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Association of routine hematological and inflammation parameters with surgical treatment results in patients with carpal tunnel syndrome

Karpal tünel sendromlu hastalarda rutin hematolojik ve inflamasyon parametrelerinin cerrahi tedavi sonuçları ile ilişkisi

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Abstract

Aim: Neutrophil/lymphocyte ratio, neutrophil/eosinophil ratio (NER), and C-reactive protein-to-albumin ratio (CAR) reflect systemic inflammation. However, their relationship with the surgical treatment of carpal tunnel syndrome (CTS) has not been studied. In the present research, the association between systemic inflammation parameters and CTS surgical treatment results was investigated in patients with neurophysiologically moderate CTS.

Methods: The present study was conducted retrospectively on patients who underwent surgical treatment owing to moderate CTS. The postoperative results were evaluated by a nerve conduction study (NCS) performed approximately 6 months after the surgery. Patients were divided into three groups based on the postoperative NCS: Patients who did not have CTS according to NCS were defined as "the group fully benefiting" from surgical treatment, patients with mild CTS were included in "the group partially benefiting," from surgical treatment, and patients with moderate or severe CTS were included in "the group with no benefit."

Results: Forty-one patients with moderate CTS were included in the study. There was a significant difference between the groups in terms of median CAR, white blood cell, neutrophil, NER, and C-reactive protein (CRP) levels (P<0.001, P=0.012, P=0.014, P=0.005 and P=0.001, respectively). There was also a statistically significant and strong positive correlation among postoperative CTS severity, CAR (rho: 0.633, P<0.001) and CRP (rho: 0.603, P<0.001).

Conclusion: In the current study, it was found that CTS patients with higher CAR levels achieved less benefit from the surgical treatment.

Keywords: C-reactive protein/albumin ratio, Surgical treatment, Carpal tunnel syndrome, Neutrophil/eosinophil ratio, Systemic inflammation

Öz

Amaç: Nötrofil/lenfosit oranı (NLO), nötrofil/eozinofil oranı (NEO) ve C-reaktif protein/albumin oranı (CAO) sistemik inflamasyonu yansıtır. Ancak, bunların karpal tünel sendromu (KTS) cerrahi tedavisi ile ilişkisi çalışılmamıştır. Bu çalışmada, nörofizyolojik olarak orta KTS'li hastalarda sistemik inflamasyon parametreleri ile KTS cerrahi tedavi sonuçları arasındaki ilişki araştırıldı.

Yöntemler: Bu çalışma, orta KTS nedeniyle cerrahi tedavi yapılmış hastalar üzerinde retrospektif olarak yapıldı. Cerrahi sonrası sonuçlar, ameliyattan yaklaşık 6 ay sonra yapılmış bir sinir iletim çalışması (SİÇ) ile değerlendirildi. Cerrahi sonrası SİÇ'e göre hastalar üç gruba ayrıldı: SİÇ ile KTS saptanmayan hastalar cerrahi tedaviden "tam faydalanan grup", hafif KTS saptanan hastalar "kısmi faydalanan grup" ve orta veya şiddetli KTS saptanan hastalar ise cerrahi tedaviden "hiç faydalanmayan grup" olarak tanımlandı.

Bulgular: Çalışmaya, 41 orta KTS'li hasta alındı. Gruplar arasında medyan CAO, beyaz kan hücresi (WBC), nötrofil, NEO ve C-reaktif protein (CRP) düzeyleri açısından anlamlı fark gözlenmiştir (sırasıyla P<0,001; P=0,012; P=0,014; P=0,005 ve P=0,001). Ayrıca, cerrahi sonrası KTS şiddeti ile CAO (rho: 0,633; P<0,001) ve CRP (rho: 0,603; P<0,001) arasında istatistiksel olarak anlamlı ve güçlü pozitif korelasyon vardı.

Sonuç: Bu çalışmada, daha yüksek CAO düzeyine sahip KTS hastalarının cerrahi tedaviden daha az fayda sağladığı bulunmuştur.

