained by the fact that Mahmoud et al.[7] used the grading criteria by Padua *et al.*[8] which diagnosed minimal affection of CTS in seven patients, whereas Karadag et al.[6] used the classification criteria, which did not include minimal cases (only mild, moderate, and severe) and Smerilli et al.[2] graded cases using the historical-objective scale based on clinical evaluation, not electrophysiology study. It may also be because of the larger sample size in their studies.

In our study, CTS in RA patients was diagnosed in 12 (20%) patients by NCS. While using U/S, a higher prevalence of CTS was diagnosed in 16 (26.7%) patients. In agreement with our finding, the meta-analysis by Zaki et al.[9] found that US had good sensitivity similar to that of electromyography and NCS; however, with slightly higher specificity. The higher sensitivity of U/S in the diagnosis of CTS in comparison to NCS can be attributed to the high rates of false negative cases observed in electromyography tests and thus US was preferred in CTS

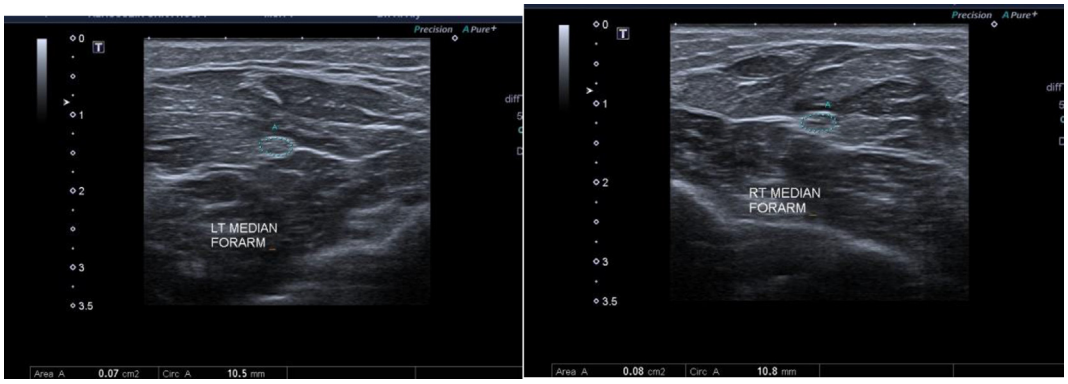

Fig. 1. CSA of the median nerve at mid-forearm. CSA, cross-sectional area.

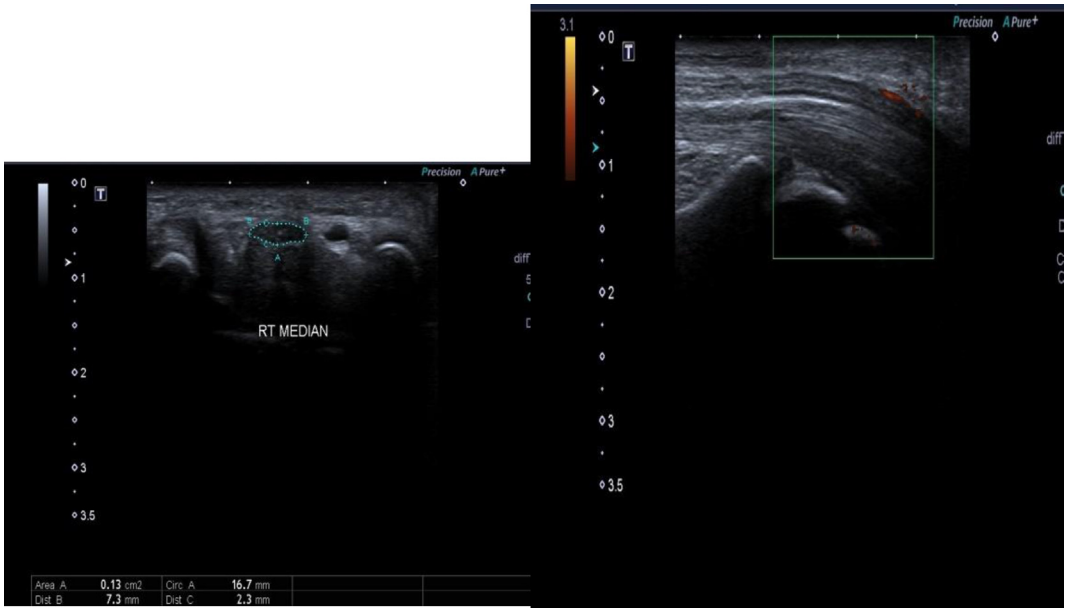

Fig. 2. CSA, flattening ratio, Doppler signal of the median nerve at the inlet of the carpal tunnel. CSA, cross-sectional area.

diagnosis. Jesus Filho et al.[10] reported that the rate of false negatives detected by electrodiagnostic tests was between 0 and 4.3%.

