

# Variations of the Median Nerve and Carpal Tunnel Syndrome: a Systematic Review of the Literature

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## ABSTRACT

**Objectives:** The purpose of this systematic review is to examine the different variations of the median nerve (MN) and the diagnostic methods used to identify carpal tunnel syndrome (CTS), a common neuropathy resulting from the entrapment of the MN within the carpal tunnel. Understanding the different variations of the MN is crucial in order to prevent injuries during surgical treatment of the syndrome.

**Material and methods:** Data were extracted from studies published in PubMed. A detailed search in PubMed was performed for studies that reviewed the variations of the MN and CTS.

**Results:** There are two main classifications of the MN, known as the Lanz and Amadio categories. Lanz's classification is the one being mostly used in the surgical literature, with group 3 (Bifid MN) being the main cause of the CTS. Additionally, there are branches and anastomosis of the MN that do not fit into either category, with the third common digital branch being the most injured nerve during carpal tunnel release surgery. Diagnostic techniques for CTS include physical examination combined with NCS tests, magnetic resonance imaging (MRI), ultrasound, or elastography. While NCS has been previously the most commonly used diagnostic method, the recent literature suggests that ultrasound and elastography are the most accurate techniques.

**Conclusions:** In order to minimize injuries during carpal tunnel release surgery, it is crucial to have knowledge on the different variations of the MN that cause CTS. Additionally, this review emphasizes the significance of the current diagnostic methods, which not only make CTS more affordable but also facilitate easier recognition of the condition.

**Keywords:** variations, median nerve, carpal tunnel syndrome.

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## SYMBOLS AND ABBREVIATIONS

CTS: carpal tunnel syndrome  
 MN: median nerve  
 TCND: third common digital branch  
 NCS: nerve conduction study  
 MRI: magnetic resonance imaging

## INTRODUCTION

Carpal tunnel syndrome (CTS) is a neuropathy that commonly occurs when the median nerve (MN) is trapped in the carpal tunnel. While the exact cause is often unknown, it can be a result of injuries, or other medical conditions such as rheumatoid arthritis, ganglia, masses and pregnancy (1, 2, 26, 31). The MN originates from the brachial plexus, specifically from C5 to T1, and is responsible for the sensitivity and movement of the thumb, index and middle fingers as well as the flexion of the wrist and opposition of the thumb. After leaving the axillary fossa, it travels through the anterior portion of the arm between the biceps brachii and brachialis muscles in the brachial canal of Cruveilhier (3, 4). In the forearm, it branches out into the anterior interosseous branch and the palmar cutaneous branch (5). As it continues into the hand, it runs alongside the palmaris longus tendon before entering the carpal tunnel. The carpal tunnel is formed by the flexor retinaculum, a ligament that connects the pisiform, hamate and trapezium bones. It contains the MN along with nine tendons and sometimes a persistent median artery. The MN divides into six branches beyond the carpal tunnel. These branches include a motor branch that splits into sensory branches and enters the thenar musculature, as well as digital nerves from both the ulnar and radial side of the thumb and index finger, which may converge into one. Two of those supply the second and third web space of the hand, one of them provides motor branches to the first lubricant muscle, and the other one gives motor branches to the second lubricant muscle. There is also a widely studied digital branch (TCDN) that is often affected during carpal tunnel release surgery (6, 7). □

## METHODS

Data utilized in this study were obtained from various research articles found in PubMed.

A comprehensive search was conducted on PubMed using the keywords "variations", "median nerve" and "carpal tunnel syndrome", resulting in a total of 213 findings. One hundred eighty-seven irrelevant articles were excluded, with inclusion criteria focusing on relevance to the topic, availability of a DOI or full text, and being written in English. Additionally, the bibliography of the above-mentioned literature was also examined to extract relevant data. □

## RESULTS

Initially, a search on the platform PubMed yielded a total of 213 studies. An additional search through the references cited in these studies produced 19 more results, bringing the total to 229 studies. After eliminating duplicate and irrelevant studies, a total of 42 articles met the inclusion criteria for this review (Figure 1). Out of these, 19 studies focused on the normal anatomy and variations of the median nerve, while 23 studies proposed different diagnostic and therapeutic procedures. Notably, different variations were mentioned in 11 papers, while the normal anatomy was discussed in four articles. In terms of diagnostic tools, ultrasonography was

