The Diagnostic Value of the Median Nerve Sonography in Chronic Phase Carpal Tunnel Syndrome Cases in Indonesia

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Abstract

Background. *Ultrasound evaluation on the median nerve in carpal tunnel syndrome (CTS) patients by measuring cross-sectional area (CSA) is widely known. However, studies have shown that CSA of the median nerve could vary in different demographical factors. Therefore, the cut-off CSA value for CTS in the Indonesian population could be significantly different. Purpose. To compare mean CSA of the median nerve between normal and CTS populations and establish a cut-off point of CSA to diagnose CTS.*
Materials and Methods. *A comparative cross-sectional study was conducted involving 40 people divided equally into CTS and normal groups. Normal and CTS subjects are determined by Electrodiagnostic study (EDx) using EMG and Nerve Conduction Study (NCS). The CSA measurement was performed at the level of the carpal tunnel inlet.*
Results. *The mean CSA value at the level of tunnel inlet of the normal group was 8.3 ± 1.4 mm2 and for the CTS group is 15.4 ± 4.4 mm2. The receiver operating characteristics (ROC) analysis showed 10.6 mm2 as the cut-off point with 95% sensitivity and 95% specificity (P<0.001).*
Conclusion. *The median nerve CSA at the tunnel inlet is significantly larger in the CTS population and the cut-off point can be recommended in detecting CTS in the Indonesian population.*

Keyword: *Nerve Conduction Study, Ultrasonography, Median Nerve, Carpal Tunnel Syndrome*

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Nilai Diagnostik Sonografi Saraf Median Pada Kasus Carpal Tunnel Syndrome Fase Kronis Di Indonesia

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Abstrak

Pendahuluan. *Ultrasonografi dikenal sebagai modalitas pilihan untuk mengevaluasi nervus medianus pada penderita sindrom terowongan karpal. Akan tetapi, penelitian sebelumnya menunjukkan luas penampang lintang nervus medianus sangat dipengaruhi oleh faktor demografis. Oleh karena itu, penelitian ini bertujuan membandingkan luas penampang lintang nervus medianus pada populasi normal dan sindrom terowongan karpal serta mencari nilai potong luas penampang lintang.*
Metode. *Studi potong lintang komparatif dengan melibatkan total 40 subjek dilakukan di Departemen Radiologi RS Cipto Mangunkusumo, Jakarta. Subjek yang dimasukkan dievaluasi dengan pemeriksaan klinis dan konduksi hantaran saraf (KHS). Luas penampang lintang nervus medianus dievaluasi dengan menggunakan ultrasonografi (USG) pada pergelangan tangan (carpal tunnel inlet). Pengukuran titik potong luas penampang lintang antar kelompok dilakukan dengan kurva ROC (Receiving Operating Characteristic Curve).*
Hasil. *Rerata dari luas penampang lintang nervus medianus kelompok normal didapatkan 8,3 ± 1,4 mm2 dan pada kelompok sindrom terowongan karpal sebesar 15,4 ± 4,4 mm2. Berdasarkan analisis dengan kurva ROC didapatkan titik potong luas penampang lintang antar kelompok yaitu 10,6 mm2 dengan sensitivitas 95% dan spesifisitas 95% (P<0.001).*
Kesimpulan. *Luas penampang lintang nervus medianus pada kelompok sindrom terowongan karpal didapatkan lebih besar secara signifikan dibanding kelompok normal dan titik potong luas penampang lintang nervus medianus dapat direkomendasikan untuk mendeteksi sindrom terowongan karpal.*

Kata Kunci: *Konduksi Hantaran Saraf, Nervus Medianus, Sindrom Terowongan Karpal, Ultrasonografi*

Introduction

Carpal Tunnel Syndrome (CTS) is a group of clinical symptoms caused by the chronic process of median nerve compression in the carpal tunnel. This frequent disease leads to sensory and motor impairment at the innervated organ. The symptoms are night wrist pain, paresthesia, numbness, and stiffness in the finger, as well as reduced grip power and thenar muscle atrophy.[1-3]

CTS is found in approximately 3.8% of the general population. 2010 National Health Interview Survey (NHIS) reported that CTS affected 4.8 million US workers of which 67.1% were medical officers. In Indonesia, Tana L, et al. found that 20.3% of garment workers in Jakarta were affected by CTS. Following this high incidence, early detection of CTS is crucial.[4]

Electrodiagnosis (EDx) using a combined needle EMG and Nerve Conduction Study (NCS) or electroneurography has become the standard diagnosis and screening tool to assess median nerve functional status. However, it could not visualize the anatomical structure of the nerve and its surrounding tissue, so another adjunct tool is required to establish the diagnosis, such as ultrasound and MRI.[5]

