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Differences in characteristics of carpal tunnel syndrome between male and female patients

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Corresponding Author: Tatsunori Mitake

First Author: Tatsunori Mitake

Order of Authors: Tatsunori Mitake, Katsuyuki Iwatsuki, Hitoshi Hirata

ABSTRACT

Background:

Sex difference is known to be a risk factor of carpal tunnel syndrome. However, sex differences with regard to the clinical presentation of carpal tunnel syndrome have not received much attention. Thus, this study aimed to detect any difference in the characteristics of carpal tunnel syndrome between male and female and thereby add new insights into disease prevention.

Methods:

A total of 647 patients (male 193 hands and female 454 hands) with carpal tunnel syndrome who underwent endoscopic or open carpal tunnel release were retrospectively reviewed. The average age at time of surgery was 66 years. Clinical and electrophysiological data of all patients were collected. Six medical conditions, including trigger finger, diabetes mellitus, hemodialysis, hyperlipidemia, hypertension, and obesity were also investigated.

Results:

A significant difference was found in the distribution of comorbidities between the male and female groups. Particularly, the prevalence of diabetes mellitus, hemodialysis, and hypertension were significantly higher in the male group than in the female group.

Meanwhile, the presence of thenar muscle atrophy was significantly higher in the female group than in the male group.

Conclusions:

Women are more likely to experience carpal tunnel syndrome even though they have no comorbidities. We suggest that carpal tunnel syndrome especially in male patients may be reduced by early intervention for diabetes mellitus. Prospective studies are needed to validate the causal relationship between diabetes mellitus and carpal tunnel syndrome.

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common compressive neuropathy of the upper extremity. Balci and Utku were the first to report the association between CTS and metabolic syndrome [1]. Moreover, patients with metabolic syndrome had a higher incidence of CTS and more severe disease stage. Its occurrence is related to numerous medical and nonmedical conditions with uncertain causality. Medical condition correlates of CTS include age, sex, pregnancy, obesity, diabetes mellitus (DM), hemodialysis (HD), hypothyroidism, and rheumatoid arthritis (RA) [2, 3].

Specifically, sex difference is known to be a risk factor of CTS; however, sex differences with regard to diagnostic and prognostic value in the clinical presentation of CTS have not received much attention. Moreover, similar studies have not yet investigated the correlation between comorbidities and sex differences in CTS patients. In this study, we hypothesized that the condition of female CTS patients is different from that of male CTS patients. This study aimed to detect any difference in the characteristics between male and female CTS patients and to add new insights into CTS prevention.

MATERIALS AND METHODS

Patients

We retrospectively reviewed 829 hands of 829 patients who underwent endoscopic carpal tunnel release (ECTR) or open carpal tunnel release (OCTR) for CTS between 2008 and 2018 at Anjo Kosei Hospital, Hachiya Orthopaedics, Nagoya University Hospital, and Tokai Hospital. Patients who had malunited fractures of the distal radius were excluded. The Institutional Review Board of each hospital approved this study. Informed consent was not required because this retrospective study does not require intervention. However, refusal opportunity was guaranteed by information disclosure. Patients who decided to refuse study participation can notify the researcher.

The diagnosis of CTS was based on a history of dysesthesias along the distribution of the median nerve and a positive provocative test. To confirm the diagnosis, nerve conduction studies were carried out. Patients were first treated conservatively with splinting, medication, and/or intra-carpal tunnel steroid injection. ECTR or OCTR was performed for refractory patients [4, 5]. Moreover, we distinguished patients between the improved group and unimproved group after surgery to ensure the diagnosis of CTS. We analyzed only improved patients for the comparison between male and female patients.

Outcome Assessment

The following data were collected: age, sex, presence of nocturnal pain, thenar muscle atrophy, and preoperative pinch power. Based on a literature review, we selected six medical conditions, including trigger finger, DM, HD, hyperlipidemia (HL), hypertension (HT), and obesity, as possible comorbidities of CTS [6].

