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Carpal tunnel syndrome and prediabetes: Is there a true association?

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ABSTRACT

Background: Carpal tunnel syndrome (CTS) is probably associated with diabetes mellitus, but its link to prediabetes (PD) is unknown.
Objective: To determine prevalence of PD and others risk factors in CTS.
Methods: A cross-sectional study including 115 idiopathic CTS patients and 115 age-, gender-and body mass index (BMI)-matched controls was performed. Clinical, laboratory and neurophysiological evaluations were conducted in all subjects to confirm CTS diagnosis. CTS severity was graded on a standardized neurophysiological scale. PD was defined using strict criteria.
Results: The prevalence of PD was similar in CTS and control groups (27% vs. 21.7%, respectively $P = 0.44$). Nocturnal symptoms (91.3%) and moderate CTS (58.3%) were most frequently observed in CTS patients. In logistic regression analysis, PD was significantly correlated with age (odds ratio [OR] 1.05, 95% confidence interval [CI] 1.01–1.09; $P = 0.006$) and BMI (OR 1.08. 95% CI 1.01–1.16; $P = 0.026$), but not with CTS (OR 0.82, 95% CI 0.43–1.53; $P = 0.537$). CTS patients with PD had a significantly higher mean age compared to those without PD (53.8 ± 10.2 vs. 49.5 ± 8.6 years, respectively $P = 0.027$). The frequency of age >60 years was significantly higher in CTS with PD than in CTS without PD (29.0% vs. 8.3%, respectively $P = 0.04$) as was BMI >30 kg/m^2 (64.5% vs. 33.3%, respectively $P = 0.03$). No significant differences were observed between the two CTS groups with respect to gender, BMI, symptoms, and neurophysiological severity of CTS.
Conclusions: Our findings indicated that CTS is not associated with PD, but that PD is closely linked to age and overweight.

1. Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy and has a wide spectrum of severity [1]. Although broadly recognized, its etiology remains unclear because idiopathic CTS is the most common diagnosis in patients with this condition [2]. Despite this observation, diabetes mellitus (DM) is probably linked to CTS since electrophysiologically proven CTS is identified in up to one-third of DM patients [3]. Conversely, it has been demonstrated that CTS patients have a threefold risk of DM compared to normal controls [4].

Prediabetes (PD) is an intermediate stage where plasma glucose falls between normal levels and those of type 2 DM, and can be identified by detecting impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) [5]. PD is an important risk factor for the development of type 2 DM, micro and macrovascular involvement [6].

Previous studies have demonstrated the association of peripheral neuropathies with PD [7,8]. However, there is no definitive evidence that CTS is also linked to PD since only two studies have addressed this issue [9,10].

Hence, this is the first study specifically designed to determine the prevalence of PD and its associated risk factors in CTS patients and compare the date to those of healthy controls matched for age, gender, and body mass index (BMI).

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2. Patients and methods

2.1. Patients

One hundred sixty-two consecutive CTS patients who were regularly followed at the Outpatient Clinic of Rheumatology of Hospital Getúlio Vargas da Universidade Estadual do Piauí and at one private clinic of Rheumatology in Teresina – Piauí, Brazil were evaluated between January 2010 and February 2012. The inclusion criterion was age 25–74 years. Exclusion criteria were DM, hypothyroidism, pregnancy, rheumatoid arthritis, wrist fracture, peripheral neuropathy, cervical radiculopathy, CTS release, having an occupation associated with the development of CTS [11,12], and having conditions or taking drugs that potentially influence blood glucose levels. CTS diagnosis was made according to characteristics symptoms and distal conduction delay of the median nerve [13].

This cross-sectional study had included 115 patients with idiopathic CTS after the exclusion of 47 patients. One hundred and fifteen healthy individuals paired by age, gender and body mass index (BMI) were selected for the control group after evaluating 1136 subjects in the community. Controls were recruited by advertising in schools and hospitals during a six months period. All volunteers with current or previous upper limbs symptoms were excluded. Clinical and neurophysiological evaluations were negative for CTS diagnosis in all controls. This study was approved by the Local Ethics Committee and written informed consent was obtained from all subjects.

2.2. Study protocol

All participants underwent a standard protocol that included a clinical examination, interview, and laboratory and neurophysiological evaluation. Demographic and anthropometric data were recorded. BMI was calculated as weight divided by the square of height (kg/m^2).

