The Egyptian Journal of Hospital Medicine (October 2025) Vol. 101, Page 5221-5230

# Rheumatoid Arthritis and Carpal Tunnel Syndrome: Clinical Characteristics, Evaluation and Relation to Disease Parameters

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## ABSTRACT

**Background:** Carpel tunnel syndrome (CTS) is one of the most prevalent extra-articular manifestations of rheumatoid arthritis (RA). The inflammatory and autoimmune nature of RA can predispose patients to this nerve entrapment neuropathy.

**Objective:** This study aimed to assess the presence and severity of carpel tunnel syndrome (CTS) in a cohort of RA patients and explore its relationship with disease parameters.

**Subjects** and **methods:** The study was conducted on 30 RA patients with clinical suspicion of CTS. Nerve conduction studies (NCS) were performed for the median nerve at wrist. Ultrasonography was used to measure the cross-sectional-area (CSA) and flattening ratio (FR) of median nerve and to assess the presence of local causes of compression.

**Result:** This study included 30 RA patients, the mean age was 43.87± 11.99 years. The ultrasound measured CSA greater than 10 mm² at the wrist showed a statistically significant positive correlation with patient age (r=0.442, p=0.000), RA disease duration (r=0.237, p=0.032), CTS symptoms duration (r=0.363, p=0.004), CRP (r=0.386,p=0.002), RF (r=0.575, p=0.000) and anti-cyclic citrullinated peptide (ACCP) positivity (r=0.707, p=0.000). This assessment also showed a negative correlation with hemoglobin percentage (r=-0.256, p=0.047). CSA at wrist > 10 mm exhibited much higher specificity (85.7%) compared to FR > 3 (14.3%) in positive NCS, and the FR > 3 demonestrated higher sensitivity (78.3%) compared to CSA at wrist > 10 (39.1%).

**Conclusion:** The frequency of CTS in RA patients was found to be higher than that observed in the general population, particularly in individuals with additional risk factors. There was significant relationship between CTS and current RA disease activity. CTS in RA patients was associated with longer disease duration suggesting that CTS is a consequence of the chronic course of RA disease.

**Keywords:** Rheumatoid arthritis, Carpal tunnel syndrome, US.

## INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune disorder characterized by chronic synovial inflammation, progressive joint destruction and extra-articular manifestations including neuropathies. Among these, carpal tunnel syndrome (CTS) is one of the most prevalent entrapment neuropathies with studies reporting a higher incidence in RA patients compared to the general population due to synovial proliferation and tenosynovitis within the carpal tunnel [(1)]. The prevalence of CTS in RA ranges widely depending on disease duration, activity and diagnostic method used [(2)].

CTS manifests clinically with paresthesia, pain, and weakness in the distribution of the median nerve, often leading to significant impairment in daily functioning. These symptoms, however may overlap with generalized RA-related discomfort and joint involvement, posing diagnostic challenges [(3)]. Therefore, accurate assessment and differentiation of CTS in RA patients is crucial for timely intervention and improved outcomes.

The pathophysiology of CTS in RA involves both mechanical compression and inflammatory processes. Inflammatory cytokines contribute to synovial hypertrophy, increasing pressure within the carpal tunnel and compromising median nerve function. Additionally, microvascular ischemia, fibrosis, and autoimmune-mediated nerve damage may also play contributory roles [(4)]. Identifying these mechanisms underscores the importance of utilizing reliable diagnostic modalities in RA-associated CTS.

Nerve conduction studies (NCS) remain the gold standard for CTS diagnosis by assessing the functional integrity of the median nerve. However, NCS has limitations including patient discomfort, operator dependence and inability to visualize anatomical changes. On the other hand, musculoskeletal ultrasound (US) has emerged as a non-invasive, cost-effective modality capable of detecting structural changes such as nerve swelling, measure cross-sectional area (CSA), and flattening ratio at the carpal tunnel inlet [(5)]. Combining functional and morphological assessments offers a comprehensive diagnostic strategy [(6)]. Several studies have explored the diagnostic performance of US versus NCS in CTS, reporting variable sensitivity and specificity depending on cut-off values and patient populations. For RA patients in particular, where inflammation and joint deformities are confounding factors, there is a pressing need to validate these tools in terms of accuracy, disease correlation and practicality [(7)]. Additionally,



Received: 07/05/2025
Accepted: 09/07/2025

understanding whether ultrasound and NCS parameters correlate with clinical features and RA-related indices such as ESR, CRP, RF and ACCP titer can enhance their diagnostic and prognostic utility [8].

This study aimed to investigate the prevalence, laterality, and severity of CTS among RA patients using both ultrasound and NCS as gold standard for diagnosis, and to determine their diagnostic performance in relation to RA disease characteristics and serological markers. By comparing unilateral and bilateral CTS cases, and analyzing associated inflammatory profiles, this research provided evidence for the optimal diagnostic approach to CTS in RA and its clinical implications.

## PATIENTS AND METHODS

This observational cross-sectional study included 30 consecutive rheumatoid arthritis (RA) patients with clinical suspicion of Carpal Tunnel Syndrome (CTS), visiting Ain Shams University Rheumatology department. Patients were diagnosed according to ACR/EULAR 2010 criteria [9].

**Exclusion criteria:** Other rheumatologic disorders (SLE & Spondyloarthropathy), endocrine [Diabetes mellitus & obesity (BMI >30)], hypothyroidism, pregnancy, and neurological disorders with median nerve neuropathy (e.g., polyneuropathy).

Patients underwent detailed history and thorough clinical/musculoskeletal examination, emphasizing CTS symptoms (pain, paresthesia, sensory loss, motor weakness & muscle wasting), age, sex, risk factors and disease duration. Body Mass Index (BMI) was calculated (weight/height$^2$ in kg/m$^2$). RA activity was assessed using DAS28 ESR score (0-9.4) [10].

