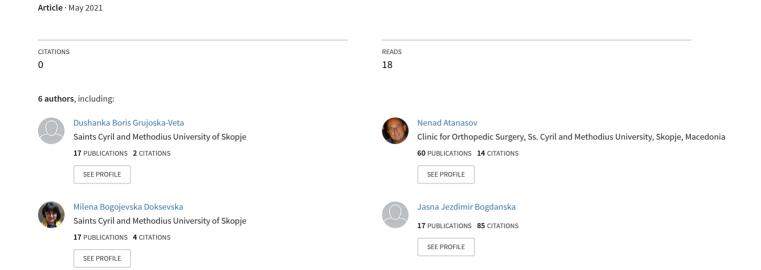
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THE ROLE OF OBESITY AS NONOCCUPATIONAL RISK FACTOR IN PATIENTS WITH CARPAL TUNNEL SYNDROME

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Abstract

Introduction: Carpal tunnel syndrome (CTS) is one of the most common peripheral neuropathies caused by chronic compression of the median nerve in the area of the carpal tunnel. The purpose of our study was to evaluate the demographic data in patients with carpal tunnel syndrome and determine the association between obesity and CTS severity.

Material and methods: A total of 116 surgically treated patients with established diagnosis of CTS (clinically and by electrophysiological examination), were included according to inclusion criteria in this prospective study, which was conducted at the University Clinic for Orthopedic Diseases in Skopje. Demographic data, findings of history of the disease, clinical, electrophysiological examination and BMI measurements were recorded and analyzed.

Results: Eighty-seven patients were female and 29 male, with a mean age of 55.41 ± 10.7 years (age range 27-75). The body mass index (BMI) had an average value of 27.7 ± 5.6 kg/m² and ranged from 27.7 to 46.5 kg/m². A statistically significant difference (p = 0.017) was found between higher grades of CTS severity (very severe and extremely severe) and higher values of BMI (overweight and obese patients), compared to patients with normal body weight.

Conclusion: Our findings have determined significant association between CTS severity and BMI values over 30kg/m². Our study has identified the possible role of obesity as an individual risk factor in the etiology of carpal tunnel syndrome.

Keywords: carpal tunnel syndrome, body mass index, CTS severity

УЛОГАТА НА ПРЕКУМЕРНО ЗГОЛЕМЕНА ТЕЛЕСНА ТЕЖИНА КАКО МОЖЕН РИЗИК-ФАКТОР ЗА ПОЈАВА НА СИНДРОМ НА КАРПАЛЕН ТУНЕЛ

Апстракт

Вовед:Синдром на карпален тунел е една од најчестите периферни невропатии причинета од хронична компресија на средишниот нерв во предел на карпалниот тунел. Целта на оваа студија беше да ги евалуира демографските податоци на

пациентите со синдром на карпален тунел и да ја одреди поврзаноста помеѓу прекумерната тежина и степенот на оштетување на средишниот нерв кај пациенти со синдром на карпален тунел.

Материјал и методи: Вкупно 116 оперирани пациенти со дијагноза на синдром на карпален тунел (потврдена со клинички и електрофизиолошки испитувања) беа вклучени според одредени критериуми за вклучување во оваа проспективна студија која се спроведе на Универзитетската клиника за ортопедски болести во Скопје. Сите демографски податоци, наоди од историја на болеста, клиничките, електрофизиолошките испитувања и вредностите на индексот на телесна маса беа регистрирани и статистички обработени.

Резултати: Во студијата беа вклучени 87 пациентки и 29 пациенти со просечна старост $55,41 \pm 10,7$ години (27-75 години). Средната вредност на индексот на телесна маса кај пациентите беше $27,7 \pm 5,6$ kg/m² (7 до 46,5 kg/m²). Беше утврдена статистички сигнификантна разлика (р = 0,017) помеѓу појаките степени на оштетување на средишниот нерв (многу тешки и екстремно тешки) и повисоките вредности на индексот на телесна маса (зголемена и прекумерно зголемена телесна тежина), споредена со пациентите со нормална телесна тежина.

Заклучок: Наодите од нашето истражување утврдија значајна поврзаност помеѓу степенот на оштетување на средишниот нерв вопределот на карпалниот тунел и индексот на телесна маса над 30 kg/m². Според нашите резултати, може да се заклучи дека прекумерно зголемената телесна тежина е можен индивидуален ризик-фактор за појава на синдром на карпален тунел.