Electrophysiological studies were also performed. Sensory conduction studies were performed using antidromic methods by stimulating the wrist and using ring electrodes in the index finger for recording. Sensory conduction velocity (SCV) of the median nerve was measured. Motor conduction studies used supramaximal stimulation at 50 mm proximal of the abductor pollicis brevis (APB). The distal electrode was placed on the skin overlying the APB. The motor distal latency (distal latency) was recorded with a surface electrode from the APB; 20 and 500 cycles were utilized, permitting the detection of signals up to 0.2 μV. Distal latency more than 4.5 ms was used as cutoff to determine abnormal results. SCV was expressed in meters per second (m/s). Distal latency and SCV of the male group and female group were compared.

Electrophysiological studies were assessed according to Padua classification [7].

Statistical Analysis

Data are presented as means ± standard deviation or as numbers and percentages. Group

differences were evaluated using the Mann-Whitney U test for non-normally distributed variables (such as age). The chi-square test or Fisher's exact test was used for categorical variables, such as sex and comorbidities. Statistical analysis was conducted using SPSS version 24J (IBM Japan, Tokyo, Japan). A P value<0.05 was considered statistically significant.

RESULTS

This study identified 829 hands that underwent carpal tunnel surgery. A total of 156 hands were excluded because electrophysiological data were lacking. Thus, a total of 673 patients and 673 hands (male, 200 hands; female, 473 hands) were enrolled. The average age at the time of the surgery was 66 (range, 30-99) years.

In our series, 26 patients were unimproved after surgery, and characteristics of 647 improved patients are summarized in Table 1. No significant difference in age was found between the male and female groups. In addition, no significant differences in the prevalence of trigger finger, HL, and obesity were found between the two groups. The prevalence of DM, HD, and HT were significantly higher in the male group than in the female group (P<0.01, P<0.01, P=0.03, respectively). On the contrary, the prevalence of DM in the unimproved group was 42.9% in male and 31.6% in female. The rate of

nocturnal pain occurrence was 39.4% in the male group and 31.5% in the female group (P=0.06). Meanwhile, the presence of thenar muscle atrophy was significantly higher in the female group than in the male group (P<0.01).

Figure 1 shows the number of comorbidities, and a significant difference was found in the distribution of the number of comorbidities.

Preoperative electrophysiological examination results are shown in Table 2. Of the 454 female patients, 263 (57.9%) were distributed in the moderate subgroup of the Padua classification, and male patients were distributed in the moderate subgroup at 48.7% and in the severe subgroup at 31.6%.

DISCUSSION

This study investigated the prevalence of comorbidities in CTS patients, while paying attention to the sex difference. A significant difference was found in the distribution of comorbidities between the male and female groups. Especially, the prevalence of DM, HD, and HT were significantly higher in the male group than in the female group. Meanwhile, the presence of thenar muscle atrophy was significantly higher in the female group than in the male group.

Comparison with previous studies about comorbidities

We believe that increased intra-carpal tunnel pressure due to swelling of the flexor tenosynovium is the most probable pathological mechanism of CTS. The most significant socio-demographic characteristics associated with CTS were female sex and advance age (>40 years) [2, 6]. The most significant concurrent medical conditions were RA, DM, obesity, gout, HT, and hypothyroidism [6]. The correlation of female sex with CTS has been well documented [2, 6]. In a systematic review, van Dijik et al. reported that the prevalence of concurrent RA, DM, and hypothyroidism was higher in CTS patients than in controls [8]. Positive correlations between DM and CTS and between obesity and CTS have been observed in several studies [8-10]. Advanced glycation end products (AGEs) have been observed to accumulate in various organs, especially in joint tissue, and damage the joint tissue during aging and DM. In the report of Ying-Ju et al., AGEs significantly induced synovial angiogenesis and inflammation [11]. Another possibility was that DM causes tenosynovitis in the carpal tunnel. HT is also a common medical problem associated with CTS. Edwards et al. reported that HT could impair the sensory nerve conduction through elevation of cutaneous sensory thresholds and reduction in sensory action potential amplitudes [12].

Uremia is a metabolic disorder caused by chronic renal dysfunction. Studies have

shown that uremia is associated with CTS in patients undergoing HD and peritoneal dialysis [13, 14]. Another study reported that comorbidities were more strongly associated with CTS in the younger population [15]. The causes of the CTS are thought to be not only β2-microglobulin but also compression in the carpal tunnel due to synovitis and amyloidosis.