**Laboratory –work up:** Included complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), kidney and liver function tests, Anti-cyclic citrullinated peptide (A-CCP), and rheumatoid factor (RF IgM).

**Imaging and neurophysiology:** Median nerve ultrasonography was conducted by the first author using an E-zaote MyLab 6 device equipped with a high-frequency linear transducer (6–18 MHz). The cross-sectional area (CSA) of the nerve was measured at the carpal tunnel inlet, with values exceeding 10 mm² considered abnormal.

Additionally, the flattening ratio was assessed at the distal tunnel by calculating the longitudinal-to-transverse diameter ratio, with a ratio > 3 indicating abnormal morphology [11].

Nerve conduction studies (NCS) were performed using the Neuropack S1 (MEB-9400K) system. Both sensory and motor assessments were conducted for the median, radial, and ulnar nerves. Sensory responses were recorded from the index finger (digit 3) for the median nerve and from the thumb for the radial nerve. Motor responses were recorded from the abductor pollicis brevis (APB) for the median nerve and the abductor digiti minimi (ADM) for the ulnar nerve. Stimulations were applied at standard distal and proximal points.

Parameters including distal latency, amplitude, and conduction velocity were automatically generated. Additional comparative tests, such as median–radial antidromic sensory studies and segmental median sensory conduction velocity, were also included in the evaluation [12].

**Ethical approval: The study was approved from The Ethical Committee, Faculty of Medicine, Ain Shams University with ethical committee number of FMASU MSO15/2025. Formal informed consent was obtained from each patient. The study followed the ethical guidelines of Helsinki Declaration.**

### *Statistical analysis*

Data were analyzed using IBM SPSS version 23.0 Quantitative data were presented as mean ± SD/range or median/IQR; qualitative as number/percentages. Chi-square or Fisher exact test (if expected count < 5) compared qualitative groups. Quantitative parametric data used Independent t-test (two groups) or One Way ANOVA with Post Hoc LSD (multiple groups). Non-parametric data used Mann-Whitney test. Spearman correlation assessed quantitative parameters. Receiver Operating Characteristic (ROC) curve determined sensitivity, specificity, PPV, NPV, and accuracy for differentiating hands by NCS. Significance was set at $p \leq 0.05$, with $p \leq 0.01$ indicating high significance.

## RESULTS

The present study included 30 RA patients with a mean age of 43.87 ± 11.99 years. The cohort was predominately females (96.7%). The characteristics of the patients are shown in table (1).

**Table (1):** Characteristics of RA patients

| | | Total no. = 30 |
|---|---|---|
| **Age (years)** | **Mean ± SD** | **43.87 ± 11.99** |
| | **Range** | **25 – 60** |
| **Sex** | **Females** | **29 (96.7%)** |
| | **Males** | **1 (3.3%)** |
| **Weight (kg)** | **Mean ± SD** | **72.87 ± 6.39** |
| | **Range** | **60 – 85** |
| **Height (cm)** | **Mean ± SD** | **161.17 ± 4.77** |
| | **Range** | **154 – 176** |
| **BMI (kg/m$^2$)** | **Mean ± SD** | **27.72 ± 1.92** |
| | **Range** | **21.77 – 30.04** |
| **Duration of symptoms (months)** | **Mean ± SD** | **5.43±2-87** |
| | **Range** | **1-12** |
| **Disease duration of RA (years)** | **Mean ± SD** | **8.63 ± 5.72** |
| | **Range** | **1 – 20** |
| **DAS 28 score** | **Mean± SD** | **5.94 ±1.11** |
| | **Range** | **3.48 – 7.67** |
| | **Moderate activity** | **10 (33.3%)** |
| | **Severe activity** | **20 (66.7%)** |
| **ESR (mm/hour)** | **Mean ± SD** | **54.27 ± 12.55** |
| | **Range** | **33 – 80** |
| **CRP (mg/l)** | **Mean ± SD** | **29.93± 20.61** |
| **RF titre Positive> 14 (Iu/mL)** | **Positive** | **30 (100.0%)** |
| | **Mean ± SD** | **23.83 ± 5.19** |
| **Anti-CCP titre Positive> 20 (IU/ml)** | **Positive** | **16 (53.3%)** |
| | **Mean ± SD** | **26.3 ± 7.3** |
| **Hb (g/dL)** | **Mean ± SD** | **10.32 ± 1.09** |
| **PLT ($10^3$/mm$^3$)** | **Mean ± SD** | **215.60 ± 48.07** |
| **TLC ($10^3$/mm$^3$)** | **Mean ± SD** | **8.77 ± 2.93** |

**BMI:** body mass index, **RA:** rheumatoid arthritis, **DAS 28 score:** Disease Activity Score in 28 joints, **ESR:** Erythrocyte Sedimentation Rate, **CRP:** C - reactive protein, **RF:** Rheumatoid Factor, **Anti-CCP:** Anti-cyclic citrullinated peptide antibodies, **Hb:** Haemoglobin, **PLT:** Platelets, **TLC:** Total leukocyte Count.

All patients had clinical CTS, and 26 patients of them had positive CTS by NCS. Median nerve's clinical presentation, nerve conduction study (NCS) findings, and ultrasound measurements (figures 1 & 2) for 60 hands (30 right & 30 left) are presented in table (2).

