

## Carpal Tunnel Syndrome in Obstructive Sleep Apnea Patients Obstrüktif Uyku Apnesi Hastalarında Karpal Tünel Sendromu

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### ABSTRACT

**Introduction:** Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper extremity. It is usually associated with the compression of the median nerve in the median groove. Because the main symptoms of CTS pain and numbness worsen at night, sleep disorders in CTS patients and the impact of preferred sleeping position on CTS development have been formerly studied. However, to the best of our knowledge, this is the first study assessing the frequency of CTS in obstructive sleep apnea (OSA) patients. This study aimed to determine the frequency of CTS in OSA patients and evaluate the causative relation between the two diseases.

**Methods:** Records of individuals who were admitted to our sleep laboratory were retrospectively scanned. Eighty patients who were diagnosed with OSA and did not have comorbidities that might cause OSA (e.g., diabetes mellitus, hypothyroiditis, rheumatic diseases, and cervical radiculopathy) were included in the study along with 80 healthy controls who matched for age, sex, and BMI of OSA patients. To maintain observer blindness, patients were not questioned regarding their symptoms or the clinical data that would be used in the study. All participants underwent

nerve conduction studies. Those who were diagnosed with CTS were questioned regarding CTS symptoms and the preferred sleeping position. Subsequently, patients were given the Boston CTS questionnaire.

**Results:** CTS frequency in OSA patients was found to be 27.5%. There was no significant relation between preferred sleeping position or being a manual worker and having CTS.

**Conclusion:** CTS frequency in OSA patients is significantly higher than that in healthy individuals. In contrast to previous studies that have been performed in the absence of polysomnographic and electrophysiological data, in our study biomechanical factors were not associated with CTS presence. Therefore, we conclude that intermittent hypoxemia is the main etiological factor for CTS in OSA patients. Inflammation may be a common factor for etiopathogenesis for both diseases, but this hypothesis needs further investigation.

**Keywords:** Obstructive sleep apnea, carpal tunnel syndrome, nerve entrapment, PSG, nerve conduction study

### ÖZ

**Amaç:** Karpal tünel sendromu (KTS) üst ekstremitenin en sık görülen tuzak nöropatisidir. En sık olarak median sinirin, karpal tünel içinde baskıya uğramasıyla ilişkilendirilir. Ana semptomları olan ağrı ve uyuşma özellikle geceleri kötüleştiğinden KTS hastalarında uyku bozuklukları ve uykuda yatış pozisyonunun KTS oluşumu üzerine etkileri daha önce çeşitli araştırmacılar tarafından incelenmiştir. Ancak obstrüktif uyku apnesi (OUA) hastalarında KTS varlığı bildiğimiz kadarıyla ilk kez tarafımızdan çalışılmıştır. Bu çalışmadaki amacımız, OUA hastalarında KTS sıklığını belirlemek ve iki hastalık arasındaki olası nedensel ilişkiyi incelemektir.

**Yöntem:** Uyku laboratuvarımıza başvuran hastaların dosyaları retrospektif olarak incelenmiştir. OUA tanısı konmuş hastalar içinden KTS için yatkınlık oluşturabilecek ko-morbiditeleri (diabetes mellitus, hipotiroidi, romatizmal hastalıklar, servikal radikulopati) olmayan 80 hasta ve hastalarla yaş, cinsiyet, vücut kitle indeksi açısından uyumlu olan 80 sağlıklı kontrol çalışmaya dahil edilmiştir. Araştırmacıların körlüğünü sağlamak açısından hastalar çalışma öncesinde klinik bilgiler ve çalışmada kullanılacak bilgiler açısından sorgulanmamıştır. Tüm hasta ve kontrollere sinir iletim

çalışması uygulanmıştır. KTS tesbit edilen hastalar KTS semptomları ve tercih ettikleri yatış pozisyonları açısından sorgulanmış ve Boston KTS sorgulama ölçeği verilmiştir.

**Bulgular:** OUA hastalarında KTS sıklığı %27,5 bulunmuştur. Yatış pozisyonu ve el gücü ile çalışmanın KTS varlığı ile bir bağlantısı bulunmamıştır.

