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Comparison of ultrasonographic parameters in the diagnosis of carpal tunnel syndrome in pregnancy

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ABSTRACT

Aims: The aim is to evaluate sonographic parameters in pregnant women diagnosed with carpal tunnel syndrome compared to electrodiagnostic tests, to determine whether these parameters have sufficient accuracy to allow their use in clinical practice.

Methods: This retrospective study examines pregnant women aged 18-40 in the 3rd trimester who received a final diagnosis of carpal tunnel syndrome between 2021-2023 at Prof. Dr. Cemil Taşçıoğlu City Hospital. Pregnant women with symptomatic complaints were divided into two groups: those with positive electrodiagnostic test results indicating carpal tunnel syndrome and those with negative electrodiagnostic test results, forming the control group. All pregnant women participating in the study had their median nerve cross-sectional area, flexor carpi radialis, cross-sectional area, wrist-to-forearm ratio, and MN-CSA/FCR ratio (expressed as a percentage called NTR) values examined.

Results: In pregnant women with carpal tunnel syndrome, the median nerve cross-sectional area values were observed to surpass those in the control cohort (10.06±3.24 vs. 7.84±2.52)($p<0.001$). The wrist-to-forearm ratio in pregnant women with carpal tunnel syndrome (2.1±0.5) was statistically higher compared to the control group (1.0±0.1)($p<0.001$). The NTR values in the pregnant women with carpal tunnel syndrome (CTS) were also higher than those in the control group (0.92±0.36 vs. 0.80±0.23) ($p=0.036$). The best cut-off for median nerve cross-sectional area values was calculated to be >8.6 mm². The best cut-off point for MN-CSA/FCR values was found to be >0.84%. The best cut-off for wrist-to-forearm ratio values was calculated as >1.4 mm². A receiver operating characteristic curve was generated, and the wrist-to-forearm ratio cut-off point of 1.4 showed a sensitivity of 97.1% and a specificity of 69.2%.

Conclusion: Ultrasonography is useful in the diagnosis of pregnancy-related CTS. It has provided comparable results to electrodiagnostic tests and is additionally practical, cost-effective, and swift.

Keywords: Carpal tunnel syndrome, cross-sectional area, ultrasonography

INTRODUCTION

The first records related to carpal tunnel syndrome (CTS) date back to the 1850s; Paget described this syndrome as trap neuropathy in those years, and a century later, in the 1960s, Phalen brought up the much more common form known as idiopathic CTS, increasing recognition of this syndrome.[1] Today, CTS is recognized as the most common peripheral neuropathy, with a reported prevalence ranging from 0.2% to 4% in the general population.[2] While CTS is often idiopathic, various factors have been associated with it, including chronic diseases (such as diabetes mellitus, rheumatoid arthritis, gout, and hypothyroidism) or strenuous repetitive hand movements. Nowadays, vibration occurring in the palm base and chronic mechanical stress, particularly in occupational branches that extensively use the wrist, can lead to CTS.[3]

The exact cause of pregnancy-related carpal tunnel syndrome (PRCTS) is unknown, but it is believed to be related to hormonal changes and local edema in the carpal tunnel.[4] PRCTS symptoms are often bilateral and typically more common in the third trimester.[5] Diagnosis of CTS is made based on history, clinical symptoms, and physical examination. The prevalence of PRCTS based on clinical symptoms ranges from 31% to 62%, while electrodiagnostically confirmed PRCTS ranges from 7% to 43%.[6] Clinical findings may include numbness in the distribution of the median nerve, sometimes accompanied by sensory disturbances, brachialgia paresthetica nocturna, thenar muscle atrophy, and occasionally swelling on the palmar aspect of the wrist. Provocative clinical tests (Phalen/Tinel) can strengthen the diagnosis.[7] Electrodiagnostic (EDx) tests are considered the gold standard, particularly useful when the diagnosis is uncertain, or when there are confusing neurological disorders like radiculopathy or polyneuropathy, or to assess the severity of the disease. However, the invasiveness and false-negative rate of EDx tests have led to the exploration of other, less invasive, and more suitable diagnostic options.[8] Our study aims

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to evaluate practical non-invasive sonographic parameters in pregnant women diagnosed with CTS compared to EDx tests, determining whether these parameters have sufficient accuracy to allow their use in clinical practice.

