

PREVALENCE OF CARPAL TUNNEL SYNDROME IN PATIENTS WITH MULTIPLE SCLEROSIS

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Objective: The aim of the study was to determine the prevalence of carpal tunnel syndrome (CTS) in patients with multiple sclerosis (MS). **Patients and Methods:** The study included MS patients older than 18 that underwent inpatient rehabilitation at the Lipik Hospital in the period from November 1, 2017 to 31 May 31, 2018. Those patients that had clinical symptoms of CTS were referred to neurologist for electrodiagnostic evaluation. **Results:** Out of 75 study patients, 21 (28.0%) had CTS. There were no statistically significant differences between the groups of patients with and without CTS according to age ($t=0.582$, $p=0.562$), gender ($t=0.43$, $p=0.669$), disease duration ($t=0.669$, $p=0.506$), level of disability ($t=0.094$, $p=0.926$), and course of disease ($t=0.572$, $p=0.569$). There was positive correlation between CTS prevalence and EDSS score ≥ 6 ($rs=0.34$, $p=0.030$) and between CTS severity and age ($rs=0.464$, $p=0.034$). **Conclusion:** Given the high prevalence and the fact that CTS symptoms could be misunderstood as MS symptoms, there is the need to actively look for CTS in patients with MS, especially those using assistive walking devices.

Key words: multiple sclerosis, carpal tunnel syndrome, electrodiagnostic evaluation

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INTRODUCTION

Carpal tunnel syndrome (CTS) is a common medical problem caused by compression of the median nerve as it passes beneath the transverse carpal ligament at the wrist (1). CTS is estimated to occur in 1%-4% of the general population, with the reported annual incidence of up to 276/100,000 population (2-5). Its more frequent occurrence in women has also been noted, with the female/male distribution of two-thirds to one-third in most studies (2). Although CTS has been observed in all age groups, it occurs within the peak range of 40-60 years (4,5). The usual presentation includes paresthesias affecting the thumb and the second, third and half of the fourth finger, while some patients may complain of paresthesias affecting the whole hand, or pain and paresthesias radiating up the arm to the shoulder (6), and less commonly, weakness and muscle wasting in the median nerve innervated muscles. In the majority of patients, the exact cause and pathogenesis of CTS is unclear, although some risk factors have been associated with it (7). CTS is sometimes caused by physical occupational activities

such as repeated and forceful movements of the hand and wrist, or the use of hand-held, powered, vibratory tools (8-11). Carpal tunnel is narrower in some people than in others (12,13). Various space occupying lesions such as persistent median artery, ganglion cyst, or tumor can increase interstitial fluid pressure in the carpal tunnel (14). Trauma may also cause CTS because of canal volume restriction as a result of hemorrhage, distorted anatomy, or scar formation (15). Furthermore, CTS can be associated with a number of medical conditions, including obesity, drug toxicity, alcoholism, diabetes, hypothyroidism, rheumatoid arthritis, primary amyloidosis, and renal failure (2,14,16). Thorough history and physical examination are key to making the diagnosis, but their results should be confirmed by electrophysiological testing (2,3,17). Prolonged motor latency of the median nerve and reduced sensory conduction velocity in properly performed electrophysiological testing are accepted as diagnostic criteria for CTS (18).

The aim of the study was to determine the prevalence of CTS in patients with MS.

PATIENTS AND METHODS

The study included 75 patients with MS that underwent inpatient rehabilitation at the Lipik Special Hospital for Medical Rehabilitation in the period from November 1, 2017 to May 31, 2018. Participating in the study were patients older than 18 and diagnosed with MS according to the revised McDonald criteria (19). The exclusion criteria were serious cognitive impairment, diabetes mellitus, positive history of alcoholism, hypothyroidism, rheumatoid disease, positive history of polyneuropathy, prolonged ulnar nerve distal latency and/or ulnar sensory and motor nerve conduction velocity slowing, feet numbness, previous wrist fracture, and carpal tunnel surgery. Data on patient age, gender, degree of disability, clinical course of MS, and time elapsed from MS diagnosis were collected. The degree of disability for all study subjects was based on the Expanded Disability Status Scale (EDSS) (20) and assessment of cognitive status was performed using the Mini Mental Status Exam (MMSE) (21). Those patients with suspected CTS symptoms (hand paresthesias ± hand pain with or without arm paresthesias and pain) were referred to neurologist for electrodiagnostic evaluation. Both median and ulnar nerve motor and sensory conduction studies were done on the affected hand. Electrodiagnostic studies were performed on the Natus UltraPro S 100 machine. The settings of electromyography are as follows: pulse duration: 0.1 ms; stimulus speed: 2 ms/division; sensitivity: 10 μ V/division for sensory, 1 mV/division for motor; filter settings were 3 Hz to 10 kHz in motor and 10 Hz to 3 kHz in sensory study. Median motor nerve conduction was recorded by a surface electrode placed at the center of the abductor pollicis brevis muscle and through stimulation at the hand wrist (8 cm distance) and antecubital fossa. Distal motor latency and combined muscle action potential (CMAP) amplitude were measured and motor conduction velocity was calculated. The sensory nerve conduction study was done from the second finger by recording orthodromically from the wrist. Ulnar motor nerve conduction was recorded by a surface electrode placed at the center of the abductor digiti V muscle and through stimulation at the hand wrist and above the elbow. The sensory nerve conduction study was done from the fifth finger by recording orthodromically from the wrist. All measurements were taken at room temperature and when skin temperature was above 32 °C. Bland's neurophysiological grading scale was used to assess existence and degree of median nerve compression (22). The scale is as follows: normal finding (grade 0); very mild CTS (grade 1); CTS demonstrable only with the most sensitive tests, mild (grade 2); sensory nerve conduction velocity slow on finger/wrist measurement, normal terminal motor latency, moderate (grade 3); sensory potential preserved with motor slowing, distal motor latency to