**Sonuç:** OUA hastalarında KTS sıklığı genel popülasyona göre çok yüksek bulunmuştur. Ancak polisomnografik ve elektrofizyolojik veriler olmadan yapılmış daha önceki çalışmaların aksine OUA hastalarında KTS varlığının biyomekanik faktörler ile bir bağlantısı bulunmamıştır. OUA' da meydana gelen aralıklı hipokseminin KTS oluşumuna yatkınlık oluşturan ana faktör olduğunu düşünmekteyiz. İki hastalığın ortak etyopatogenezi olarak inflamasyon da suçlanabilir ancak bu faktörle ilgili karar vermek için daha ileri çalışmalar gereklidir.

**Anahtar kelimeler:** Obstrüktif uyku apnesi, karpal tünel sendromu, sinir tuzaklanması, PSG, sinir iletim çalışması

**Cite this article as:** Bilgin Topçuoğlu Ö, Oruç Ö, Saraç S, Çetintaş Afşar G, Uluç K. Carpal Tunnel Syndrome in Obstructive Sleep Apnea Patients. Arch Neuropsychiatry 2017; 54:307-311.

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**Received / Gelış tarihi:** 23.02.2016

**Accepted / Kabul tarihi:** 07.04.2016

**Available Online Date / Çevrimiçi Yayın Tarihi:** 15.04.2016

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## INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common compressive neuropathy of the upper extremity with an estimated prevalence of 3%–6% of the general population (1,2,3). CTS is a clinical syndrome most often related to mechanical distortion produced by a compressive force on the median nerve in the carpal tunnel segment (4). Multiple factors including genetic predisposition, injury, and workplace biomechanical factors have been blamed for etiology (5,6,7,8). Furthermore, there are consistent and strong associations between CTS and age, gender, body mass index (BMI), diabetes mellitus (DM), pregnancy, and wrist morphology (2,9,10,11,12). Clinical findings of CTS are pain and dysesthesia in the median nerve distribution, in the region of the thumb, index, middle and the lateral half of the ring finger, which may worsen during sleep (13).

Obstructive sleep apnea (OSA) is characterized by recurrent partial and complete airway obstruction episodes during sleep resulting in repetitive apneas and hypopneas (14) with an estimated prevalence of 3%–10% in the adult population (15,16,17). CTS is known to affect almost all systems in the body including the neurological system. Despite a limited number of studies determining axonal damage and peripheral neuropathy in sleep apnea patients (18,19) and those describing sleep disturbances in CTS patients (20,21), no studies have analyzed CTS in OSA. To the best of our knowledge, this is the first study assessing CTS in OSA patients.

In this study, we investigated the frequency of CTS in OSA. Because of its relation with waning productivity that causes work disability and high-cost treatments, CTS is an important issue particularly in the workplace (22,23,24). The study also aimed to explore the link between the two syndromes depending on polysomnographic and electrophysiologic data, supported by the use of Boston CTS questionnaire (BCQ), so that early diagnosis, preventive, and/or therapeutic approaches may be possible for OSA patients.

## METHODS

A retrospective review of the polysomnography records of 476 individuals who were admitted to our sleep laboratory between March 2015 and December 2015 was performed. Medical records of 423 subjects (88.9%) who were diagnosed with OSA were reviewed. The severity of OSA was decided by the apnea/hypopnea index (AHI) and total number of respiratory events per hour of sleep, which is supposed to be  $\geq 5$  for diagnosis (25). Patients who had HbA1C  $>6.5\%$ , did regular alcohol consumption, or had a prior diagnoses of DM, hypothyroidism, rheumatic diseases, cervical radiculopathy were excluded. Eighty OSA patients between the age of 28–75 years, meeting the inclusion criteria were included in the study and underwent nerve conduction studies (NCSs). No information about the participants was gathered before NCSs. To provide observer blindness, those who were diagnosed with CTS were then questioned about symptom presence and symptom sides (right, left, or bilateral) and sleeping position (none, right, left, supine) and given the BCQ to investigate the clinical compatibility of electrophysiological findings. The results of the questionnaires have been calculated as the mean values.

