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SYMPATHETIC SKIN RESPONSE AND BOSTON QUESTIONNAIRE IN CARPAL TUNNEL SYNDROME

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We aimed to determine relations between the sudomotor efferent nerve fiber function and Boston questionnaire (BQ) in idiopathic carpal tunnel syndrome (CTS). Median nerve-induced sympathetic skin responses (SSRs) evoked by wrist stimulation were recorded in 108 CTS patients and compared with those in 88 healthy volunteers. The Boston questionnaire form (BQF) was applied to the subjects. All patients and healthy individuals were questioned about the autonomic symptoms in the hand (red or purple skin coloration, excessive sweating, and feeling cold). The average SSR latencies of the patients with CTS were significantly longer than those in the control group ($P < 0.001$). Positive significant, while weak, correlations were found between the SSR latency, autonomic symptoms, and total sympathetic system scores. No statistically significant relationship was found between the Boston symptom severity, functional capacity scores, and SSR latency. The latter obtained through wrist stimulation was sensitive to support the sudomotor sympathetic dysfunction in patients with CTS. No relationship between the BQF and SSR can be related to the fact that these indices evaluate different aspects of CTS.

Keywords: carpal tunnel syndrome, sympathetic skin response, sympathetic activity, sudomotor activity, Boston questionnaire.

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most frequently observed peripheral nerve entrapment neuropathy [1]. Although many factors may increase the pressure on the median nerve, as it passes through the carpal tunnel, idiopathic CTS cases far outnumber all other types [1]. Idiopathic CTS often occurs in middle-aged women without other known pathologies [2].

Median sensory and motor nerve conduction studies (NCSs) are valid and reproducible clinical laboratory techniques that can confirm clinical diagnosis of CTS with a high degree of sensitivity and specificity [3]. Autonomic nerve fibers constitute an important component in the peripheral nerves [4]. However, only the function of myelinated (fast-conducting) fibers can usually be examined using NCS; the responses of unmyelinated fibers, such as C afferents and postganglionic sympathetic fibers, can be detected with significant difficulties.

The sympathetic skin response (SSR) has been frequently used in polyneuropathies and dysautonomic disorders in the studies carried out upon sympathetic fiber functions [5, 6]. In terms of the electrical potential of the skin, the SSR is a transient change. It can be spontaneous or can also be caused by several internal or external stimuli [5]. The SSR was analyzed in several studies related to autonomic involvement in CTS; however, findings of these studies considerably differed from each other [4, 5, 7-11]. Moreover, the relationship of the SSR data with clinical scales, such as the Boston questionnaire form (BQF) used to evaluate the severity of the symptoms and functional status in CTS, has not been known.

The studies searching for the CTS and SSR relationship have up to present been carried out with maximum 76 patients [10]. In our study, the number of patients was greater, and we aimed to clarify the controversial CTS-SSR relationship and analyze the relationship of SSR data with BQF, which have not been evaluated before.

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METHODS

One hundred-eight patients showing symptoms and clinical signs suggesting unilateral or bilateral CTS and 88 healthy volunteers were included in the study. The study was carried out upon the patients with idiopathic CTS. Therefore, the patients with *diabetes mellitus*, rheumatoid arthritis, hypothyroidism, wrist fracture, renal failure, and dialysis history were not included in the study. Also, the patients with cardiac failure, severe hypertension, and hereditary autonomic system diseases that can cause involvement of the autonomic system were also not examined. Symptoms of CTS and data on age, gender, occupation, spare time activities, height, and body mass were evaluated, and neurological examinations were performed. The body mass index (BMI) was calculated as the body mass (kg) divided by the square of the height (m) [12]. The patients filled the BQF including the "functional capacity scale" and "symptom severity scale". The following symptoms related to hands were asked to all patients and healthy individuals: red or purple skin coloration, excessive sweating, and feeling cold. Any of the patients did not have any symptoms or signs of a peripheral neuropathy rather than CTS. Points from 0 to 3 were marked according to the existence of red or purple coloration, excessive sweating, or feeling cold for the sympathetic symptoms in the symptomatic hands of the patients (one point for each symptom) [4, 5].

The NCS and SSR recordings were performed on the more symptomatic hand, if the patient was bilaterally symptomatic for CTS, and on the symptomatic hand, if the patient was unilaterally symptomatic for this pathology [12, 13]. These procedures were also performed on the dominant hand in the control group. Diagnosis of CTS was based on the practice parameter for electrodiagnostic studies established by the American Academy of Neurology, American Association of Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation [14].