Using U/S, the BMN was reported in three (5.0%) cases in our study. Higher prevalence was found in 20 (54%) wrists in the Mahmoud et al.[7] study. Furthermore, Walker et al.[11] and Chen et al.[12] reported the likelihood of the coexistence of BMN with CTS. Bayrak et al.[13] and Bagatur et al.[14] have considered a BMN and a PMA as potential risks for CTS.

Gassner et al.[15] and Kim et al.[16] showed that the utilization of color Doppler US at high frequencies is a valuable tool in diagnosing CTS cases as it evaluates PMA. In our work, PMA was found in two (3.3%) wrists. It was found in four (5.4%) wrists in the Mahmoud et al.[7] study. Furthermore, PMA could coexist with thrombosed PMA as in a case study of a female (aged 39 years) with CTS with thrombosed PMA as a cause of compression as reported by Rzepecka-Wejs et al.[17] The PMA is an uncommon etiology of CTS as it increases the pressure on the MN.[18] US of the wrists should be performed before surgery to avoid injury of the PMA, thus improving surgical outcomes.[19]

Regarding radio-carpal joint by ultrasonography, synovial hypertrophy was found in 39 (65.0%) wrists, effusion in 32 (53.3%) wrists, bone erosion in 31 (51.7%) wrists, and PD in 23 (38.3%) wrists. In the Mahmoud et al.[7] study, inflammatory changes were prominent features detected by U/S in RA cases with CTS, while Smerilli et al.[2] showed that synovial tissue inflammation at the carpal tunnel level was the most characteristic US feature in those patients.

As regards the etiology of CTS, tenosynovitis flexor tendons were the most commonly reported in 19 (31.7%) wrists in the present study. In line with our finding, Mahmoud et al.[7] reported that most of the hands (85.1%) had flexor tendon tenosynovitis at wrists and radio-carpal joint synovitis. Furthermore, Smerilli et al.[2] found a higher rate of inflammatory changes at the carpal tunnel level in RA wrists with CTS in comparison to RA wrists without CTS (39.1 vs. 15.4%).

The current study showed significantly higher CSA of MN at the level of tunnel inlet (mm^2), at the level of tunnel (mm^2), and CSA at the level of tunnel outlet in RA cases in comparison with controls. Similarly, Mahmoud et al.[7] reported increased CSA of the MN in CTS wrists when compared with those without CTS. Moreover, Smerilli et al.[2] found that the mean CSA in RA cases without CTS was 8.6 ± 2.1, while in those with CTS, it was 10.6 ± 4.2. Also, Karadag et al.[6] reported a median CSA of 9 for RA wrists without CTS and 13.0 for those with CTS.

In the present work, there were significantly increased F-wave responses (FR) in motor nerve conduction of MN at the level of tunnel inlet (mm^2), at the tunnel level, and at the level of tunnel outlet in the RA group compared with the control group. Also, patients in the RA group had significantly decreased amplitude in motor nerve conduction of MN. In accordance with our finding, Aktürk et al.[4] found that MN mobility was reduced among CTS patients in comparison with controls. Aktürk et al.[4] attributed this to the gradual increase in pressure leading to endo-neural edema manifested by increased CSA by neuromuscular U/S and segmental demyelination, which is observed in motor and sensory NCSs. In addition, reduced MN mobility was found in 21 (28.4%) wrists in the Mahmoud et al.[7] study.

RA patients had significantly higher sensory latency of the MN on both sides compared to the control group. In line with our findings, Chang et al.[20] found that the specificity was 100% by using a distal sensory latency cutoff of 2.9 ms, while Tseng and Wang[21] found that the specificity was 100% by using a distal sensory latency cutoff of 4.0 ms.

RA patients had a significantly lower amplitude of sensory conduction in the MN as compared with controls, and significantly lower CV of sensory nerve conduction when compared with the control group. Similarly, Lee et al.[22] reported decreased amplitude of the sensory nerve action potential in CTS patients when compared with normal individuals.

RA patients in our study had significantly increased motor latency of MN. This agrees with the Lee et al.[22] study, which reported delayed sensory peak latency in CTS patients when compared with normal individuals.

4.1. Conclusion

Although CTS in RA patients can be first diagnosed by NCS, U/S imaging was found to be of value for diagnosing CTS even in those with normal NCS. U/S can demonstrate the etiology of CTS in RA as a ganglion cyst, BMN, and PMA. U/S is a noninvasive, rapid, and nonpainful method for the assessment of CTS in RA patients.

Conflicts of interest

None declared.

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