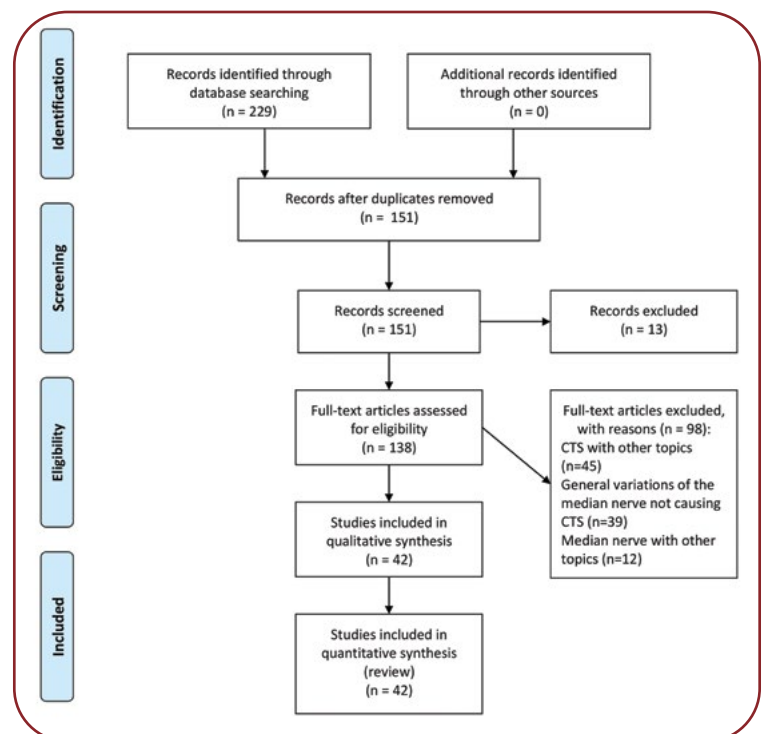


FIGURE 1. PRISMA flow chart

mentioned in 15 studies, NCS and MRI in three articles each and sonoelastography in two. ■

## DISCUSSION

Carpal tunnel syndrome may be developed without a known cause, known as idiopathic, or as a secondary condition. The main reason for this condition is variations of the MN. The most common classification system used in the literature is the one introduced by Lanz (8), which categorizes these variations into four groups (Table 1). In 2009, Al Qattan *et al* further classified the appearance of a bifid median nerve into six subgroups based on the presence of a persistent median artery or a nearby muscle. Subgroups I and III are typically asymptomatic (9).

Lanz did not incorporate the palmar cutaneous branch in his classification. As a result, in 1988, Amadio released a widely accepted classification of median nerve abnormalities that consisted of five groups. These included abnormalities in the division near the ligament, abnormalities in the motor branch, abnormalities in the palmar-cutaneous branch, abnormalities in the median-ulnar communicating sensory branch and other unclassified abnormalities.

### Variations

While Lanz's classification is the most commonly mentioned in the surgical literature (Table 1, Figure 2), there are also other variations related to the CTS that have not been classified by him.

Martin-Gruber anastomosis is a commonly found connection between the median and ulnar nerves in the forearm, as described in the literature (10, 6). However, it is quite rare for a connection to exist from the ulnar to the median nerve, and it usually indicates abnormalities (Marinacci anastomosis) (11). It is possible to classify Martin-Gruber anastomosis into two groups based on the number of anastomotic branches present. In cases where only one branch exists, there are three additional subgroups based on the origin of that branch. Specifically, it can originate from either a branch of the MN, passing through the superficial muscles of the forearm, directly from the MN itself, or from the terminal motor branch of the MN.

In 2008, a study conducted by Nitin J. Engineer *et al* assessed the different variations of the origin of the third common digital branch (TCDN),

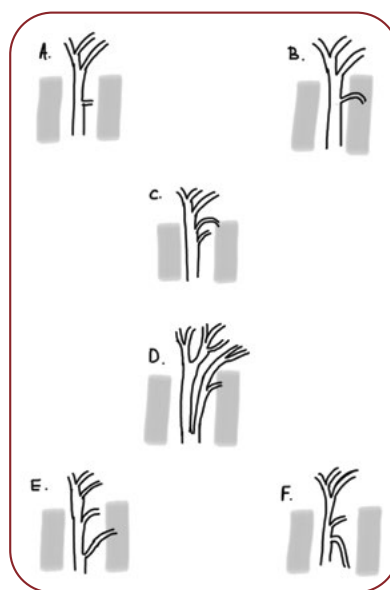
**TABLE 1.** Lanz's groups of variations

