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# On the Severity of Carpal Tunnel Syndrome: Metabolic Syndrome or Obesity

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**Abstract**

**AIM:** This study aimed to determine the relationship between CTS, metabolic syndrome and obesity and to compare the severity of CTS between patients with or without metabolic syndrome (MS) and patients with or without obesity.

**METHODS:** In this prospective study, patients with clinical and electrophysiological confirmed diagnosis of CTS were included. The waist circumference, blood pressure, fasting blood glucose, fasting triglycerides and high/low density lipoprotein cholesterol levels were recorded. Patients were categorized having metabolic syndrome according to Adult Treatment Panel III definition, while body mass index was used to identify obesity.

**RESULTS:** A total of 65 patients with a mean age of 58.91 ± 12.49 years were included. MS was found in 39 (60%) patients and obesity in 27 (41.5%) patients. The CTS was described as mild, moderate and severe in 8, 12 and 19 hands of those with MS and in 2, 6, and 18 of those without MS respectively ($p = 0.207$). There were no statistically significant results observed between BMI and the severity of CTS ($p > 0.05$). The mean waist circumference was 94.75 ± 7.36, 98.78 ± 9.64, 106.42 ± 10.78, 86.41 ± 6.77 for patients with $MS^+O^-$, $MS^-O^+$, $MS^+O^+$ and $MS^-O^-$ respectively ($p < 0.002$).

**CONCLUSION:** CTS appears to be more severe in patients with MS than in patients with obesity. Central obesity is one of the well-known risk factors for CTS, but components of MS may have a greater effect on the severity of CTS.

## Background

Carpal tunnel syndrome (CTS) is the most common upper limb entrapment neuropathy, which ranges from 2.7% to 5.8% in the general population [1]. CTS is more common in women with a male-to-female ratio between 1:3.1 and 1:10.1 [2]. Although its exact cause and pathogenesis are unclear, it is commonly associated with several conditions, such as obesity, hypothyroidism, diabetes mellitus, amyloidosis, and pregnancy [3], [4]. The metabolic syndrome (MS) is referred to the cooccurrence of several known cardiovascular risk factors, including insulin resistance, central obesity, atherogenic dyslipidemia, and hypertension [3]. The first definition attempt was made in 1999 by the World Health Organization (WHO), which proposed that MS may be defined by the presence of insulin resistance or its surrogates. In 2001, the National Cholesterol Education Program Adult Treatment Panel III (NCEP:ATPIII) published a new set of criteria that included waist circumference, blood lipids, blood pressure, and fasting glucose [5]. The previous epidemiological studies have shown that constitutional (obesity and smoking), hormonal, and musculoskeletal risk factors are associated with CTS and recent research indicated that MS plays an important role in CTS [3], [4].

The aim of the present study was to determine the relationship between CTS, MS, and obesity (body mass index [BMI] ≥30 kg/m$^2$). Furthermore, the severity of CTS was compared between patients with or without central obesity and patients with or without MS.

## Methods

### *Participants and data collection*

All patients (n = 65) diagnosed with CTS at the Department of Orthopaedic Surgery in the General Hospital of Katerini from January 2019 to December 2019 were included in the study. They were referred to the electrophysiology laboratory with sensory or motor complaints in the upper limbs. The variables recorded were age, gender, height, weight, BMI, additional comorbidities (diabetes mellitus, hypertension, hypothyroidism, dyslipidemia, cardiovascular disease, nephropathy, etc.), and upper extremities trauma history were documented. Patients who previously received corticosteroid or hormone replacement treatments, had a history of rheumatoid arthritis or wrist fracture were excluded from the study. Patients conforming to polyneuropathy, cervical radiculopathy, and thoracic outlet syndrome as a result of EMG were also excluded from the study. The protocol was reviewed and approved by the Scientific Committee of the General Hospital of Katerini. All participants had signed the written informed consent.

Patients were divided into two groups according to the presence or the absence of MS. According to the NCEP ATP III definition, MS is present if three or more of the following five criteria are met: Waist circumference over 102 cm (males) or 88 cm (females), blood pressure over 130/85 mmHg (or taking anti-hypertension medication), fasting triglyceride (TG) level over 150 mg/dL, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dL (males) or 50 mg/dL (females), and fasting blood sugar over 100 mg/dL [5]. According to the WHO, obesity is a medical condition, which is defined as abnormal or excessive fat accumulation. BMI, which is calculated by dividing the body weight in kilograms by height in meters squared (kg/m$^2$), was used to identify obesity. A person with a BMI of 30 or more is generally considered obese [6].

