

Is The Visceral Adiposity Index an Indicator of Carpal Tunnel Syndrome?

Visseral Adipozite İndeksi Karpal Tünel Sendromu İçin Bir Gösterge midir?

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Abstract

Introduction: Carpal tunnel syndrome (CTS) is the most common peripheral focal mononeuropathy caused by compression of the median nerve in the carpal tunnel.

Objective: We aimed to investigate inflammation parameters, body mass index (BMI), visceral adiposity index (VAI), and their relationship with disease severity in patients diagnosed with CTS in our study.

Method: This prospective study included 147 patients with CTS and 85 healthy volunteers. We grouped the patients by CTS severity as severe, moderate, or mild based on electroneuromyography findings. We recorded demographic characteristics and the test results of complete blood count and inflammation parameters and calculated BMI and VAI for the subjects included in the study.

Results: Of the patients with CTS, 78.9% were women and 26.5% had severe disease. C-reactive protein (CRP), triglycerides, the neutrophil-lymphocyte ratio (NLR), waist circumference, and VAI were statistically significantly higher in the CTS group compared to the control group ($p<0.05$). CRP, NLR, BMI, VAI, and the proportion of obese individuals were statistically significantly higher in the severe CTS group compared to the moderate and mild CTS groups ($p<0.05$).

Conclusion: We showed that VAI, waist circumference, CRP, and NLR were higher in CTS patients compared to the control group. The high values of VAI and NLR in patients with CTS and severe CTS indicate that these parameters are useful markers to demonstrate the risk of developing CTS and predict prognosis.

Keywords: Carpal Tunnel Syndrome, Visceral Adiposity Index, Neutrophil-Lymphocyte Ratio.

Özet

Giriş: Karpal tünel sendromu (KTS), median sinirin karpal tünel içinde sıkışması ile oluşan ve en sık görülen periferik fokal mononöropatidir.

Amaç: Çalışmamızda KTS tanısı alan hastalarda, inflamasyon parametrelerini, vücut kitle indeksi (VKİ), visceral adiposite indeksi (VAİ) değerlerini ve hastalık şiddeti ile ilişkilerini araştırmayı amaçladık.

Yöntem: Bu prospektif çalışma KTS tanısı alan 147 hasta ve 85 sağlıklı gönüllü ile yapıldı. Elektroneuromiyografi sonuçlarına göre KTS şiddeti ağır, orta ve hafif olarak sınıflandırıldı. Hastaların demografik özellikleri, hemogram, inflamasyon değerleri kayıt edildi ve VKİ, VAİ ölçümleri hesaplandı.

Bulgular: KTS tanılı hastaların %78,9'u kadındı ve %26,5'nin şiddeti ağırdı. KTS tanısı alan hastaların C reactive protein (CRP), neutrophil lymphocyte ratio (NLO), trigliserid, bel çevresi, VAİ düzeyleri kontrol grubundan istatistiksel olarak anlamlı derecede daha fazlaydı ($p<0,05$). KTS şiddeti ağır olanlarda CRP, NLO, VKİ, VAİ ve obezite oranları, orta ve hafif olanlardan istatistiksel olarak anlamlı derecede daha fazla bulundu ($p<0,05$).

Sonuç: VAİ, bel çevresi, CRP, NLO oranlarının KTS'li hastalarda kontrol grubuna göre daha yüksek oranda olduğunu gösterdik. KTS tanılı hastalarda ve şiddeti ağır olanlarda VAİ ve NLR gibi göstergelerin yüksek olması, bu parametrelerin KTS geliştirme riski ve prognozu göstermede yararlı belirteçler olduklarını göstermektedir.

Anahtar Kelimeler: Karpal Tünel Sendromu, Visseral Adipozite İndeksi, Nötrofil Lenfosit Oranı.