Eighty healthy individuals perfectly matching the age, sex, and BMI of OSA patients, without comorbidities like DM, hypothyroidism, cervical radiculopathy, rheumatic diseases and whose HbA1Cs were  $<6.5\%$  and did not regularly consume alcohol were included in the study as control subjects.

BMI of the patients and the controls was calculated as the weight (kg) divided by the height squared ( $m^2$ ).

All experiments were performed in compliance with the relevant institutional guidelines. The study was approved by the Local Ethics Committee of our Institution and was conducted in accordance with the ethical principles stated in the Declaration of Helsinki. A written informed consent form was obtained from each participant included in the study.

## Polysomnography

All patients were monitored with a nocturnal PSG that was performed with multichannel monitoring that included neurophysiological electrodes (electroencephalography electrodes), chest wall motion, abdominal motion, arterial oxygen saturation, and electrocardiography electrodes (Grass-Telefactor Cephalo, An Astro-med Inc. Product Group, 2005, USA). Oronasal airflow was measured using a thermistor. The oxyhemoglobin saturation was monitored with a finger pulse oximeter with a sampling rate of 1 Hz. The body position was measured by a position sensor attached to the anterior chest wall. Signals recorded in the sleep period were manually analyzed (25). Apneas were scored when the airflow decreased by at least 90% from baseline for at least 10 s and were classified as central, mixed, or obstructive depending on the occurrence of thoracoabdominal movements (25). Hypopneas were scored when airflow decreased by at least 30% for  $\geq 10$  s and was associated with an oxygen saturation ( $SpO_2$ ) fall of  $\geq 3\%$ . AHI was calculated as the average number of apneas and hypopneas per hour of recording in the sleep period. An AHI of  $\geq 5$  was used to diagnose OSA (26).  $SpO_2$  during the sleep period was automatically analyzed, and after the manual elimination of possible artifacts, mean  $SpO_2$  and lowest nocturnal  $SpO_2$  values were detected. According to their overall AHIs OSA patients were grouped as mild (5–14.9/h) and moderate to severe ( $>15/h$ ) (25).

## Nerve conduction studies

Eighty patients and eighty healthy control subjects underwent NCSs. Two investigators who were blinded to the patient and control groups assessed all of the electrophysiological studies. All median motor and sensory NCSs were performed using a Medelec Synergy electromyography device (Medelec Synergy EMG, Oxford Instruments Medical, Old Working, UK) and surface bar recording and bipolar surface recording electrodes (Teca Corp.). Median sensory NCSs were performed using the antidromic technique; the recording electrode was placed over the palmar surface of the second digit and the nerve was stimulated from the wrist at 13 cm. The normative value in our laboratory for median motor latency is  $<4.5$  milliseconds and median sensory distal peak latency is  $<3.5$  milliseconds. For motor NCSs, the median motor nerve was stimulated at the wrist 6.5 cm proximal to the active recording electrode. Diagnostic criteria for CTS were accepted as the nerve conduction velocity of the sensory and/or motor median nerves to be  $<50$  m/s.

Filter settings were 5 Hz to 10 kHz for motor NCSs and 20 Hz to 2 kHz for sensory NCSs. During testing procedures the room temperature was maintained at an average of 25°C, and the skin temperature was maintained above 33°C in all participants.

## Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences statistical software version 18.0 (IBM SPSS Statistics, New York, USA). Categorical variables were expressed using percentages. Shapiro–Wilk normality test was used to test the distribution of numerical variables. Categorical variables were compared using the chi-square test. For continuous variables, parametric Student's t-test and non-parametric Mann–Whitney U test were used. Analysis of descriptive variables was presented

**Table 1.** Demographic features of all study participants

	OSA patients (n:80)	Healthy controls (n:80)	p
Age (years)	49.35 (28–74)	47.63 (35–70)	0.147
Gender (f/m)	9 f (11.25%), 71 m (88.75%)*	7 f (8.75%), 73 m (91.25%)*	0.92
Mean BMI (kg/m <sup>2</sup> )	30.27 (21.3–40)	29.13 (23–41.4)	0.328
*f: female; m: male; BMI: body mass index			