Nerve conduction studies and electromyography were performed to resolve diagnostic uncertainty and to quantify and stratify disease severity. According to Padua's classification [7], patients were divided into five groups (Table 1). For statistical convenience and significance, we modified this classification into three groups: (a) Minimal to mild CTS (Group I); (b) moderate CTS (Group II); and (c) severe to extremely severe CTS (Group III). The patients were divided into the following four groups according to the presence or absence of MS and/or obesity: (1) Metabolic syndrome only (MS$^+$O$^-$), (2) obesity only (MS$^-$O$^+$), (3) metabolic syndrome and obesity together (MS$^+$O$^+$), and (4) neither metabolic syndrome nor obesity (MS$^-$O$^-$). The demographic characteristics, the severity of CTS according to the electrophysiological findings of the subjects, were analyzed and compared among these four groups.

**Table 1: Neurophysiological classification of CTS**

| Grade | Neurophysiological findings |
|---|---|
| Minimal CTS | "Standard negative" hands with abnormal comparative or segmental (<7 – 8 cm) tests |
| Mild CTS | Slowing of median digit-wrist segment and normal DML |
| Moderate CTS | Slowing of median digit-wrist segment and abnormal DML |
| Severe CTS | Absence of median SNAPS (digit-wrist segment) and abnormal DML |
| Extreme severe CTS | Absence of thenar motor (and sensory) response |

DML: Distal motor latency, SNAPS: Sensory nerve action potentials.

### *Statistical analysis*

Collected data were analyzed with SPSS (Version 24.0). The Kolmogorov–Smirnov test was utilized for normality analysis. Student's t-test and Mann–Whitney U-test were utilized for the comparison of the quantities-continuous variables in our independent samples, for parametric and non-parametric distribution, respectively, in population divided into two categories. The one-way ANOVA test and the Kruskal–Wallis test were utilized for the comparison of the quantities-continuous variables in our independent samples, for parametric and non-parametric distribution, respectively, in population divided into more than 2 categories. Pearson-$\chi^2$ (cross-tabulation) was utilized for the comparison of the categorical variables. The level of significance was set at $p < 0.05$.

## Results

Among the 65 patients included in the study, 16 (24.6 %) were male and 49 (75.4%) were female. The average age was 58.91 ± 12.49 years (56.75 ± 12.28 for females and 65.5 ± 11.03 for males). Unilateral CTS was present in 30 (46.2%) patients, while 35 (53.8%) patients had bilateral CTS. Thirty-nine (60%) of the patients were diagnosed with MS, while 26 (40%) did not meet the diagnostic criteria. There was a statistically significant difference between patients with and without MS and age (62.03 ± 11.57 years vs. 54.23 ± 12.56 years, p = 0.013), while there was no difference between the two genders (females/males: 30/9 vs. 19/7, p = 0.724). Bilateral CTS was present in 22 (56.4%) of the 39 patients with MS and in 13 (50%) of the 26 patients without MS (p = 0.612). The CTS was described as mild, moderate, and severe in 8, 12, and 19 hands of those with MS and in 2, 6, and 18 of those without MS, respectively (p = 0.207) (Table 2). The proportion of patients who had moderate and severe CTS was higher

**Table 2: Age, gender, severity of CTS, and comorbidities in patients with or without MS**

| Variables | All patients | Patients with MS | Patients without MS | p-value* |
|---|---|---|---|---|
| Age | 58.91 ± 12.49 | 62.02 ± 11.57 | 54.23 ± 12.56 | 0.013 |
| Gender (F/M, n) | 16/49, 65 | 9/30, 39 | 7/19, 26 | 0.724 |
| Bilateral CTS (n, %) | 35 (53.8%) | 22 (56.4%) | 13 (50%) | 0.612 |
| Severity of CTS | | | | |
| Mild (n, %) | 10 (15.4%) | 8 (20.5%) | 2 (7.7%) | 0.207 |
| Moderate (n, %) | 18 (27.7%) | 12 (30.8%) | 6 (23.1%) | |
| Severe (n, %) | 37 (56.9%) | 19 (48.7%) | 18 (69.2%) | |
| Comorbidities | | | | |
| Hypertension (n, %) | 34 (52.3%) | 28 (71.8%) | 6 (23.1%) | < 0.001 |
| Dyslipidemia (n, %) | 17 (26.6%) | 17 (43.6%) | | < 0.001 |
| Hypothyroidism (n, %) | 10 (15.4%) | 5 (12.8%) | 5 (19.2%) | 0.483 |
| DM (n, %) | 7 (10.8%) | 6 (15.4%) | 1 (3.8%) | 0.142 |
| CVD (n, %) | 7 (10.8%) | 5 (12.8%) | 2 (7.7%) | 0.513 |
| GERD (n, %) | 3 (4.6%) | | 3 (11.5%) | 0.030 |
| BPH (n, %) | 1 (1.5%) | 1 (2.6%) | | 0.411 |
| Anemia (n, %) | 1 (1.5%) | | 1 (3.8%) | 0.217 |
| Nephropathy (n, %) | 1 (1.5%) | | 1 (3.8%) | 0.217 |