In a basic research, Jinrok et al. studied the subsynovial connective tissue of the tendon sheath in 10 idiopathic CTS patients [16]. They reported that the typical pathologic findings of CTS patients included vascular proliferation, vascular hypertrophy, and vascular obstruction with wall thickening. In the present study, the prevalence of DM, HD, and HT was significantly higher in the male group than in the female group. According to a report in 2016 from the Ministry of Health, Labor and Welfare, the prevalence of DM in normal population was 16.3% in male and 9.3% in female individuals. In our study, the prevalence of DM in CTS patients was 41.5% in the male group and 19.6% in the female group, and these were about two-fold of that in the normal population. Although the prevalence of DM was higher in CTS patients than in the normal population, the prevalence of HT in normal population was 34.6% for men and 24.8% for women, so it was not specific in CTS patients.

Possible cause of female CTS

Because of the higher CTS incidence in women particularly around menopause, the role of specific risk factors for women and hormonal changes related to menopause has been proposed [17]. Kim et al. observed increased expressions of estrogen receptor alpha and beta (ERα and ERβ) in the tenosynovial tissues of postmenopausal women with CTS [18]. Although Toesca et al. observed expression of ERα in both transverse carpal ligaments (TCL) and synovial tissues and progesterone receptor (PR) in TCL samples from CTS patients, no statistically significant difference was found between male and female groups in the number of ER- and PR-positive cells within TCL or synovial tissues of CTS patients, except patients aged 50-70 years [19]. In addition, Mohammadi et al. reported that ER expression in TCL and serum estrogen levels were not significantly different in the case group compared to the control group [20]. In the present study, although an association between CTS and female sex hormonal changes is still controversial, women are more likely to suffer from CTS even though they have no comorbidities.

Electrophysiological and clinical findings: comparison with previous studies about sex difference

One previous study has shown that the severity of electrophysiological testing in men was significantly higher than that in women [21]. Edema might signify an earlier stage of CTS, with epineural thickening being a sign of chronic changes to the nerve [22, 23]. Men have been shown to have a worse post-surgical outcome than women, similar to elderly patients and smokers [24]. Bland et al. reported that CTS was more prevalent in women, although it was more severe in men and elderly [17]. Our finding was consistent with that of Bland et al.

Our study indicated that the Padua classification showed significant difference in the severity of CTS between the male and female groups. The severe subtype was greater in men than in women. When we considered the prevalence of DM was higher in male group, poor nerve conduction velocity (NCV) in men may be related to DM neuropathy. On the contrary, edema in the tenosynovium due to hormonal changes could cause increased intra-carpal tunnel pressure in female patients. In this case, there would be less neurodegenerative change. The presence of thenar muscle atrophy was significantly higher in the female group than in the male group despite its less severity in the Padua classification. Although severe NCV was considered the cause of the thenar muscle atrophy, this result may be called a false positive in male DM neuropathy.

Limitations

Several limitations of our study must be acknowledged. Although we investigated the association between CTS and several risk factors in this cross-sectional study, the reason for the higher number of female CTS patients remains unknown. To determine the causal relationship with regard to the onset of CTS, a prospective cohort study is needed. Second, our results cannot be extrapolated to mild cases of CTS as some of these patients may show a normal pattern velocity. Third, we cannot provide functional data on patient-based assessments, such as the Disability of the Arm, Shoulder, and Hand score or Hand20 [25]. Fourth, original electrophysiological procedures of Padua et al. were slightly different from that commonly used in Japan. For example, we used ring electrodes from the index finger, whereas Padua et al. used middle finger in their original article. Finally, we could not evaluate female sex hormones, because serum estradiol levels change dramatically during the menstrual cycle. We require a reliable assessment kit for permanent estrogen level, such as hemoglobin A1c against DM.

Conclusion

We believe that increased intra-carpal tunnel pressure is the most probable pathological mechanism of CTS. Flexor tenosynovitis, microvascular proliferation, and neuropathy

due to DM, HD (including amyloidosis), and HT were considered the main causes of CTS in men. Our findings might provide evidence-based data on the differences in the characteristics of male and female patients with CTS. It can help the clinician be more acquainted with these characteristics and would form a basis for prevention of future CTS. In particular, DM neuropathy was extremely higher in male CTS patients and this may be the cause of worse NCV. Prospective studies are needed to validate the causal relationship between DM and CTS.

