Asymptomatic carpal tunnel syndrome in obese and overweight patients with metabolic syndrome

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Carpal tunnel syndrome (CTS) is the most frequent type of compressive neuropathy. It results from the entrapment of the median nerve at the level of the carpal tunnel. The most important independent risk factors are female gender, obesity, square wrists, rheumatoid arthritis, diabetes, wrist fracture, and hypothyroidism.[1] The diagnosis of CTS is based on a collection of clinical symptoms and signs including pain and numbness in the territory of the median nerve in the hand, and electrophysiological findings. The clinical significance of asymptomatic electrophysiological (E)-CTS is its ability to change into the symptomatic type due to the vulnerability of the median nerve. Balci and Utku[2] reported that metabolic syndrome is 3 times more prevalent in patients with CTS, and CTS is more severe when compared with cases without metabolic syndrome. Azizi et al[3] reported that the unadjusted prevalence of metabolic syndrome in their study was 30% in Iran. There are different definitions for metabolic syndrome, however, it was reported by the WHO in 1999 for the first time. A European group developed a modified version in the same year, but 2 years later the United States National Cholesterol Education Program Adult Treatment Panel (ATP-III) reported simple criteria for defining metabolic syndrome and a revised version was reported in 2005.[4] The aim of this study is to investigate the frequency of asymptomatic E-CTS among obese and overweight patients with metabolic syndrome and compare the severity of CTS in those groups of an Iranian population.

Patient selection. After obtaining institutional ethics committee approval, we conducted a case-control study from June 2010 to November 2011 at the Zahedan University of Medical Sciences, Zahedan, Iran. We studied a local population in the southeastern province of Iran. Eighty patients with functional pain and a confirmed diagnosis of obese metabolic syndrome (body mass index [BMI] >30), and 59 cases with functional pain and overweight metabolic syndrome (BMI: 25-30) entered into the study consecutively. The diagnosis of metabolic syndrome was based on a revised version of the ATP-III, which was released by the International Diabetes Federation in 2005.[4] Patients with functional pain did not have clinical criteria for referred, radicular or mechanical pain. In this situation, patients did not complain of any radiation from the neck or any neural (median or ulnar) territory pain; however, nonspecific musculoskeletal complaints were occasional. Patients with osteoarthritis, disc herniation, fractures and radiculopathies were not included in the study. Routine neurological and rheumatological examinations did not reveal any abnormal findings. The researcher explained the nature of the work, and after obtaining informed consent for the study, the examiner filled out a questionnaire on the demographic characteristics of the participants such as age, gender, occupation, any associated disorder like pregnancy, diabetes, trauma, and fractured wrists. The patients had no history or clinical signs suggesting systemic disease, and no clinical and/or electrophysiological signs suggesting pathological conditions such as polyneuropathy, radiculopathy, weakness or atrophy of muscles or previous median nerve surgery.

Electrophysiological study. The diagnosis of E-CTS was based on previously validated electrodiagnostic criteria according to the American Academy of Neurology (AAN) consisting of neurographic evidence of slowing of distal median nerve conduction. One of the researchers carried out all electrodiagnostic studies with a Medtronic-Keypoint® 4 apparatus (Medtronic A/S, Skovlunde, Denmark) on subjects lying on a bed in a quiet and warm room. All studies were carried out in the same room and in similar temperature using a surface temperature recorder. All nerve stimulations were delivered with a constant current standard bipolar surface stimulator (cathode distal). The sweep speed was set at 2 ms/division and the recording of the median nerve compound muscle action potential (CMAP) was performed using a standard bar electrode supplied by the equipment, which was placed on the thenar muscle at a distance of 8 cm from the stimulator. The CMAP for the median nerve had been measured from the baseline to the negative peak. The interelectrode distance (between active and reference electrodes) was 4 cm. Supramaximal stimulation was used for motor conduction studies, while up to 50 mA stimulation intensity was delivered for sensory nerves. The obtained sensory responses were averaged. Maximum antidromic sensory conduction

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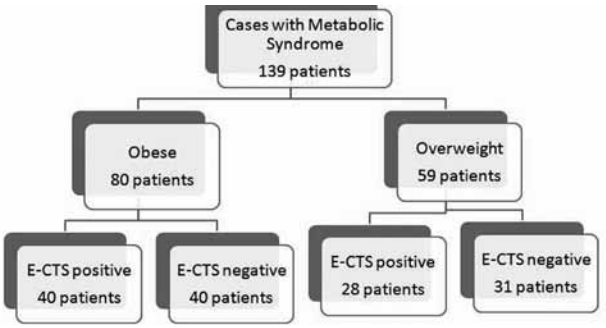

