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Carpal Tunnel Syndrome in Rheumatoid Arthritis: Assessment of Different Anatomical Causes in Non-Clinically Deformed Wrist

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ABSTRACT

Background: Carpal tunnel syndrome (CTS) can affect 4-50% of rheumatoid arthritis (RA) patients. Pain and paresthesia in the first three digits are the commonest symptoms of CTS and can progress to hand weakness in the late stage.

Objective: This study aimed to determine the most prevalent anatomical cause of CTS in non-clinically deformed RA.

Patients and methods: This case-control study included convenience sample of 100 female RA patients with CTS and clinically non-deformed wrists who were recruited from the Outpatient Clinics, Faculty of Medicine, Ain Shams University Hospitals over a period of three months.

Results: The patients' average age was 44.68 ± 6.97 years. Musculoskeletal ultrasound showed that 42% of the patients had tenosynovitis, 30% of the patients had thickened flexor retinaculum, 22% of the patients had increased power Doppler (PD) signal, and 6% of the patients had bone erosions. There was a significant association between tenosynovitis and age, duration of RA, and moderate CTS, compared to patients with thickened flexor retinaculum, increased PD signal, and bone erosions.

Conclusion: There was an inflammatory pattern present in the ultrasound spectrum of CTS in RA patients, such as tenosynovitis and/or synovitis. Tenosynovitis was a key factor in the onset of CTS in RA.

Keywords: RA, CTS, Tenosynovitis.

INTRODUCTION

Carpal tunnel syndrome (CTS), the most common form of entrapment neuropathy in the general population, is caused by the compression of the median nerve in the carpal tunnel at the level of the wrist [1]. It is accompanied by discomfort, pain, numbness, and paresthesia in the first three digits, as well as hand weakness in a late stage [2].

Rheumatoid arthritis (RA), a chronically progressive systemic autoimmune inflammatory disorder, primarily affects the synovial lining of synovial joints and tendon sheaths, particularly in the hands and feet [3]. RA is characterized by pathological damage to the peripheral joints and surrounding tissue. Chronic RA can cause severe dysfunction and disability in the hand and wrist. RA can also lead to changes in the wrist, such as narrowed joint space, scapholunate dislocation, synovial inflammation of tendons, thickened flexor retinaculum, and production of pannus, which can lead to secondary CTS [4].

The prevalence of CTS in rheumatoid patients varies from 4% to 50%, depending on ethnicity and disease duration [5]. The patient's medical history, clinical symptoms, physical examination, and electrophysiological tests are used to diagnose CT [2]. Although, patients find this procedure painful and invasive, it is the main reference for diagnosing CTS with a specificity greater than 95% and a sensitivity greater than 90% [6].

Ultrasonography is a frequently used imaging technology that is non-invasive, quick, and sensitive. It can be used to diagnose CTS and monitor the joint status and subclinical abnormalities of surrounding soft tissues [7].

The most common ultrasound features of CTS are median nerve swelling, wrist synovitis, and flexor tendon tenosynovitis. Persistent synovitis is a risk factor for further bone erosions, cartilage degradation, and tendon tears [8]. Intraneural power Doppler (PD) signals have been observed in a small number of studies [9]. The objective of our research was to identify the most prevalent anatomical cause of CTS in non-clinically deformed rheumatic patients.

PATIENTS AND METHODS

Study design and setting: This was case-control research conducted at Outpatient Clinics, Faculty of Medicine, Ain Shams University Hospitals It included a convenience sample of RA patients with CTS and clinically non-deformed wrists over a period of three months.

Participants: One hundred RA patients with CTS and clinically non-deformed wrists were enrolled in this study. The patients met the 2010 American College of Rheumatology/European League Against Rheumatism (EULAR) criteria for RA [10].

Exclusion criteria: Patients with active RA, active synovitis on ultrasound, severe CTS, overlapping syndromes, cancer, active infections, obesity, diabetes, pregnancy, local steroid injection, acromegaly, and severe uncontrolled illness were excluded.

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A total of 100 healthy controls without any known musculoskeletal disorders were recruited from hospital employees or visitors.

All patients underwent:

1- **Clinical assessment:** Age, body mass index (BMI), occupation, RA duration (years), joint involvement, cardiovascular, renal, liver, and endocrine systems. Each patient was on regular disease-modifying antirheumatic drugs (DMARDs). The Disease Activity Score-28 joints (DAS-28) was used to measure the disease activity [11]. Patients with inactive disease were enrolled in the study. Neurological examination was performed for all participants for Tinel, Phalen tests, and thenar atrophy.

