

Case-control study on individual risk factors of carpal tunnel syndrome

WENJIE GUAN¹, JIE LAO^{1,2}, YUDONG GU¹⁻³, XIN ZHAO^{2,3}, JING RUI¹⁻³ and KAIMING GAO¹⁻³

¹Department of Hand Surgery, Huashan Hospital, Fudan University; ²Key Laboratory of Hand Reconstruction, Ministry of Health; ³Shanghai Key Laboratory of Peripheral Nerve and Microsurgery, Shanghai 200040, P.R. China

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Abstract. This study was conducted to observe the characteristics of the risk factors of carpal tunnel syndrome (CTS) in Chinese population. CTS of 1,512 outpatients aged 41-70 years were without any other diseases which could cause numbness as a case group, and 4,536 non-CTS outpatients as a control group were involved in the study in 2013-2014. Both groups received a questionnaire and the case group received another electrical physiological examination. The results showed the odds ratio (OR) of age is 0.990 (95% CI, 0.984-0.996). The OR of BMI is 1.096 (95% CI, 1.077-1.115). The OR of smoking is 4.862 (95% CI, 3.991-5.925). The OR of wrist injury is 1.313 (95% CI, 1.019-1.691). The OR of diabetes mellitus is 1.837 (95% CI, 1.557-2.168). The OR of hypertension is 0.805 (95% CI, 0.688-0.942). The OR of hypothyroidism is 1.385 (95% CI, 1.119-1.715). The OR of rheumatic disease is 4.450 (95% CI, 3.712-5.215). The results showed that sex, age, smoking, wrist injury, diabetes mellitus, hypothyroidism and wrist working are all risk factors of CTS. Hypertension could be a protection factor of CTS in early phase but will increase the risk in a long-term high blood pressure. Smoking, alcohol and diabetes mellitus can be predictors of moderate and severe CTS.

Introduction

Carpal tunnel syndrome (CTS), or median neuropathy in the wrist, is a medical condition in which the median nerve is compressed in the wrist, leading to paresthesia, numbness and muscle weakness in the hand. It is the most common neuro-compressive disease. With the development of the modern life, the morbidity of CTS is also increased (1). As a common disease, the study on etiology is very important in CTS, which can improve the life quality of patients with CTS. The risk factors include individual factors such as age (2), sex (3),

diabetes (4), hypothyroidism (5), obesity (6), complication of systematic diseases (7-9), tobacco (5), injury (7) and occupational factors (10-12).

As most of the study were based on the population in Western countries and the life style and the ethnicity between Chinese people and Western country people is quite different, there may be some similarities and differences in epidemiology. There is lack of similar research in China so that this study was conducted to observe the characteristics of these risk factors in Chinese population.

Materials and methods

Study design. The present case-control study was based on a single medical center in Shanghai, China, in which more than 5,000 CTS patients per year are treated. The hospital involved in the study is a University Teaching Hospital. Cases were recruited from the surgical wards and appropriate outpatient clinics, while the controls were recruited from the outpatient clinics. Both groups filled out a standardized questionnaire, and a standardized patient record was filled out by a hand surgeon. In addition, participants with jobs involving lifting and carrying of loads were interviewed. The study was approved by the Ethics Committee of Huashan Hospital (Shanghai, China).

Sex is widely mentioned in the study on etiology of CTS. Nathan *et al* (3) found that sex is a clear and important factor in 2005. The incidence of CTS in middle aged women was significantly higher than that in men. Similar results were found in the study by Geoghegan *et al* (7), and Lam and Thurston (13). In our hospital, 83% are female patients of the total patients who received surgical therapy. Islam *et al* (14) stated that sex factor is rarely affected by other factors. Therefore, it was chosen as a match factor to reduce the effect in this study.

Clinical evaluation

Standardized questionnaire. The questionnaire was based on the Boston Carpal Tunnel Questionnaire (BCTQ) (15) and Quick DASH questionnaire to investigate the life quality of the patients.

Patient record. The patients' history and the physicians' findings were recorded including information on general health status, general use of wrist and hands. All the persons who

Correspondence to: Dr Jie Lao, Department of Hand Surgery, Huashan Hospital, Fudan University, 12 Wulumuqizhong Road, Shanghai 200040, P.R. China
E-mail: laojie633@sina.com

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were suspected of CTS received the neural electrophysiological examination to diagnose the disease.