abductor pollicis brevis (APB) <6.5 ms, severe (grade 4); sensory potentials absent but motor response preserved, distal motor latency to APB <6.5 ms, very severe (grade 5); and terminal latency to APB >6.5 ms, sensory and motor potentials effectively unrecordable (surface motor potential from APB <0.2 mV amplitude), extremely severe (grade 6). The cut off value for median nerve terminal latency was ≥ 3.9 ms, and for sensory nerve slowing <50 ms.

All respondents were divided into two groups according to the presence or absence of median nerve compression, and into the groups with EDSS score ≥ 6 and 6. The study was approved by the Hospital Ethics Committee and patients were required to provide written consent for their participation. Independent t-test was used to determine if difference existed between the groups of patients, and Spearman's correlation coefficient as a measure of strength of the association between variables. In all analyses, the level of significance was set at $p < 0.05$. Statistical analysis was performed using the SOFA Stat. for Windows.

RESULTS

The study included 75 patients, 62 (82.7%) female and 13 (17.3%) male, mean age 49.4 years, age range 31-68 years. The mean time elapsed from MS diagnosis was 9.9 years (range, 1 year to 32 years). The relapsing-remitting course of the disease (RRMS) was diagnosed in 55 (73.3%), secondary progressive MS (SPMS) in 16 (21.3%), and primary progressive MS (PPMS) in four (5.4%) patients. The median EDSS was 4.45, range 1 to 7. Out of 75 study patients, 45 had hand paresthesias ± hand pain with or without arm paresthesias and pain, and they were referred to neurologist for electrodiagnostic evaluation.

Electrodiagnostic evaluation confirmed CTS in 21 of them, which means that 21 (28%) of 75 study patients had electrophysiologically confirmed CTS (34 hands). Thirteen (17.3%) patients had bilateral positive finding.

There were no statistically significant between-group differences according to age ($t=0.582$, $p=0.562$), gender ($t=0.43$, $p=0.669$), disease duration ($t=0.669$, $p=0.506$), level of disability ($t=0.094$, $p=0.926$), and course of disease ($t=0.572$, $p=0.569$).

The number of affected hands according to relative frequency distribution of CTS with regard to severity is shown in Table 1. Moderate (grade 3) level of compression was most common.

There was positive correlation between CTS prevalence and EDSS score ≥ 6 ($r_s=0.34$, $p=0.030$) and between CTS severity and age ($r_s=0.464$, $p=0.034$).

Table 1.
Relative frequency distribution of carpal tunnel syndrome according to severity

Bland's scale level	1	2	3	4	5	6
Affected hand, n (%)	0 (0)	4 (11.8)	24 (70.5)	4 (11.8)	2 (5.9)	0 (0)

Correlation of CTS severity with the level of disability ($r_s=0.269$, $p=0.238$) and duration of illness ($r_s=0.062$, $p=0.415$) did not reach statistical significance.

Due to the small number of patients that suffered from PPMS, only patients with RRMS and SPMS were included in the analysis of the relationship of CTS and MS course.

DISCUSSION

In our study, the prevalence of CTS in MS patients was 28%. There were no significant differences between patient groups with and without CTS according to age. The mean age of patients with CTS was 50.2 years, which is in the age range when CTS reaches its peak prevalence in the general population in most of studies (4,5). CTS occurs within the peak range of 41-60 years in Croatia (23). Therefore, the absence of between-group differences was an expected finding, since the mean age of patients in the CTS negative group was similar, 49.4 years.