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INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common peripheral focal mononeuropathy caused by compression of the median nerve in the carpal tunnel. The highest incidence of CTS is in the age range of 40-60 years and the disease is more common in women (1). CTS impairs hand function, reduces grip strength, and causes numbness, pain, and tingling in the areas innervated by the median nerve. The most common causes include a history of repetitive wrist movements, genetic predisposition, pregnancy, rheumatoid inflammation, and obesity (2).

Recent studies have reported that a high body mass index (BMI) and hypercholesterolemia are the risk factors for the development of CTS (3). Central fat accumulation in obesity is associated with metabolic syndromes, which may result in peripheral neuropathy. Moreover, it is suggested that adipose tissue accumulation in the carpal tunnel in obese individuals results in narrowing and increased pressure inside the carpal tunnel (4). The examinations of the biopsy specimens of patients with CTS have revealed inflammatory and proliferative changes leading to tendon degeneration and hypertrophy of the synovial tissue (5). The roles of immune dysfunction, oxidative stress, and chronic inflammation were previously described in obesity. Adipose tissue inflammation has been shown to be the cause of complications, affecting distant organ functions adversely (6). Thus, in addition to adipose tissue accumulation, it is suggested that many interrelated inflammatory, vascular, and oxidative factors take part in the etiology of CTS (5).

Obesity is a risk factor for many diseases, but it has been reported that the distribution pattern of adipose tissue is more important than the total amount for the development of vascular complications (7). The visceral adiposity index (VAI) is currently a commonly used parameter, which includes not only anthropometric measurements but also high-density lipoprotein (HDL) and triglyceride (TG) levels, indicating abdominal fat distribution and adipose tissue function (8). To the best of our knowledge, the relationship between VAI and CTS was not investigated previously in the literature. In our study, we aimed to investigate the relationship between complete blood count, inflammation parameters, BMI, VAI, and disease severity in patients with CTS.

METHOD

This prospective study was approved by Ankara Şehir Hastanesi Ethics Committee (E2-22-2957). All procedures were carried out in accordance with the principles of the Declaration of Helsinki. Informed consent forms were obtained from all subjects, who agreed to participate in the study. The study included 147 patients, who were admitted to the neurology outpatient clinic of our hospital, and who were diagnosed with CTS based on clinical and electroneuromyography (ENMG) examination findings. Eighty-five healthy subjects, who were admitted to the outpatient clinics for routine check-up examinations, and who had no diagnosis of any disease, were included as the control group in the study. Patients with a history of medication use or diabetes mellitus, rheumatoid disease, hypertension, immune deficiency, acute or chronic inflammatory disease, diseases of the heart or lung, hematologic diseases, or oncologic diseases were not included. Subjects with chronic alcohol use, pregnant women, and individuals diagnosed with polyneuropathy, radiculopathy/plexopathy or ulnar neuropathy based on electrodiagnostic test findings were excluded. The control group included subjects with no medication use and no history of systemic disease or recent infection.

We recorded demographic characteristics, complete blood count, and C-reactive protein levels of all patients and subjects. We calculated the neutrophil-lymphocyte ratio (NLR) by dividing

the neutrophil count by the lymphocyte count. We calculated BMI as the subject's weight in kilograms divided by the square of height in meters. We grouped subjects with a BMI value of ≥ 30 kg/m² under the obese category (9). The equation for VAI calculation included waist circumference in cm, and HDL and TG levels in mmol/L. We used the following equations to calculate VAI for men and women, respectively (10):

- For men: $VAI = \text{waist circumference} / (39.68 + (1.88 \times \text{BMI})) \times (\text{TG} / 1.03) \times (1.31 / \text{HDL})$
- For women: $VAI = \text{waist circumference} / (36.58 + (1.89 \times \text{BMI})) \times (\text{TG} / 0.81) \times (1.52 / \text{HDL})$

Electrophysiologic Examinations

We used the Nicolet EDX device for electrophysiological examinations. We maintained the limb skin temperatures of subjects in the range of 31-36°C. We carried out the electrophysiologic examinations by using standard nerve conduction techniques in accordance with the protocol recommended by the American Electrodiagnostic Medical Association (11). We examined both of the upper limbs of the patients in this study. We examined the median and ulnar nerve conduction in one extremity, but we examined median nerve conduction and ignored ulnar nerve conduction in the other.