2- **Laboratory studies:** Rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and anti-citrullinated antibodies (anti-CCP) were recorded.

3- **Electrophysiological studies:** All RA patients underwent nerve conduction studies according to the American Association of Electrodiagnostic Medicine's (AAEM) criteria for the detection of CTS [12]. Patients were classified as mild, moderate, or severe. A total of 134 hands were impacted by the study's 100 individuals with unilateral or bilateral CTS.

4- **Musculoskeletal ultrasound (MSU):** The sonographic examination was carried out by a radiologist with 7 years of experience in the field of musculoskeletal imaging. A high-resolution linear transducer (6–15 MHz; LOGIQ 9 pro series; GE Medical Systems, USA) that operated between 6 and 15 MHz. The patients were lying supine on the examination bed when the wrists were evaluated using ultrasound in the palmar and dorsal views. With their fingers in a neutral posture, the patients' forearms were propped up on the bed in a comfortable position. Each wrist was scanned in transverse and longitudinal views in accordance with the 2017 EULAR recommended standards for MSU imaging in rheumatology [13]. By using both B mode and color Doppler examination in transverse and longitudinal planes, the radiocarpal joint, intercarpal joints, flexor and extensor tendons were examined. Findings were defined according to the following:

- Tenosynovitis is characterized by thicker tissue that is hypoechoic or anechoic in two perpendicular planes, as well as by the presence or absence of fluid in the tendon sheath and a Doppler signal [14].
- Bone erosion: An intra-articular bone surface discontinuity. It was supported by data showing at least two perpendicular bony cortical discontinuities larger than 1 mm in size [3].
- Using a color or power Doppler test, the median nerve's intraneural vascularity was assessed. The presence or absence of the intraneural PD signal was determined [15].
- In the longitudinal plane, the flexor retinaculum was measured at the level of the Hamate hook. Scores for thickened flexor retinaculum of equal to or more than 2 mm were given as present or absent [16].

Ethical approval: The Ethics Committee of Faculty of Medicine, Ain Shams University granted the study approval. All participants signed an informed consent after a thorough explanation of the goals of the study. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analyses

Statistical Package for Social Science version 20 (SPSS-V20) was applied to update, code, tabulate, and import the obtained data into a computer. According to the type of data that was obtained for each parameter, the results were displayed and examined. For non-numerical data, frequency and percentage were utilized and for numerical data, mean ± standard deviation (SD), and range. Using the Student's t-test, quantitative data was compared between two groups. To compare qualitative and quantitative data, the chi-square test was performed. For the purpose of comparing several times in time within the same group, the analysis of variance (ANOVA) test was performed. A p-value ≤ 0.05 was regarded significant.

RESULTS

100 female rheumatoid patients and 100 female h ealthy controls were involved in the study. The control group's age ranged from 35 to 60 years, whereas the rh eumatic group's age ranged from 33 to 57 years. The control group's body mass index (BMI) ranged from 1 9.5 to 27 kg/m^2, whereas the rheumatic group's BMI ranged from 19 to 27.5 kg/m^2.

The RA patients' CTS lasted from 1 to 11 months, but t he RA patients' disease duration ranged from 5 to 17 y ears. In 66 cases, CTS was unilateral, and in 34 patients, it was bilateral. It was determined that 48 patients had mild CTS and 86 had significant CTS. Musculoskeletal ultrasound revealed that 8 patients had bone erosions, 30 patients had elevated PD signal of the median nerve, 40 patients had thickened flexor retinaculum, and 56 patients had tenosynovitis of the flexor tendons (Table 1 and Figures 1, 2, 3 and 4).

Table (1): Clinical and demographic information for RA patients and controls

	Patient			Control
Age (years)	44.68± 6.976			44.88±7.056
BMI (kg/m^2)	23.65±2.497			23.62±2.346
RA Disease duration (years)	10.98±3.288			-
Duration of CTS (months)	7.34±3.052			-
		N	**%**	
Laterality	*Unilateral*	66	66	-
	Bilateral	34	34	
		N	**%**	
NCS	*Mild*	48	35.82	-
	Moderate	86	64.18	
		N	**%**	
Ultrasound Findings	*Tenosynovitis of flexor tendons*	56	41.79	-
	Thickened FR	40	29.85	
	Increased PD of the median nerve	30	22.39	
	Erosions	8	5.97	

BMI: Body Mass Index, RA: Rheumatoid arthritis, SD: Standard duration, CTS: carpal tunnel syndrome, NCS: Nerve conduction study, %: percentage, FR: flexor retinaculum, PD: Power Doppler.