Before electrophysiological examination, SSR was recorded in accordance with the technique described by Shahani et al. [15] and Verghese et al. [10]. In order to prevent habituation, single 0.1-msec square-wave pulses slightly exceeding the motor threshold intensity were five times applied with irregular intervals upon the median nerve at the wrist level. The obtained effects were recorded using standard surface electrodes attached to the palmar and dorsal surfaces of the hand. The latency was measured with respect to the onset of the response (negative or positive deflection), and peak-to-peak response amplitudes were estimated. Average amplitudes and latencies were also calculated from the obtained five records.

The NCS data obtained included the thumb (M1), index (M2), and middle (M3) finger sensory conduction velocity to the wrist, median distal motor latency, and median motor conduction velocity of the patients and controls. Patients and controls with abnormalities in the ulnar motor nerve and sensory conduction were not included in the study.

All recordings were performed on subjects lying supine on a bed in an air-conditioned room at room temperature of 24°C and avoiding external stimuli. The skin temperature during the electrophysiological examinations was kept at or above 32°C. Standard surface recording and stimulating electrodes were used during electrophysiological studies. The Medelec-Oxford EMG equipment (Great Britain) was used in all tests.

The clinical severity of CTS was assessed according to a 6-stage scale: stage 0, no evidence suggesting the presence of CTS; stage 1, only nocturnal paresthesias; stage 2, diurnal paresthesias; stage 3, sensory deficit; stage 4, strength loss in the thenar muscles, and stage 5, complete atrophy or complete plegia [12, 16, 17]. Electrophysiological abnormalities of patients with CTS were evaluated on a 5-stage scale: stage 1, abnormal results of segmental or comparative studies; stage 2, abnormal finger/wrist sensory conduction velocities; stage 3, abnormal finger/wrist sensory conduction velocities and abnormal distal motor latencies; stage 4, absence of the sensory response and an abnormal distal motor latency, and stage 5, absence of the sensory and motor responses [12, 16-18].

Descriptive analysis was performed for the studied groups in order to inform on general features of the studed groups. For evaluation distributions of the variables, the Kolmogorov – Smirnov test was used. For comparison of the constant variables in the groups, the independent-sample *t*-test or Mann–Whitney U-test were used in the case of normal distributions. For comparison of the categorical variables, the χ^2 test was used. Pearson's and Spearman's correlation analyses were employed in the analysis of the relationship between variables. The data related to the constant variables were presented as means ± s.d., and the data related to the categorical variables were presented as normalized values (%). The *P* values below 0.05 were considered indications of statistically significant

intergroup differences. The calculations were made using statistical software packages, IBM SPSS Statistics 20 and SPSS inc. (IBM Co. and Somers, USA).

RESULTS

The mean age of 108 patients included in the study was 45.96 ± 8.93 years, and the respective value in the control group was 43.51 ± 9.48 years. Ninety-seven patients (89.8%) were women, and 11 (10.2%) were men; in the control group, the respective figures were 73 (83%) and 15 (17%). There were no significant differences between the patient and control groups in terms of age and gender ($P > 0.05$).

Most examined subjects (87.9% of the CTS patients and 78.4% of the control persons) were housewives. The most frequently performed leisure activity after house works was handworks (29.6% in the patients and 53.5% in the control subjects).

In terms of the clinical stage, 33 (30.6%) of the CTS patients were at stage 1, 64 (59.3%) were at stage 2, 10 (9.3%) were at stage 3, and one (0.9%) was at stage 4. In terms of the electrophysiological stage, 11 (10.2%) patients were at stage 1, 40 (37%) patients were at stage 2, 47 (43.5) patients were at stage 3, 5 (4.6%) patients were at stage 4, and 5 (4.6%) patients were at stage 5. The mean Boston symptom severity score of the patients with CTS was 33.03 ± 9.01, and their functional capacity score was 23.88 ± 7.25.

Most (70.4%) of the patients with CTS complained about red or purple coloration on their hands, 84.3% complained about sweating, and 33.3% complained about feeling cold; the respective rates for the control group were 20.5, 30.7, and 9.1%. There was a statistically significant difference between the control and patient groups in terms of these autonomic symptoms ($P < 0.001$). The average values of sympathetic system scores obtained through the total of these three complaints were 1.88 ± 0.94 in CTS group and 0.59 ± 0.70 in the control group ($P < 0.001$).

The mean SSR latency of the patients with CTS was 1.39 ± 0.18 sec, and in the control group it was 1.25 ± ± 0.14 sec. the mean SSR latency of the patients with CTS was significantly longer than that in the control group ($P < 0.001$). The average SSR amplitude of the patients with CTS was 833.9 ± 782.5 μV, and it was 718.8 ± 439.0 μV in the control group. No statistically significant difference was found between the patient and control groups in terms of the SSR amplitudes ($P = 0.823$). The SSR could not be obtained in three patients.