Due to its impracticality and high cost, MRI is less recommended to assess peripheral nerves. Ultrasound is favored for its benefits of zero radiation, low cost, and non-invasive

method, with a sensitivity of 70 – 90 % and specificity of 57 – 100% in diagnosing CTS. The measurement of the CSA of the median nerve is considered a sensitive indicator in wrist ultrasound.[6]

Previous wrist or forearm ultrasound studies to determine the CSA of the median nerve in the normal and CTS patients have been conducted. At the wrist, the measurement is performed at the height of scaphoid and pisiform bone, known as the inlet, and at the height of trapezium bone and hamate bone groove, known as the outlet. The CSA of the median nerve ranges from 7 to 10 mm2 and 9 to 15 mm2 in CTS patients.[6-9] Hobson-Webb, et al was comparing the wrist-to-forearm ratio (WFR) of median nerve area between normal population and CTS patients and found significant differences between wrist cross-sectional median nerve area (10.0 ± 2.3 (7-14) in controls and 14.3 ± 4.1 (8-34) in CTS patients), forearm cross-sectional median nerve area (9.8 ± 2.4 (7-14) in controls and 6.9 ± 1.6 (3-10) in CTS patients), and WFR between these population (1.0 ± 0.1 (0.8-1.3) in controls and 2.1 ± 0.5 (1.5-3.8) in CTS population).[10] Another study by Burg, et al discovered that CSA normal values for the median nerve could vary in different demographical factors, including race, age, height, and weight. In Dutch subjects, CSA of the median nerve in both left (8.3±1.9mm2) and right wrist (8.1±2.0mm2) was significantly bigger compared to Indian subjects' CSA of the median nerve, which is 7.0±1.1mm2 for the left wrist and 7.2±1.1mm2 for the right wrist.[11] There were potentially different CSA normal values for the median nerve among Indonesian. However, currently, there is no data regarding the CSA of the median nerve in normal and CTS populations in Indonesia. This study aims to find the cut-off value of CSA of median nerve sonography to diagnose CTS.

Methods

A comparative cross-sectional study using primary data was conducted from February to March 2017. Clinical examination and NCS were performed in the Neurophysiology Clinic, Department of Neurology, Dr. Cipto Mangunkusumo Hospital, Jakarta. The median nerve ultrasound examination was conducted in the Department of Radiology. A total of 40 subjects fulfilled the inclusion criteria and did not possess any exclusion criteria included in this study by consecutive sampling and were taken written informed consent to participate in this study. The participant was divided into CTS and normal subject groups and both consisted of 20 subjects. This study was approved by the Ethical Committee of Research in Health from the Faculty of Medicine, University of Indonesia (No. 136/UN2. F1/ETIK/2017).

The inclusion criteria of CTS participants were adults aged 20 – 60 years old with dominant affected hand and had any CTS clinical symptom's severity ranging from grades 1 to 4. The inclusion criteria of the normal subjects were adults aged 20 – 50 years old with no CTS clinical symptoms found on the dominant hand. The exclusion criteria of normal and CTS subjects were patients who had a history of surgery on the median nerve or the wrist, median nerve tumor, post-trauma patient, fracture in the wrist area, pregnant, polyneuropathy, carpal tunnel inflammation, cutaneous and subcutaneous wrist edema or had median nerve anatomical variation following ultrasound. Additional exclusion criteria for CTS subjects were patients who had received CTS treatment for at least two weeks, whether it was oral conservative therapy, injection therapy, or median nerve surgery.

NCS and nerve ultrasound were performed on the subjects. CTS diagnosis was established and graded based on physical examination and NCS using Bland Criteria. This study used a 15 MHz linear transducer with adjusted gain, magnification, and depth for each subject. A muskuloskeletal radiologist with more than ten years of experience examined the cross-sectional area of the median nerve from the inlet using an elliptical line measured inside the hyperechoic layer. Median nerve vascularization was also evaluated using Color Doppler Ultrasonography (CDUS) PRF 147 Hz. Other data obtained in this study were median nerve echogenicity and the notch sign.

Data obtained were then analyzed by 2010 SPSS. We performed an independent T-test for normally distributed data and a Mann-Whitney U test for abnormally distributed data. The cut-off point was determined by creating the Receiving Operating Characteristic Curve (ROC Curve).

Results

Subject Characteristics

From a total of 40 participants included in this study, the mean age of normal and CTS group was 38.0 ± 9.1 and 45.5 ± 8.2 years old, respectively (p = 0.01). The subject characteristics of each group are shown in Table 1.