Anahtar kelimeler: C-reaktif protein/albumin oranı, Cerrahi tedavi, Karpal tünel sendromu, Nötrofil/eozinofil oranı, Sistemik inflamasyon

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Introduction

Surgical treatment of moderate and advanced carpal tunnel syndrome (CTS) is known as the most effective method of treatment [1,2]. However, not all patients benefit from this approach [3]. It is emphasized that the underlying causes of surgical failure stem from the surgeon and the patient [4,5]. Patient-related causes of unsuccessful carpal tunnel surgery are identified as follows: Tenosynovitis of flexor tendons, necrosis of palmar fascia after surgery, development of fibrous proliferation in the carpal tunnel, infections developing in the surgical site, and compression of the palmar cutaneous branch of the median nerve. Surgeon-related causes include incomplete transection of the transverse carpal ligament and, in rare cases, iatrogenic median nerve incisions [4,5]. According to a recently published study, obesity and advanced age also have a role in surgical failure [6]. In many recent studies, C-reactive protein/albumin ratio (CAR) [7], neutrophil/eosinophil ratio (NER) [8], neutrophil/lymphocyte ratio (NLR) [9], and increased levels of neutrophils [10] have been established to reflect systemic inflammation and to play a role in the prognosis of many diseases [7-10]. To the best of our knowledge, the role of systemic inflammation in the success of CTS surgery has never been studied. Therefore, the present study investigates the relationship between surgical treatment results of CTS and CAR, NER, NLR, white blood cells (WBC), neutrophils, and C-reactive protein (CRP).

Materials and methods

This study was performed retrospectively on patients who underwent surgical treatment owing to moderate CTS between July 2014 and August 2019. First, patients with moderate CTS were identified through a nerve conduction study (NCS) in our neurophysiology laboratory. Among them, 852 had moderate CTS, 475 of whom had been already operated. Of the patients who had been operated, 41 had preoperative laboratory results and a report of NCS conducted nearly 6 months after the operation. The study was done with this group of 41 patients for whom complete data were available.

Those with missing data, those with moderate CTS patients who had not undergone surgical treatment, and patients less than 18 years of age were excluded from the study. None of the patients included herein were pregnant. Also, those who had cervical radiculopathy, brachial plexopathy, and generalized peripheral neuropathy were not included in the study.

In our clinic, the diagnosis of CTS is confirmed by a neurophysiologically-performed NCS along with the presence of clinical symptoms of CTS. During the neurophysiological examination, the hand temperature of the patients is kept above 32°C. During NCS, the median and ulnar nerves are bilaterally examined. The sensory conductions are performed antidromically using surface recording electrodes on the 2nd and 5th fingers, respectively, while the NCS of the median motor is performed with surface recording electrodes on the muscle of the abductor pollicis brevis. The motor and sensory conduction amplitudes, distal latencies (ms), and nerve conduction rates (m/s) of the bilateral median and ulnar nerves are measured. Accordingly, the patients diagnosed with moderate CTS were included in the study. The patients were classified as (neurophysiologically) mild, moderate, and severe CTS [9]. Two-channel electroneuromyography device (Micromed SpA-Via Giotto, 2-31021 Mogliano Veneto-Italy, 2014) was used for neurophysiological diagnosis.

The patients were divided into three groups based on postoperative NCS: Patients who did not have CTS according to NCS were defined as "the group fully benefiting" from the surgical treatment, patients with mild CTS as "the group partially benefiting" from surgical treatment and patients with moderate or severe CTS as "the group with no benefit."

The patients' blood sample analysis was performed using an autoanalyzer (Sysmex XN-1000 hematology analyzer, Kobe, Japan) installed in our hematology laboratory. CAR was calculated by dividing the amount of C-reactive protein by the albumin level, while NER was calculated by dividing the neutrophil count by the eosinophil count, and NLR by dividing the neutrophil count by the lymphocyte count.

This study was approved by Aksaray University Human Research Ethics Committee (October 21, 2020, Number: 2020/09-15), and the study was conducted in accordance with the Helsinki Declaration.

Statistical analysis

Results are presented as mean (SD) or median (min-max). The distribution pattern of the data was investigated using Kolmogorov-Smirnov normality test. Age, neutrophil, WBC, BMI, NLR, NER, CRP, and CAR were compared using Kruskal-Wallis test. Mann-Whitney U test was used for post-hoc comparisons. Correlations of postoperative CTS severity with the other parameters were checked using Spearman non-parametric correlation test because postoperative CTS severity was ordinal. The correlation results were interpreted according to the principles set by Cohen [11]. SPSS 23.0 (SPSS Inc., Chicago, IL) was used for all statistical analysis. A P-value <0.05 was considered statistically significant. Additionally, for non-parametric post-hoc comparisons, Bonferroni correction was applied and a P-value under 0.05/3=0.017 (triple combination) was considered statistically significant.