**Table (2):** Description of median nerve clinical presentation, NCS findings and ultrasound measurements in 60 hands

| | | | Total | Right | Left |
|---|---|---|---|---|---|
| | | | No. = 60 | No. = 30 | No. = 30 |
| Median Nerve related clinical finding | Duration (months) | Median (IQR) | 3 (2 – 7) | 3.5 (2 – 7) | 3 (2 – 7) |
| | | Range | 1 – 24 | 1 – 12 | 1 – 24 |
| | Pain | Negative | 1(1.7%) | 0 (0.0%) | 1 (3.3%) |
| | | Positive | 59 (98.3%) | 30 (100.0%) | 29 (96.7%) |
| | Parathesia | Negative | 1 (1.7%) | 0 (0.0%) | 1 (3.3%) |
| | | Positive | 59 (98.3%) | 30 (100.0%) | 29 (96.7%) |
| | Sensory loss | Negative | 10 (16.7%) | 5 (16.7%) | 5 (16.7%) |
| | | Positive | 50 (83.3%) | 25 (83.3%) | 25 (83.3%) |
| | Motor weakness | Negative | 51 (85.0%) | 26 (86.7%) | 25 (83.3%) |
| | | Positive | 9 (15.0%) | 4 (13.3%) | 5 (16.7%) |
| | Wasting | Negative | 44 (73.3%) | 23 (76.7%) | 21 (70.0%) |
| | | Positive | 16 (26.7%) | 7 (23.3%) | 9 (30.0%) |
| Ultrasound Findings | CSA at wrist >10 | Mean ± SD | 10.42 ± 4.74 | 11.21 ± 5.41 | 9.63 ± 3.90 |
| | | Range | 3 – 24.2 | 3 – 24.2 | 4 – 21 |
| | | Negative | 40 (66.7%) | 18 (60.0%) | 22 (73.3%) |
| | | Positive | 20 (33.3%) | 12 (40.0%) | 8 (26.7%) |
| | Flattening ratio >3 | Mean ± SD | 4.19 ± 1.57 | 4.46 ± 1.87 | 3.92 ± 1.15 |
| | | Range | 1.52 – 9.67 | 2.32 – 9.67 | 1.52 – 6.25 |
| | | Negative | 12 (20.0%) | 6 (20.0%) | 6 (20.0%) |
| | | Positive | 48 (80.0%) | 24 (80.0%) | 24 (80.0%) |
| | Local causes | Normal | 57 (95.0%) | 28 (93.3%) | 29 (96.7%) |
| | | TS | 2 (3.3%) | 1 (3.3%) | 1 (3.3%) |
| | | Low MTS | 1 (1.7%) | 1 (3.3%) | 0 (0.0%) |
| Nerve conduction study | Motor | Normal | 50 (83.3%) | 25 (83.3%) | 25 (83.3%) |
| | | Mild | 3 (5.0%) | 1 (3.3%) | 2 (6.7%) |
| | | Moderate | 5 (8.3%) | 2 (6.7%) | 3 (10.0%) |
| | | Severe | 2 (3.3%) | 2 (6.7%) | 0 (0.0%) |
| | Sensory | Normal | 14 (23.3%) | 7 (23.3%) | 7 (23.3%) |
| | | Mild | 32 (53.3%) | 15 (50.0%) | 17 (56.7%) |
| | | Moderate | 10 (16.7%) | 5 (16.7%) | 5 (16.7%) |
| | | Severe | 4 (6.7%) | 3 (10.0%) | 1 (3.3%) |

CSA: cross sectional area.

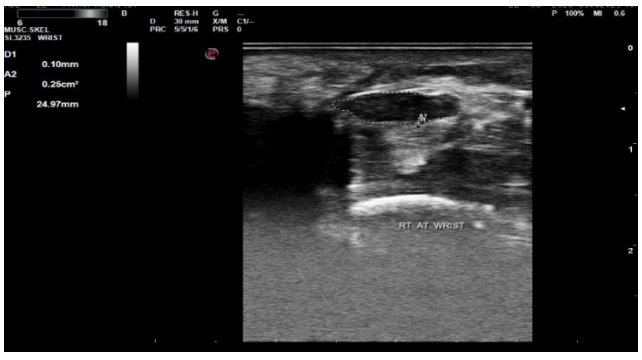


**Figure 1: Rt median nerve surface area measurement by trace at wrist. CSA=25 mm**

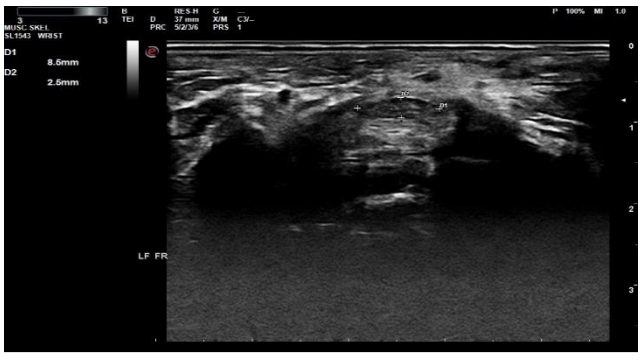


**Figure 2: Lt median nerve flattening ratio at level of hook of hamate (FR= 3.4)**

Comparison of various parameters between RA patients clinically presented with unilateral (10 patient) versus bilateral (20 patients) sensory loss as a manifestation of CTS are listed in table (3). Significant differences were observed in age, with patients experiencing bilateral CTS being older (mean age 47.95 ± 10.46 years) compared to those with unilateral CTS (mean age 35.70 ± 11.02 years) (p=0.006). Disease duration of RA was also significantly longer in the bilateral CTS group (10.20 ± 5.85 years) compared to the unilateral group (5.50 ± 4.09 years) (p=0.031). Regarding sensory NCS, there was a statistically significant difference (p=0.008) where bilateral CTS patients had abnormal sensory NCS results (95.0%) compared to unilateral CTS patients (40.0%), and only RA patients with bilateral CTS by NCS was found to have motor abnormality.

