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An evaluation of gender, obesity, age and diabetes mellitus as risk factors for carpal tunnel syndrome

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Abstract

Objectives: The aim of this study is to identify gender, high body mass index (BMI), age and diabetes mellitus (DM) as independent risk factors (RF) for carpal tunnel syndrome (CTS) and to analyse the strength of association of these factors, both globally and in individual subgroups.

Methods: We performed a case–control study with 791 CTS cases and 981 controls. Patients were selected from those referred to nerve conduction studies and electromyography in 3 university hospitals and two private services. We calculated the odds ratio between the two groups to analyse the RF. Possible sources of bias were studied using stratified and multivariate analyses.

Results: The mean BMI and age were greater in the case group than in the control. Female gender, BMI > 30, age of 41–60 years and DM were significantly more frequent in the case group. Males tend to have a more severe CTS and DM was a significant RF for bilateral lesions. Stratified analysis showed female gender, obesity and age of 41–60 years as independent RF. DM, when stratified by BMI category, was not significantly associated with CTS.

Conclusions: Our study confirms that female gender, obesity and age are independent RF for CTS. DM may be a weak RF, especially among women.

Keywords: Carpal tunnel syndrome; Risk factors; Gender; Body mass index; Age; Diabetes mellitus

1. Introduction

Carpal tunnel syndrome (CTS) is the most commonly observed neuropathy in the general population (Dumitru and Zwarts, 2001; Kouyoumdjian et al., 2002), resulting from a compression of the median nerve at the level of the carpal tunnel (Tanaka et al., 1997; Leclerc et al., 1998; Lam and Thurston, 1998; Kouyoumdjian et al., 2000a,b; Dumitru and Zwarts, 2001). The estimated prevalence of this condition, calculated in a Dutch population, is about 6.8% in women and 0.6% in men (De Krom et al., 1992).

The most typical symptoms are pain and paresthesia, occurring especially at night, at the territory of the median nerve in the hands, although they can extend to the area innervated by the ulnar nerve, or eventually to all of the upper limb. It is also very common for patients to wake up with hypoesthesia in their hands, to feel paresthesia while reading or driving, to drop objects, and to obtain temporary relief of their symptoms by shaking hands (Stallings et al., 1997; Lam and Thurston, 1998; Stevens et al., 1999; Bland, 2000; Kouyoumdjian et al., 2000a,b; Dumitru and Zwarts, 2001). According to Nathan et al. (1998) and Salerno et al. (1999), the most reliable method to obtain objective diagnosis of CTS is electrodiagnostic studies.

Some epidemiological studies have been performed to identify risk factors for CTS. Although they present some contradicting data, the most consistent risk factors in these studies have been female gender, obesity, a high body mass index (BMI), age above 30 years, repetitive motor activity and a number of systemic diseases, such as diabetes mellitus (DM), rheumatoid arthritis and hypothyroidism (Werner et

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Tanaka et al., 1997; Lam and Thurston, 1998; Leclerc et al., 1998; Buschbacher, 1999; Stevens et al., 1999; Sungpet et al., 1999; Bland, 2000; Kouyoumdjian et al., 2000a,b; Dumitru and Zwarts, 2001; Kouyoumdjian et al., 2002). The possibility of a confusion bias among these variables, as well as the strength of each of these associations in various subgroups, however, have not been well studied.

After performing both stratified and multivariate analyses of their data, Werner et al. (1994) found that BMI > 29, gender and age were all independent RF for CTS. Stallings et al. (1997) also identified a high BMI as an independent risk factor. However, even though DM is associated both with obesity and CTS, no study has analysed this possible source of confusion bias.

In order to identify independent risk factors for CTS and to analyse the strength of association of these factors, both globally and in individual subgroups, we performed an epidemiological study in a population of patients undergoing nerve conduction studies and electromyography in southern Brazil.

2. Methods

We studied all patients who were referred to nerve conduction studies and electromyography with sensory or motor complaints in the upper limbs in the 7-month period between February and August of 2001. Data were gathered by 4 neurologists specializing in clinical neurophysiology. The study was performed in the neurophysiology units of 3 university hospitals and two private services in Rio Grande do Sul state, Brazil.