Клучни зборови: синдром на карпален тунел, индекс на телесна маса, степени на оштетување на средишниот нерв

Introduction '

Carpal tunnel syndrome (CTS) is one of the most common peripheral neuropathies caused by chronic compression of the median nerve in the area of the carpal tunnel. The diagnosis of the syndrome is mainly based on the history of the disease, clinical findings, findings of provocative tests and electroneuromyographic examination (ENMG) of the median nerve (1,2).

With the technological advancement of visualization methods and equipment, ultrasonography and magnetic resonance imaging were introduced as additional diagnostic tests for carpal tunnel syndrome 20 years ago (3,4). The clinical picture depends on the duration and intensity of pressure on median nerve, which is a mixed type of nerve with sensitive and motor nerve fibers. At the beginning, the discomfort is in the form of sensory disturbances (numbness, paresthesia and/or pain in the fingers from the thumb to the radial side of the ring finger, tingling and burning pain even radiating to the elbow or shoulder, nocturnal pains). Nocturnal pains and paresthesia are of gradual onset and they are reported to be 51-96% sensitive and 27-68% specific (5). Later, in more severe cases, when motor component of the median nerve is involved, decreased muscle power, dropping objects and clumsiness during everyday activities are observed. Hypotrophy of tenor muscles is a significant sign of serious functional loss. Characteristic clinical findings are usually absent in milder cases with CTS. In order to establish diagnosis of CTS more accurately many provocative tests are in use with reported sensitivity between 10% and 100% and specificity between 33% and 100% (6).

The exact incidence and prevalence vary depending on the diagnostic criterion. The highest incidence is in patients aged 50-60 years and more often in females, i.e.female: male ratio is 3:1. (7). The exact prevalence of people with complaints is from 13.0% to 15.8% in the general population, and according to the clinical picture and confirmed by ENMG examinations varies from 2.7% to 5.8% (8,9).

The etiology of the syndrome is multifactorial. The disease is most commonly associated with a variety of genetic factors (10), physiological conditions (pregnancy) (11), systemic and metabolic diseases(12,13). Risk factors for carpal tunnel syndrome include female gender, age (40-70 years), smoking, diabetes, hypothyroidism and obesity(14). Among anthropometric factors, body mass index is a well-known determinant of CTS(15).

Bearing this in mind, the purpose of our study was to evaluate the demographic data in CTS patients and determine the association between obesity and carpal tunnel syndrome.

Material and methods

Our study is a prospective clinical study conducted at the University Clinic for Traumatology, OrthopedicDiseases, Anesthesiology, Reanimation and Intensive Care Medicine and Emergency Department, Clinical Center Mother Theresa, Skopje, RNM, during a 3-year period. One hundred and sixteen patients included in the study were with clinical diagnosis of CTS and previously examined by ENMG examination. All patients were admitted for surgical procedure of open carpal tunnel release (CTR), at the University Clinic for Orthopedic Diseases in Skopje. Medical history of the disease and previous injuries and treatments were recorded. Findings of patient's weight, height, examination of hands (muscle strength, ROM of wrist metacarpophalangeal joints), signs of thenar hypotrophy as well as findings of provocative tests (Phalen, Durkan and hand elevation test) were noted. All patients were asked to fulfill questionnaires concerning their perception of his/her symptoms and hand function, dominant hand, level of education, profession, weight, height, cigarette smoking and consumption of alcohol.

Inclusion criteria for the group of participants:

- persons aged 25-75 years
- anamnestic data on tingling and/or pain in the thumb, second, third and radial part
 of the fourth finger, nocturnal paresthesia, clumsiness with the fingers of the
 affected hand
- · positive provocative tests
- confirmed diagnosis of CTS by ENMG

Exclusion criteria for the group of participants:

- persons under 25 years of age and older than 75 years
- pregnant women
- people with reduced cognitive abilities
- · detainees and prisoners
- · previous hand surgery
- soft-tissue injuries or fractures of the bones of the forearm and wrist
- · polyneuropathy, hereditary neuropathy

For the grading of median nerve impairment by nerve electroneuromyographic examination (ENMG), Canterbury Severity Scale for CTS was used (16). According to

this scale, grades are:normal (grade 0); very mild (grade 1), CTS demonstrable only with 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), terminal latency to APB > 6.5 ms; extremely severe (grade 6), sensory and motor potentials effectively unrecordable (surface motor potential from APB < 0.2 mV amplitude).

Weight and height were measured in all CTS patients in order to calculate theirbody mass index (BMI).BMI is the same for both sexes and for all ages of adults. It was calculated for all the examined subjects as a person's weight in kilograms divided by the square of his/her height in meters (kg/m²)(17).