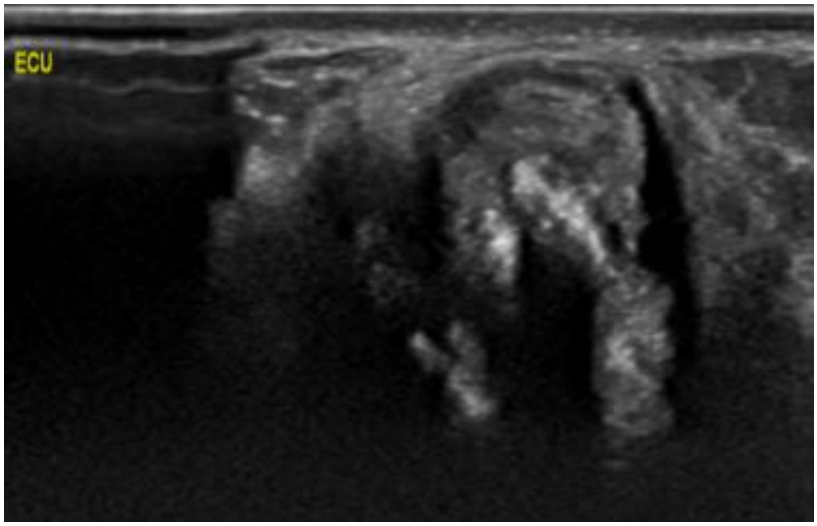

Figure (1): Longitudinal and transverse sections of mild tenosynovitis of flexor tendons

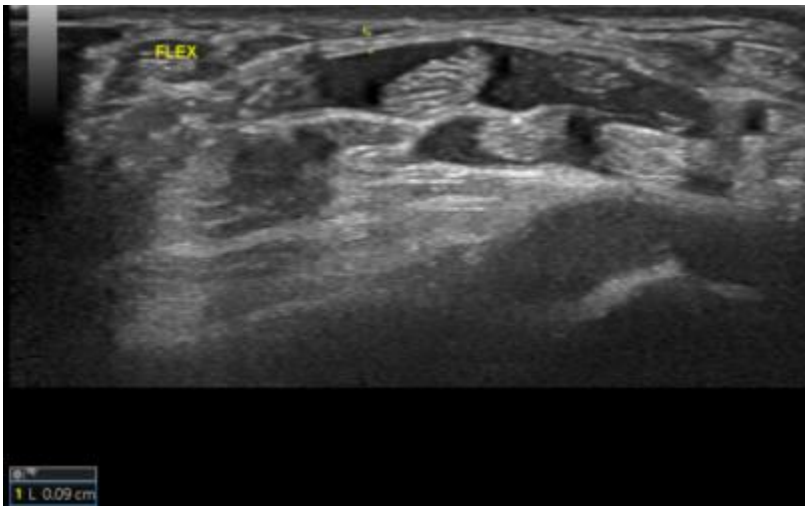

Figure (2): Sonographic measurement of flexor retinaculum (B mode)