**Table (3):** Comparison between RA patients with unilateral and bilateral clinical CTS

| | | Laterality by sensory loss | | Test value | P-value | Sig. |
|---|---|---|---|---|---|---|
| | | Unilateral | Bilateral | | | |
| | | No. = 10 | No. = 20 | | | |
| Age (years) | Mean±SD<br>Range | 35.70 ± 11.02<br>25 – 60 | 47.95 ± 10.46<br>28 – 60 | -2.973 | 0.006 | HS |
| Height (cm) | Mean ±SD<br>Range | 161.00 ± 3.62<br>155 – 166 | 161.25 ± 5.34<br>154 – 176 | -0.133 | 0.895 | NS |
| Weight (kg) | Mean ±SD<br>Range | 69.90 ± 5.80<br>60 – 80 | 74.35 ± 6.28<br>62 – 85 | -1.875 | 0.071 | NS |
| BMI (kg/m$^2$) | Mean ±SD<br>Range | 26.82 ± 2.31<br>21.77 – 29.3 | 28.18 ± 1.56<br>24.52 – 30.04 | -1.910 | 0.066 | NS |
| Disease duration of RA (years) | Mean ±SD<br>Range | 5.50 ± 4.09<br>1 – 12 | 10.20 ± 5.85<br>2 – 20 | -2.268 | 0.031 | S |
| DAS 28 score | Mean ±SD<br>Range | 5.90 ± 1.30<br>3.48 – 7.67 | 6.34 ±1.12<br>4.16 – 7.6 | 0.96. | 0.344 | NS |
| Activity | Moderate activity<br>High activity | 3 (30.0%)<br>7 (70.0%) | 7 (35.0%)<br>13 (65.0%) | 0.075 | 0.784 | NS |
| Duration of symptoms (months) | Mean ±SD<br>Range | 4.00 3.27<br>1 – 12 | 5.05 3.39<br>1 – 12 | -1.755 | 0.079 | NS |
| ESR (mm/hour) | Mean ±SD<br>Range | 49.10 ± 13.86<br>33 – 76 | 56.85 ± 11.33<br>40 – 80 | -1.640 | 0.112 | NS |
| CRP (mg/l) | Mean SD | 15.9±1.78 | 37± 3.36 | -3.30 | 0.003 | S |
| RF titre positive > 14 (IU/mL) | Positive<br>Mean ±SD | 10 (100.0%)<br>22.60 ± 5.88 | 20 (100.0%)<br>24.45 ± 5.05 | -<br>0.652 | -<br>0.520 | -<br>NS |
| Anti-CCP titre positive > 20 (IU/mL) | Positive<br>Mean ±SD | 3 (30.0%)<br>17.9±4.81 | 13 (65.0%)<br>36.55 ±1.18 | 1.071<br>3.56 | 0.301<br>0.002 | NS<br>S |
| CSA at wrist | Mean ±SD<br>Range | 9.00 ± 6.32<br>3 – 24 | 12.31 ± 4.68<br>5 – 24.2 | -1.622 | 0.116 | NS |
| Flattening ratio | Mean SD<br>Range | 5.62 ± 2.35<br>2.32 – 9.67 | 3.88 ± 1.29<br>2.5 – 7.4 | 2.629 | 0.014 | S |
| Motor | Normal<br>Mild<br>Moderate<br>Severe | 10 (100.0%)<br>0 (0.0%)<br>0 (0.0%)<br>0 (0.0%) | 15 (75.0%)<br>1 (5.0%)<br>2 (10.0%)<br>2 (10.0%) | 3.000 | 0.392 | NS |
| Sensory | Normal<br>Mild<br>Moderate<br>Severe | 6 (60.0%)<br>3 (30.0%)<br>1 (10.0%)<br>0 (0.0%) | 1 (5.0%)<br>12 (60.0%)<br>4 (20.0%)<br>3 (15.0%) | 11.743 | 0.008 | HS |
| Nerve conduction by hand | Negative<br>Positive | 6 (60.0%)<br>4 (40.0%) | 1 (5.0%)<br>19 (95.0%) | 11.273 | 0.001 | HS |

BMI: body mass index, RA: rheumatoid arthritis, DAS 28 score: Disease Activity Score in 28 joints, ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive protein, RF: Rheumatoid Factor, Anti-CCP: Anti-cyclic citrullinated peptide antibodies, Hb: Haemoglobin, CSA: cross sectional area.

Table (4) compared RA patients with unilateral and bilateral carpal tunnel syndrome based on sensory nerve conduction findings by NCS of the 30 RA patients where no significant statistical differences were observed in demographic characteristics (age and BMI), disease activity markers and duration of symptoms between the two groups, with all p-values exceeding 0.05, except for CRP. CRP levels were significantly higher in patients with bilateral CTS by NCS compared to those with unilateral CTS (p=0.021).