Classification of BMI scores are:

< 18.5	(Underweight)
18.5 - 24.9	(Normal weight)
25 - 29.9	(Overweight)
30 - 34.9	(Obesity class I)
35 - 39.9	(Obesity class II)
> 40	(Obesity class III)

Statistical analysis

A descriptive-analytical statistical method was used for the statistical processing of the obtained results from the clinical study. Statistical analysis was carried out by using the software SPSS, version 22.0. Descriptive data are presented as mean \pm standard deviation (SD), or as median. Percentages are given for categorical variables. The threshold for statistical significance was set at p<0.05.

Results

One hundred and sixteen patients were enrolled in this study according to the inclusion criteria. They were examined by ENMG examination prior to admittance for surgical procedure of CT release at the University Clinic for Orthopedic Diseases-Skopje. Eighty-seven patients were female and twenty-nine male, with a mean age of 55.41±10.7 years (age range 27-75). In the distribution according to the level of education, most of the patients had completed secondary education - 62.9% (73). 86.2% (100) of CTS patients were of Macedonian ethnicity, followed by patients of Albanian - 6% (7), and Serbian ethnicity - 4.3% (5). Two patients were of Turkish and one patient was of Roma ethnicity.

Female patients with CTS were younger than male patients, but the mean age was not statistically significant (p=0.16). The mean age of female patients was 54.6 ± 10.4 and of male patients 57.83 ± 10.9 .

Table 3 presents the most common symptoms and duration of symptoms. Results obtained showed that all patients complained on paresthesia and numbness. Twenty (17.2%) CTS patients had pain during daytime. Nocturnal pains were predominant symptoms in this group of patients - 47.4% (55), 35.35% (41), respectively. Sleep disturbance and clumsiness with the handswere positive in 41(35.35%) patient, who also had hypotrophy of thenar and muscle weakness. Duration of characteristic symptoms of more than 2 years was noted in 50.9% (59) of CTS patients.

Table 1 Demographic ch	Demographic characteristics of CTS patients					
Variable						
Gender	n (%)					
Female	87 (75)					
Male	29 (25)					
Total	116 (100)					
Age (mean \pm SD)	(55.41 ± 10.7)					
Level of education	n (%)					
Elementary school	10 (8.62)					
Secondary school	73 (62.93)					
College / Faculty	33 (28.45)					
Nationality						
Macedonian	100 (86.21)					
Albanian	7 (6.03)					
Serbian	5 (4.31)					
Turkish	2 (1.72)					
Roma	1 (0.86)					
other	1 (0.86)					

Table 2	Gender an	i mean age	of CTS	patients
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C 1	Descriptiv	e Statistics	n loval		
Gender n	mean ± SD	p-level			
Female	87	54.61 ± 10.4	t=1.43		
Male	29	57.83 ± 10.9	p=0.16 ns		

p (Student t-test for independent samples)

Table 3 Symptoms, duration of symptoms, symptomatic hand	l, surgery
Variable	
Symptoms	n (%)
Numbness, paresthesia	116 (100)
Numbness, paresthesia, pain	20 (17.24)
Numbness, paresthesia, nocturnal pains,	55 (47.41)
Numbness, paresthesia, nocturnal pains, sleep disturbance, weakness	41 (35.35)
Duration of symptoms	n (%)
6 – 12 months	15 (12.93)
12 – 24 months	42 (36.21)
> 24 months	59 (50.86)
Symptomatic hand	n (%)
Right hand	38 (32.76)
Left hand	26 (22.41)

Both hands		51 (43.96)
Dominant hand		n(%)
Right	*	111 (95.69)
Left	-3	5 (4.31)
Carpal tunnel release	w	n(%)
Right hand		66 (56.9)
Left hand		50 (43.1)

Table 4 presents classification of BMI values in relation to the gender of CTS patients. The body mass index (BMI) had an average value of 27.7 ± 5.6 kg/m² and ranged from 27.7 to 46.5 kg/m². Two patients were slender (underweight), 39 patients had normal weight, 40 patients were overweight, and 35 patients were obese. The body mass index did not differ significantly between patients according to their gender (p=0.71).