Table 1. Subject Characteristics of CTS and Normal Group

Subject Characteristics	Groups		*P-value*
	CTS	Normal	
	N (%)	N (%)	
Gender			
Men	4 (44.44)	5 (55.56)	>0.999
Women	16 (51.61)	15 (48.39)	
Age group (years)			
≤ 40	5 (31.25)	11 (68.75)	0.053
> 40	15 (62.50)	9 (37.50)	

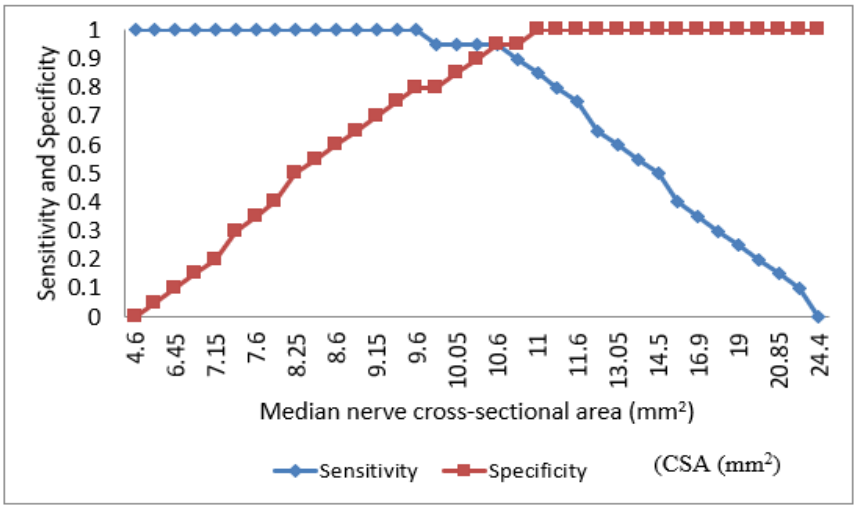

Figure 1. Determination of Median Nerve Cross-sectional Area's Cut-off Value Based on Sensitivity and Specificity

The mean cross-sectional area of the median nerve in normal and CTS group was 8.3 ± 1.4 mm2 and 15.4 ± 4.4 mm2, respectively (p <0.001). From the ROC curve, as shown in Figure 1, we found a cutoff point of median nerve cross-sectional area of 10.6 mm2 with 95% (95%CI: 75.13-99,87%) sensitivity, 95% (95%CI: 75.13-99,87%) specificity, 95% (95%CI: 75.13-99,87%) Positive Predictive Value (PPV) and 95% (95%CI: 75.13-99,87%) Negative Predictive Value (NPV) (p <0.001). Table 2 shows the cutoff point between both groups. This study also found a reduction in median nerve echogenicity in 12 CTS subjects and a notch sign in 3 CTS subjects, as shown in Table 3. Vascularization was not detected in any group. Median nerve ultrasound analysis

Table 2. Cut off Point of Median Nerve Cross-sectional Area Between CTS and Normal Group

Cut off point of the cross-sectional area	Groups		Total N (%)
	CTS	Normal	
	N (%)	N (%)	
Above cut-off point (≥ 10,6mm2)	19 (95)	1 (5)	20 (100)
Below cut-off point (< 10,6mm2)	1 (5)	19 (95)	20 (100)
Total	20 (50)	20 (50)	40 (100)

Table 3. Additional Evaluation of Median Nerve Ultrasound

Ultrasound Parameter	Groups		*P-value*
	CTS	Normal	
	N (%)	N (%)	
Echogenicity reduction			
Yes	12 (100)	0 (0)	<0.001
No	8 (28.57)	20 (71.43)	
Notch sign			
Present	3 (100)	0 (0)	
Not present	17 (45.95)	20 (54.05)	0.231
Vascularization detection			
Present	0 (0)	0 (0)	
Not present	20 (50)	20 (50)	>0.999

Discussion

There was a significant difference in the mean CSA between the normal group (8.4 ± 1.4 mm2) and the CTS group (15.4 ± 4.4 mm2, p<0.001). Hobson-Webb, et al[6] found the mean cross-sectional area of the median nerve at the level of wrist inlet was 10.0 ± 2.3 mm2 in the normal group and 14.3 ± 4.1 mm2 in the CTS group with a sample size comprised of 18 normal and 44 CTS subjects. The mean cross-sectional area of the median nerve found by Fu, et al5 was 8.7 ± 1.2 mm2 in the normal subject and 14.69 ± 1.2 mm2 with a sample size comprised of 44 normal and 46 CTS subjects. Sample composition, sample size, and cross-sectional area taken at the inlet level were thought to cause differences in results compared to this study. Another study conducted by Shim, et al[9] found the mean cross-sectional area of the median nerve at the inlet level of the bilateral wrist was 7.7 ± 1.2 mm2 in normal subjects and 13.6 ± 4.8 mm2 in CTS subjects with a sample size comprised of 36 normal and 60 CTS subjects. The different result compared to this study was thought due to the sample which did not include non-dominant hand as exclusion criteria.