After informed consent was obtained for the study, patients were asked about their symptoms, age, gender, weight, height and associated diseases. The electrodiagnostic studies (Uncini et al., 1993; Campion, 1996; Stevens, 1997; Dumitru and Zwarts, 2001) included the following techniques: (a) sensory orthodromic conduction of the median and ulnar nerves, registered at the wrist, with stimulation at the third and fifth digits, respectively, and at the palm of the hand (8 cm distally to the recording (E-1) electrode) in both nerves' territories; (b) motor conduction of the median nerve, registered at the abductor pollicis brevis muscle (APB), with stimulation at the wrist (8 cm to E-1) and antecubital fossa; (c) sensory antidromic conduction of the median and radial nerves, registered at the thumb, with stimulation (10 cm to E-1) at the nerves' trajectory, if there was a conduction abnormality in the ulnar nerve; (d) distal motor latencies (DML) from the median nerve to the second lumbrical and from the ulnar nerve to the second interosseous muscle with equal distances, in the presence of borderline differences in the 'a' portion of the study or in the absence of response at the APB; and (e) electromyography and other neurophysiological studies required for individual cases. Surface electrodes were used for registering the data below 32°C. Studies were performed in one or both of the upper limbs, depending on the referring physician's request. All studies were performed using either Medelec-Oxford Synergy or Nihon-Kohden Neuropack 4 equipment.

The study had a case–control design. The case group included patients with sensory deficits in the affected hand, sometimes with symptoms involving the whole upper limb or tenar atrophy. All individuals in this group had a neurophysiologic diagnosis of CTS. The control group included patients with or without upper limb symptoms, but not fulfilling neurophysiologic criteria for CTS. Diagnosis of CTS was made through the presence of any one of the following criteria: (a) a difference greater than 10 m/s between the conduction velocities of the ulnar and median nerves in the palm–wrist segment; (b) a difference greater than 0.5 ms between the peak latencies of the palm–wrist segments of the median and ulnar nerves; (c) a difference greater than 0.5 ms between the sensory peak latencies of the median and radial nerves; (d) absence of a sensory or mixed response of the median nerve, when a diagnosis of polyneuropathy, brachial plexus injury and median nerve injury proximally to the wrist could be excluded; and (e) a difference greater than 0.4 ms between the DML from the median and ulnar nerves to the second lumbrical and interosseous muscles, respectively.

Cases which met the criteria described above were divided into 3 groups of severity according to the following criteria: mild CTS, with sensory amplitude after digital stimulation greater in the median than in the ulnar nerve, and with a DML from the median nerve to the APB of 4.5 ms or less; moderate CTS, with sensory amplitude after digital stimulation greater in the ulnar than in the median nerve (or with an amplitude either lower than 8 μV or lower than half of the amplitude in the contralateral median nerve, in cases where comparison with the ulnar nerve was not possible), and with a DML from the median nerve to the APB of 4.5 ms or less; and severe CTS, with a DML from the median nerve to the APB greater than 4.5 ms, reduced amplitude (below 5.0 mV baseline-to-peak) or absent response. Patients with bilateral lesions were classified according to their most severe lesion.

The control group comprised all patients in which criteria for a diagnosis of CTS were not met, excluding those with age inferior to 18 years (as there were no cases found in this age group), and those in which nerve conduction studies were performed only on one side (due to the possibility that they might have undiagnosed CTS on the opposite side). Patients with previous median nerve surgery were excluded in both groups.

BMI was calculated as weight/height^2. Patients were classified as being slender (BMI ≤ 21 kg/m^2), medium (BMI > 21 and < 25 kg/m^2), overweight (BMI ≥ 25 and < 30 kg/m^2), obese (BMI ≥ 30 and < 35 kg/m^2) or morbidly obese (BMI ≥ 35 kg/m^2) (Stallings et al., 1997).

Demographic, clinical and neurophysiological informa-

using Microsoft Access® 97 and data were analysed using SPSS® version 6. For comparisons between mean age and BMI between the two groups, we used Student's t test for different variances, with these being previously compared by the F test. A P value of 0.05 or less was considered statistically significant. For the analysis of risk factors for CTS, we calculated the odds ratio (OR) between the two groups, with a confidence interval of 95%. For the evaluation of possible confounding variables, we used both stratified and multivariate analysis. In stratified analysis, the OR was calculated by the Mantel–Haenszel method (OR_{MH}) to verify interactions among independent variables. Multivariate analysis was carried out through logistic regression, using second- and third-order interactions in the model.