Results

Forty-one patients who had undergone surgery for CTS were eligible for this study. While no patients were present in the severe-CTS group, the moderate-CTS group (the group with no benefit) consisted of 15 patients [4 males and 11 females, mean age: 53.7 (11.2) years], the mild-CTS group (the group partially benefiting) consisted of 9 patients [9 females, mean age: 47.7 (6.7) years], and the non-CTS group (the group fully benefiting) consisted of 17 patients [7 males and 10 females, mean age: 47.1 (12.8) years]. The groups were age and gender-matched (P=0.240 and P=0.084, respectively).

The comparison of inflammatory parameters among the three groups is presented in Table 1. According to the Kruskal-Wallis test, the median NLR did not significantly differ among the three groups (P=0.069), but the median WBC, neutrophil, BMI, NER, CRP, and CAR did (P=0.012, P=0.014, P=0.001, P=0.005, P=0.001, and P<0.001, respectively). Post-hoc tests revealed that the median neutrophil and NER were not significantly different between the mild-CTS group and the non-

CTS group (*P*=0.133 and *P*=0.535, respectively), but the median BMI, WBC, CRP and CAR were significantly higher in the mild-CTS group than in the non-CTS group (*P*=0.004, *P*=0.045, *P*=0.015, and *P*=0.014, respectively). In addition, the median BMI, WBC, neutrophil, NER, CRP, and CAR were significantly higher in the moderate-CTS group than in the non-CTS group (*P*<0.001, *P*=0.006, and *P*=0.014, respectively). Median NER was significantly higher in the moderate-CTS group than in the mild-CTS group (*P*=0.002), however, median BMI, WBC, neutrophil, CRP, and CAR were similar between the moderate and mild-CTS groups (*P*=0.482, *P*=0.29, *P*=0.123, *P*=0.144, and *P*=0.074, respectively).

Table 1: The comparison of median inflammatory parameters among the groups defined according to post-surgical nerve conduction study results

	Non-CTS (the group fully benefiting) (n=17)	Mild-CTS (the group partially benefiting) (n=9)	Moderate-CTS (the group with no benefit) (n=15)	*P*-value[#]
Neutrophil, 10^9/L	3.23 (2.04-6.39)	4.3 (3.11-6.73)	5.65 (2.09-12.46)	0.014
WBC, 10^9/L	7.24 (4.53-9.2)	8.87 (6.34-10.28)	9.23 (4.26-14.06)	0.012
BMI, kg/m^2	29.3 (24.8-34)	36.3 (28.1-39)	37 (24.3-48.3)	0.001
NLR	1.45 (0.82-3.39)	1.51 (1.17-3.32)	2.41 (1.17-10.4)	0.069
NER	22.08 (7-169.2)	19.22 (12.53-40.4)	48.26 (19.13-778.75)	0.005
CRP, mg/dL	1.44 (0.11-6)	4.2 (1.02-8.59)	5.7 (1.4-30)	0.001
CAR	0.36 (0.03-1.31)	0.87 (0.24-1.86)	1.16 (0.29-7.14)	<0.001

[#] Kruskal Wallis test, CTS: Carpal tunnel syndrome, WBC: White blood cell, BMI: Body mass index, NLR: Neutrophil/lymphocyte ratio, NER: Neutrophil/eosinophil ratio, CRP: C- reactive protein, CAR: C- reactive protein/albumin ratio, NOTE: Since no patients with severe-CTS were detected after surgical treatment, the severe-CTS group was not included in the study.

Spearman correlation analysis revealed that the severity level of CTS (after surgery) was positively, strongly, and significantly correlated with CAR (rho: 0.633 and *P*<0.001; Figure 1), CRP (rho: 0.603 and *P*<0.001; Figure 2), and BMI (rho: 0.578 and *P*<0.001). In addition, the severity level of CTS (after surgery) was positively, moderately, and significantly correlated with NLR (rho: 0.351 and *P*=0.024), NER (rho: 0.389 and *P*=0.012), WBC (rho: 0.467 and *P*=0.002), and neutrophil count (rho: 0.461 and *P*=0.002).