We studied median motor nerve conduction by standard techniques, using a surface electrode placed in the center of the abductor pollicis brevis muscle and stimulating the wrist and the antecubital fossa. We measured the combined muscle action potential amplitude and the distal motor latency and calculated the motor conduction velocity. We orthodromically measured mixed nerve conduction from the palm and sensory nerve conduction from the second finger. In addition, we measured the sensory latency, sensory nerve action potential, and sensory nerve conduction velocity. We recorded the results and grouped patients under three categories based on the findings from electrophysiological examinations as follows (12):

Mild CTS: A slow median sensory nerve conduction velocity (< 50 m/s from palm/wrist and digit II segments)

Moderate CTS: A prolonged distal latency of the median motor nerve (> 4.0 ms) and a slow median sensory nerve conduction velocity

Severe CTS: Prolonged motor and sensory distal latencies, a significant reduction in the motor conduction velocity, and a reduced/absent median nerve sensory action potential amplitude

Statistical Analysis

We performed the statistical analysis by using the IBM SPSS Statistics 26 program. We used descriptive statistics (mean \pm SD) and frequency distributions for numerical and categorical variables, respectively. To select statistical analysis tests for numerical variables, we used the Kolmogorov-Smirnov normality test. Because the test results showed that the variables did not conform to the normality assumption, we used non-parametric tests. We used the Mann-Whitney U Test to check whether there was a difference in variables between two independent groups. We used the Kruskal-Wallis test to examine differences in variables between more than two independent groups. We examined relationships between two independent categorical variables by chi-square analysis. We took statistical significance as 0.05 in the statistical analysis.

RESULTS

Out of the 176 CTS patients examined during the study period, we included 147 patients in the statistical analysis (Fig. 1).