**Table (4):** Comparison between RA patients with unilateral and bilateral CTS by NCS

| | | Laterality by sensory NCS | | Test value | P-value | Sig. |
|---|---|---|---|---|---|---|
| | | Unilateral | Bilateral | | | |
| | | No. = 6 | No. = 20 | | | |
| Age (years) | Females<br>Males | 6 (100.0%)<br>0 (0.0%) | 19 (95.0%)<br>1 (5.0%) | 0.312* | 0.576 | NS |
| Height (cm) | Mean±SD<br>Range | 162.33 ± 2.73<br>160 – 166 | 161.00 ± 5.52<br>154 – 176 | 0.566• | 0.577 | NS |
| Weight (kg) | Mean±SD<br>Range | 73.83 ± 6.94<br>68 – 85 | 72.95 ± 6.68<br>60 – 80 | 0.282• | 0.781 | NS |
| BMI (kg/m$^2$) | Mean±SD<br>Range | 27.51 ± 1.67<br>25.71 – 29.8 | 27.80 ± 2.06<br>21.77 – 30.04 | -0.312• | 0.758 | NS |
| Disease duration of RA (years) | Mean±SD<br>Range | 8.00 ± 5.37<br>2 – 15 | 9.50 ± 6.08<br>1 – 20 | -0.542• | 0.593 | NS |
| DAS 28 score | Mean± SD<br>Range | 6.00 ± 1.17<br>3.48– 7.67 | 6.10 ±0.96<br>4.16 – 7.51 | 0.24 | 0.81 | NS |
| Duration of symptoms (months) | Mean± SD<br>Range | 4.5 ±3.02<br>1 – 7 | 5.13±4.3<br>1- 12 | -0.711‡ | 0.477 | NS |
| ESR (mm/hour) | Mean±SD<br>Range | 49.33 ± 11.79<br>33 – 67 | 58.30 ± 11.70<br>40 – 80 | 1.644 | 0.113 | NS |
| CRP (mg/l) | Mean± SD | 18.67±3.91 | 37.9± 2.95 | 3.06 | 0.0057 | HS |
| RF titre positive > 14 (IU/mL) | Positive | 6 (100.0%) | 20 (100.0%) | - | - | - |
| | Mean±SD | 25.00 ± 6.16 | 24.00 ± 7.40 | 0.300• | 0.767 | NS |
| Anti-CCP titre positive > 20 (IU/mL) | Positive | 2 (33.3%) | 14 (70.0%) | 2.622 | 0.105 | NS |
| | Mean±SD | 19.67±13.01 | 31.3±19.22 | -1.62‡ | 0.127 | NS |
| CSA at wrist | Mean±SD<br>Range | 9.83 ± 4.96<br>3 – 16 | 12.46 ± 5.56<br>5 – 24.2 | 1.037• | 0.310 | NS |
| Flattening ratio | Mean±SD<br>Range | 4.67 ± 1.70<br>2.32 – 7.4 | 3.77 ± 1.02<br>2.5 – 6.25 | 1.603 | 0.122 | NS |
| Motor | Normal<br>Mild<br>Moderate<br>Severe | 6 (100.0%)<br>0 (0.0%)<br>0 (0.0%)<br>0 (0.0%) | 14 (70.0%)<br>1 (5.0%)<br>3 (15.0%)<br>2 (10.0%) | 2.340 | 0.505 | NS |
| Sensory | Normal<br>Mild<br>Moderate<br>Severe | 0 (0.0%)<br>5 (83.3%)<br>1 (16.7%)<br>0 (0.0%) | 0 (0.0%)<br>11 (55.0%)<br>6 (30.0%)<br>3 (15.0%) | 1.807 | 0.405 | NS |

**BMI:** body mass index, **RA:** rheumatoid arthritis, **DAS 28 score:** Disease Activity Score in 28 joints, **ESR:** Erythrocyte Sedimentation Rate, **CRP:** C-reactive protein, **RF:** Rheumatoid Factor, **Anti-CCP:** Anti-cyclic citrullinated peptide antibodies, **Hb:** Haemoglobin, **CSA:** cross sectional area.

Table **(**5) presented a comparison between RA patients with negative and positive nerve conduction study (NCS) results concerning various RA-related parameters. Statistically significant differences ($p < 0.05$) were found for duration of symptoms, ESR, CRP, ACCP positivity, Hb (g/dL) and CSA at wrist. Patients with positive NCS results showed higher ESR and CRP levels. Patients with positive NCS showed higher percentage of positive ACCP titre. Additionally, patients with positive NCS exhibited lower Hb levels and larger CSA at the wrist, which is consistent with median nerve involvement.

**Table (5):** Comparison between RA patients with negative NCS and patients with positive NCS regarding RA related parameters

| | | Nerve conduction study | | Test value | P-value | Sig. |
|---|---|---|---|---|---|---|
| | | Negative | Positive | | | |
| | | No. = 4 | No. = 26 | | | |
| Age (years) | Females<br>Males | 4 (100.0%)<br>0 (0.0%) | 25 (96.2%)<br>1 (3.8%) | 0.159* | 0.690 | NS |
| Height (cm) | Mean ± SD<br>Range | 160.25 ± 3.06<br>157 – 164 | 161.31 ± 4.94<br>154 – 176 | -0.585• | 0.561 | NS |
| Weight (kg) | Mean ± SD<br>Range | 71.00 ± 4.60<br>65 – 77 | 73.15 ± 6.55<br>60 – 85 | -0.894• | 0.375 | NS |
| BMI (kg/m2) | Mean ± SD<br>Range | 27.66 ± 1.84<br>24.77 – 29.21 | 27.73 ± 1.93<br>21.77 – 30.04 | -0.097• | 0.923 | NS |
| Duration of symptoms (months) | Mean ± SD<br>Range | 2.5±1.12<br>1-4 | 5.31±3.03<br>1-12 | 2.46 | 0.022 | S |
| Disease duration of RA (years) | Mean ± SD<br>Range | 5.25 ± 3.33<br>2 – 10 | 9.15 ± 5.80<br>1 – 20 | -1.849• | 0.070 | NS |
| DAS 28 score | Mean± SD<br>Range | 6.275± 1.39<br>4.88 – 7.27 | 6.08 ± 1.05<br>4.17 – 7.6 | 0.183 | 0.855 | NS |
| | Moderate activity<br>Severe activity | 1 (25.0%)<br>3 (75.0%) | 9 (34.6%)<br>17 (65.4%) | 0.144 | 0.704 | NS |
| ESR (mm/hour) | Mean ± SD<br>Range | 71.50 ± 7.05<br>33 – 50 | 56.23 ± 12.11<br>33 – 80 | 2.350 | 0.026 | S |
| CRP (mg/l) | Mean ± SD | 7. 25 ±0.96 | 32.22± 1.86 | 5.08 | 0.0005 | HS |
| RF titre positive > 14 (IU/mL) | Positive | 4 (100.0%) | 26 (100.0%) | - | - | - |
| | Mean±SD | 21.25 ± 4.63 | 24.23 ± 5.96 | 1.093• | 0.279 | NS |
| Anti-CCP titre positive > 20 (IU/mL) | Positive | 0 (0.0%) | 16 (61.5%) | 5.275 | 0.022 | S |
| | mean± SD | 9.5 ±2.38 | 34.3 5±7.58 | 4.17 | 0.0003 | HS |
| Hb (g/dL) | Mean ± SD | 11.05 ± 1.27 | 10.21 ± 1.01 | 2.116• | 0.039 | S |
| PLT ($10^3$/$mm^3$) | Mean ± SD | 215.75 ± 28.96 | 215.58 ± 50.13 | 0.009• | 0.992 | NS |
| TLC ($10^3$/$mm^3$) | Mean ± SD | 7.25 ± 1.73 | 9.01 ± 2.73 | -1.614• | 0.112 | NS |
| CSA at wrist | Mean ± SD<br>Range | 8.00 ± 3.68<br>3 – 16 | 11.16 ± 4.82<br>4 – 24.2 | 2.254• | 0.028 | S |
| | < 10<br>> 10 | 12 (85.7%)<br>2 (14.3%) | 28 (60.9%)<br>18 (39.1%) | 2.981* | 0.084 | NS |
| Flattening ratio | Mean ± SD<br>Range | 5.14 ± 2.35<br>1.52 – 9.67 | 3.90 ± 1.12<br>2.32 – 7.4 | 2.724• | 0.009 | HS |
| | < 3<br>> 3 | 2 (14.3%)<br>12 (85.7%) | 10 (21.7%)<br>36 (78.3%) | 0.373* | 0.542 | NS |