Table 4	Classi	ification	of BMI values i	in relation to gende	er of CTS pa	atients
		Ger	p-level			
Variable BMI		Female n (%)				Male n (%)
mean ± SD	AND THE PERSON NAMED IN COLUMN TWO PERSONS NAMED IN COLUMN TRANSPORT NAMED IN COLUMN TRANSPORT NAMED IN COLUMN TRANSPORT NAMED IN COLUMN TRANS		27.77 ± 5.5	27.34 ± 6.0	t=0.36	p=0.72 ns
<18.5		2	2 (2.3)	0		
18.5 - 24.9		39	29 (33.33)	10 (34.48)	Z=0.37	p=0.71 ns
25 - 29.9		40	26 (29.89)	14 (48.28)		
30 - 34.9		23	23 (26.44)	0		
35 - 39.9		7	5 (5.75)	2 (6.9)		
>40		5	2 (2 3)	3 (10.34)		

p (Wilcoxon Matched Pairs Test

Table 5	Comparison of clinical findings in relation to BMI values
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Clinical findings	BMI (kg/m²)						
	< 18.5	18.5 . –	25 –	30 – 34.9	35 –	> 40	
	N=2	24.9	29.9	N=23	39.9	N = 5	
	n (%)	N=39	N=40	n (%)	N=7	n	
		n (%)	n (%)	•	n (%)	(%)	
Positive provocative tests	0	24(61.54)	26(65)	14(60.87)	5(71.43)	3(60)	
Hypotrophy of thenar	2(100)	15(38.46)	14(35)	9(39.13)	2(28.57)	2(40)	
p-level	H=3.7p	=0.6 ns					

H (Kruskal-Wallis test)

Table 5 presents the relation between clinical findings (positive provocative tests and hypotrophy of thenar) and BMI in CTS patients. The clinical findings preoperatively did not differ significantly between patients according to their body mass index (p = 0.6). Patients with normal body weight (BMI = $18.5 - 24.9 \text{ kg/m}^2$), overweight(BMI = $25 - 29.9 \text{ kg/m}^2$) and obese patients(BMI $\geq 30 \text{ kg/m}^2$) more often had positive provocative

test on clinical examination- 61.5% (24), 65% (26), 60.9% (14), 71.4% (5) and 60% (3) patients, respectively(**Table 5**).

Table 6 presents the relation between the severity of the electroneuromyographic findings and BMI in CTS patients. Astatistically significant difference of electroneuromyographic findings in patients with carpal tunnel syndrome in relation to the body mass index was found (p = 0.017).

The higher grade of severity of electroneuromyographic finding (very severe and extremely severe) was detected more often in overweight and obese patients, compared to patients with normal body weight - 12.8% (5), 25% (10), 34.8% (8), 28.6% and 80% (4) patients, respectively (Table 6).

Table 6	Comp	arison of CTS	severity in r	elation to BM	II values		
		¥ = = =					
C/D/C	BMI (k	g/m²)	•				
CTS severity scale	<18.5 N=2	18.5 – 24.9 N=39	25 – 29.9 N=40	30 – 34.9 N=23	35 – 39.9 N=7 n (%)	> 40 N =5 n (%)	n
	n (%)	n (%)	n (%)	n (%)	0	0	+
normal very mild	0 1(50)	0	1(2.5) 0	0	0	1(20)	2
mild	1(50)	6(15.38)	1(2.5)	1(4.35)	0	0	9
moderate	0	20(51.28)	24(60)	11(47.83)	3(42.86)	0	58
severe	0	8(20.51)	4(10)	3(13.04)	2(28.57)	0	17
very severe	0	0	3(7.5)	6(26.09)	0	1(20)	10
extremely severe	0	5(12.82)	7(17.5)	2(8.7)	2(28.57)	3(60)	19
p-level	H=15.4	p=0.017 sig		F			

A statistically significant correlation was found between electroneuromyographic findings in patients with carpal tunnel syndromeand their body mass index (p = 0.0096)(Figure 1).

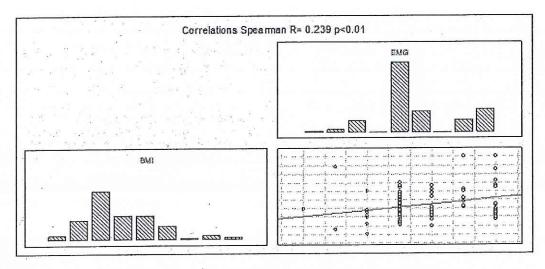


Figure 1 Correlation between CTS severity (ENMG) and BMI

The value of the Spearman's correlation coefficient of R=0.239 showed that this correlation was positive. This leads to the conclusion that the higher values of body mass index, the higher values of severity of carpal tunnel syndrome in electroneuromy ographic findings, and vice versa.