Recruitment and inclusion criteria of cases and controls. The inclusion criteria were as follows: age 41-70 years. People in the case group with the symptom 'numbness' were clinically and neural-electrophysiologically diagnosed as CTS. People in the control group were excluded the symptom 'numbness'. The case group included clinically diagnosed CTS which was divided into 4 parts at every 10 years of age. The sex of the patients of the control group was matched to the case group and divided into 4 parts by age.

Statistical analysis. The study evaluated the risk factors of CTS to obtain the odds ratio (OR) and the P-value of these factors. Then all the data were imported to the database by Epidata Ver. 3.1 and processed by SPSS Ver. 20.0 for regression analysis. The average value and standard deviation were expressed as Avg. \pm Std.

Results

Description of the sample. During 2013 and 2014, there were 3,223 patients who were diagnosed in the Huashan Hospital and 85.1% of patients were aged 41-70 years. Among these patients, there were 1,512 CTS patients aged 41-70 years without any other diseases which could cause numbness as the case group. Then there were 4,536 non-CTS outpatients involved as the control group (Table I).

There were 200 as mild patients (13.22%), 1,202 moderate patients (79.89%) and 104 severe patients (6.88%) in this study according to the classification by Luchetti *et al* (16). BCTQ score in the case group is 41.32 \pm 16.94 while in control group 14.28 \pm 1.38. Quick DASH score in case group is 22.35 \pm 7.42 while in the control group 15.66 \pm 1.94. Both scores in the two groups have a statistically significant level ($P < 0.01$).

Predictors of CTS. The risk ratio of 51-60 age group is OR 1.334 (95% CI, 1.178-1.059) based on 41-50 as age group, while there was no statistical significance in 61-70 age group, which shows that 51-60 years of age in this study is the highest risk age (Table II).

The average BMI in case group was 22.79 \pm 2.60 and 21.49 \pm 5.03 in control group with significant difference ($P < 0.01$).

There were 192 patients (12.70%) who were educated in the primary school in case group and 32 patients (0.71%) in the control group. The number of patients who were educated up to secondary school was 672 (44.44%) in the case group and 1,360 (29.98%) in the control group. The number of high school patients was 304 (20.11%) in the case group and 1,576 (34.74%) in the control group. The number of college patients was 344 (22.75%) and 1,568 (34.57%). This showed that patients in control group were more educated. The OR of patients in primary school education is 25.328 (95% CI, 17.16-37.392) ($P < 0.01$). The OR of patients in secondary school education is 2.227 (95% CI, 1.918-2.585) ($P < 0.01$). The OR of patients in high school education is 0.880 (95% CI, 0.743-1.042) ($P > 0.05$) (Table III).

The investigated factors in the case group and control group as listed (Table IV). The OR of age is 0.990 (95% CI,

Table I. General information of the persons involved in the study.

Sex	Age (years)	Case group	Control group
Male	41-50	112	271
	51-60	64	140
	61-70	88	371
Female	41-50	544	1046
	51-60	336	879
	61-70	368	1819

Table II. The relationship between age and CTS.

Item	P-value	OR	95% CI
Age (year)	0.001	0.990	0.984-0.996
41-50 years	0.043	0.981	0.963-0.999
51-60 years	<0.001	1.412	1.337-1.490
61-70 years	<0.001	1.239	1.187-1.292

CTS, carpal tunnel syndrome; OR, odds ratio; CI, confidence interval.

Table III. The relationship between education level and CTS.

Education level	P-value	OR	95% CI
Primary school	<0.001	25.328	17.16-37.392
Secondary school	<0.001	2.227	1.918-2.585
High school	0.139	0.880	0.743-1.042
College		1.000	

CTS, carpal tunnel syndrome; OR, odds ratio; CI, confidence interval.

0.984-0.996). The OR of BMI is 1.096 (95% CI, 1.077-1.115). The OR of smoking is 4.862 (95% CI, 3.991-5.925). The OR of wrist injury is 1.313 (95% CI, 1.019-1.691). The OR of diabetes mellitus is 1.837 (95% CI, 1.557-2.168). The OR of hypertension is 0.805 (95% CI, 0.688-0.942). The OR of hypothyroidism is 1.385 (95% CI, 1.119-1.715). The OR of these factors in each age group is listed (Tables V-VII).