BMI: body mass index, RA: rheumatoid arthritis, DAS 28 score: Disease Activity Score in 28 joints, ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive protein, RF: Rheumatoid Factor, Anti-CCP: Anti-cyclic citrullinated peptide antibodies, Hb: Haemoglobin, PLT: Platelets, TLC: Total leukocyte Count, CSA: cross sectional area.

Table (6) illustrated the correlation of cross-sectional area (CSA) at the wrist and flattening ratio by ultrasound with various clinical and laboratory parameters. Significant positive correlations were found between CSA at the wrist and age (r=0.442, p<0.001), disease duration of RA (r=0.278, p=0.032), duration of symptoms (r=0.363, p=0.004), TLC (r=0.336, p=0.009), CRP (r=0.386, p=0.002), RF titre (r=0.575, p<0.001) and ACCP titre (r=0.707, p<0.001). Conversely, a significant negative correlation was observed between CSA at the wrist and Hb (r=-0.258, p=0.047).

**Table (6):** Correlation of CSA &Flattening ratio by ultrasound and different parameters

| | CSA at wrist | | Flattening ratio | |
|---|---|---|---|---|
| | r | P-value | r | P-value |
| **Flattening ratio** | **-0.246** | **0.079** | **-** | **-** |
| **CSA at rest** | **-** | **-** | **-0.246** | **0.079** |
| **Age (years)** | **0.442**** | **0.000** | **-0.160** | **0.222** |
| **Height (cm)** | **-0.266*** | **0.040** | **0.097** | **0.459** |
| **Weight (kg)** | **0.042** | **0.753** | **-0.006** | **0.966** |
| **BMI (kg/m$^2$)** | **0.237** | **0.068** | **-0.064** | **0.626** |
| **Disease duration of RA (years)** | **0.278*** | **0.032** | **0.054** | **0.683** |
| **DAS 28 score** | **0.243** | **0.196** | **0.148** | **0.435** |
| **Duration of symptoms (months)** | **0.363**** | **0.004** | **-0.209** | **0.110** |
| **Hb (g/dL)** | **-0.258*** | **0.047** | **0.325*** | **0.011** |
| **PLT ($10^3$/mm$^3$)** | **-0.188** | **0.151** | **-0.066** | **0.615** |
| **TLC ($10^3$/mm$^3$)** | **0.336**** | **0.009** | **-0.145** | **0.269** |
| **ESR (mm/hour)** | **0.249** | **0.055** | **-0.128** | **0.331** |
| **CRP (mg/l)** | **0.386**** | **0.002** | **-0.305*** | **0.018** |
| **RF titre positive > 14 (IU/mL)** | **0.575**** | **0.000** | **-0.188** | **0.149** |
| **ACCP titre positive> 20 (IU/mL)** | **0.707**** | **0.000** | **-0.161** | **0.220** |

BMI: body mass index, RA: rheumatoid arthritis, DAS 28 score: Disease Activity Score in 28 joints, ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive protein, RF: Rheumatoid Factor, Anti-CCP: Anti-cyclic citrullinated peptide antibodies, Hb: Haemoglobin, PLT: Platelets, TLC: Total leukocyte Count, CSA: cross sectional area.

Table **(**7) evaluated the diagnostic accuracy of CSA at wrist > 10 mm² and flattening ratio > 3 in differentiating between negative and positive hands by nerve conduction study. The flattening ratio > 3 demonstrated higher sensitivity (78.3%) in detecting positive NCS compared to CSA at wrist > 10 mm² (39.1%). However, CSA at wrist > 10 mm² exhibited much higher specificity (85.7%) compared to the flattening ratio > 3 (14.3%). When both CSA and flattening ratio were considered together ("CSA and Flattening"), the sensitivity improved to 89.1%, but the specificity remained low at 14.3%. Overall accuracy was highest when both parameters were combined (71.7%).

**Table (7):** Diagnostic accuracy of CSA at wrist>10 and flattening ratio >3 in differentiation between negative and positive hands by nerve conduction study

| | TP | TN | FP | FN | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|---|---|---|---|
| **CSA at wrist >10** | **18** | **12** | **2** | **28** | **39.1%** | **85.7%** | **90.0%** | **30.0%** | **50.0%** |
| **Flattening ratio >3** | **36** | **2** | **12** | **10** | **78.3%** | **14.3%** | **75.0%** | **16.7%** | **63.33%** |
| **CSA and Flattening** | **41** | **2** | **12** | **5** | **89.1%** | **14.3%** | **77.36%** | **28.6%** | **71.7%** |

CSA: cross sectional area.