<b>Group 1</b>	<i>Variations of the course of the thenar branch: the thenar branch instead of leaving the median nerve after passing through the carpal tunnel, it leaves inside it and sometimes it can penetrate the ligament (7).</i>
<b>Group 2</b>	<i>Accessory branches arising either from the ulnar or the radial part of the median nerve distal to the carpal tunnel: most of the times, those branches are sensory, but there are also studies indicating the existence of motor branches too.</i>
<b>Group 3</b>	<i>High division or duplication of the median nerve/Bifid median nerve: Group 3 is widely reported in the surgical literature. When a bifid median nerve is present, the risk of developing CTS is higher than any other variation of the median nerve due to its higher cross-sectional area. It has a rate of appearance of 2.8% that is no different from men to women, from the left to right wrist and in different age groups. There is also some reference for a trifid median nerve but it is not that common (10).</i>
<b>Group 4</b>	<i>Accessory branches arising close to the carpal tunnel: they can either pass through the ligament or perforate it so that they can join other branches.</i>

which is frequently injured during carpal tunnel release surgery. The study classified the variations into three types based on their proximity to the carpal ligament – either close to it, distal to it and close to the palmar arch, or distal to both the carpal ligament and the palmar arch (12).

During the release surgery, another variation that is frequently compromised is known as the Johnson and Strewsbury variation. A study conducted by those researchers in 1988 revealed that, in 80% of their patients, the median nerve followed a distinct pathway when passing through the carpal ligament (6).

Steinberg *et al* noted a recurrent nerve perforating the carpal ligament, as well as the presence of an extra branch that originated near the carpal tunnel and either passed through it or beyond it,



**FIGURE 2.** Lanz's groups of variations. A) GROUP 1: Thenar branch leaving inside the carpal tunnel; B) GROUP 1: Thenar branch perforating the carpal tunnel; C) GROUP 2: Distal accessory branches; D) GROUP 3: Bifid median nerve; E) GROUP 4: Proximal accessory branch perforating the ligament; F) GROUP 4: Proximal accessory branch passing through the ligament

similar to Lanz group 4. Additionally, they identified an accessory branch originating from the recurrent branch of the MN, which could be found either close or distant to the carpal tunnel.

A single study has demonstrated the presence of a distinct variant of the MN possessing both Lanz's group 1 and group 3 attributes. This variant involves a branch originating proximal to the transverse carpal ligament and subsequently passing through it to access the thenar musculature (13, 14).

In addition to the presence of various branches, the position of the MN can also differ. When the MN travels through the carpal tunnel, it may either have a curved or straight path. If it follows a straight path, it can be shifted to either the radial or ulnar side of the tunnel, or it can pass through the center of the tunnel. Alternatively, if the nerve curves, it can be split towards either the ulnar or radial side of the tunnel (6).

## Diagnosis

Patient's history plays a crucial role in diagnosing CTS, just like in any other clinical examination. This is because certain occupations involving heavy manual labor, like construction, and prolonged repetitive hand movements, such as computer work, increase the risk of developing CTS (15, 16). The initial indicators of compression on the MN include pain, tingling and eventually numbness in the affected fingers (17). Considering these symptoms, a physical examination is highly significant (18).

Currently, the hand elevation test is regarded as the most precise examination. During this assessment, patients are instructed to raise their hand as high as possible. If any symptoms occur within the first minute, the test is deemed positive. To enhance the accuracy of this test, patients can further flex their wrist and have the doctor apply pressure to it, in addition to bending their head in the opposite direction.

Another widely used orthopedic test is the Phalen test, in which the patient flexes their wrists by touching the back of their hands together. If the patient experiences pain and paresthesia within the first 60 seconds, the test is deemed positive, indicating a strong possibility of CTS. This test can also be adapted by having the patient extend their hand and flex their wrist while tilting their head in the opposite direction. In this modified version of the test, pain is

expected to occur within approximately 60 seconds for a positive result.

In addition to these, another test called the "carpal compression test" involves the doctor exerting pressure on the patient's MN using both thumbs. If the patient experiences pain within 20-30 seconds, the test is considered positive and suggests a higher risk for CTS.

The final test in the series is called the "tethered median nerve stress test." During this test, the patient maintains their wrist in extension and applies pressure to the index finger, causing it to hyperextend. If the patient experiences pain or paresthesia within one minute, the test is interpreted as positive. Combining this test with one of the previously mentioned tests from this review, significantly enhances its accuracy.