METHODS

The study was approved by the institutional review board of Prof. Dr. Cemil Taşçıoğlu City Hospital Clinical Researches Ethics Committee (Date:06.02.23 Decision No:87). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study is a retrospective review of pregnant women in their third trimester, aged 18-40, who received a final diagnosis of CTS and presented to the neurophysiology (EMG) laboratory at Prof. Dr. Cemil Taşçıoğlu City Hospital between 2021 and 2023. Our institutional standard for pregnant women with carpal tunnel symptoms relies on a definitive diagnosis based on EDx tests. Patients with clinical symptoms but normal EDx results constituted the control group for our study. Routine wrist ultrasound is performed for patients with a diagnosis. Patients with incomplete clinical examinations or unavailable wrist ultrasound data were excluded from the retrospective data review. Symptomatic evaluations of 76 wrists meeting the study criteria were assessed through the hospital's electronic information system.

Pregnant women presenting with numbness or pain in their wrists undergo routine wrist examinations following regular prenatal check-ups in obstetrics clinics. This examination includes assessment of upper extremity muscle strength, sensation, muscle stretch reflexes, and provocative tests (Phalen and Tinel). A clinical diagnosis of CTS is made based on the presence of symptoms such as wrist pain, tingling in the fingers, numbness, weakness in the abduction or opposition of the thumb, especially in the first three fingers, or positive provocative test results, along with sensory disturbances in the hands. Symptomatic CTS findings referred to the neurophysiology unit undergo routine administration of the Boston Carpal Tunnel Questionnaire (BCTQ). Pregnant women with severe CTS symptoms, including thenar muscle atrophy or a difference of at least 8 mm in two-point discrimination in at least one finger, those who have used a wrist splint in the dominant hand within the past year, received steroid injections for CTS, have inflammatory joint disease, polyneuropathy, experienced trauma to the dominant hand in the past 12 months, undergone CTS surgery, have a bifid median nerve, inability to complete questionnaires due to speech difficulties or cognitive impairment, multiple pregnancies, hypothyroidism, or severe obstetric diseases (uncontrolled gestational diabetes, severe preeclampsia, eclampsia, premature rupture of membranes, or medical conditions requiring urgent delivery), and women with known substance abuse (alcohol or drug) are excluded from the study.

EDx Testing

All nerve conduction studies (NCS) were performed at a skin temperature of 32 °C. For CTS, a minimum of median motor response over the abductor pollicis brevis, median mixed nerve action potential, and ulnar mixed nerve action potential recordings were performed. The median motor nerve conduction study was obtained by placing recording electrodes over the abductor pollicis brevis and stimulating the nerve 6.5 cm proximally at the wrist. Median and ulnar mixed NCS were obtained by stimulating the nerves in the palm and recording 8 cm proximally over the respective nerves. A diagnosis of CTS was defined by a distal motor latency of >4.3 ms, a median mixed nerve latency of >2.2 ms, or a difference between median and ulnar mixed latencies of ≥0.4 ms. Distal median motor latency, median motor compound muscle action potential amplitude, median mixed nerve latency, and median and ulnar mixed inter-latency differences were recorded for all patients.[9]

Ultrasound

Ultrasound examinations were performed within 1 week after electrodiagnostic study. The ultrasound examinations were performed by a neuroradiologist with 25 years of experience in the field of ultrasonography and specialization in musculoskeletal radiology. In the examination, anatomical structures were assessed using a high-resolution US device. These included the median nerve cross-sectional area (MN-CSA), the flexor carpi radialis (FCR) cross-sectional area at the carpal tunnel entrance at the same level, the carpal tunnel inlet (CTI) cross-sectional area, and the cross-sectional areas of the median nerve in the forearm, 12 cm proximal to the wrist. In the measurements, once the location of these specified structures was identified, their circumferences were marked in the axial plane, and the cross-sectional areas were noted in square millimeters (mm^2). US findings were reviewed for median nerve CSA at the distal wrist crease and 12 cm proximal to the distal wrist crease. The wrist to forearm ratio (WFR) of CSA (wrist CSA/forearm CSA) was calculated. This process was performed separately for both wrists (Figure). Patients were assessed with a high-resolution ultrasound device (7-11MHz linear probe, Toshiba Aplio 500, 2017 model, Toshiba Medical System Corporation, Japan).