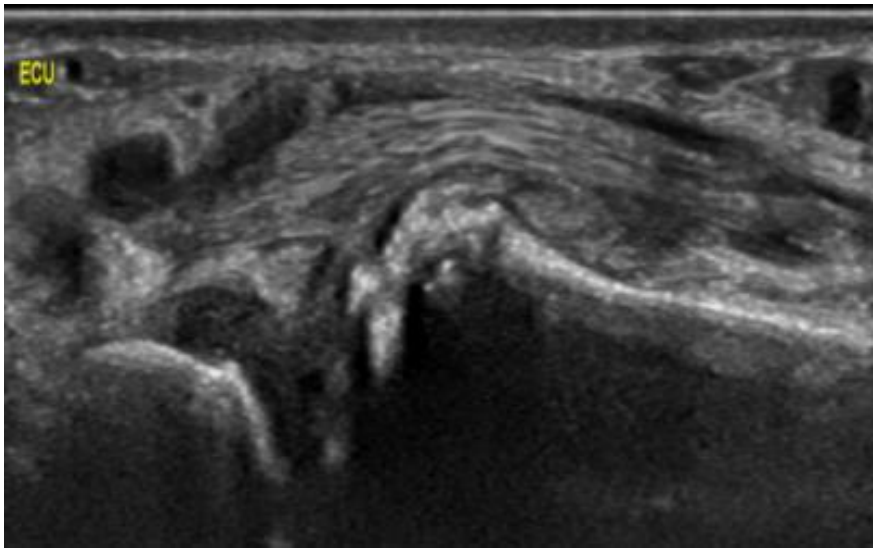

Figure (3): Ulnar styloid process erosions

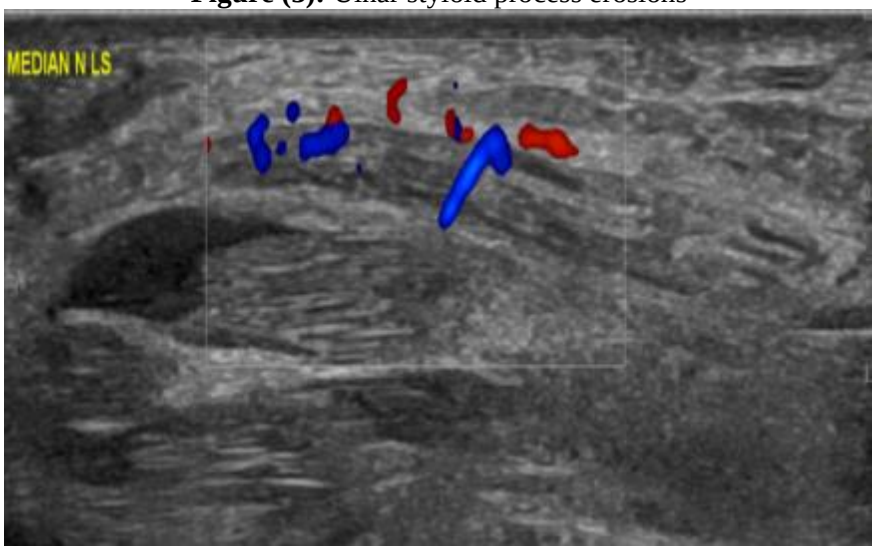

Figure (4): Longitudinal section of the median nerve showed predominant vascularity on color Doppler examination

Age, the length of RA, and the length of CTS all significantly correlated with tenosynovitis of the flexor tendons, as opposed to thicker flexor retinaculum, higher PD signal of the median nerve, and bone erosions. BMI and patients with any of the four illnesses, however, did not have a statistically significant association (Table 2). In patients with RA and CTS, the MSU findings were most strongly correlated with the duration of CTS, according to the linear regression analysis. The longer the duration of CTS, the more likely the patient is to have MSU findings (Table 3). In contrast to the other three conditions, there was a significant correlation between moderate CTS and the presence of flexor tendon tenosynovitis (Table 4).

Table (2): Relation between each of age, BMI, RA duration, CTS duration, and musculoskeletal ultrasound findings

		U/S				ANOVA	
		Tenosynovitis (Flexor)	**Thick Flexor Retinaculum**	**PD of the median nerve**	**Erosion**	**F**	**P**
Age	**Range**	40-57	33-55	33-57	36-43	10.022	<0.001*
	Mean	48.238±5.587	44.000±6.726	40.364±6.987	39.000±3.225		
BMI	**Range**	20-27	19-27.5	19-27.5	21-25.5	0.834	0.478
	Mean	24.024±2.172	23.667±2.346	23.136±3.281	22.833±2.113		
Duration RA	**Range**	7-17	6-14	5-15	5-9	17.866	<0.001*
	Mean	13.000±2.811	10.533±2.432	8.909±2.877	6.667±1.862		
Duration CTS	**Range**	3-11	2-9	1-7	1-5	44.942	<0.001*
	Mean	9.524±2.155	7.467±1.814	4.273±1.956	2.667±1.862		

U/S: ultrasound, PD: Power Doppler, RA: Rheumatoid arthritis, CTS: carpal tunnel syndrome, P-value ≤0.05: Significant (S), * P-value ≤0.01: Highly significant (HS).

Table (3): Regression analysis between age, disease duration, nerve conduction studies and musculoskeletal ultrasound findings

	Unstandardized Coefficients		Standardized Coefficients	t	P
	B	Std. Error	Beta		
Age	-0.027	0.016	-0.201	-1.720	0.089
Duration RA	0.054	0.044	0.190	1.232	0.221
Duration CTS	-0.272	0.043	-0.885	-6.264	<0.001*
NCS	0.227	0.207	0.117	1.098	0.275
Dependent Variable: U/S					

U/S: ultrasound, RA: Rheumatoid arthritis, CTS: carpal tunnel syndrome, NCS: nerve conduction study, P-value ≤0.05: Significant (S), * P-value ≤0.01: Highly significant (HS).