We found no significant between-group gender difference. The more frequent presentation of CTS in women has been noted in most of studies (2,23); however, there is a study which concluded that gender was not a risk factor in the prevalence of CTS in obese subjects (24). CTS has multifactorial etiology, and systemic, idiopathic, and ergonomic factors could be significant in its pathogenesis. Certain conditions such as hypothyroidism, rheumatoid arthritis, obesity and pregnancy can predispose to CTS (25-27). Some of these conditions, which have a higher prevalence in female gender, were among the exclusion criteria in our study (hypothyroidism and rheumatoid arthritis), while others were not analyzed or were not represented in the sample (body mass index and pregnancy).

The prevalence of CTS in the general population varies in published studies between 1% and 4% (2-5). On systematic search of medical databases ([PubMed](#), [Current Contents](#), [Web of Science](#), [Scopus](#), [Cochrane Database of Systematic Reviews](#)), we found no articles investigating the prevalence of CTS in patients with MS, although there are studies which suggest the presence of motor or sensorimotor polyneuropathy in MS patients, ranging from 5% to 45.5% (28-32). In our study, we excluded

patients with known polyneuropathy and conditions in which polyneuropathy could be expected (diabetes, hypothyroidism, feet numbness, prolonged ulnar nerve distal latency and ulnar motor and sensory nerve conduction velocity slowing). Compared with the prevalence of CTS in the general population, it is obvious that CTS was by far more common in our MS patients. We can only speculate about the reasons for the increased prevalence in our study. Prolonged postures in extremes of wrist flexion or extension and repetitive use of flexor muscles are known risk factors for CTS development (8-10). It has also been reported that the prevalence of CTS among long-term manual wheelchair users with spinal cord injury is 49%-73% (33-36). According to the findings of these studies, we can assume that the use of crutches or walker could be a predisposing factor for development of CTS symptoms. Patients with EDSS 6, 6.5 and 7 have to use crutch/crutches, walker or wheelchair by definition, and we found positive correlation between CTS prevalence and EDSS score ≥ 6 . We did not have patients with EDSS >7 among our respondents.

The absence of difference between the groups according to the duration and course of the disease when these two parameters were observed independently of other parameters was expected, since MS is a disease of the central nervous system but not a disease characterized by progressive peripheral nervous system involvement. The absence of difference between the groups according to the level of disability as measured by EDSS could be explained by the fact that the mean EDSS score was very similar in both patient groups. However, there was positive correlation between CTS prevalence and EDSS score ≥ 6 , as mentioned above. Our study demonstrated a statistically significant relationship between age and CTS severity, with CTS severity increasing with advancing age. This finding is compatible with other studies (37,38). There are statements with respect to the potential CTS risk increase with the loss of axons and vascular abnormalities due to aging (38-40).

Our study suffered from some limitations, which could have had an impact on the results. Our respondents were MS patients referred for inpatient rehabilitation, which means that the analysis excluded some of those with short disease duration associated with low functional deficit, younger age, and RRMS because these patients are rarely treated as inpatients. Furthermore, we did not use provocative test for development of CTS symptoms (Tinel's, Phalen's and reverse Phalen's test) as inclusion criteria for the study. The reasons for that was the fact that some patients had wrist contracture due to inactivity or severe arm weakness, which hampers proper performance of these tests, and difficulties in explaining negative findings of provocative tests in patients who have hypoesthetic arm due to

central lesions. Hypoesthesia in the skin areas of the hand innervated by median nerve was not an inclusion criterion for electrodiagnostic evaluation because of the possible presence of whole arm hypoesthesia due to central lesion, which would interfere with interpretation of hypoesthesia due to median nerve compression.

We also have to mention that the number of patients with CTS may have been underestimated because electrodiagnostic evaluation was only performed in patients with paresthesia or pain, thus asymptomatic individuals with CTS were not included in the group of patients with CTS.

Finally, out of 75 study patients, 45 had hand paresthesias ± hand pain with or without arm paresthesias and pain. We confirmed CTS in 21 of them, which means that 46.7% of patients with suspected CTS symptoms had electrophysiologically confirmed CTS. In the rest of patients with suspected CTS, the possible causes of symptoms suggestive of CTS most likely were central lesions due to MS, cervical radiculopathy or mild form of CTS, which cannot be proven by electrodiagnostic evaluation.

CONCLUSION

In the present study, the prevalence of CTS in patients with MS was 28%. Given the high prevalence and the fact that hand paresthesias and pain could be misunderstood as MS symptoms, there is the need to actively look for CTS in patients with MS, especially those using assistive walking devices.