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## DISCUSSION

Carpel tunnel syndrome (CTS) in patients with rheumatoid arthritis (RA) represents a multifactorial complication, driven by a complex interplay of mechanical, inflammatory, and immunological mechanisms. In this study, bilateral clinical CTS was the most prevalent clinical presentation, particularly observed among older patients who had a longer duration of RA. This finding is consistent with the work of **George *et al.*** [13], who demonstrated that disease chronicity and cumulative joint pathology significantly elevate the risk for bilateral median nerve compression. The protracted inflammatory process can lead to structural changes within the carpal tunnel that progressively narrow the space, predisposing the nerve to compression.

RA patients with bilateral clinical CTS had NCS-detected motor abnormalities and severe sensory abnormalities, reflecting association between CTS severity and bilaterality. Furthermore, elevated C - reactive protein (CRP) levels and a longer duration of symptoms were significantly associated with bilateral CTS in the patient cohort. These observations are in agreement with **Dede *et al.*** [14] who underscored that the development of CTS in RA is not merely a consequence of local anatomical factors but often reflects the overall systemic inflammatory burden. This systemic inflammation can drive fluid extravasation and edema around the median nerve, contributing to its compression. The findings are also corroborated by **Smerilli *et al.*** [15] who reported that synovial proliferation and chronic tenosynovitis, hallmark features of RA, directly narrow the carpal tunnel and promote compression neuropathy.

The diagnostic performance of ultrasound parameters revealed distinct capabilities with the flattening ratio proving to be more sensitive, while

the cross-sectional area (CSA) was more specific for identifying CTS. These findings align with **Yoshii *et al.*** [16] who reported that synovial proliferation and chronic tenosynovitis, hallmark features of RA, directly narrow the carpal tunnel and promote compression who noted that morphological flattening of the median nerve often occurs in the early stages of compression, making it a valuable marker for early detection. Additionally, the observations are consistent with **Kaya *et al.*** [17] who emphasized that a CSA greater than 10 $mm^2$ is a reliable and specific indicator of significant median nerve pathology. The decision to combine both criteria improved overall diagnostic accuracy, thereby supporting the recommendations of **Hirsiger *et al.*** [18] who advocated for a multimodal approach when evaluating entrapment neuropathies.

In the current cohort, patients with positive nerve conduction study (NCS) results had significantly higher erythrocyte sedimentation rate (ESR), CRP, and anti-citrullinated protein antibody (ACCP) titres. This finding strongly underscores the established relationship between systemic inflammation and peripheral nerve involvement in RA. The results reinforce findings from **Tulbă *et al.*** [19] who showed that ACCP-positive RA patients are at an increased risk for extra-articular and neurologic manifestations. Similarly, the study is in agreement with **Tang *et al.*** [20] who previously found that peripheral neuropathies were more prevalent in seropositive RA patients. They observed positive correlation between CSA and systemic inflammatory markers including CRP, rheumatoid factor (RF) and ACCP, which further supports the pivotal role of systemic inflammation in the pathogenesis of CTS. This finding is consistent with the work of **Dede *et al.*** [14] who similarly documented that nerve swelling observed through ultrasound is significantly associated with the overall inflammatory burden in various autoimmune conditions. An inverse correlation was also observed between hemoglobin and CSA, which may reflect the influence of anemia of chronic disease on peripheral nerve health. This is supported by **Paunikar *et al.*** [21] who reported that lower hemoglobin levels were linked to worsened nerve conduction and an increased risk of neuropathy in RA.

The development of CTS in RA is driven by a two-pronged attack of both localized mechanical compression and systemic immunologic activity. Elevated levels of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) induce fibroblast proliferation, compromise vascular function, and promote perineural fibrosis, all of which cumulatively impair nerve function. This intricate interplay was previously discussed by **Tanaka *et al.*** [22] who emphasized that both mechanical and immunologic mechanisms are crucial contributors to the development of neuropathies in inflammatory arthritis. Carpal tunnel syndrome (CTS) is a prevalent yet under recognized complication in patients with rheumatoid arthritis (RA), closely linked to prolonged disease duration, active systemic inflammation, and seropositivity. In summary, this investigation reaffirms that carpal tunnel syndrome (CTS) in rheumatoid arthritis (RA) is intricately linked to systemic inflammation, disease duration, and seropositivity. The incorporation of a dual-modality diagnostic approach, integrating both nerve conduction studies (NCS) and ultrasound, substantially enhances diagnostic precision by capturing both the functional and anatomical changes associated with the condition. This comprehensive approach should therefore be routinely considered in the clinical evaluation of all RA patients with suspected CTS to ensure accurate and timely management.

## CONCLUSION

CTS is a common, underdiagnosed complication in RA patients, linked to long disease duration, active inflammation and seropositivity. This study highlighted that combining NCS and ultrasound enhances diagnostic accuracy. The flattening ratio is a sensitive indicator, while the cross-sectional area (CSA) is highly specific. The correlation with inflammatory markers suggested that systemic disease burden causes CTS, advocating for routine screening in high-risk RA patients.

## RECOMENDATION

Screening patients with RA complaining of persistent hand pain for CTS by US assessing CSA of median nerve. Proper control of disease activity in RA patients helps to decrease incidence, severity and disability caused by CTS. Repetition of the work using large sample size to assess all other parameters for CTS by US Doppler sign, palmer bowing, wrist/forearm ratio of CSA and motility as diagnostic tools separately and collectively.

## LIMITATION

Investigation was subject to several limitations that may affect the generalizability of its findings. First, the sample size was relatively small, which could reduce the statistical power of the analysis. Furthermore, the absence of a healthy control group made it impossible to directly compare the frequency of carpal tunnel syndrome (CTS) and specific median nerve measurements obtained via ultrasound (US) to a non-diseased population. The study also encountered technical and machine-related limitations that compromised the accuracy of flattening ratio (FR) measurements at the distal carpal tunnel. Methodologically, the cohort was restricted to clinically symptomatic rheumatoid arthritis (RA) patients, thus precluding a random

assessment of both symptomatic and asymptomatic individuals. Lastly, the patient cohort was predominantly composed of individuals with moderate to high disease activity, which may account for the non-significant statistical values observed when comparing these groups.