The traditional method of diagnosing CTS involves physical tests and a Nerve Conduction Study (NCS). During the NCS, electrodes are placed on the wrist and elbow to stimulate the median nerve. One electrode is placed over the dorsum of the hand (ground electrode), another on the thenar eminence of the MN (active electrode detecting motor responses), and additional electrodes are placed over the first or the fifth metacarpophalangeal joint and some others on the fingers. If the nerve responds with sensory impulses, the test is considered negative, indicating that the patient does not have compression of the MN. The range of responses can vary from normal sensory and motor responses, indicating a negative test, to complete absence of motor and sensory responses, indicating an extreme result (19).

There is evidence suggesting that, although NCS is the most used technique for diagnosis, it has a significant rate of false negative cases (16-34%). Additionally, it is both costly and a painful, invasive, and uncomfortable procedure for patients (20-22). As a result, there has been an increasing number of studies that recommend the use of MRI or ultrasound as more accurate diagnostic techniques, always taking into consideration the results of the physical examination (23).

Magnetic resonance imaging provides a clear view of the MN within the carpal tunnel, aiding doctors in identifying any abnormalities or variations in the nerve's structure, such as flattening, compression, or other morphological changes (5, 9, 24, 25). Additionally, doctors may employ

an advanced MRI technique, called Diffusion-Weighted Imaging (DWI), to further enhance the visualization of the nerve, making it easier to detect tumors, trauma, or signs of neuritis (26). While MRI is a convenient and cost-effective diagnostic tool, it does require a significant amount of time to complete.

Ultrasound is a commonly mentioned and highly reliable method for diagnostic procedures. It is considered to be the most accurate and affordable tool, with a significantly lower error rate (6-11%) compared to other diagnostic methods. Additionally, ultrasound is painless and provides quick results. This procedure allows doctors to assess various parameters of the MN, including its size (high-resonance ultrasound HRNU), blood flow (through doppler), and mobility (through dynamic ultrasound) (27, 28, 29, 11). Enlargement of the nerve increased cross-sectional area, and palmar bowing of the flexor retinaculum are expected indications of CTS during ultrasound examinations (30). While many researchers favor this technique (31-37, 29), it should always be compared to the results of a physical examination since it cannot differentiate the stages of CTS (38).

Some studies (39, 20) suggest using dynamic ultrasound as a diagnostic tool for CTS. Dynamic ultrasound is a modified version of normal ultrasound where patients are instructed to move their fingers in standard motions during the scanning process. This allows doctors to differentiate between the flexor tendons (which move) and the MN (which does not move). The advantage of this technique is that it does not require a separate diagnostic machine; rather, doctors can use a commercial ultrasound machine, similar to the one used in the unmodified procedure. However, in cases where patients experience extreme discomfort in moving their fingers, this technique cannot be employed as it may result in images with artifacts, leading to inaccurate diagnosis.

Sonoelastography (SEL) is a newly developed method to evaluate the elasticity of soft tissue during ultrasound scanning. The diagnostic image is color-coded based on the tissue elasticity. Soft tissue is represented by the color red, medium elasticity by green and yellow, and hard tissue by blue. This technique can accurately

diagnose the CTS by identifying the stiffer transverse carpal ligament in affected individuals (40) compared to healthy ones (41, 42). □

## CONCLUSIONS

The occurrence and seriousness of CTS are closely related to differences in the structure of the MN, which is primarily responsible for providing feeling to the thumb, index, middle and ring fingers, and controlling certain hand muscles. Variations in the anatomy of the MN can have a significant impact on the likelihood and progress of CTS. One important factor is the size and shape of the carpal tunnel, a narrow passage in the wrist formed by the wrist bones that the MN travels through. People with naturally narrower carpal tunnels have less room for the nerve, making them more prone to compression and irritation. Additionally, deviations in the path and branches of the MN can affect the development of CTS. In some instances, the nerve may take an unusual route, increasing the risk of being trapped or squeezed within the tunnel. These variations contribute to the build-up of pressure on the nerve, leading to the distinctive symptoms of CTS.