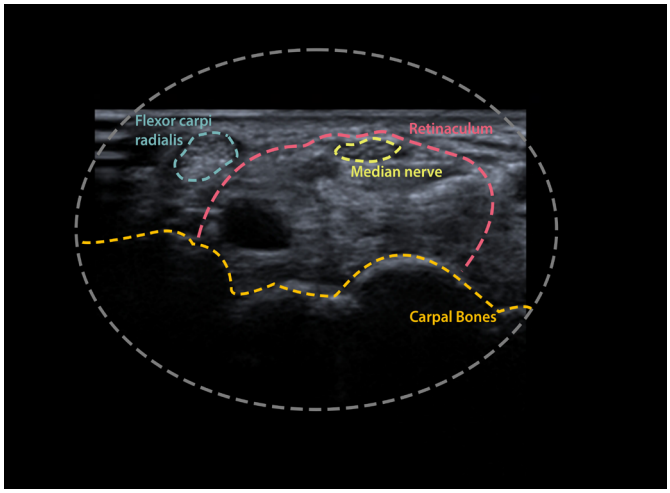

Figure. On the US image obtained at the entrance level of the carpal tunnel in the wrist; flexor carpi radialis and the median nerve were measured. Evaluation was also performed by measuring the wrist circumference at the same wrist.

The patients were seated on a chair opposite the radiologist on the examination table to ensure their comfort. The patient's

arms were positioned on the examination table in a supine position, with their hands placed in a free and neutral position. The radiologist examined while sitting across from the patient on the other side of the examination table. The radiologist was not permitted to ask the volunteers or patients about symptoms to minimize observer bias. Sonographers were blinded to the clinical and NCS outcomes.

Boston Carpal Tunnel Syndrome Questionnaire (BCTQ)

The BCTQ is a questionnaire consisting of a total of 19 questions used to evaluate the severity of symptoms and functional status in patients with CTS. The answers are multiple-choice, and each question is assessed with at least one and up to five points. One point corresponds to the mildest symptom or the best functional capacity, while five points correspond to the most severe symptom or the worst functional status. A high average score for the patient indicates that their complaints are severe or their functional capacity is inadequate. The symptom severity score is the total score obtained from 11 questions. The average symptom severity score is obtained by dividing the total score obtained for all questions by the current number of questions. The functional capacity score is the total score obtained from eight questions. The average functional capacity score is obtained by dividing this total score by eight.[10] The survey has been validated in Turkish.[11]

Statistical Analysis

Descriptive statistics were provided for continuous data, including mean, standard deviation, median, minimum, maximum values, and for discrete data, counts and percentage values were presented. To assess the normal distribution of continuous data, the Shapiro-Wilk test was utilized. For comparing continuous data and ultrasound measurements with the EDx result, the student's T-test was used for normally distributed data, and the Mann-Whitney U test was used for data that did not follow a normal distribution. Group comparisons of nominal variables (in contingency tables) were performed using the Chi-squared test and Fisher's exact test. The diagnostic performance of US measurement values was evaluated using the area under the ROC curve (AUC). The optimal cut-off point was determined using Youden's Index. The diagnostic accuracy criteria for US values (sensitivity, specificity, positive predictive value, negative predictive value) were assessed. For comparing wrist US measurements in patients with pathological results in the EDx, the Kruskal-Wallis variance analysis was used to evaluate differences among those with mild, moderate, and severe conditions. The source of differences was examined through the Kruskal-Wallis multiple comparison test. IBM SPSS for Windows 20.0 (SPSS Inc. Chicago, IL) software was used for the analysis, and a significance level of $p<0.05$ was considered statistically significant.

RESULTS

In our study, the mean ages of the two groups mentioned in the methods section were 32.79±5.38 for the control group with normal EDx results and 33.33±4.41 for pregnant women with CTS. There was no significant difference in age between the groups. There were no differences observed between the groups regarding BMI and parity. Although complaints started earlier in pregnant women with CTS in our study, as only third-trimester pregnant women were included, this difference is not clinically significant from an obstetric standpoint.