Figure 1 - Trial profile showing how Iranian patients with metabolic syndrome and electrophysiological carpal tunnel syndrome (E-CTS) were entered into the study.

velocity (SCV) and maximum sensory action potential amplitude (SAP) were determined. The mean values of distal latencies, conduction velocities, and amplitudes were calculated for motor and sensory branches of the median nerve. Normal reference values for age and gender were based on a previous local population study of healthy subjects in this region. Distal and peak latencies for sensory branches of the median nerve in CTS and non-CTS patients were measured.

Statistical analysis. After an evaluation of the assumption of normal distribution by using the Statistical Package for Social Sciences software for Windows, version 15 (SPSS Inc., Chicago, IL, USA), arithmetic mean values and standard deviations (SD) of the data were calculated. Then we carried out an unpaired 2-sample t-test and chi-squared test comparing age and gender between overweight and obese groups. A 2-sided significance level of 0.05 was used.

We studied a total of 139 patients (120 females), aged between 22-60 years (mean: 44.4 years); 80 patients had a BMI of more than 30, and the remaining 59 cases (42.4%) had BMI between 25-30 (**Figure 1**). Although the female/male ratio in this study was too high (more than 6 times); we did not find any significant difference between the 2 groups of overweight and obese female cases (p=0.239). Only one hand (painful hand) from each patient was analyzed. Seventy-one patients (51.1%) did not have E-CTS, in which 31 had BMI score less than 30, and 40 cases had a BMI score more than 30. Chi-squared analysis between obese and overweight patients with metabolic syndrome according to presence or absence of asymptomatic E-CTS did not reveal any significant difference (p=0.45). One hundred and 2 patients had hypertension (73.3%). The other defining parameters were compared in the 2 groups. The means of age, 46.6±8.9 years for overweight (confidence interval [CI] 95%: 44.3-48.9) and 44.9±9.3 years for obese patients (CI 95%: 40.7-44.9) (p=0.107), height, 159.1±8.0 cm for overweight (CI 95%: 157.0-161.2) and 157.3±8.7 cm for obese cases (CI 95%: 153.3-159.2) (p=0.206), high-density lipoprotein (HDL)-cholesterol, 41.0±8.4 mg/dL for overweight (CI 95%: 38.8-43.3) and 40.7±10.0 mg/dL for obese patients (CI 95%: 38.4-42.9) (p=0.252), low-density lipoprotein cholesterol, 131.4±37.3 mg/dL for overweight (CI 95%: 121.7-141.1), and 131.9±30.4 mg/dL for obese patients (CI 95%: 121.2-138.9) (p=0.926) and triglycerides (TG), 211.7±88.7 mg/dL for overweight (CI 95%: 188.6-234.9), and 191.5±74.8 mg/dL for obese patients (CI 95%: 174.9-208.2) (p=0.159) were found not to be significant in the 2 groups. However, means of weight, 70.4±7.9 kg for overweight (CI 95%: 68.3-72.4) and 85.0±10.8 kg for obese patients (CI 95%: 82.6-87.4) (p<0.001), waist circumference, 95.6±7.5 cm for overweight (CI 95%: 92.7-96.6) and 103.9±8.4 cm for obese patients (CI 95%: 102.0-105.7) (p<0.001) and fasting blood sugar, 144.0±70.7 mg/dL for overweight (CI 95%: 125.6-162.5) and 117.8±45.9 mg/dL for obese patients (CI 95%: 107.7-128.1) (p=0.009) were found to be significant.

According to the nerve conduction studies, 30 (21.6%) patients had mild, and 38 (27.3%) patients had moderate to severe CTS. Seventy-one cases did not have CTS. Thirteen patients from the mild CTS group, 15 from the moderate, and 31 cases from the last group were included in the overweight patients, and

Table 1 - Comparison of the conduction parameters of the median nerve in overweight and obese Iranian patients with electrophysiological carpal tunnel syndrome.