It is crucial to comprehend these anatomical differences in order to diagnose and treat the CTS accurately. Medical professionals often use nerve conduction studies and physical examinations to assess the severity and underlying causes of CTS. If conservative treatments do not yield positive results or if CTS is severe, surgery may be necessary to relieve pressure on the MN and alleviate symptoms. The correlation between variations in the MN and the development of CTS emphasizes the significance of personalized diagnosis and treatment plans. It is essential to identify these anatomical variances to deliver appropriate care to individuals affected by this prevalent and potentially debilitating condition. □

*Availability of data and materials: Data used in this systematic review are available in the PubMed database, using the above-mentioned keywords.*

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# REFERENCES

1. Bianchi S, Hoffman DF, Tamborini G, et al. Ultrasound Findings in Less Frequent Causes of Carpal Tunnel Syndrome. *J Ultrasound Med* 2020;39:2469-2482.
2. Kaya Subaşı P, Güler T, Yurdakul FG, et al. Carpal tunnel syndrome in patients with rheumatoid arthritis and psoriatic arthritis: an electrophysiological and ultrasonographic study. *Rheumatol Int* 2021;41:361-368.
3. Encarnacion M, Nurmukhametov R, Barrientos RE, et al. Anatomical Variations of the Median Nerve: A Cadaveric Study. *Neurol Int* 2022;14:664-672.
4. Soubeyrand M, Melhem R, Protais M, et al. Anatomy of the median nerve and its clinical applications. *Hand Surg Rehabil* 2020;39:2-18.
5. Pierre-Jerome C, Smitson RD Jr, Shah RK, et al. MRI of the median nerve and median artery in the carpal tunnel: prevalence of their anatomical variations and clinical significance. *Surg Radiol Anat* 2010;32:315-322.
6. Demircay E, Civelek E, Cansever T, et al. Anatomic variations of the median nerve in the carpal tunnel: a brief review of the literature. *Turk Neurosurg* 2011;21:388-396.
7. Kadar IA, Virág TH, Matei IR, et al. High Division of the Median Nerve with Unusually High Origin of the 3rd Space Common Digital Nerve. *Injury*. 2020;51 Suppl 4:S96-S102.
8. Lanz U. Anatomical variations of the median nerve in the carpal tunnel. *J Hand Surg Am* 1977;2(1):44-53.
9. Tountas CP, Bihrlé DM, MacDonald CJ, et al. Variations of the median nerve in the carpal canal. *J Hand Surg Am* 1987;12(5 Pt 1):708-712.
10. Sur A, Sinha MM, Ughade JM. Prevalence of Martin-Gruber Anastomosis in Healthy Subjects: An Electrophysiological Study from Raigarh, Chhattisgarh. *Neurol India* 2021;69:950-955.
11. Chang YT, Chen CL, Lai CH. Marinacci anastomosis (reverse Martin-Gruber anastomosis): A case report. *Medicine (Baltimore)* 2021;100:e25073.
12. Engineer NJ, Hazani R, Mowlavi A, et al. Variations in the anatomy of the third common digital nerve and landmarks to avoid injury to the third common digital nerve with carpal tunnel release. *Eplasty* 2008;8:e51.
13. Mullin EP 3rd, Deal JB Jr, Krul KP. A Preligamentous Variant of the Thenar Motor Branch of the Median Nerve. *J Am Acad Orthop Surg Glob Res Rev* 2020;4:e20.00029.
14. Neumann M, Suchomlinov A. Pilot Cadaveric Study of Anatomical Variations of the Median Nerve at the Wrist in the Lithuanian Population. *Cureus* 2023;15:e39282.
15. Genova A, Dix O, Saefan A, et al. Carpal Tunnel Syndrome: A Review of Literature. *Cureus* 2020;12:e7333.
16. Mohammad WS. Work-related risk factors for Carpal Tunnel Syndrome among Majmaah University female touchscreen users. *Pak J Med Sci* 2019;35:1221-1226.
17. Osiak K, Elnazir P, Walocha JA, et al. Carpal tunnel syndrome: state-of-the-art review. *Folia Morphol (Warsz)* 2022;81:851-862.
18. Chong HH, See A, Kulkarni K. National trends in the initial diagnosis and management of carpal tunnel syndrome: results from the ELECTS (ELEctrophysiology in Carpal Tunnel Syndrome) study. *Ann R Coll Surg Engl* 2022. doi:10.1308/rcsann.2022.0087.