In pregnant women with symptoms, the BTCQ scores were found to be 30.59±9.60 in the group with CTS and 14.11±2.49 in the control group. BTCQ scores were significantly higher in the CTS group ($p<0.001$). When evaluated in terms of clinical provocative tests, there was no statistically significant difference observed in Phalen and Tinel signs ($p=0.644$, $p=0.613$, respectively). A family history was more frequently observed in pregnant women with CTS ($p<0.001$). Characteristic features are summarized in Table 1.

Table 1. Demographic data and characteristic features of groups

	EDx normal (n=38) Mean±SD Median; (IQR)	EDx pathologic (n=38) Mean±SD Median; (IQR)	p value
Age (years)	32.79±5.38 (20-43)	33.33±4.41 (20-43)	0.073[a]
BMI (kg/m²)	28.67±4.45 29 (25.21-31.17)	29.23±4.52 28.72 (25.30-31.60)	0.540[c]
Parity median (IQR)	1 (1-2)	1 (1-2)	0.879[c]
Complaint start week	30.99±1.65 31 (30-32)	30.19±1.39 30 (29-31)	0.002[c]
Pregnancy week	31.81±11.89 32 (32-34)	32.86±2.28 33 (32-36)	<0.001[c]
Weight gained during pregnancy	11.86±3.01 13 (11-15)	11.42±3.51 11 (10-13)	0.540[c]
Previous type of birth			
NSD	33 (49.3)	50 (86.2)	<0.001[b]
C/S	34 (50.7)	8 (13.8)	
Family history			
Absent	81 (100)	61 (77.2)	<0.001[b]
Present	0 (0)	18 (22.8)	

EDx: Electrodiagnostic, SD: Standart deviation, BMI: Body mass index, a: Student's T test, b: Chi-square test/Fisher's exact test, c: Mann-Whitney U test

In our study, there was no difference in wrist measurements between the groups. The MN-CSA in the CTS group was found to be 10.06±3.24 mm², which was statistically higher than in the control group ($p<0.001$). The WFR in pregnant women with CTS was 2.1±0.5, statistically higher than in the control group ($p<0.001$). The MN-CSA/FCR (NTR) % values were higher in the CTS group compared to the control group, respectively (0.92±0.36 vs. 0.80±0.23, $p=0.036$). The findings are summarized in Table 2.

Table 2. Comparison of EMG results with wrist ultrasound findings between groups

	EDx normal (n=38) Mean±SD Median (IQR)	EDx pathologic (n=38) Mean±SD Median (IQR)	p value
Wrist circumference	15.43±0.79	15.51±1.03	0.791[c]
Forearm median nerve mm²	4.64±0.75	5.06±1.40	0.100[c]
MN-CSA mm²	7.84±2.52	10.06±3.24	<0.001[c]
FCR mm²	9.66±1.36	11.26±3.28	0.001[c]
WFR	1.0±0.1	2.1±0.5.	0.001[c]
MN-CSA/FCR (NTR) %	0.80±0.23	0.92±0.36	0.036[c]

SD: Standart deviation, c: Mann-Whitney U test, EDx: Electrodiagnostic test, FCR: Flexor carpi radialis, MN-CSA: Median nerve cross-sectional area

The best cut-off for MN-CSA values was calculated as >8.6 mm². A receiver operating characteristic curve was generated, and the MN-CSA cut-off point of 8.6 showed a sensitivity of 58.3% and a specificity of 65.3%. The positive predictive value and the negative predictive value were 71.9% and 72.9%, respectively, with the mentioned point as the diagnostic threshold (area under the curve [AUC), 0.592 (95% confidence interval (CI), 0.637-0.801)]. The best cut-off for WFR values was calculated as >1.4 mm². A receiver operating characteristic curve was generated, and the WFR cut-off point of 1.4 showed a sensitivity of 97.1% and a specificity of 69%. The positive predictive value and the negative predictive value were 56.4% and 78.1%, respectively, with the mentioned point as the diagnostic threshold [area under the curve, 0.582 (95% CI, 0.491-0.673)]. The best cutoff for MN-CSA/FCR values was found to be >0.84%. A receiver operating characteristic curve was generated, and the NTR cut-off point of 0.84% showed a sensitivity of 51.9% and a specificity of 67.9%. The positive predictive value and the negative predictive value were 61.2% and 59.1%, respectively, with the mentioned point as the diagnostic threshold [area under the curve, 0.592 (95% CI, 0.503–0.680)]. The findings are summarized in Table 3.