**Conflict of interest:** The authors declared no conflict of interest.

**Funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## RERERENCES


1. **Sakini R, Abdul-Zehra I, Al-Nimer M (2005)**: Neuropathic manifestations in rheumatoid arthritis: a clinical and electrophysiological assessment in a small sample of Iraqi patients. Ann Saudi Med., 25 (3): 247–49.
2. **Bîrsanu L, Vulpoi G, Cuciureanu D *et al.* (2024)**: Carpal tunnel syndrome related to rheumatic disease (Review). Exp.Ther. Med., 28 (4): 389.
3. **Joshi A, Patel K, Mohamed A *et al.* (2022)**: Carpal tunnel syndrome: pathophysiology and comprehensive guidelines for clinical evaluation and treatment. Cureus, 14 (7): e27053.
4. **Miller L, Hammert W, Rekant M *et al.* (2024)**: Diagnostic accuracy of neuromuscular ultrasound vs. electrodiagnostic studies for carpal tunnel syndrome: systematic review and meta-analysis of paired accuracy studies. Hand (N.Y). Doi: 10.1177/15589447241278972.
5. **Diao E, Nwawka OK, Jablonowski L *et al.* (2022)**: Diagnostic accuracy of ultrasound versus electrodiagnostic studies in carpal tunnel syndrome: A systematic review and meta-analysis. Skeletal Radio., 51 (8): 1401–1412.
6. **El-Maghraby A, Almalki Y, Basha M *et al.* (2024)**: Diagnostic accuracy of integrating ultrasound and shear wave elastography in assessing carpal tunnel syndrome severity: a prospective observational study. Orthop Res Rev., 16: 111–123.
7. **Bayat M, Bagheri Z, Raeissadat S *et al.* (2022):** Diagnostic value of ultrasound for detecting carpal tunnel syndrome in patients with rheumatoid arthritis: a three arm cross sectional study. Ultrasound Med Biol., 48 (7): 1372-1379.
8. **Abd El Rahman H, Badawy F, Haggag A (2024):** Role of high-resolution grey scale and power Doppler ultrasonography in the evaluation of synovial activity of wrist and hand joints in rheumatoid arthritis. Ain Shams Med J., 75 (3): 720–732.
9. **Aletaha D, Neogi T, Silman A *et al.* (2010):** Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis., 62 (9): 1580–8.
10. **Siemons L, Vonkeman H, ten Klooster P *et al.*(2014):** Interchangeability of 28-joint disease activity scores using the erythrocyte sedimentation rate or the C-reactive protein as inflammatory marker. Clin Rheumatol., 33 (6): 783–89.
11. **Mahmoud W, Mansour M, El-Naby H *et al.* (2022):** Carpal tunnel syndrome in rheumatoid arthritis patients: the role of combined ultrasonographic and electrophysiological assessment. Egypt Rheumatol Rehabil., 49: 62.
12. **American Association of Electrodiagnostic Medicine (2002)**: Practice parameter for electrodiagnostic studies in carpal tunnel syndrome. Muscle Nerve., 25 (6): 918–22.
13. **George R, Frechette N, Oviedo M *et al.* (2025):** Carpal tunnel syndrome (CTS) as an early under recognized feature of rheumatoid arthritis (RA): a population-based study of CTS occurrence before and after RA incidence. Arthritis Care & Research, Epub ahead of print. Doi: 10.1002/acr.25566.
14. **Dede B, Oğuz M, Bulut B *et al.* (2023):** Carpal tunnel syndrome evaluation with ultrasound in rheumatoid arthritis patients. ARP Rheumatol., 2 (4): 330–7.
15. **Smerilli G, Di Matteo A, Cipolletta E *et al.* (2021):** Ultrasound assessment of carpal tunnel in rheumatoid arthritis and idiopathic carpal tunnel syndrome. Clin Rheumatol., 40 (3): 1085–92.
16. **Yoshii Y, Zhao C, Amandio P (2020):** Recent advances in ultrasound diagnosis of carpal tunnel syndrome. Diagnostics (Basel), 10 (8): 596.
17. **Kaya Subaşı P, Güler T, Yurdakul F *et al.* (2021):** Carpal tunnel syndrome in patients with rheumatoid arthritis and psoriatic arthritis: an electrophysiological and ultrasonographic study. Rheumatol Int., 41 (2): 361–68.
18. **Hirsiger S, Schlimme N, Rossel J *et al.* (2023):** The inlet and outlet ratio:retrospective and prospective study on an improved diagnostic ultrasound tool for carpal tunnel syndrome. J Hand Surg Glob Online, 5 (3): 303-9.
19. **Tulbă D, Popescu B, Manole E *et al.* (2021):** Immune axonal neuropathies associated with systemic autoimmune rheumatic diseases. Front Pharmacol., 12: 610585.
20. **Tang Z, Liu C, Gao L *et al.* (2022):** Prognostic value of inflammatory biomarkers for surgical outcomes in carpal tunnel syndrome: a systematic review. J Orthop Surg Res., 17 (1): 305.
21. **Paunikar V, Rawekar A, Barapatre S (2023):** Assessment of peripheral nerve conduction in iron-deficiency anemia patients in Indian rural adult population attending a tertiary care hospital. Int J Nutr Pharmacol Neurol Dis., 13 (3): 173–80.
22. **Tanaka Y, Sakaguchi N, Yamanaka H *et al.* (2021):** Cytokine Networks in the Pathogenesis of Rheumatoid Arthritis. International Journal of Molecular Sciences, 22 (20): 10922.