3. Results

The study lasted 7 months, and in this period we performed 2555 nerve conduction studies and electromyography involving at least one of the upper limbs, with a total of 4153 hands examined. Of these, 791 (31%) studies (1339 hands) filled diagnostic criteria for CTS. Among the 1764 patients who did not have a diagnosis of CTS, 1050 had a bilateral study, and 981 were older than 18 years, and were therefore included in the study.

3.1. Case population

Of those patients with a diagnosis of CTS, nerve conduction studies and electromyography were performed in both upper limbs in 548 (69.2%). Of these, 420 (76.6%) had bilateral CTS, 94 (17.1%) had CTS only on the right side, and 34 (6.2%) on the left side. Of the remaining patients with CTS, in 174 the study was performed only on the right side, and in 69 only on the left side. Among all cases, we found a female:male ratio of 7.4:1. Age varied from 18 to 87 years, with a mean of 49.1 ± 11.9 and a median of 49. The majority of cases (62%) were found in the age group between 41 and 60 years. Of the patients with CTS, 7.3% mentioned having a systemic disease, most commonly DM (4.6%), rheumatic disease (1.6%) and thyroid dysfunction (0.5%). In 5.3% of cases, a second neurophysiologic diagnosis was found, with ulnar neuropathy being the most common one.

Of the 981 patients in the control group, 777 (79.2%) had a normal examination. Among the others, the most frequent neurophysiologic findings were polyneuropathy (6.9%), cervical radiculopathy (5.2%) and ulnar neuropathy (1.7%). Approximately two-thirds (67%) of controls were female, and age varied between 18 and 90 years, with a mean of 45.9 (±13.5) and a median of 45. In this group, 6.8% of people mentioned a systemic disease, with DM (2.4%), neoplasia (1.4%) and rheumatic disease (1.3%) being the most frequent.

3.3. Risk factors studied

The mean BMI was greater in the case group (27.5 ± 4.8) than in the control group (25.2 ± 4.1) ($P < 0.0001$). Mean age was also greater among cases ($P < 0.0001$). Age group distribution showed that the proportion of patients in age between 41 and 60 years was greater in the case group, with this age group being later analysed as a risk factor. With respect to BMI, an increase in the frequency of CTS was seen with a BMI greater than 25; however, this difference was significant only when BMI was above 30. Among the associated diseases studied, only DM was prevalent enough to be studied as a risk factor or as a possible confusion factor.

The conditions studied as possible risk factors for CTS, therefore, were female gender, age between 41 and 60 years, obesity (BMI > 30) and DM. All of these were shown to be statistically significant when analysed separately, with gender and BMI having the strongest association (Table 1). When analysing if any of the factors predisposed to more severe CTS, we found that only gender was significantly correlated with severity, as the female predominance was less marked in the patients with severe lesions (Table 2). Only DM was a significant risk factor for the presence of bilateral lesions (OR = 9.42; CI 95% = 1.27–69.84).

3.4. Stratified and multivariate analyses

Stratified analysis of the data showed that the independent risk factors for CTS were female gender (OR_{MH} = 3.66–3.76), obesity (OR_{MH} = 2.73–2.87) and age between 41 and 60 years (OR_{MH} = 1.81–1.92). The presence of DM, when stratified by BMI category, was not significantly associated with CTS (Table 3), although a non-significant trend

Table 1
Prevalence of risk factors in the studied groups, with the respective odds ratio and its 95% confidence interval presented for each association[a]

Risk factor in study	Cases (791) (%)	Controls (981) (%)	OR	CI 95%
Female gender	88.1	67.0	3.66	2.84–4.71
BMI > 30	26.8	11.2	2.90	2.25–3.73
Age between 41 and 60 years	62.1	46.2	1.91	1.58–2.31
Diabetes mellitus	4.6	2.5	1.82	1.08–3.06

[a] OR, odds ratio; CI 95%, 95% confidence interval; BMI, body mass index.