Discussion

Carpal tunnel syndrome is the most common neurocompressive disease with multifactorial etiology. The diagnosis is mainly based on characteristic symptoms, clinical signs and electroneuromyographic findings. Several risk factors such asgender, age, genetic and anthropometric factors are associated with development of CTS.

The results obtained in our study haveshown that majority of participants were of female gender at themean age of 54.61 ± 10.4 years. This is in correlation with most of the epidemiological studies which have reported a higher risk of CTS among women than among men(18). English *et al.* from New Zealand, reported in their retrospective study including2,313 patients who underwent CTR that 1,419 (61%) were female and 890 (39%) were male(19). In a study conducted by Farioli*et.al.* in Italybetween 1997 and 2000, analmost 4-fold increase in the risk of surgically treatedCTS was observed in women compared with menamong non-manual workers(20).

Female patients in our study were younger than male patients, but the mean age was not found to be statistically significant (p=0.16). This finding is consistent with other studies(21).

Female patients in our study group were in reproductive and menopausal period. This means that hormonal changes during these periods might be responsible for the onset of tissue edema, thus causing an increased pressure in the region of the carpal tunnel and on the median nerve (22,23). Greater incidence of surgically treated female patients with CTS might also be explained by repetitive movements in taking care of small children and during housework (24).

Not only hormonal variations in females, but also many risk factors in both females and males are associated with different metabolic changes (dyslipidemia, hypercholesteremia), with long-term effect on cardiovascular system. Microvascular changes might lead to reduction of nutrients and oxygen to the nerves and development of ischemia. Such alterations are more expressed in nerves placed in narrow osteofibrous tunnels like median nerve (25, 26).

BMIis one of the anthropometric factors commonly associated with CTS patients. It is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. In our study, 116 patients with CTS had the body mass index (BMI) of an average value of $27.7 \pm 5.6 \text{ kg/m}^2$. The majority of the study group was with increased BMI. Forty patients were overweight, and 35 patients were obese (over 30 kg/m²). The body mass index did not differ significantly between patients according to their gender (p=0.71).

The clinical findings preoperatively did not differ significantly between patients according to their body mass index (p = 0.6). But overweight and obese patients more often had a positive provocative test on clinical examination- 61.5% (24), 65% (26), 60.9% (14), 71.4% (5) and 60% (3) patients, respectively. These results are consistent with other studies(27).

Our results have shown that the body mass index showed a statistically significant impact on the electroneuromyographic findings in patients with carpal tunnel syndrome

(p = 0.017). Overweight and obese patients had higher grades of severity on severe).A electroneuromyographic finding (very severe and extremely statisticallysignificant correlation was found between electroneuromyographic findings in patients with carpal tunnel syndrome and their body mass index (p = 0.0096). This leads to aconclusion that the higher values of body mass index, the higher values of severity of carpal tunnel syndrome on electroneuromyographic findings, and vice versa. These findings are consistent with other studies. Nathan et al.in a longitudinal study published in1992 evaluated weight and body mass index (BMI) as risk factors for slowing of sensory conduction of the median nerve and concluded that the risk for abnormal nerve conduction averaged 3.5-fold and 4.1-fold greater, respectively, in the obese workers than in the slender workers (28).

In 2012Spahnet al. published their results from a meta-analysis for the evaluation of risk factors for CTS. Two of real risk factors (results from longitudinal studies) were female gender and overweight or obesity (29). Overweight increased the risk of CTS or carpal tunnel release 1.5-fold and obesity two-foldas reported in a study by Shiri et al. (30). Female sex and high BMI are reported in many studies to be independent risk factors and the most important predictors of surgical release in patients with CTS (31,32).

The relationship between increased BMI and CTS severity had been explained by increased fat deposits outside and inside carpal tunnel. The increased carpal tunnel pressure is thought to cause ischemia of the median nerve and subsequent changes according to the duration of pressure (demyelination and axonal degeneration)(33).

There are many studies on etiology and pathophysiology of CTS and yet there are many cases of CTS considered to be idiopathic.

The limitation of our study is the small number of participants, which consequently does not represent the characteristics of the general population. Further studies are necessary to investigate the role of other non-occupational and anthropometric risk factors responsible for the development of CTS.

Conclusion

Over the past few years, the morbidity of CTS has increased. Our study has identified the female gender as an individual risk factor. Also, a significant relationship between the CTS severity and obesity has been identified as a non-occupational risk factor in the etiology of carpal tunnel syndrome. Since the prevalence of overweight and obesity is increasing globally, overweight-related CTS is expected to increase, too.

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