**Table 2.** Polysomnographic findings of CTS patients vs. non-CTS patients

	CTS patients (n:22)	Non-CTS patients (n:58)	p
Epworth Sleepiness Scale	7.72 (±5.04)	9.06 (±5.60)	0.305**
Sleep latency (min)	10.78 (±10.59)	14.79 (±21.99)	0.457**
Sleep efficiency (%)	82.07 (±19.40)	86.67 (±8.09)	0.694**
NREM1 stage sleep (%)	5.35 (±4.64)	5.76 (±5.87)	0.966**
NREM2 stage sleep (%)	55.29 (±15.05)	57.15 (±12.02)	0.567*
NREM3 stage sleep (%)	17.90 (±13.09)	20.42 (±10.27)	0.369*
REM stage sleep (%)	13.90 (±5.04)	13.48 (±6.85)	0.769*
AHI (/h)	27.54 (±22.46)	29.18 (±19.56)	0.730**
Mean oxygen saturation%	93.18 (±2.32)	93.00 (±2.80)	0.926**
Minimum oxygen saturation%	77.90 (±11.36)	76.19 (±12.99)	0.726**

\*independent samples t test, \*\*Mann-Whitney U. NREM: non rapid eye movement; REM: rapid eye movement; AHI: apne hypopnea index

**Table 3.** Classification of OSA severity in CTS patients vs. non-CTS patients

	CTS patients (n:22)	Non-CTS patients (n:58)	p
Mild (AHI 5–14.9/h)	27.3% (n:6)	29.3% (n:17)	0.857
Moderate to severe (AHI >15/hour)	72.7% (n:16)	70.7% (n:41)	

CTS: carpal tunnel syndrome; AHI: apne hypopnea index

as mean ± SD, whereas the analysis of categorical variables was presented as percentile. Statistical significance was set at a p value of <0.05.

## RESULTS

Eighty OSA patients and eighty healthy controls were included in the study. There were no significant differences between the study groups with respect to age, sex distribution, or BMI. Demographic features of the study participants are presented in Table 1.

CTS was detected in 27.5% (n:22) of the OSA patients. CTS and non-CTS patients revealed no significant difference in sleep statistics (Table 2).

There were no significant differences between the mean AHIs of CTS and non-CTS patients ( $p=0.730$ , 27.54/h vs. 29.18/h, consecutively). Comparison of CTS patients with mild vs. moderate to severe OSA revealed no significance difference ( $p=0.86$ ). Categorization of OSA severity and its relation with CTS presence have been summarized in Table 3. No relation between the side of CTS and the preferred sleeping position was found ( $p=0.727$ ).

Ten patients (45.5%) with CTS had CTS symptoms, whereas 12 patients (54.5%) were asymptomatic. The mean Boston scaling value of CTS patients was 1.59. However, the scale showed no correlation between the severities of OSA and CTS ( $p=0.104$ ).

Occupations of the CTS patients were questioned. Ten patients (45.5%) were manually working, whereas twelve (54.5%) were not manually working.

## DISCUSSION

This study showed that CTS was highly frequent in OSA patients than in the general population. However, the presence of CTS in OSA was independent of OSA severity and formerly described factors such as sleeping position and manual working.

Demographic and polysomnographic characteristics of the study group were consistent with the literature (27,28,29,30).

Despite the lack of polysomnographic data, previous studies have reported sleeping problems, mainly insomnia and night-wakings in CTS patients (20,31). Our patients did not complain about insomnia or night-wakings due to CTS symptoms but this may be because of OSA comorbidity of our sample, which already causes repeated awakenings during sleep.

Our aim in this study was to assess the prevalence of CTS in OSA. We found that 27.5% of the OSA patients had CTS. This highly significant finding compared with normal population developed a question regarding the causative relation between the two syndromes. Although CTS is the most common entrapment neuropathy, currently there is no unifying theory that links the multiple known associations of CTS into a common mechanism.