Except where indicated otherwise, the data are mean ± SD. *The threshold for statistical significance was p < 0.05. CTS: Carpal tunnel syndrome, MS: Metabolic syndrome, F: Female, M: Male, DM: Diabetes mellitus, CVD: Cardiovascular disease, BPH: Benign prostate hyperplasia, GERD: Gastroesophageal reflux disease.

in those with MS than in those without (*p* = 0.160). A majority (69.2%) of patients, with or without MS, had at least one comorbidity, with hypertension being the most common 1 (52.3%), followed by dyslipidemia (26.6%), hypothyroidism (15.4%), diabetes mellitus (10.8%), and cardiovascular disease (10.8%) (Table 2).

Based on the BMI, there were 7 patients (10.8%) with normal weight (BMI: less than 25), 31 patients (47.7%) were overweight (BMI: 25–29.9), and 27 patients (41.5%) were obese (BMI: 30 and higher). In the first category, there was one patient with mild CTS, one patient with moderate CTS, and five patients with severe CTS. In the overweight category, there were 6 patients with mild CTS, 9 patients with moderate CTS, and 16 patients with severe CTS. In the patients with BMI of 30 and higher, there were 3 patients with mild CTS, 8 patients with moderate CTS, and 16 patients with severe CTS. There were no statistically significant difference observed between BMI and the severity of CTS (p > 0.05) (Figure 1).

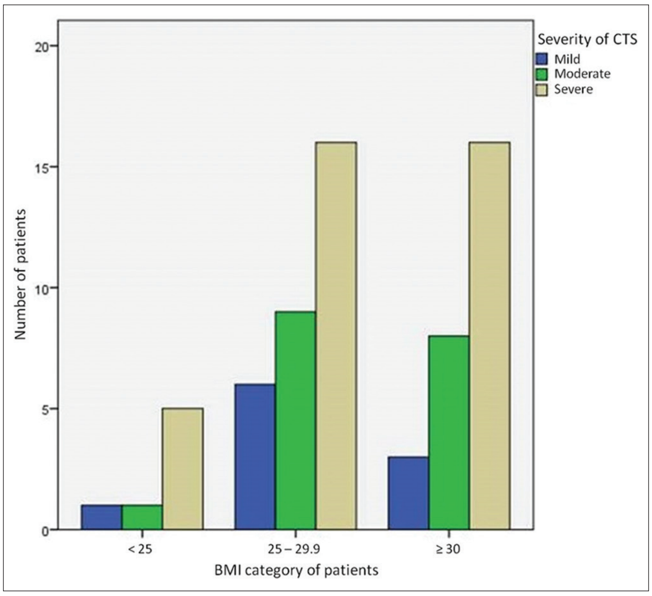


*Figure 1: Stratification of body mass index based on the severity of carpal tunnel syndrome*

Stratification of the patients according to the presence/absence of MS/obesity yielded the following CTS patient distribution: $MS^+O^-$, n = 4; $MS^-O^+$, n = 14; $MS^+O^+$, n = 35; and $MS^-O^-$, n = 12. Comparison of the electrophysiological findings of these four patient groups revealed that the severity of CTS was worse in $MS^-O^+$ patients than in $MS^+O^-$ patients (p = 0.369). The severity of CTS was worse in $MS^+O^+$ patients than in $MS^+O^-$, $MS^-O^+$, and $MS^-O^-$ patients (p = 0.265). The electrophysiological findings in the four groups and the relationships between them are listed in Table 3.

**Table 3: Severity of carpal tunnel syndrome according to the presence/absence of metabolic syndrome and/or obesity**

| Group | Mild, n (%) | Moderate, n (%) | Severe, n (%) | p value* |
|---|---|---|---|---|
| $MS^+O^-$ | 1 (25) | 2 (50) | 1 (25) | 0.510 |
| $MS^-O^+$ | 2 (14.3) | 3 (21.4) | 9 (64.3) | |
| $MS^+O^+$ | 7 (20) | 10 (28.6) | 18 (51.4) | |
| $MS^-O^-$ | 0 (0) | 3 (25) | 9 (75) | |

*The threshold for statistical significance was p < 0.05. $MS^+O^-$: CTS patients with metabolic syndrome only, $MS^-O^+$: CTS patients with obesity only, $MS^+O^+$: CTS patients with both metabolic syndrome and obesity, $MS^-O^-$: CTS patients with neither metabolic syndrome nor obesity; MS: Metabolic syndrome, O: Obesity.