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Figure 1

Figure 1 Distribution of comorbidities

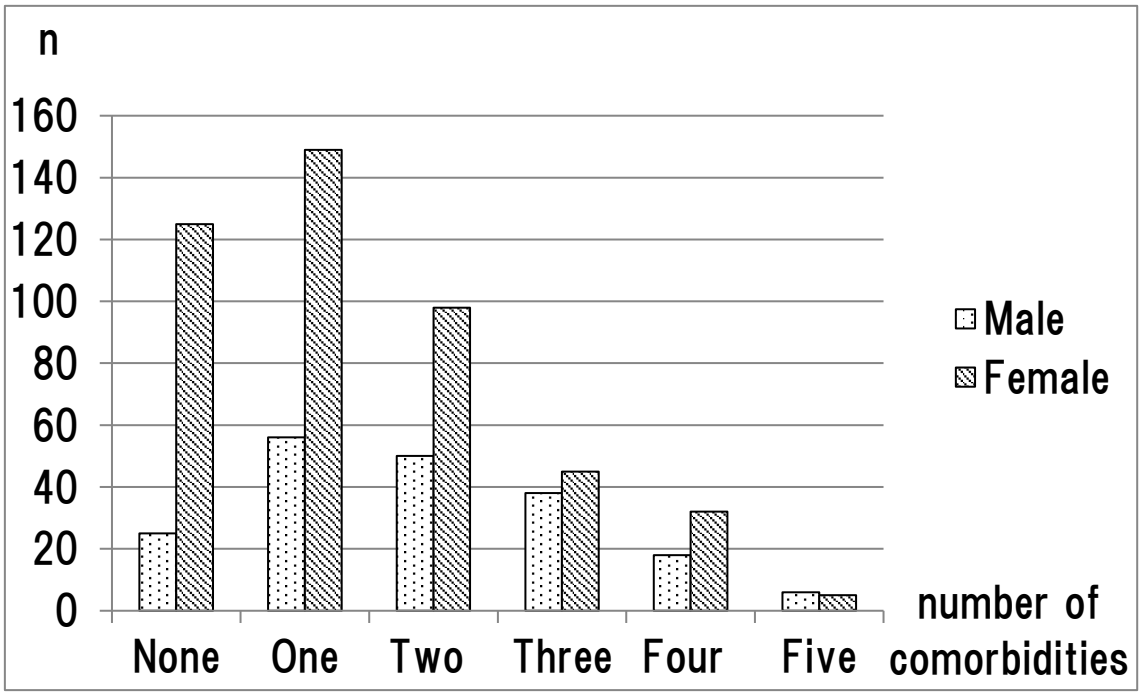

Table 1 Patients' characteristics

		Male (n=193)	Female (n=454)	P
Age (years)		66±10	66±13	0.38
Trigger finger		62	134	0.51
DM		80 (41.5%)	89 (19.6%)	<0.01
HD		38 (19.7%)	29 (6.4%)	<0.01
HL		52	102	0.23
HT		74 (38.3%)	134 (29.5%)	0.03
BMI (kg/m^2)	<18.5	9	35	0.58
	18.5-24.9	119	271	
	25-29.9	49	111	
	>30	16	37	
Nocturnal pain		76 (39.4%)	143 (31.5%)	0.06
Atrophy of the thenar eminence		58 (30.1%)	220 (48.5%)	<0.01
Preoperative pinch power (kg)		5.9±3.4	3.9±1.8	0.19

BMI, body mass index; DM, diabetes mellitus; HD, hemodialysis; HL, hyperlipidemia, HT, hypertension

Table 2 Padua classification

	Male (n=193)	Female (n=454)	P
Normal	5	11	
Minimal	4	12	
Mild	6 (3.1%)	27 (5.9%)	
			0.004
Moderate	94 (48.7%)	263 (57.9%)	
Severe	61 (31.6%)	79 (17.4%)	
Extreme	23 (11.9%)	62 (13.7%)	