Prevalence of studied factors among patients with severe and mild/moderate CTS, with the respective odds ratio and its 95% confidence interval presented for each association[a]

Risk factor in study	Severe (400)[b] %	Mild/moderate (364)[b] %	OR	CI 95%
Female gender	85.5	91.8	0.53	0.33–0.84
BMI > 30	28.3	25.5	1.15	0.83–1.58
Age between 41 and 60 years	62.0	62.4	0.98	0.73–1.32
Diabetes mellitus	5.5	3.6	1.57	0.78–3.17

[a] Twenty-seven patients were not classified with respect to CTS severity.
[b] OR, odds ratio; CI 95%, 95% confidence interval; BMI, body mass index.

of association was found in this stratified analysis ($OR_{MH} = 1.66$, CI 95% = 0.94–2.95). The strength of the association between female gender and CTS was similar among all ages, but it was greater among non-obese patients (OR = 4.26) and among diabetic patients (OR = 7.37). Obesity was shown to be a stronger risk factor among male patients (OR = 5.64). No association was seen between age and CTS among obese and diabetic patient subgroups, while DM was a significant risk factor only among females (OR = 3.13).

Among patients with CTS, female gender ($OR_{MH} = 0.53$; CI 95% = 0.33–0.87), was shown in stratified analysis to be an independent protection factor for severe disease (i.e. there was a strong inverse association with female gender and cases with severe CTS). The presence of DM, meanwhile, was an independent risk factor for bilateral lesions in stratified analysis ($OR_{MH} = 9.32$–9.36; CI 95% = 1.52–57.47).

The final logistic regression model (Table 4) confirmed that obesity, female gender and age between 41 and 60 years were independent and highly significant risk factors for CTS. The association between obesity and male gender was also identified as a risk factor, but not that between female sex and DM. In this analysis, differently from what was found through stratified analysis, DM was found to be a statistically significant independent risk factor.

4. Discussion

The findings of our study confirm that female gender, obesity and age are independent risk factors for CTS, as

Table 3
Stratified analysis of risk factors for CTS[a]

Risk factor	Stratifying factor	*n* (RF/no RF)	OR	CI 95%	OR_{MH}	CI 95%
Female gender	BMI > 30	265/57	1.81	0.97–3.38	3.66	2.84–4.71
	BMI ≤ 30	1089/361	4.26	3.21–5.66		
	Age 41–60 years	735/209	3.84	2.77–5.34	3.65	2.85–4.68
	Other age groups	619/209	3.43	2.35–5.02		
	With diabetes	38/23	7.37	2.22–24.43	3.76	2.94–4.81
	Without diabetes	1316/395	3.65	2.83–4.70		
BMI > 30	Female gender	265/1089	2.39	1.80–3.18	2.75	2.14–3.53
	Male gender	57/361	5.64	3.22–9.89		
	Age 41–60 years	203/741	2.33	1.68–3.24	2.73	2.13–3.50
	Other age groups	119/709	3.51	2.37–5.21		
	With diabetes	18/43	3.34	0.79–14.09	2.87	2.24–3.68
	Without diabetes	304/1407	2.85	2.21–3.68		
Age 41–60 years	Female gender	735/619	1.95	1.57–2.43	1.91	1.57–2.33
	Male gender	209/209	1.74	1.07–2.84		
	BMI > 30	203/119	1.29	0.76–2.20	1.81	1.49–2.21
	BMI ≤ 30	741/709	1.94	1.57–2.41		
	With diabetes	31/30	2.10	0.59–7.45	1.92	1.58–2.32
	Without diabetes	913/798	1.91	1.57–2.32		
Diabetes mellitus	Female gender	38/1316	3.13	1.46–6.68	2.45	1.36–4.41
	Male gender	23/395	1.55	0.44–5.44		
	BMI > 30	18/304	1.87	0.44–8.06	1.66	0.94–2.95
	BMI ≤ 30	43/1407	1.60	0.82–3.13		
	Age 41–60 years	31/913	1.98	0.86–4.57	1.89	1.09–3.28
	Other age groups	30/798	1.80	0.79–4.09		

[a] RF, risk factor; OR, odds ratio; OR_{MH}, Mantel–Haenszel odds ratio; CI 95%, 95% confidence interval; BMI, body mass index.