2.3. Clinical CTS diagnosis

Clinical evaluation was performed blinded by two trained rheumatologists who had good agreement on CTS diagnosis between them (Kappa = 0.74). CTS diagnosis was confirmed in subjects who reported one or more of the following criteria (for at least once a week in the prior month) [14]: (1) numbness, nocturnal paresthesia and pain in the hand that awakened the patient; (2) activity-related numbness, paresthesia or pain involving the palmar aspects (at least two of the first four fingers) that was relieved by hand-shaking; (3) spontaneous numbness, paresthesia or pain involving the palmar aspects (at least two of the first four fingers).

2.4. Nerve conduction studies (NCS)

Standardized bilateral NCS were blindly performed by the same investigator using a Nicolet Compass Portabook machine (Nicolet Biomedical, WI, USA). Antidromic sensory NCS were performed in the right and left median (wrist – digit 2), ulnar (wrist – digit 5) and superficial radial nerves (distal radius – snuffbox) for CTS diagnosis. The latency was measured to the peak of the evoked sensory nerve potential. In the motor NCS, supramaximal stimulation was delivered at the wrist and proximally at the elbow to evaluate median and ulnar nerves. The distal motor latency and motor conduction velocity were recorded. The amplitude was measured from baseline to the negative peak of the evoked sensory and motor nerve potentials. Hand skin temperature (index) was at least 32 °C during all tests. Nerve conduction techniques and reference values of neurophysiologic parameters were those described by Preston and Shapiro [15]. Diagnosis of median neuropathy at the wrist was based on the practice parameters established by the American Academy of Neurology, American Association of Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. Median sensory NCS was performed across the wrist with a conduction distance of 13 cm and an internal-comparison test of median sensory conduction across the wrist with ulnar sensory (ring finger) conduction across the wrist in the same limb [16]. Severity was defined according to the neurophysiological classification of CTS proposed by Padua et al. [17]. One of the six degrees of severity was recorded for each hand and the final CTS classification was defined according to the worse affected hand.

2.5. Laboratory evaluation

A 12-hour fasting non-gestational oral glucose tolerance test using a 75 g oral dextrose load was performed in all subjects. A baseline fasting venous plasma glucose level (FPGL) was collected followed by oral administration of glucose load within a 5-min period. Blood samples to determine venous plasma glucose levels were subsequently collected at 120 min after the glucose load (2h-OGTT). Impaired fasting glucose (IFG) was confirmed if the FPGL was 100–125 mg/dL and impaired glucose tolerance (IGT) was confirmed if the 2h-OGTT was 140–199 mg/dL. PD was defined as the presence of IFG and/or IGT [5]. Criteria for new-onset DM were an FPGL $\geq$ 126 mg/dL and/or a 2h-OGTT $\geq$ 200 mg/dL [18].

2.6. Statistical analysis

Demographic, anthropometric, clinical, laboratory and neurophysiologic characteristics are expressed as mean $\pm$ standard deviation for continuous variables or as percentages for categorical variables. The median was calculated for continuous variables not normally distributed. Data were compared using Student's *t*-test or the Mann–Whitney test for continuous variables, as appropriate. For categorical variables, differences were assessed by the chi-squared test or Fischer's exact test. Logistic regression analysis with PD as a dependent variable and age, BMI and CTS as independent variables was performed. Results for the logistic regression were presented as odds ratios (OR) with a 95% confidence interval (CI). Data were analyzed using statistics software (SPSS 15.0, Chicago, USA). *P* values <0.05 were considered significant.

3. Results

One hundred and fifteen CTS patients and healthy controls paired by age, gender and BMI were studied. CTS patients and controls had similar mean ages (50.6 $\pm$ 9.2 and 50.1 $\pm$ 8.9 years respectively, $P = 0.980$) and BMIs (29.2 $\pm$ 4.6 and 28.3 $\pm$ 4.1 kg/m^2 respectively, $P = 0.330$) and female gender frequency ($P = 0.826$). The proportion of non-Caucasians in CTS patients was significantly lower than in controls (61.7% vs. 71.3% respectively, $P = 0.003$).

The main clinical and neurophysiological CTS data are summarized in Table 1. The median duration of CTS symptoms was 12.0 months (1–144 months). In the CTS group, nocturnal symptoms were most frequently reported (91.3%), followed by activity-related (78.3%) and spontaneous daytime symptoms (72.2%).

NCS revealed that median mononeuropathy at the wrist (CTS) was predominantly bilateral (82.6%). According to the neurophysiological classification, moderate CTS (58.3%) and mild CTS (20.9%) classes were most frequently observed whereas minimal and severe classes were detected in 13.0% and 7.8%, respectively. No case of extreme CTS was identified.