The occurrence of abdominal obesity, hypertension, hyperglycemia, and dyslipidemia (hypertriglyceridemia, high serum LDL, low serum HDL, and high serum cholesterol) was compared among the four groups (Table 4). The waist circumferences in the $MS^+O^-$, $MS^-O^+$, $MS^+O^+$, and $MS^-O^-$ groups were 94.75 ± 7.36, 98.79 ± 9.64, 106.42 ± 10.78, and 86.41 ± 6.78 cm, respectively (p < 0.001) (Table 4). The mean waist circumference of the $MS^+O^-$ group was lower than in the $MS^-O^+$ group (p = 0.670) and $MS^+O^+$ group (p = 0.015). The frequencies of hypertension in the $MS^+O^-$, $MS^-O^+$, $MS^+O^+$, and $MS^-O^-$ groups were 100%, 35.7%, 91.4%, and 66.7%, respectively (p = 0.123). The frequency of hypertension was lower in the $MS^-O^+$ group than in the other three groups (p < 0.001). The frequencies of dyslipidemia in the $MS^+O^-$ and $MS^+O^+$ groups were 75% and 40%, respectively (p = 0.001). The frequencies of diabetes mellitus in the $MS^+O^+$ and $MS^-O^-$ groups were 17.1% and 8.3%, respectively (p < 0.001).

## Discussion

Carpal tunnel syndrome is the most common entrapment neuropathy with a prevalence of 2.7–5.8 in the general population [1], [8]. Clinical studies have shown that MS was found to be approximately 3 times more common in patients with CTS, while CTS was found to be more severe in patients with MS [9], [10]. A possible reason why CTS is more common in MS is that MS is a condition driven by inflammation with a variety of biomarkers and cell types are emerged as significant mediators of this inflammation. Mast cells in subcutaneous adipose tissue seem to play a crucial role

**Table 4: Body mass index, presence of hypertension, dyslipidemia, hyperglycemia, and waist circumference in the carpal tunnel syndrome patients stratified according to the presence/absence of metabolic syndrome and/or obesity**

| Variables | $MS^+O^-$ | $MS^-O^+$ | $MS^+O^+$ | $MS^-O^-$ | p-value* |
|---|---|---|---|---|---|
| BMI (kg/m²) | 26.4 ± 1.28 | 29.17 ± 2.7 | 32.24 ± 5.39 | 24.92 ± 2.78 | < 0.001 |
| SBP (mmHg) | 148.75 ± 17.42 | 132.78 ± 19.53 | 145.42 ± 15.5 | 139.5 ± 20.89 | 0.123 |
| DBP (mmHg) | 87.75 ± 14.75 | 82.28 ± 12.07 | 87.68 ± 11.59 | 87.66 ± 10.78 | 0.366 |
| TG (mg/dL) | 175.25 ± 38.9 | 106.64 ± 40.53 | 145.14 ± 51.85 | 93.08 ± 25.6 | 0.001 |
| HDL (mg/dL) | 42.15 ± 6.51 | 63.57 ± 13.36 | 56.05 ± 19.5 | 63.1 ± 17.45 | 0.017 |
| LDL (mg/dL) | 125.3 ± 36.52 | 134.56 ± 18.32 | 110.47 ± 31.85 | 109.19 ± 25.62 | 0.045 |
| Cholesterone (mg/dL) | 202.5 ± 42.58 | 219.42 ± 26.34 | 198.28 ± 36.54 | 190.75 ± 37.34 | 0.179 |
| Glucose (mg/dL) | 129 ± 14.25 | 91.6 ± 8.76 | 123.57 ± 45.11 | 106.66 ± 36.01 | < 0.001 |
| Waist circumference (cm) | 94.75 ± 7.36 | 98.78 ± 9.64 | 106.42 ± 10.78 | 86.41 ± 6.77 | < 0.001 |

*The threshold for statistical significance was p < 0.05. $MS^+O^-$: CTS patients with metabolic syndrome only, $MS^-O^+$: CTS patients with obesity only, $MS^+O^+$: CTS patients with both metabolic syndrome and obesity, $MS^-O^-$: CTS patients with neither metabolic syndrome nor obesity, MS: Metabolic syndrome, O: Obesity, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, TG: Triglyceride, HDL: High-density lipoprotein, LDL: Low-density lipoprotein.

in promotion both of inflammation and fibrosis around and within the median nerve resulting in the inhibition of nerve gliding [5], [9], [11].