Table 3. The diagnostic performance of ultrasound findings in predicting carpal tunnel diagnosis (pathological in EDx results)

	AUC (SE) 95% CI	p	Cutoff	Sensitivity 95% CI	Specificity 95% CI	PPV	NPV
MN-CSA mm²	0.719	<0.001	>8.6	0.583	0.653	0.719	0.729
FCR mm²	0.656	0.001	>11.3	0.481	0.901	0.826	0.640
WFR	0.582	<0.001	>1.4	0.971	0.692	0.564	0.781
MN-CSA/FCR (%)	0.592	0.045	>0.84	0.519	0.679	0.612	0.591

FCR: Flexor carpi radialis, WFR: Wrist to forearm ratio MN-CSA: Median nerve cross-sectional area, BCTQ: Boston carpal tunnel questionnaire

DISCUSSION

In our study, we found that WFR, NTR and MN-CSA measurements gave comparable results to electrodiagnostic test results in preganancy CTS.

Our study demonstrated the usefulness of ultrasound measurements in PRCTS due to its non-invasive and practical nature. Pregnancy, with its inherent nature and changing hormonal effects, often leads to CTS. In this context, the impact of pregnancy itself and potential neuropathies on daily life can lead to depressive symptoms in pregnant women.[12] The commonly expressed belief that CTS symptoms will alleviate after childbirth is not always accurate and has been shown in studies. In one study, it was observed that these symptoms could persist for up to 3 years postpartum.[13] This may be attributed to the frequent active use of the wrist during breastfeeding, potentially contributing to edema and inflammation. Another study investigating possible risk factors found that symptoms starting before the third trimester, an increase in the severity of CTS symptoms during pregnancy, and ongoing CTS postpartum were identified as risks.[14]

Although the best diagnostic strategy for CTS remains uncertain, clinical symptoms and physical examination continue to form the basis of diagnosis, but their diagnostic accuracies vary. Our literature review revealed a prevalence of clinically suspected PRCTS ranging from 30% to 60%, while the prevalence of electrodiagnostically confirmed PRCTS varies between 7% and 43%.[15] This variability stems from differences in methodological approaches used across studies, such as the lack of confirmation with EDx testing in PRCTS and widely varying sample sizes (ranging from 15 to 10,000) in systematic analyses.[15] Another crucial point is that clinical parameters and used provocative tests alone may not be sufficient. It has been shown that combining multiple provocative tests enhances the sensitivity and specificity in diagnosing CTS.[16] Although our study did not find a statistical difference between groups in terms of Phalen and Tinel tests, we agree with the literature that these tests strengthen the clinical symptoms for diagnosis.

Especially in cases of PRCTS, alternative ultrasound studies have been of interest for diagnosis or treatment monitoring.[17] Particularly in groups involving pregnant women, familiarity with obstetric ultrasound and the perception of its harmlessness is crucial, especially in populations such as pregnancy that require special attention. In recent years, there has been significant heterogeneity in MN-CSA ranging from 9 to 16.8 mm² in many studies.[18] In a recent study, the diagnostic threshold value was found to be optimal at 11.75 mm².[19] Similarly, in another study, MN-CSA was found to be higher than 9.44±2.68 mm² in the control group, although not confirmed with EDx.[20] In a meta-analysis focusing on this topic, 2292 wrists were examined, with MN-CSA being 11.64 mm² for mild CTS, 13.74 mm² for moderate CTS, and 16.80 mm² for severe CTS (20). In our study, consistent with the literature, MN-CSA >8.6 was found to have a sensitivity of 58% and specificity of 65% for diagnosing CTS in pregnant women. In our literature review, the most commonly studied parameter in CTS is WFR. A WFR of ≥1.4 provided 100% sensitivity for detecting patients with CTS, while using solely the median nerve area at the wrist yielded a sensitivity of 45-93%, contingent on the chosen cut-off value.[21] In another study, a WFR cut-off value of 1.53 mm² resulted in sensitivity and specificity of 60% and 92.5%, respectively, for diagnosing CTS.[22] In our study, consistent with the literature, WFR >1.4 mm² was found to have a sensitivity of 97.1% and specificity of 69% for diagnosing CTS in pregnant women. NTR is a relatively new parameter that has not been extensively studied in pregnant women. In a study conducted in a non-pregnant population, NTR was found to be 0.83%.[23] Especially, the origin of this parameter stems from the search for a new parameter independent of anthropometric measurements, as wrist measurements in CTS are influenced by wrist thickness and a person's height and weight measurements. In this context, it is promising as a new parameter in the face of differences in weight and edema between trimesters in pregnant women. In our study, similar to the relevant study, we found that NTR >84% had a sensitivity and specificity of 52% and 68%, respectively, for diagnosing CTS. Especially in more severe cases requiring postpartum or invasive treatment, examining the performance of NTR will allow us to better test the clinical sensitivity of the relevant parameter in the future. Today, ultrasound has aroused interest as an alternative diagnostic test for CTS.[24] Studies have used EDx or clinical diagnosis as the reference standard while determining the sensitivity and specificity of ultrasound in diagnosing CTS.[25] A meta-analysis revealed that ultrasound exhibited a sensitivity of 77.6% and a specificity of 86.8% in diagnosing