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SAŽETAK

UČESTALOST SINDROMA KARPALNOG KANALA KOD OBOLJELIH OD MULTIPLE SKLEROZE

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Cilj rada: Cilj rada bio je odrediti učestalost sindroma karpalnog kanala kod oboljelih od multiple skleroze (MS). **Ispitanici i metode:** Ispitivanjem su obuhvaćeni bolesnici s MS stariji od 18 godina koji su bili u razdoblju od 1. studenoga 2017. do 31. svibnja 2018. god. na stacionarnoj rehabilitaciji u Bolnici Lipik. Dijagnoza MS postavljena je sukladno revidiranim McDonaldovim kriterijima. Prikupljeni su podaci o dobi, spolu, stupnju onesposobljenosti, kliničkom tijeku MS i vremenu proteklom od postavljanja dijagnoze MS. Bolesnici koji su imali kliničke simptome sindroma karpalnog kanala (parestezije u šaci ± bolovi u šaci s parestezijama ili bez parestezija i bolova u ruci) upućeni su neurologu na elektrofiziološku procjenu. Ispitanike smo podijelili u skupine ovisno o prisutnosti ili odsutnosti kompresije medijalnog živca u karpalnom kanalu i na skupine sa zbrojem na ljestvici EDSS ≥ 6 i < 6 . Za procjenu postojanja i stupnja težine sindroma karpalnog kanala rabili smo Blandovu neurofiziološku ljestvicu prema kojoj se sindrom karpalnog kanala dijeli u stupnjeve 0-6. **Rezultati:** Ukupan broj ispitanika bio je 75, od kojih je 21 (28,0 %) imao elektrofiziološki potvrđen sindrom karpalnog kanala. Trinaest (17,3 %) ispitanika imalo je obostrano pozitivan nalaz. Nije nađena statistički značajna razlika između skupina bolesnika sa sindromom karpalnog kanala i bez njega u odnosu na dob ($t=0,582$, $p=0,562$), spol ($t=0,43$, $p=0,669$), trajanje bolesti ($t=0,669$, $p=0,506$), stupanj onesposobljenosti ($t=0,094$, $p=0,926$) i klinički tijek bolesti ($t=0,572$, $p=0,569$). Nađena je pozitivna korelacija između učestalosti sindroma karpalnog kanala i zbroja na ljestvici EDSS ≥ 6 ($r_s=0,34$, $p=0,030$) te između stupnja težine sindroma karpalnog kanala i dobi ($r_s=0,464$, $p=0,034$). Najčešće je bio dijagnosticiran umjeren stupanj (3. stupanj) kompresije živca. **Rasprava:** Učestalost sindroma karpalnog kanala među ispitanicima bila je 28 %. Nije nađena razlika između skupina ispitanika sa sindromom karpalnog kanala i bez njega u odnosu na dob i spol. Prosječna dob u skupini ispitanika sa sindromom karpalnog kanala bila je 50,2 godine, što je u okviru dobne granice kada se sindrom karpalnog kanala najčešće javlja i u općoj populaciji (40-60 godina). Stoga je nepostojanje razlike između skupina očekivano, jer je prosječna životna dob u objema skupinama bila slična (50,2:49,4 godine). U većini studija sindrom karpalnog kanala češći je u žena, ali neka od stanja koja su češća u žena bila su isključni kriteriji za ulazak u našu studiju (hipotireoza, reumatoidni artritis), neka stanja nisu analizirana (indeks tjelesne mase), a neka nisu bila zastupljena u uzorku (trudnoća). Nepostojanje razlika između skupina u odnosu na zbroj na ljestvici EDSS može se objasniti činjenicom da je u objema skupinama srednja vrijednost zbroja bila gotovo jednaka (4,48:4,44). Veća učestalost sindroma karpalnog kanala u odnosu na opću populaciju, gdje se učestalost procjenjuje na 1 %-4 %, mogla bi biti uzrokovana upotrebom pomagala za hod (štap, štake, hodalica, invalidska kolica), budući da je učestalost sindroma karpalnog kanala bila značajno viša u onih sa zbrojem 6 i više na ljestvici EDSS. Radi se o bolesnicima koji moraju koristiti pomagalo za hod (6 - štap ili štaka, 6,5 - dvije štake ili hodalica, 7 - invalidska kolica). U uzorku nismo imali zastupljene bolesnike sa zbrojem na ljestvici EDSS većim od 7. Nepostojanje razlika između skupina s obzirom na trajanje bolesti i tijek bolesti očekivani je nalaz, budući da je MS bolest središnjega živčanog sustava, a ne progresivna bolest perifernoga živčanog sustava. Pozitivna korelacija između stupnja sindroma karpalnog kanala i porasta životne dobi u skladu je s rezultatima drugih istraživanja s obzirom na gubitak aksona i poremećaje u krvnim žilama živca sukladno s porastom dobi. **Zaključak:** S obzirom na visoku učestalost i činjenicu da simptomi sindroma karpalnog kanala mogu biti zamijenjeni simptomima MS potreban je aktivan pristup u dijagnostici sindroma karpalnog kanala kod oboljelih od MS, osobito onih koji koriste pomagala za hod.

Cljučne riječi: multipla skleroza, sindrom karpalnog kanala, elektrofiziološko testiranje