The present study analyzed the impact of MS and obesity on the severity of CTS and evaluated the association between MS with or without obese people and CTS. The rate of MS in patients with CTS has been found to be between 48% and 75% in the previous studies [9], [10]. These reported different prevalence rates of MS in the patients with CTS may be the result of genetic factors, environmental/occupational conditions, the different age of the studied populations, and the lifestyle of the populations concerned. In agreement with these findings [9], [10], in the present study, MS was also found in 60% of patients with CTS with a mean age of 62.03 ± 11.57 years. CTS was also more severe in the patients with MS than in those without. Nowadays, MS is a major public health problem and is characterized by abdominal obesity, hypertension, dyslipidemia, and hyperglycemia [5].

Female patients and patients aged between 40 and 60 years are more likely to develop CTS. One study involved 107 patients with CTS (mean age 53.9 ± 8.9), of whom 89.7% were female [10]. Yurdakul *et al*. included 200 patients with CTS (mean age 51.61 ± 11.86), of whom 140 (70%) were female [9]. In a descriptive cross-sectional study of 112 patients with a mean age of 54 ± 5 years, 65% were female [11]. Similar to these findings, 49 (75.4%) of the patients in the present study were female.

Previously, Werner *et al*. reported that only 16% of individuals with a BMI below 20 kg/m$^2$ had CTS compared with 39% of individuals with BMI of 29 kg/m$^2$ and higher [12]. They reported that CTS patients are 2 times more likely to be obese than slender ones and female patients are 2 times more likely to be obese. Nordstrom *et al*. demonstrated that a weight gain of about six pounds increased the risk of developing CTS by 8% [13]. This trend was also observed in the patients of the present study, while 42.5% of the patients had a BMI of ≥30 kg/m$^2$. Female patients were also 3 times more likely to be obese than male patients. We also identified a relationship between severity of CTS and obese population, with the highest BMI in patients with severe CTS. In another study by Kouyoumdjian *et al*., they studied the influence of higher BMI in the severity of CTS and found that CTS had a significant correlation with higher BMI when compared to control subjects [14].

Hyperglycemia, obesity, and dyslipidemia, which are the components of MS, have been proposed as possible risk factors for CTS [3]. In the present study, comparisons between patients with or without MS and obesity revealed significantly higher waist circumference in patients with $MS^+O^+$. Moreover, lipid profile including HDL and serum TG was significantly different in those with $MS^+O^-$ compared to those with $MS^-O^+$. Hyperglycemia was significantly higher in patients with $MS^+O^-$ compared to $MS^-O^+$ patients. El Gharieb *et al*. recruited 103 female patients of CTS with a mean age between 31 and 42 years (according to the severity of CTS) and found mean triglycerides levels 159.02 ± 53.7 mg/dL, mean LDL cholesterol levels 140.45 ± 47.74 mg/dL, and mean HDL cholesterol levels 54.34 ± 8.62 mg/dL [15]. In the present study, the patients' mean triglycerides levels were elevated 175.25 ± 38.9 mg/dL and their mean LDL/HDL cholesterol levels were lower 125.3 ± 36.52/56.05 ± 19.5 mg/dL. These differences could be due to differences in ethnicity, geographic distribution, dietary habits, and/or lifestyle modifications.

In the current study, a significant association was detected between hypertension, dyslipidemia, and cardiovascular diseases and the development of CTS. High percentages of patients with CTS had one or more of these diseases. These findings might be explained by the reported high rates of CTS among the studied population. In accordance with this, Alotaibi *et al*. reported higher incidence (36.4%) of hypertension in CTS patients compared to control group [16]. In addition, Sharief *et al*. demonstrated hypertension in 25% and dyslipidemia 24% of patients who were diagnosed with CTS [17]. Küçükakkas and Yurdakul demonstrated that among patients with CTS, 14% had hypertension [18].

The present study has some limitations. First, this was a public hospital-based study conducted on patients of specific socioeconomic status having a different clinical and risk factor profile, so these results cannot be applied to the general population. Second, the number of cases is small, thus the need of more studies with larger samples is needed to confirm and improve precision of the results.

## Conclusion

Despite the small number of included patients with CTS, the results of the present study suggest that CTS appears to be more severe in patients with MS than patients with obesity. Central obesity is one of the well-known risk factors for CTS, but components of MS may have a greater effect on the severity of CTS. However, further research with larger samples is needed to enforce these results.

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