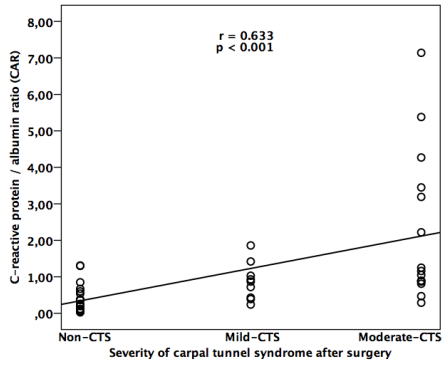

Figure 1: Graph showing the correlation between C-reactive protein/albumin ratio and the (neurophysiological) severity of carpal tunnel syndrome after the surgical treatment

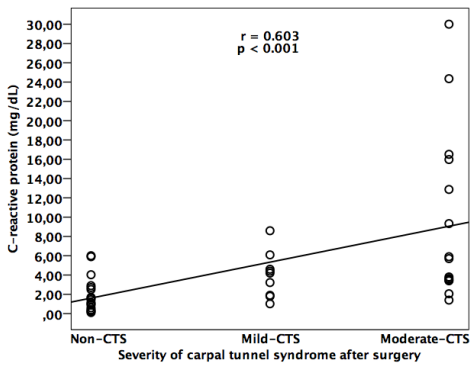

Figure 2: Graph showing the correlation between C-reactive protein and the (neurophysiological) severity of carpal tunnel syndrome after the surgical treatment

Discussion

This study concludes that patients with failed CTS surgery had higher WBC, BMI, NER, CRP, and CAR. There was also a positive correlation between the severity of CTS and these parameters after surgical treatment. To the best of our knowledge, the current study has been the first one to investigate the relationship between systemic inflammation parameters and surgical treatment results in CTS.

NER, CRP, WBC, NLR, and CAR are the blood parameters that reflect systemic inflammation [7-9,12,13]. In recent years, these parameters have been associated with the prognosis of various diseases such as ischemic stroke [8,12], hemorrhagic stroke [7,14], and CTS [9] or the severity of the disease.

Surgical treatment has a prominent place in the treatment of patients with moderate and advanced CTS [2]. However, it was emphasized that one out of four patients undergoing surgical treatment (25%) did not benefit from it [3]. The underlying reasons for the failure of surgical treatment might be attributed to the patient or the surgeon [5]. However, systemic inflammation in unsuccessful CTS surgery has not been studied at all. A recent study [9] emphasized that there is a positive correlation between NLR and severity of CTS. It is not exactly known why CTS is more severe in patients with a higher level of systemic inflammation. Therefore, systemic inflammation may be associated with the severity of CTS as well as with the surgical treatment outcomes in CTS. It has been determined in this study that patients with higher WBC, NER, CRP, and CAR achieve less benefit from the surgical treatment or no benefit at all, which supports the presence of this correlation. The underlying pathophysiological mechanisms are not yet fully known. Further studies are needed to clarify them.

NLR is a hematological parameter that reflects systemic inflammation [9,13,14]. NLR has been associated with diabetic polyneuropathy [15] and Guillain-Barré Syndrome [16-18] in several studies conducted in recent years. In the present study, patients who did not benefit from CTS surgery had higher NLR compared to those who benefited from it. However, there was no statistically significant difference between the groups. It is believed that this may be due to the small number of patients in the groups.

A recent study found that advanced age and high BMI had adverse effects on surgical treatment success in CTS [6]. Similar to this study, it was found that patients with higher BMI derived less benefit out of the surgical treatment. Thus, the determination of the presence of a positive correlation between BMI and severity of CTS was consistent with the study [6] in literature. Losing weight before the surgical treatment might increase the chances of success in patients with high BMI [6].

Limitations

Although this study is considered to contribute novel information to the literature, it has some limitations. First, this study is a monocentric retrospective study. Secondly, the present study was conducted with a small number of patients. Thirdly, owing to its retrospective nature, patients with moderate CTS who had elevated levels of inflammation were not administered anti-inflammatory treatments to lower the levels of inflammation

in combination with surgical treatment; therefore, they were not included in a particular follow-up process.

Conclusion

The presence of an elevated level of systemic inflammation in patients with CTS can adversely affect its surgical treatment. Long-term use of systemic anti-inflammatory treatments in combination with surgical treatment in such patients can offer additional benefit. The role of systemic inflammation in the success of surgical treatment of CTS can be clarified by further prospective studies.

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