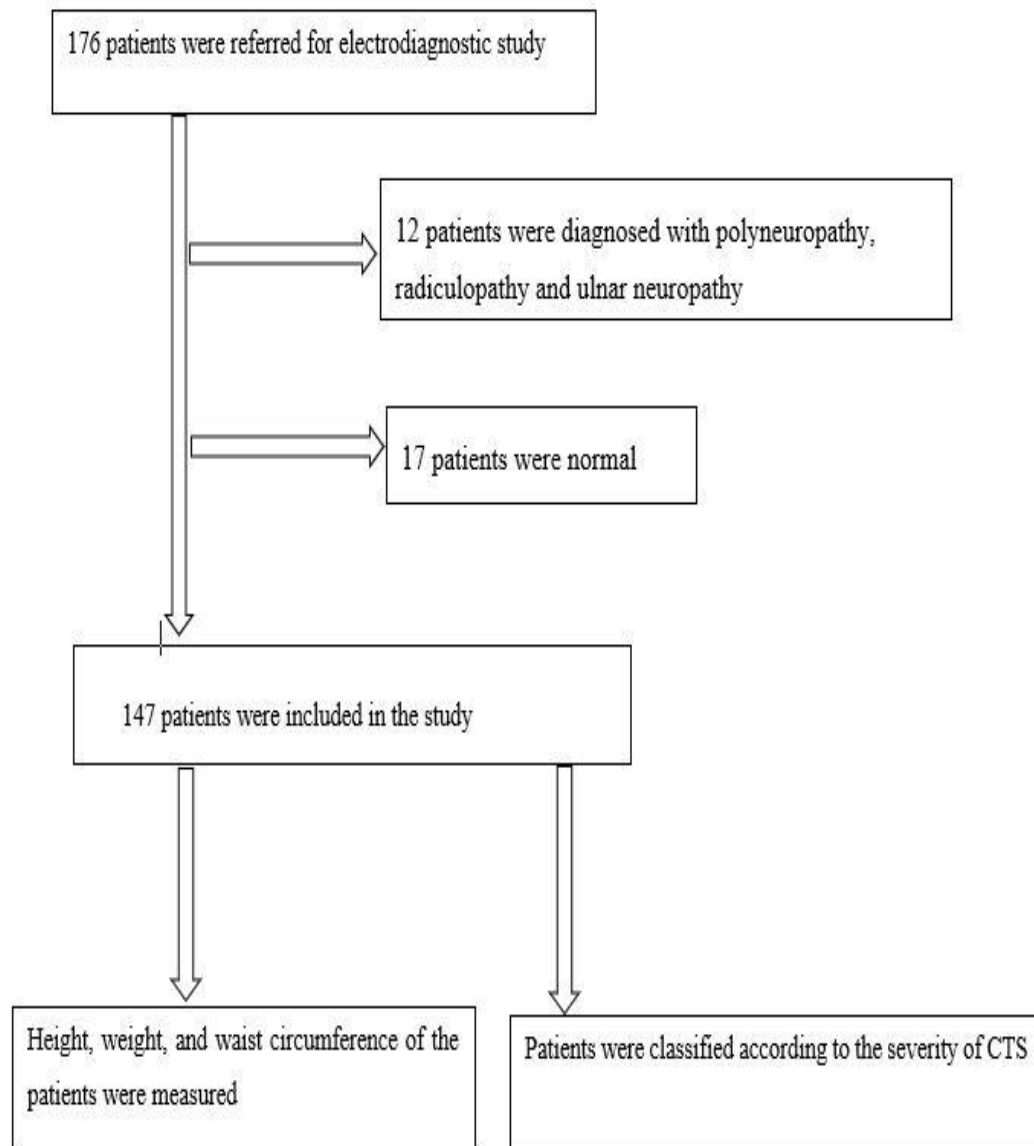


Figure 1. Case Selection Criteria

The mean age was 47.90 ± 8.87 years and there was a female preponderance in the group of CTS patients. Based on ENMG findings, CTS severity was mild in 36.1%, moderate in 37.4%, and severe in 26.5% of the patients (Table 1).

Table 1. Demographic Characteristics of Patients by Groups

| | CTS (n=147) n(%) | Control (n=85) n(%) | Chi-square | p |
|---------------------|---------------------|------------------------|------------|----------|
| Gender | | | 1.521 | 0.217 |
| Female | 116(78.9) | 61(71.8) | | |
| Male | 31(21.1) | 24(28.2) | | |
| CTS Severity | | | - | - |
| Severe | 39(26.5) | | | |
| Moderate | 55(37.4) | | | |
| Mild | 53(36.1) | | | |
| | Mean±SD | Mean±SD | U | p |
| Age | 47.90±8.87 | 45.68±10.22 | 9189.5 | 0.147 |

U: Mann Whitney U, *:p<0.05, CTS: Carpal Tunnel Syndrome.

The Mann-Whitney U tests showed statistically significantly higher values of CRP, NLR, TG, waist circumference, VAI, and counts of neutrophils in CTS patients compared to the control group (p<0.05). BMI and the percentage of obese subjects were not statistically significantly different between the groups (p>0.05) (Table 2).