19. Yu G, Chen Q, Wang D, et al. Diagnosis of carpal tunnel syndrome assessed using high-frequency ultrasonography: cross-section areas of 8-site median nerve. *Clin Rheumatol* 2016;35:2557-2564.
20. Liao YY, Wu CC, Kuo TT, et al. Carpal tunnel syndrome diagnosis by a self-normalization process and ultrasound compound imaging. *Med Phys* 2012;39:7402-7411.
21. Sasaki T, Nimura A, Kuroiwa T, et al. Assessment of Pain During Nerve Conduction Studies in Patients With Carpal Tunnel Syndrome. *J Hand Surg Glob Online* 2022;4(2):89-92.
22. Wright AR, Atkinson RE. Carpal Tunnel Syndrome: An Update for the Primary Care Physician. *Hawaii J Health Soc Welf* 2019;78(11 Suppl 2):6-10.
23. Kleggetveit IP, Jørum E. Diagnosis of carpal tunnel syndrome. *Scand J Pain* 2018;18:333-337.
24. Ng AWH, Griffith JF, Tong CSL, et al. MRI criteria for diagnosis and predicting severity of carpal tunnel syndrome. *Skeletal Radiol* 2020;49(3):397-405.
25. Naik S, Mahanty S, Bhoi SK, et al. MRI of wrist and diffusion tensor imaging of the median nerve in patients with carpal tunnel syndrome. *J Neurosci Rural Pract* 2023;14:302-307.
26. Bao H, Wu C, Wang S, et al. Diffusion-weighted magnetic resonance neurography for the diagnosis of carpal tunnel syndrome: a pilot study. *Clin Radiol* 2017;72:165-169.
27. Gervasio A, Stelitano C, Bollani P, et al. Carpal tunnel sonography. *J Ultrasound* 2020;23(3):337-347.
28. Petrover D, Hakime A, Silvera J, et al. Ultrasound-Guided Surgery for Carpal Tunnel Syndrome: A New Interventional Procedure. *Semin Intervent Radiol* 2018;35:248-254.
29. Linehan C, Childs J, Quinton AE, et al. Ultrasound parameters to identify and diagnose carpal tunnel syndrome. A review of the literature. *Australas J Ultrasound Med* 2020;23:194-206.
30. Park JS, Won HC, Oh JY, et al. Value of cross-sectional area of median nerve by MRI in carpal tunnel syndrome. *Asian J Surg* 2020;43:654-659.
31. Aktürk S, Büyükcavcı R, Ersoy Y. Median nerve ultrasound in carpal tunnel syndrome with normal electrodiagnostic tests. *Acta Neurol Belg* 2020;120:43-47.
32. Ting BL, Blazar PE, Collins JE, et al. Median Nerve Ultrasonography Measurements Correlate With Electrodiagnostic Carpal Tunnel Syndrome Severity. *J Am Acad Orthop Surg* 2019;27:e17-e23.
33. Chen J, Fowler JR. Ultrasound Findings in Patients with Normal Nerve Conduction despite Clinical Signs and Symptoms Consistent with Carpal Tunnel Syndrome. *Plast Reconstr Surg* 2022;150:1025e-1032e.
34. Padua L, Cuccagna C, Giovannini S, et al. Carpal tunnel syndrome: updated evidence and new questions. *Lancet Neurol* 2023;22:255-267.
35. Yoshii Y, Zhao C, Amadio PC. Recent Advances in Ultrasound Diagnosis of Carpal Tunnel Syndrome. *Diagnostics (Basel)* 2020;10:596.
36. Tai TW, Wu CY, Su FC, et al. Ultrasonography for diagnosing carpal tunnel syndrome: a meta-analysis of diagnostic test accuracy. *Ultrasound Med Biol* 2012;38:1121-1128.
37. Georgiev GP, Karabinov V, Kotov G, et al. Medical Ultrasound in the Evaluation of the Carpal Tunnel: A Critical Review. *Cureus* 2018;10:e3487.
38. Nam K, Peterson SM, Wessner CE, et al. Diagnosis of Carpal Tunnel Syndrome using Shear Wave Elastography and High-frequency Ultrasound Imaging. *Acad Radiol* 2021;28(9):e278-e287.
39. Stoianov AG, Patrascu JM, Hoge BG, et al. Static and Dynamic Ultrasound Evaluation of the Median Nerve Morphopathology in Carpal Tunnel Syndrome Diagnosis. *Maedica (Bucur)* 2022;17:591-595.
40. Uz C, Umay E. Ultrasonographic measurement of median nerve and wrist skin thickness in patients with carpal tunnel syndrome: relationship with clinical, electrophysiologic and functionality. *Acta Orthop Belg* 2023;89:167-172.
41. Wee TC, Simon NG. Shearwave Elastography in the Differentiation of Carpal Tunnel Syndrome Severity. *PM R* 2020;12:1134-1139.
42. Klausner AS, Miyamoto H, Martinoli C, et al. Sonoelastographic Findings of Carpal Tunnel Injection. *Ultraschall Med* 2015;36:618-622.