Discussion

CTS and general factors. Atroshi *et al* (2) found CTS incidence rate from age 45-65 years increased significantly both in male and female patients in a sample survey in Sweden, and the incidence of reported clinical and electrophysiological dual diagnosis of CTS was at the rate of 2.7% (95% CI, 2.1-3.4%). There are similar results in the study by Nathan *et al* (3) and Lam and Thurston *et al* (13). Therefore, it can be considered that there is a close relationship between the middle aged and elders and the occurrence of CTS. This result is similar to the age distribution of the patients mentioned above.

Table IV. Exposed parameters in case and control group.

Exposed parameters	Case group				Control group			
	Exposed	%	Unexposed	%	Exposed	%	Unexposed	%
Alcohol	432	28.57	1080	71.43	724	15.96	3812	84.04
Cigarette	320	21.16	1192	78.84	268	5.91	4268	94.09
Injury	114	7.54	1398	92.46	336	7.41	4200	92.59
Diabetes	265	17.53	1247	82.47	560	12.35	3976	87.65
Hypertension	305	20.17	1207	79.83	1126	24.82	3410	75.18
Hypothyroidism	128	8.47	1384	91.53	264	5.82	4272	94.18

Table V. The relationship between living habits and CTS.

Variables	P-value	OR	95% CI
Cigarettes	<0.001	4.862	3.991-5.733
41-50 years	<0.001	1.614	1.327-1.962
51-60 years	<0.001	4.264	2.303-7.894
61-70 years	1.000	1.000	<0.001
Alcohol	0.584	1.023	0.881-1.165
41-50 years	0.584	1.089	0.802-1.480
51-60 years	<0.001	1.512	1.265-2.376
61-70 years	0.996	<0.001	<0.001

CTS, carpal tunnel syndrome; OR, odds ratio; CI, confidence interval.

Table VI. The relationship between wrist injury and CTS.

Item	P-value	OR	95% CI
Wrist injury	0.035	1.313	1.019-1.691
41-50 years	<0.001	2.525	1.625-3.337
51-60 years	0.995	<0.001	<0.001
61-70 years	1.000	<0.001	<0.001

CTS, carpal tunnel syndrome; OR, odds ratio; CI, confidence interval.

In this study, the study subjects were selected in the age range of 41-70 years. At this age, the increase of the age and the incidence of CTS does not have a strong positive correlation. Patients in 51-60 years of age should pay more attention to the incidence of CTS during the diagnosis and treatment (Table II).

The low education level proportion in case group is significantly higher than in the control group, the primary school education level (OR=25.328; 95% CI, 17.16-37.392) and the junior school education (OR=2.227; 95% CI, 1.918-2.585) showed a strong positive correlation with the occurrence of CTS. There have been no studies in Western countries, which may be related to the higher average education level in the developed countries and the lesser extreme low education level. This phenomenon is related to the current social situation in China. The higher education level of the population

Table VII. The relationship between related diseases and CTS.

Variables	P-value	OR	95% CI
Diabetes	<0.001	1.837	1.557-2.168
41-50 years	0.201	1.540	1.067-2.223
51-60 years	<0.001	5.632	3.096-10.245
61-70 years	<0.001	1.535	1.207-1.951
Hypertension	0.007	0.805	0.688-0.942
41-50 years	<0.001	0.219	0.134-0.358
51-60 years	<0.001	0.753	0.525-0.902
61-70 years	0.007	1.695	1.534-1.904
Hypothyroidism	<0.001	4.450	3.712-5.215
41-50 years	0.996	1.000	<0.001
51-60 years	<0.001	4.579	2.474-8.473
61-70 years	1.000	<0.001	<0.001

CTS, carpal tunnel syndrome; OR, odds ratio; CI, confidence interval.

in the case group was lower but the difference between the two did not have statistical significance. Therefore, the impact of education on the incidence of CTS is more reflected in the low educational level. On the other hand, the low education level for the acceptance and understanding defects in the progress of health education, further weakened the ability of self-protection of their wrist in the process of work, which increased the risk of CTS occurrence. The different severity of CTS in patients with the factors of education degree was not significantly different, so that the level of education is not the indicative factor for the severity of carpal tunnel (Table III).