T a b l e 1. Correlations between the SSR Latency and Clinical/ Electrophysiological Features in CTS Patients

Кореляції між латентним періодом шкірної симпатичної відповіді та клінічними електрофізіологічними особливостями у пацієнтів із синдромом зап'ястного каналу

Features	SSR latency	
	r	***P***
Age	0.221	**0.024**
BMI	0.044	0.656
Mean SSS	0.361	**<0.0001**
Skin coloration	0.237	**0.015**
Excessive sweating	0.308	**0.001**
Feeling cold	0.254	**0.009**
DML–M	0.276	**0.005**
MCV–M	–0.165	0.097
M1 SCV	–0.148	0.148
M2 SCV	–0.085	0.406
M3 SCV	–0.084	0.413
Clinical severity scores	0.186	0.059
Electrophysiological severity scores	0.272	**0.005**
BSSS	–0.034	0.734
BFCS	0.028	0.783

Foonotes. BMI, body mass index; SSS, sympathetic symptom score; M1–M3, conductions, thumb to wrist (M1), index finger to wrist (M2), and middle finger to wrist (M3); SCV, sensory conduction velocity; DML-M, median distal motor latency; MCV-M, median motor conduction velocity; BSSS, Boston symptom severity score, and BFCS, Boston functional capacity score. *P* values shown in bold indicate cases of statistical significance of correlation.

A positive significant (but weak) correlation was estimated between the SSR latency and obtained autonomic symptoms and total sympathetic system scores (Table 1). The SSR latency was also in a positive significant (but also weak) correlation with electrophysiological staging of CTS, median nerve motor latency, and age (Table 1). No statistically significant difference was found between the Boston symptom severity, functional capacity scores, and SSR latency (Table 1).

DISCUSSION

In our study, the SSR latencies measured after stimulation of the median nerve at the wrist level were found to be statistically significantly longer in patients

with CTS than those in the control group; beside this, the SSR latencies were found to correlate with the intensity of autonomic symptoms. The findings obtained earlier in the SSR studies on patients with CTS were not consistent with each other [4, 5, 7-11]. Verghese et al. [10] using the same technique in 76 patients with CTS reported that SSR abnormality significantly correlated with the presence of autonomic symptoms, and the latter significantly correlated with the severity of electrophysiological abnormality. Reddeppa et al. [9] observed abnormalities in the SSR values in 30 patients with CTS who had no serious autonomic disorders. Kanzato et al. [7] recorded SSRs simultaneously from four different points. Electrodes were placed on the palmar surface of the hand; at the wrist level (W) at the metacarpo-phalangeal joint (J), on the middle phalanx (M), and on the distal phalanx (D) of the index finger. At all recording sites except of point D, the SSR amplitude in normal hands was significantly higher than this parameter in CTS patients. A weak but significant correlation was clear between the SSR amplitude at points W and J and the clinical grade [7].

In the study of Bayrak et al. [5], the SSR was evoked by suprasternal stimulation in 50 hands of 31 patients and 50 hands of 25 healthy controls. The groups were investigated in terms of the sympathetic symptoms, and sympathetic system scores (SSS) were calculated. Although there was no significant difference between the groups in terms of SSS values, there was also no difference in terms of the SSR. No relationship was found between the SSR and SSS parameters and the electrophysiological stage. The authors, therefore, did not recommend SSR recording as a sensitive method to evaluate autonomic involvement in CTS [5]. Sener et al. [4] recorded the median and ulnar SSRs by stimulating the sternum in 31 patients with CTS comparing the findings with those in 21 healthy controls. It was reported that the SSR was not sensitive to reveal sudomotor sympathetic dysfunction even in the patients with autonomic symptoms of CTS. As in the study by Sener et al. [4], peripheral effects of the somatic fiber involvement might be neglected by giving suprasternal stimulation. In the study of Zyluk and Kosovets [11], bilateral capillaroscopy and sternally stimulated SSRs were performed in patients with unilateral CTS, and no significant difference was found between the SSR parameters and capillaroscopy values in affected and unaffected hands.

In examination of the SSRs, there is no agreement in the recording methods or in attention to different SSR parameters (the mean or the shortest latency, the mean amplitude or the area, etc.) [8]. Therefore, it is difficult to compare the results of the above-cited SSR studies. Kiylioglu et al. [8] mentioned that the discrepancies might be caused by the use of different stimulation and recording methods. The common point in these studies is the following. As the distance between the recording and stimulation points increases, the possibility for identification of an abnormality decreases [7].