CTS. Notably, these values remained competitive when using EDX as the benchmark (80.2% sensitivity and 78.7% specificity).[26] Technological advancements in ultrasound provide more detailed pathophysiological information about the median nerve and surrounding structures. This information not only enhances diagnostic accuracy but also enriches and complements our understanding of CTS pathology by providing additional insights. However, there are still some challenges in ultrasound assessment. One of these challenges is the need for standardized protocols. Additionally, difficulties arise due to variations in race, gender, and physique, which are important for the diversity of studies, especially when dealing with the median nerve. Investigating the diagnostic significance of ultrasound in patients with diabetes and chronic kidney disease, apart from the pregnant population, will expand our knowledge in this area.[27] Another consideration is the variability in carpal tunnel characteristics, which may necessitate different threshold values for patients with CTS due to these conditions. Furthermore, the relationship between ultrasound findings and the progression of the disease remains unclear. These findings may reflect the pathological anatomy and kinetics associated with CTS. However, it is still unknown whether it is possible to predict outcomes or identify risk factors based on ultrasound findings, and the role of ultrasound examination in decision-making for treatment options remains uncertain. Looking at it from another perspective, when comparing open and endoscopic procedures in compressive carpal tunnel surgery, ultrasound-guided procedures offer advantages in visualizing all important anatomical structures with a small incision and minimal soft tissue damage.[28]

Nerve ultrasound has gained importance in the diagnosis of CTS alongside traditional neurophysiological tests, and emerging imaging techniques such as ultrasound elastography and magnetic resonance tractography further corroborate these findings.[29] We believe that ultrasound radiomics applications, which have recently entered our lives, will continue to be prominent in the future. In a recent meta-analysis, ultrasound radiomics demonstrated superior diagnostic performance in detecting CTS compared to evaluations by radiologists. Additionally, ultrasound radiomics showed minimal variability in diagnostic accuracy even during the training and testing phases, highlighting its potential as a strong diagnostic tool in CTS.[30] While clinical assessment, neurophysiology, and imaging provide supportive evidence, the selection of the most appropriate approach for diagnosis and treatment depends on the clinician's experience. Evaluating the response to treatment based on ultrasound parameters should also be considered in the future.

Among the strengths of our study is the unbiased and comprehensive application of diagnostic tests. Blinding the radiologist and their expertise in the neuromuscular field strengthened our findings.

Despite the introduction of numerous new methods for the diagnosis and treatment of CTS, there is a continued need for well-designed longitudinal studies in the future. These studies are necessary to confirm the effectiveness of these new approaches and evaluate their feasibility in clinical research settings.

Limitations

A limitation of our study arises from the small sample sizes for each group and its retrospective nature. The lack of division into groups based on mild, moderate, and severe CTS is relatively limiting, with the most significant reason being the insufficiently large sample size.

CONCLUSION

Ultrasound applications in PRCTS are non-invasive, practical, cost-effective, and beneficial. MN-CSA, WFR, and NTR have provided comparable results to electrodiagnostic tests.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the institutional review board of Prof. Dr. Cemil Taşçıoğlu City Hospital Clinical Researches Ethics Committee (Date:06.02.23 No:87).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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