In 2004 Boz *et al* (6) reported BMI (95% CI, 1.048-1.198; OR=1.120) was an independent factor that increased the risk of CTS. For the mechanism of obesity and CTS, it may be associated with an increase in fat tissue in the carpal tunnel of obese people that can cause increased pressure and stress in the median nerve in the carpal tunnel.

In this study, OR of BMI was 1.096, 95% CI (1.077-1.115), which had statistical significance (P<0.01). 0.9<OR<1.1 indicated that BMI did not have a clear increase in the risk of CTS, but OR >1 showed that it had a trend to increase the risk of CTS. This difference may be related to the incidence of obesity worldwide, however, the study results of OR difference

is not large, which may be related to the differences in the study sample and random population.

Luchetti *et al* (16) proposed the CTS classification of patients with CTS severity of mild, moderate and severe. According to this classification, the BMI index had a weak correlation between the occurrence of the syndrome in patients with moderate carpal tunnel, that is to say that the risk of obesity in patients with moderate CTS was higher, but for the mild and severe CTS, the results were not statistically significant. This study still had limitation, the moderate CTS patients in the case group were the largest proportion while mild and severe CTS patients were significantly less, which may also caused some impact on the results.

CTS and living habits. Previous studies had indicated that smoking could affect the local microcirculation (17), which could lead to local hypoxia, injury of vascular endothelium and micro-thrombus. According to the microcirculation ischemia theory of CTS, smoking could affect the occurrence of CTS, which was mentioned in the study in Nathan *et al* (18), while different opinions exist (5). In this study, 320 cases were smokers of whom 268 were in the control group. The proportion of smokers in the case group was higher. By regression analysis, it was found that smoking was a risk factor (95% CI, 3.991-5.925; OR=4.862), which was in good agreement with the reported results (18) (Table V).

Long-term drinking could lead to peripheral neuropathy, which may be related to nutritional deficiency and vitamin B1 deficiency (19). Alcohol could cause nerve axonal degeneration and demyelination, often involving a fine feeling of optic nerve fibers, with axonal degeneration characterized. EMG showed the loss of NCV, and later large fiber segmental demyelination and axonal degeneration could be found, which lead to the slowing of conduction velocity. As the peripheral nerve was more sensitive to mechanical and ischemic injury, nerve paralysis could occur during the compression or traction. These symptoms appeared in long-term alcohol abuse patients. In this study, there was no clear evidence that alcohol caused the increasing risk of CTS. However, long-term and excessive drinking would lead to peripheral neuropathy, numbness and other symptoms. There are not many studies on the effects of alcohol on CTS (17,18,20). Some reported that CTS patients were less among mild and moderate drinkers but no further studies exists. We presumed that there was no significant correlation with the amount of alcohol consumption and CTS, but long-term excessive drinking could increase the risk of CTS. In this study, drinking OR was 1.023 (95% CI, 0.881-1.306) with no statistical significance which is consistent with the above studies (Table V). By age stratification, it was found that the risk of CTS in young and middle-aged smokers and drinkers was higher, especially in the 51-60 years old. Smoking and alcohol consumption are risk factors for moderate and severe CTS.

CTS and related diseases. The carpal tunnel is an osteofibral pipeline which connects the forearm and the palm. As the carpal tunnel volume ductility, any parts of the carpal tunnel damage may lead to a decline in the volume of the carpal tunnel, which can lead to the median nerve compression and the symptoms of CTS. These injuries include carpal fractures, through which the peripheral nerve and tendon is damaged and the surface of

the transverse carpal ligament injury. Wrist fracture (including distal radius fractures) has been widely reported (21-23). The first case of CTS was reported secondary to the distal radius fracture. Wrist open injury could be usually secondary cause the CTS. The case group in this study had a history of wrist trauma, 114 people, accounting for 7.54%; in the control group, there were 336 patients with wrist hand trauma history, accounting for 7.41%. OR was 1.313 (95% CI, 1.019-1.691) (Table VI). It was also confirmed that there was a positive correlation between the wrist hand injury and the risk of CTS. This is consistent with previous data. Hyperplastic fibrous connective tissues may fill the carpal tunnel or limit the expansion of the carpal tunnel because of the proliferation of fibrous connective tissue during the healing process when the wrist injury occurred, which resulted in the compression of the median nerve, however it was combined with the severity of patients with CTS analysis, no regular characteristics were found. Therefore, the wrist trauma was only a risk factor for the incidence of CTS, but could not be the indicator of the severity on CTS.