Table (4): Relation between CTS grading and musculoskeletal ultrasound findings

		U/S								Chi-Square	
		Tenosynovitis (Flexor)		Thick Flexor Retinaculum		PD of the median nerve		Erosion			
		N	%	N	%	N	%	N	%	X^2	P-value
NCS	Mild	5	8.93	13	32.5	22	73.33	6	75.00	43.494	<0.001*
	Moderate	51	91.1	27	67.5	8	26.67	2	25.00		

U/S: ultrasound, PD: Power Doppler, NCS: nerve conduction study, * P-value ≤0.01: Highly significant (HS).

DISCUSSION

RA is an autoimmune inflammatory condition that can cause autonomic and entrapment neuropathies [11]. In RA patients, CTS is the most typical upper limb entrapment neuropathy. The median nerve at the wrist is compressed, either acutely or over time [17]. Our study evaluated the most prevalent anatomical cause of CTS in non-clinically deformed RA patients.

The results of **Subasi *et al.*** [18] are consistent with our findings in that there was no discernible age difference between the two groups. Similarly, there was no significant difference in BMI between the two groups, which is in line with **Yagci *et al.*** [19], who emphasized the importance of excluding factors such as obesity that could increase median nerve compression.

Ultrasound allows for accurate visualization of morphological, structural, and perfusional changes associated with RA [3]. In accordance with the findings of **Elsaman *et al.*** [5], who came to our conclusion that tenosynovitis plays a crucial role in the development of CTS in RA patients. Tenosynovitis was found in 42% of our studied hands. Their study found that the depth of the carpal tunnel was diminished due to the presence of tenosynovitis and synovitis, which could be explained by the median nerve's location just superficial to the flexor tendons. They also stated that the carpal tunnel's depth is a more accurate assessment of canal dimension than the median nerve's actual cross-sectional area. The extensor carpi ulnaris and the II, III, and IV fingers are the tendons that are most frequently impacted by the inflammatory process, according to **Bruyn *et al.*** [20].

In our study, 30% of the hands had swollen flexor retinaculum. This is in line with the results of **Bartolome-Villar *et al.*** [21], who demonstrated that RA patients with CTS had thicker flexor retinaculums than controls. **Bartolome-Villar *et al.*** [21] also concluded that CTS is a multifactorial disorder and that thickened flexor retinaculum is not the only causative factor. Intraneural PD signal was also frequent in our study, with 22% of hands showing increased PD signal. This is in line with the findings of **Rahmani *et al.*** [22], who discovered that RA patients with CTS had a considerably greater prevalence of intraneural PD signal. The diagnostic significance of intraneural PD signal, a biomarker of median nerve compression, is currently debatable. Despite, being a clinical feature of RA, bone erosion does not play a significant role in the pathophysiology of CTS in RA patients. Only 6% of the hands in our study suffered from bone erosions. According to **Filippucci *et al.*** [3], the main issue arises when two or more erosions combine to form a single greater erosion, which can make the situation worse.

There was a statistically significant relationship between age and the incidence of tenosynovitis in CTS, which is consistent with the findings of **Hannawi *et al.*** [11] and **Kwang-Hyun Lee *et al.*** [23]. These studies concluded that age is a risk factor for CTS. In RA patients with CTS, there was no statistically significant link between BMI and tenosynovitis. This is consistent with the findings of some studies, which have shown that obesity (BMI > 29) does not affect the pressure in the carpal tunnel. However, other studies have found a correlation between high BMI and slower median nerve conduction. CTS and BMI have a positive linear association, according to **Hannawi *et al.*** [11].

In contrast, **Hammer *et al.*** [24] observed no association between RA patients' height and weight and CTS. They also reported that neither height nor weight should be considered to have a significant influence on evaluating the median nerve in RA patients.

Our study found that the duration of CTS and RA are important factors to consider when evaluating them

for MSU findings and tenosynovitis. This may be attributed to the immunological mechanism of RA, which becomes more severe with long duration of the disease. Compared to the existence of thickened flexor retinaculum, PD signal and bone erosions, tenosynovitis and the occurrence of CTS had a higher statistically significant connection. This is consistent with the findings of **Elsaman *et al.* [5],** who found that tenosynovitis is a major contributor to CTS in RA patients. According to **Smerilli *et al.* [9]**, the most distinctive sonographic hallmark of CTS in RA patients is tenosynovitis, a symptom of synovial tissue inflammation. This is corroborated by the results of our investigation, which showed that tenosynovitis affected 42% of the hands with CTS.

CONCLUSION

It is important to understand that CTS is a common neurological finding in RA. Tenosynovitis and/or joint synovitis are two examples of inflammatory patterns that are seen in the sonographic spectrum of CTS and RA. Tenosynovitis plays a crucial role in the initiation of CTS in RA. To assess the presence of these factors in distinct kinds of CTS, more investigations are necessary.

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Competing interests: Nil.

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