The polysynaptic reflex arc for the SSR contains large myelinated afferent sensory fibers, central relays localized in the posterior hypothalamus and/or upper brainstem reticular formation, and an efferent pathway through the spinal cord, sympathetic preganglionic fibers, and postganglionic nerve fibers, with sweat glands as crucial effectors [8]. Certain changes have been expected in CTS because postganglionic unmyelinated C fibers are present in the median nerve [5, 8]. Myelinated nerve fibers are less resistant to compression than unmyelinated ones. The latter can be damaged by prolonged local compressions, and patients in chronic stages can have obvious autonomic symptoms [5]. For this reason, a statistically significant positive relationship was found with the SSR latency in EMG stages.

Autonomic symptoms have not been encountered at a rare rate in patients with CTS. In the study of Verghese et al. [10], 57% (43 limbs) of the patients in the symptomatic group had one autonomic symptom, and 43% (33 limbs) had two or more such symptoms in the above group. In the cited study, as in ours, autonomic symptoms were significantly associated with the severity of electrophysiological abnormalities but not with the clinical severity [10]. We, however, could not find a relationship in terms of the female gender and the presence of autonomic disorders. In the study by Sener et al. [4], the mean sympathetic symptom score was 1.1 ± 0.15. Skin coloration, excessive sweating, and feeling cold scores were $0.36 \pm \pm 0.08$, 0.46 ± 0.08, and 0.26 ± 0.07, respectively [4]. In our patients, the mean SSS was 1.88 ± 0.94.

The Boston questionnaire form was developed by Levine et al. [19] in 1993. It allows the patient to evaluate the symptoms and functional status. In 2001, this form was translated into Turkish by Heybeli et al. [20], and its validity was preliminarily confirmed. In 2006, the Turkish version of BQF was found to be reliable and valid by Sezgin et al. [21]. It cannot, however, distinguish other neuropathies and disorders affiliated to upper extremity diseases from CTS. In the literature, there is a limited number of studies

analyzing the relationship between the Boston scores and median nerve conduction characteristics. Akman et al. [22] reported that there is good correlation between the BQF and median nerve characteristics. The authors suggested that only BQF application would be adequate in postoperative evaluation, and additional EMG analysis in asymptomatic patients increased the cost. Because an invasive analysis technique should be used in this case, it imposed an additional load for the patients [22]. Heybeli et al. [20] and Mondelli et al. [18] found no relationship between the Boston scores and median nerve conduction and tried to explain the reason of this finding. Heybeli et al. [23] mentioned that only the research-purpose use of the BQF was appropriate; Mondelli et al. [18] stated that electrophysiological tests and BQF should be used together for the CTS monitorization. In our study, no significant relationship was also found between the SSR parameters and BQF. The reason for this can be the following: the BQF and SSR testing evaluate different aspects of CTS, as was also mentioned by the above authors.

All procedures were in accordance with the ethical standards of the responsible Committees on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed writen consent was obtained from all patients for being included in the study.

The authors, B. Cevik, S. Kurt, D. Aksoy, and V. Solmaz, confirm that they have no conflicts with respect to any kind related to commercial or financial problems, relations with organizations or persons, which could in any way be associated with the investigation, and with the relationship of the co-authors of the article.

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ВИКОРИСТАННЯ ШКІРНОЇ СИМПАТИЧНОЇ ВІДПОВІДІ ТА БОСТОНСЬКОГО ОПИТУВАЛЬНИКА У ВИПАДКАХ СИНДРОМУ ЗАП'ЯСТНОГО КАНАЛУ

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Р е з ю м е

Ми намагалися встановити взаємовідносини судомоторної функції еферентного нерва та показників Бостонського опитувальника (BQ) у випадках ідіопатичного синдрому зап'ястного каналу (СЗК). Шкірні симпатичні відповіді (ШСВ) відводилися після стимуляції медіанного нерва на рівні зап'ястка у 108 пацієнтів із діагностованим СЗК; ці характеристики порівнювались із такими у 88 здорових добровольців. Усім суб'єктам пропонували форму BQF. Усі пацієнти та здорові особи опитувалися щодо вегетативних симптомів, які проявлялися на кисті (червоне або пурпурове забарвлення шкіри, надмірне потовиділення та відчуття холоду). Середнє значення латентного періоду ШСВ у пацієнтів із СЗК вірогідно перевищувало таке в контрольній групі ($P < 0.001$). Істотна позитивна, хоча й слабка, кореляція була виявлена між латентним періодом ШСВ, вегетативними симптомами та бальною загальною оцінкою стану симпатичної системи. Не було встановлено вірогідних відносин між показником тяжкості симптомів (згідно з BQF), оцінкою функціональної здатності та латентним періодом ШСВ. Останній параметр, отриманий при стимуляції на рівні зап'ястка, був чутливим щодо судомоторної симпатичної дисфункції у пацієнтів із цим синдромом. Відсутність зв'язку між оцінками BQF та ШСВ може бути зумовлена тим, що дані показники оцінюють різні аспекти ШСВ.

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