Final multiple logistic regression model[a]

Risk factor in study	*B*	SE	*R*	*P*	OR
Female gender	0.63	0.17	0.07	<0.001	1.87
BMI > 30	0.62	0.08	0.15	<0.001	1.85
Age between 41 and 60 years	0.30	0.05	0.12	<0.001	1.35
Diabetes mellitus	0.40	0.16	0.04	0.012	1.49
Male gender and BMI > 30	0.22	0.08	0.04	0.011	1.24
Female gender and diabetes mellitus	0.14	0.16	0.00	0.481	1.12

[a] *B*, *B* value of the logistic regression; SE, standard deviation of the *B* value; *R*, *R* value of the logistic regression; *P*, *P* value of the logistic regression; OR, odds ratio; BMI, body mass index.

has been described by other authors (Werner et al., 1994; Stallings et al., 1997; Tanaka et al., 1997; Lam and Thurston, 1998; Kouyoumdjian et al., 2002). Literature also suggests that DM is a possible risk factor for CTS. However, its influence as an independent factor is not precisely defined, as this association could also represent a confusion bias due to the association between obesity and type II DM (Werner et al., 1994). In our analysis we found that obesity and female gender were the strongest risk factors, even after stratification by the presence of DM. Other systemic diseases were not prevalent enough to be analysed as risk factors or to have an impact as confusion factors.

One should keep in mind, however, that a possible limitation of this study is the fact that it was undertaken in a population of patients referred to neurophysiologic evaluation. Although this might not represent the general population, however, both groups were probably similar in most aspects except for the outcome in study, which makes the study of risk factors a valid enterprise in this case. Another possible bias is the inclusion, in the control group, of patients with incipient CTS and borderline values in neurophysiologic analysis, as most control patients complained of sensory symptoms, which were sometimes similar to those of the syndrome. This, however, would have led us to underestimate the strength of any association in study, strengthening our belief that the risk factors we found are indeed real, and that the associations we found could be even stronger.

The association between obesity and CTS can be explained either by the accumulation of fat tissue inside the carpal tunnel or by an increase in hydrostatic pressure through this canal, exerting a compressive effect on the median nerve. Stratified analysis of obesity as a risk factor showed a similar association strength among different age groups. However, in agreement with what was found by Werner et al. (1994), obesity was shown to be a stronger risk factor among males. This could be explained by the fact that female sex is by itself a strong risk factor, making the association with obesity numerically more evident in men. Another hypothesis is that there could be a real and independent influence of the association of obesity and male gender on the risk of CTS through unknown pathophysiosis of our data.

Although female gender was an independent risk factor for CTS, this association was not shown to be significant among obese patients. This was probably due to the fact that obesity is specially strong as a risk factor among males, as was discussed above, making it more difficult to establish female gender as a risk factor in this subgroup. On the other hand, we found that the association between female gender and CTS was greater in the subgroup of diabetic patients, although this was not confirmed by multivariate analysis. More studies must be done to confirm this finding, as in our study the prevalence of diabetic women with CTS was small, leading to a wide confidence interval.

DM is mentioned as a risk factor for CTS (Dumitru and Zwarts, 2001), although De Krom et al. (1990) did not find this in their study of a Dutch population. In our analysis, the presence of DM was found to be a statistically significant risk factor by logistic regression; however, when stratified analysis was performed with obesity as the stratifying factor, this finding was not confirmed to be significant, although a trend of association was found. It is feasible that DM might not be a real risk factor, being associated with CTS only due to its strong relation to a definite risk factor (obesity). However, considering that the association between DM and CTS was significant in multivariate analysis, that a trend of association was found even when analysis was stratified by BMI category, and that our sample of diabetic patients was relatively small, it is quite possible that the lack of significance in stratified analysis was merely due to an insufficient sample size. In any case, even if DM is indeed a risk factor for CTS, it is probably not as strongly associated with the disease like the other risk factors we found, as if this association was strong it should have been proved significant by the Mantel–Haenszel analysis even in our sample. This association could also be present only in some subgroups, as stratified analysis showed an association of DM and CTS only in the female population; however, the association of these variables was not confirmed to be significant by the logistic regression model.

The cutoff point in which age begins and ceases to be a risk factor varies among the various studies, although most agree that the risk of CTS increases after the age of 30 (Werner et al., 1994; Tanaka et al., 1997; Stallings et al., 1997; Lam and Thurston, 1998). In our study, the age group between 41 and 60 years was shown to be an independent risk factor for the syndrome, although the strength of this association was small. Analysis of increasing age as a risk factor is difficult due to the fact that CTS is a chronic disease, becoming therefore more prevalent as people grow older. Our study confirmed, however, that CTS is very rare below the age of 20, as has been observed by other authors (Deymeer and Jones, 1994; Werner et al., 1994; Al-Qattan et al., 1996; Stallings et al., 1997; Tanaka et al., 1997; Cruz-Martínez and Arpa, 1998; Lam and Thurston, 1998; Dumitru and Zwarts, 2001).

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