Diabetes can cause local median nerve microcirculatory disorders, followed by chronic peripheral nerve injury. Ferry *et al* (24), reported a similar study. In this study, there were 265 patients with diabetes, accounting for 17.53%; 560 people with diabetes in control group, accounting for 12.34%. The case group was significantly higher than that of the control group, OR was 1.837 (95% CI, 1.557-2.168) by regression analysis, which fully showed the possibility of diabetic patients with CTS was higher (Table VII). Non-diabetic patients in moderate and severe patients accounted for a lower proportion, indicating that patients with diabetes had higher risk of moderate or higher CTS.

Hypertension is a clinical syndrome characterized by elevated systemic arterial pressure, which can lead to damage of target organs, and is associated with systemic metabolic changes. In this study, the OR of hypertension was 0.805 (95% CI, 0.688-0.942). Although the incidence of CTS was weakly related, it had statistical significance. Other similar studies were not found. It showed that the occurrence of CTS was a protective factor in this study. In the earlier stage the action with hypertension elevated arterial pressure, which could make tiny vasodilatation and the microcirculation blood supply could be compensated, so that the median nerve in the carpal tunnel compression performance could be temporarily relieved. Based on the regression analysis after age stratification, all OR increased gradually, 61-70 OR reached 1.695 (Table VII) becoming a high-risk factor, which may be related to the progress of small vessel disease after long-term hypertension and vascular sclerosis and the local blood supply was affected. Thus, the role of these factors in the performance of different ages varied, so that personalized treatment should be carried out based on the age level of the patients.

Hypothyroidism is a group of endocrine diseases caused by thyroid hormone synthesis, secretion or biological effect. Ferry *et al* (24), reported that hypothyroidism could increase the risk of CTS. It was supposed that the release of thyroid hormone could reduce the formation of foam-like changes. The deposition of false mucin on the surface of the median nerve can lead to median nerve injury (25,26).

In this study there were 128 patients with hypothyroidism in the case group, accounted for 8.47%, 264 people in the control group, accounting for 5.82%. Hypothyroidism patients

in case group were significantly higher than the control group, OR was 1.385 (95% CI, 1.119-1.715), also showing that the incidence of hypothyroidism was a CTS risk factor (Table VII). Palumbo *et al* (27) also reported on a study of OR=1.7 in patients with hypothyroidism in the United States. The results of this study were similar.

Effect of rheumatoid arthritis on the tissue in the wrist is obvious. Since the rheumatoid arthritis usually occurs in the wrist, RA synovial hyperplasia is obvious in the wrist. The synovial invasion of the normal space in the carpal tunnel results in the stenosis of the carpal tunnel, and then causes the entrapment of the median nerve. Combined with the median nerve of peripheral vascular invasion of rheumatoid vasculitis caused by local blood supply affected and further aggravated the injury of the median nerve. Rheumatoid arthritis and CTS is closely related with the incidence. Reported long suffering from rheumatoid arthritis patients with CTS incidence rate could reach 10.7% (OR, 2.2-2.9) (28). In this study, rheumatism OR was 4.450 (95% CI, 3.712-5.215), showing that the risk of rheumatic diseases will significantly increase the CTS, but further analysis found there was no directivity in the severity by age stratification.

In conclusion, sex, age, smoking, wrist injury, diabetes mellitus, hypothyroidism and wrist working are all risk factors of CTS. Hypertension could be a protection factor of CTS in early phase but will raise the risk in a long-term high blood pressure. Smoking, alcohol and diabetes mellitus can be the predictors of moderate and severe CTS. Elder people are effected by the working factors compared to younger people.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

WG researched the literature and designed the study, analyzed and interpreted the patient data, and was a major contributor in writing the manuscript. JL participated in the design of the research and was a major contributor in editing the manuscript. YG participated in the design and revision of the manuscript. XZ participated in the design of the methods. JR was a major contributor in data acquisition. KG mainly participated in the clinical studies. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Huashan Hospital, Fudan University (Shanghai, China). Signed written

informed consents were obtained from the patients and/or guardians.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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