Variable	Overweight patients	Obese patient	*P*-value
Median nerve distal latency-sensory (msec)	3.59±1.02	3.75±1.26	0.36
Median nerve peak latency-sensory (msec)	4.20±1.21	4.32±1.01	0.31
Median nerve peak amplitude-sensory (mV)	11.15±3.15	10.15±4.23	0.11
Median nerve distal latency-motor (msec)	4.69±1.09	4.75±1.73	0.10
Median nerve conduction velocity-motor (m/sec)	59.36±10.03	57.65±12.36	0.31

the remaining patients were obese. Electrophysiological studies did not reveal CTS in 31 cases of the overweight group, and 40 patients of the obese group (p=0.909). We did not find any significant difference between the 2 genders according to BMI (p=0.454). Comparing conduction parameters of the median nerve in overweight and obese patients with CTS did not show any statistically important difference (**Table 1**).

Increased distal latency of the median nerve is the main diagnostic feature of CTS. In patients without any objective clinical findings such as pain and/or numbness the term asymptomatic E-CTS may be used. Although they do not present typical symptoms, their neurophysiologic presentation is the same as typical symptomatic CTS. Increased carpal tunnel pressure due to obesity, squaring of the wrist, mechanical factors (jobs involving the hands), and biochemical changes in the synovial tissue are the main pathophysiological mechanisms of CTS. Werner et al[5] in their study on 949 patients reported that those individuals who were classified as obese were 2.5 times more likely than slender individuals (BMI <20) to be diagnosed with CTS. Forty-three percent of obese women and 32% of obese men had the diagnosis of CTS compared with 21% of slender women and zero percent of slender men.

In the present study, the authors examined the presence of asymptomatic E-CTS in 2 groups of overweight and obese patients according to BMI. There is a scarcity of studies that have evaluated the association between asymptomatic E-CTS and metabolic syndrome in the above-mentioned groups. Previous studies have shown that the most important risk factors of CTS are increased BMI, female gender, and increased carpal tunnel pressure due to certain jobs. The frequency of asymptomatic E-CTS was higher in women, but it was not significantly associated with obesity.

Metabolic syndrome is defined as a cluster of metabolic risk factors that come together in a person. These factors include abdominal obesity, dyslipidemia, hyperglycemia, and hypertension. According to the ATP-III criteria, metabolic syndrome has 5 major features in which obesity; high TG level, and an increased level of blood glucose are those characteristics causing increased BMI; in which, obesity is the main feature. The age adjusted prevalence rate of metabolic syndrome in adults more than 20 years is around 23-24%. Obesity is the most important risk factor for the rising prevalence of metabolic syndrome. Azizi et al[3] reported that the unadjusted prevalence of metabolic syndrome in Iran was 30%, and the age-standardized prevalence was 33.7%. The prevalence increased with age in both genders, and it is more common in women than in men. The prevalence is high in Middle Eastern countries such as Iran and Turkey, but with a large excess in females, resulting in a significant public health problem. The HDL cholesterol may be low, and it is one of the most reported metabolic abnormalities in both genders. Overall, 36.6% of men and 35.9% of women were overweight; 11.2% of men and 28.1% of women were obese. It was reported that 45% of Iranian premenopausal women in the central region of Iran had metabolic syndrome. Azizi has also shown that low HDL cholesterol was the most prevalent risk factor among men and women. Although asymptomatic E-CTS is more common in diabetic patients; being present in 22-29%. It is prevalent in urban populations, and may be due to the high content of fat in that carpal canal that may increase pressure in the canal and may play an important role as a risk factor for E-CTS.

The growing number of the obese patients, especially with diabetes, plays an important role in the increasing prevalence of CTS patients. It is estimated that 14% of patients without diabetes and 30% of those with diabetic peripheral neuropathy show symptoms of CTS. It has been postulated that a diabetic nerve is more vulnerable to extraneural pressure and more susceptible to entrapment. A combination of mechanical trauma and ischemic injury to the median nerve has been proposed. Diabetic peripheral neuropathy may aggravate the ischemic injury to the median nerve. The degree of median nerve recovery after carpal tunnel release in diabetics is less than their normal counterparts. Metabolic syndrome may lead to diabetes in a high proportion of patients. It has been found that around 25% of diabetic patients had asymptomatic CTS, but further studies revealed a lower prevalence of the disease. Symptomatic CTS has a better correlation with metabolic syndrome and it has been reported that 75% of patients with CTS are affected with metabolic syndrome.[2] However, in our study we found that metabolic syndrome is not an independent risk factor for asymptomatic E-CTS in obese and overweight patients. One should keep in mind that a possible limitation of such a study is that it was performed in a referral center and probably does not show the characteristics of the general population.

In summary, the present investigation did not confirm any positive effect of metabolic syndrome as a prerequisite for asymptomatic E-CTS, and the risk of developing asymptomatic CTS is the same in both groups of obese or overweight patients with metabolic syndrome.

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