Table 2. Biochemical Test Results and Differences by Groups

| | CTS (n=147) Mean±SD | Control (n=85) Mean±SD | U | p |
|---------------------------------|------------------------|---------------------------|-------------------|-------------------|
| WBC(×10³ µl) | 7.04±1.56 | 6.88±1.70 | 5745.0 | 0.308 |
| PLT(×10³ µl) | 260.88±57.09 | 254.27±56.28 | 5947.0 | 0.542 |
| LYM(×10³ µl) | 2.35±0.63 | 2.93±3.72 | 5352.5 | 0.069 |
| NEU (×10³ µl) | 4.16±1.13 | 3.70±1.11 | 4745.0 | 0.002* |
| CRP(mg/l) | 0.31±0.33 | 0.17±0.19 | 3709.0 | <0.001* |
| NLR | 1.88±0.67 | 1.54±0.59 | 4466.0 | <0.001* |
| TG(mg/dl) | 161.68±78.76 | 134.20±64.22 | 5003.0 | 0.012* |
| HDL(mg/dl) | 49.60±11.73 | 52.28±11.84 | 5388.5 | 0.081 |
| WC | 97.42±10.41 | 92.89±9.36 | 4816.5 | 0.004* |
| BMI | 25.34±4.39 | 24.20±3.85 | 5415.5 | 0.091 |
| VAI | 6.96±4.96 | 5.42±4.41 | 4694.0 | 0.002* |
| | n(%) | n(%) | Chi-square | p |
| BMI | | | | |
| Obese | 120(81.6) | 76(89.4) | 2.486 | 0.115 |
| Nonobese | 27(18.4) | 9(10.6) | | |

U: Mann Whitney U, *:p<0.05, WBC: White blood cell, PLT: Platelets, LYM: Lymphocytes, NEU: Neutrophils, CRP: C-reactive protein, NLR: Neutrophil/lymphocyte ratio, TG: Triglyceride, HDL: High-density lipoprotein, WC: Waist circumference, BMI: Body mass index, VAI: Visceral adiposity index.

CRP, NLR, TG, waist circumference, BMI, and VAI were statistically significantly higher in severe CTS patients compared to the patients of the mild and moderate severity groups (p<0.05))The percentage of obese patients was significantly higher in the severe CTS group compared to the CTS groups of mild and moderate severity (p<0.001) (Table 3).

Table 3. Relationship Between CTS Severity and Parameters

| | Mild (n=53) | Moderate (n=55) | Severe (n=39) | KW | p |
|----------------------------------|----------------|--------------------|------------------|------------|--------------------------|
| | Mean±SD | Mean±SD | Mean±SD | | |
| WBC($\times 10^3 \mu\text{l}$) | 6.90±1.30 | 7.17±1.62 | 7.05±1.80 | 1.524 | 0.467 |
| PLT($\times 10^3 \mu\text{l}$) | 260.45±57.29 | 258.29±63.86 | 265.10±46.98 | 1.840 | 0.398 |
| LYM($\times 10^3 \mu\text{l}$) | | 2.44±0.74 | 2.35±0.57 | 1.368 | 0.505 |
| NEU($\times 10^3 \mu\text{l}$) | 4.02±1.08 | 4.14±1.22 | 4.40±1.06 | 2.709 | 0.258 |
| CRP(mg/l) | 0.24±0.22 | 0.23±0.17 | 0.53±0.51 | 23.805 | <0.001* Dif: 3>1,2 |
| NLR | 1.88±0.67 | 1.81±0.69 | 1.98±0.64 | 2.202 | 0.332 |
| TG(mg/dl) | 143.47±62.68 | 135.22±71.23 | 223.74±76.28 | 32.187 | <0.001* Dif: 3>1,2 |
| HDL(mg/dl) | 51.81±12.10 | 52.15±11.41 | 43.00±9.08 | 19.254 | <0.001* Dif: 3<1,2 |
| WC | 95.57±7.97 | 93.73±9.44 | 105.15±10.83 | 31.123 | <0.001* Dif: 3>1,2 |
| BMI | 24.82±3.63 | 23.67±4.11 | 28.40±4.25 | 26.152 | <0.001* Dif: 3>1,2 |
| VAI | 5.66±3.78 | 5.36±3.68 | 11.00±5.74 | 35.476 | <0.001* Dif: 3>1,2 |
| | n(%) | n(%) | n(%) | Chi-square | p |
| BMI | | | | | |
| Obese | 5(9.4) | 4(7.3) | 18(46.2) | 27.419 | <0.001* |
| Nonobese | 48(90.6) | 51(92.7) | 21(53.8) | | |

KW:Kruskal Wallis, Dif.:Difference, *:p<0.05 WBC: White blood cell, PLT: Platelets, LYM: Lymphocytes, NEU: Neutrophils, CRP: C-reactive protein, NLR: Neutrophil/lymphocyte ratio, TG: Triglyceride, HDL: High-density lipoprotein, WC: Waist circumference, BMI: Body mass index, VAI: Visceral adiposity index.