With the increasing interest in sleep and sleep disorders, the possible role of sleeping position in development of CTS has been discussed with supporting results (32,33). McCabe et al. (34) described the association between sleeping on the side and CTS in their prospective study. However, the study was based on clinical findings and questionnaires without any electrophysiological data. We wanted to improve this study by adding objective diagnostic tools like PSG and NCS. We gained totally controversial results with McCabe et al. Majority of the patients (54.5%) were asymptomatic and symptom sides of the symptomatic ones had no relation with the CTS side ( $p=0.43$ ). Similarly, preferred sleeping position had no relation with the CTS side ( $p=0.73$ ). For this reason, we hypothesized that hypoxia, which is an established cause of peripheral neuropathy (35,36), was the reason for CTS tendency in OSA. Although patients with OSA are already known to have predisposition for several known risk factors for polyneuropathy (37), only a limited number of studies paid attention to the link between OSA and peripheral neuropathy. Smaller amplitudes for sensory and mixed nerve action potentials in patients with OSA have already been described (36). Subsequently, recurrent intermittent hypoxemia in OSA was described as an independent risk factor for axonal damage of the peripheral nerves, which supports our hypothesis (18).

Biomechanical factors had no effect on our CTS patients with OSA. Thus, other explanations for binding the two co-morbidities may be considered. We would propose the inflammation theory. OSA is already known to be associated with pro-inflammatory mediators (38,39). The inflammatory cytokine tumor necrosis factor- $\alpha$ , which increase ICAM-1 and VCAM-1 synthesis, platelet aggregation and activation that is measured by

P-selectin activation, neutrophils' superoxide production, is all known to increase in OSA (40,41,42). CTS can result from any cause that induces compression or irritation of the median nerve, including synovitis, thickening of the tendon or flexor retinaculum, fluid accumulation, or subsynovial connective tissue alterations (43). Hence, primary or secondary inflammation may be expected to cause CTS. Regarding the lack of published evidence supporting this hypothesis, it is necessary to conduct further studies to determine if OSA and CTS share the same of type of inflammatory pathways.

In conclusion, CTS is highly frequent in OSA patients. It is known that CTS amounts to a heavy burden on the national health service to provide care for CTS patients in the form of clinicians' time, diagnosis and treatment. We consider that in OSA patients, intermittent hypoxia is the major reason which facilitates axonal damage in the carpal tunnel. CTS starts earlier than its symptoms in OSA. In other words, OSA patients may have CTS even without any symptoms. Thus, NCSs may be suggested to all OSA patients right after the diagnosis of OSA. Furthermore, we propose that the effective treatment of OSA with positive airway pressure will result in the decrease of the frequency of CTS depending on our hypoxia theory.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Süreyyapaşa Chest Diseases and Chest Surgery Training and Research Hospital.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - Ö.B.T., K.U.; Design - Ö.B.T., K.U.; Supervision - K.U.; Resource - Ö.B.T., G.Ç.A., S.S.; Materials - Ö.B.T., G.Ç.A., S.S., Ö.O.; Data Collection and/or Processing - Ö.B.T., G.Ç.A., Ö.O.; Analysis and/or Interpretation - Ö.B.T., S.S., Ö.O.; Literature Search - Ö.B.T., G.Ç.A., S.S., Ö.O.; Writing - Ö.B.T., K.U.; Critical Reviews - Ö.B.T., K.U.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Etik Komite Onayı:** Bu çalışma için etik komite onayı Süreyyapaşa Göğüs Hastalıkları ve Cerrahisi Eğitim ve Araştırma Hastanesi Etik Kurulu'ndan alınmıştır.

**Hasta Onamı:** Yazılı hasta onamı bu çalışmaya katılan hastalardan alınmıştır.

**Hakem Değerlendirmesi:** Dış Bağlımsız.

**Yazar Katkıları:** Fikir - Ö.B.T., K.U.; Tasarım - Ö.B.T., K.U.; Denetleme - K.U.; Kaynaklar - Ö.B.T., G.Ç.A., S.S.; Malzemeler - Ö.B.T., G.Ç.A., S.S., Ö.O.; Veri Toplanması ve/veya İşlemesi - Ö.B.T., G.Ç.A., Ö.O.; Analiz ve/veya Yorum - Ö.B.T., S.S., Ö.O.; Literatür Taraması - Ö.B.T., G.Ç.A., S.S., Ö.O.; Yazıyı Yazan - Ö.B.T., K.U.; Eleştirel İnceleme - Ö.B.T., K.U.

**Çıkar Çatışması:** Yazarlar çıkar çatışması bildirmemişlerdir.

**Finansal Destek:** Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

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