DISCUSSION

The incidence of CTS is 1-5% in the general population and it is a common cause of disability resulting in high costs to society (13). CTS is characterized by tingling, numbness, and night pain in the areas innervated by the median nerve, including the radial half of the ring finger, and the palmar segments of the thumb and of the index and middle fingers (14). Of the CTS patients included in our study, 78.9% were women and the mean age was 47.90±8.87 years. CTS was mild in 36.1%, moderate in 37.4%, and severe in 26.5% of the patients included in this study.

Obesity and excessive weight gain are significant health issues globally. These conditions have been increasingly recognized as chronic diseases with growing prevalence rates recently (15). Several epidemiologic studies reported a relationship between obesity and CTS (16). The underlying pathophysiology of this relationship includes dyslipidemia, metabolic syndrome, oxidative and inflammatory mechanisms, central fat accumulation, fat accumulation around the wrist, and the direct compression of the median nerve (17). Yeo et al. examined the lipid profiles of patients by the severity of CTS and reported a positive

correlation between CTS severity and TG levels (18). However, Razavi et al. found no relationship between CTS severity, obesity, and lipid profiles in a cross-sectional study (19). In our study, we found significantly higher TG levels in CTS patients compared to the control group. Moreover, TG levels were significantly higher in the severe CTS group compared to the CTS groups of mild and moderate severity in our study. Moghtaderi et al. reported significantly high mean values of BMI and waist circumference in patients with CTS (20). In another study, Kurt et al. showed the relationship between high BMI and CTS severity (21). In our study, BMI values and the percentage of obese individuals in the CTS group were not significantly different compared to the control group. However, when we compared CTS patients by disease severity, we found that BMI and the percentage of obese individuals were significantly higher in the severe CTS group compared to the CTS groups of mild and moderate severity. We suggest that this finding is associated with fat accumulation and increased pressure in the carpal tunnel due to high BMI, which augments CTS severity.

VAI is closely associated with many metabolic conditions and has been a commonly used parameter in recent years, presenting a higher predictive value for obesity and helping distinguish between visceral and subcutaneous fat (22). In our study, we found significantly increased VAI and waist circumference in patients with CTS. VAI and waist circumference were significantly higher in patients with severe CTS compared to patients with mild and moderate CTS. Consistent with the findings in our study, Mondelli et al. previously showed that a high waist circumference increased the risk of CTS (23). However, in the literature, we could not find studies, which investigated the relationship between VAI and CTS. Significantly high VAI in the overall patient group and the severe CTS group in our study shows that VAI is an important indicator, which can be used for the diagnosis and the prediction of prognosis in CTS.

Metabolic disorders in the organism such as immune dysfunction, oxidative stress, and chronic low-grade inflammation were previously demonstrated in overweight individuals (24). Histological studies on the carpal tunnel revealed increased vascular permeability, intraneural fibrosis, and tenosynovitis in flexor tendons (13). NLR is one of the potential indicators of subclinical systemic inflammation and has gained frequent use in recent years (25). The study by Güneş et al. showed that increased CTS severity was associated with high NLR (26). Consistently, we found significantly higher NLR and CRP values in severe CTS patients compared to patients with mild and moderate CTS in our study. We suggest that NLR and CRP values in our study have indicated systemic inflammation, which takes part in the etiology of CTS.

CONCLUSION

This study showed that VAI, waist circumference, CRP, and NLR were higher in CTS patients compared to the control group. VAI, BMI, CRP, and NLR, and the percentage of obese individuals were higher in the severe CTS group compared to the CTS groups of mild and moderate severity. Indicators such as VAI and NLR are high in CTS patients and those with severe CTS, indicating that these parameters are useful markers to predict the risk and prognosis of CTS.

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