A study conducted by Burg, et al[7] involving 100 Indian subjects and 137 German subjects obtained a significant difference in the median nerve CSA of the normal population between Indians and Germans. The cross-sectional area of the Indian population was 7.261 ± 1 mm2 on the right wrist and 7.061 ± 1 mm2 on the left wrist, while the median nerve cross-sectional area of the German population was 8.162 ± 2 mm2 on the right wrist and 8.362 ± 2 mm2 on the left wrist. It was very likely that nation and sample size differences caused the different results of the median nerve cross-sectional area between the normal group of this study and the normal group of Indians and German.[7]

By using the ROC curve, this study obtained a cut-off point of 10.6 mm2 of median nerve cross-sectional area at the proximal inlet level between normal and CTS subjects, with 95% sensitivity and 95% specificity. A previous study by Chan, et al[8] obtained a cut-off point of 10 mm2 at the proximal inlet level with 81.85% sensitivity and 83.3% specificity. Fifty-four subjects were involved without considering the non-dominant hand as exclusion criteria. Shim, et al[9] obtained a cutoff point of 9 mm2 at the inlet level with 86.7 sensitivity and 88.9% specificity in the Korean population. The sample size and measurement site difference could be the reason behind the difference between the result of this study and the previous ones. This study's high sensitivity and specificity were due to the measurement performed only on the dominant hand.

Twelve out of 20 CTS subjects had reduced median nerve echogenicity, while none of the normal subjects had an abnormality in the median nerve echogenicity (Figure 2). The echogenicity evaluation was significantly different (Fisher test, p<0.001). Chan, et al[8] found 77.8% sensitivity and 96.3% specificity in the reduction of median nerve echogenicity, while Mallouhi, et al[12] found 80% sensitivity, 65% specificity, and 77% accuracy, with 206 CTS subjects.

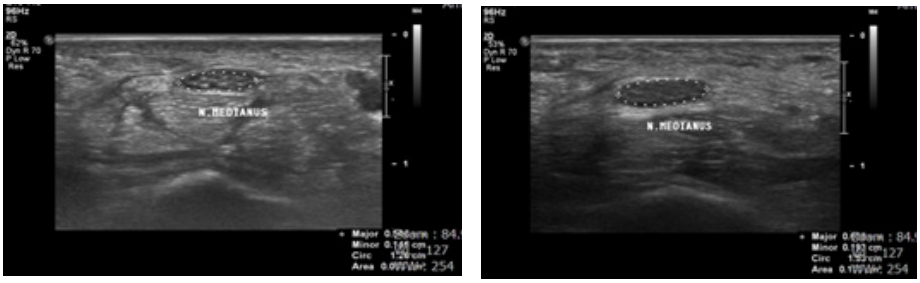

Figure 2. Transverse section of median nerve ultrasound. (a) normal subject with a cross-sectional area of 6.3 mm2, well-defined and hyperechoic fascicle structure (b) CTS subject with a cross-sectional area of 11.7 mm2 and reduced median nerve echogenicity.

Several studies mentioned that ultrasound examination of normal peripheral nerve, including the median nerve, will visualize a group of fascicles with hypoechoic echogenicity, bordered by hyperechoic septum creating a honeycomb-like appearance and surrounded by a hyperechoic layer that is epineurium.[13,14] Therefore, the absence of reduced echogenicity of the median nerve in the normal group of this study is in line with the literature. CTS is caused by median nerve compression at the level of the carpal tunnel. Long term compression leads to the structural change of median nerve micro vascularity, followed by increased endoneurial vascular permeability and fluid accumulation which develops into intra-fascicular edema.[3,15] Based on the pathophysiology, fluid accumulation and intra-fascicular edema in ultrasound examination will be visualized as dull and hypoechoic fascicle structure, as found in 12 CTS subjects in this study.

MacKinnon explained the presence of progressive histological changes in strangulated nerve vascularity, including microvascular thickening of perineurium and endoneurium with membrane reduplication, fibrosis of perineurium and epineurium, and the loss of nerve fibre related to myelin thinning, contributing to demyelination and degeneration of nerve fibre.[3] This theory explains the absence of reduced echogenicity in 8 CTS subjects.

About 3 out of 20 CTS subjects had the notch sign (Figure 3), while none of the normal subjects had the sign. The notch sign is a visualization of the shrinking median nerve at the proximal compression level.[13] Mallouhi et al[12] used a threefold increase in the nerve diameter on the longitudinal level as a standard of notch sign characteristic which was called nerve flattening, with 60% sensitivity, 76% specificity, and accuracy of 63%, obtained from 151 CTS patients. Chan, et al[8] found a cutoff point of flattening ratio between compression level at the carpal tunnel and median nerve enlargement on the longitudinal section of 2.65, with 70% sensitivity and 53.7% specificity. This study used a 3:1 flattening ratio as

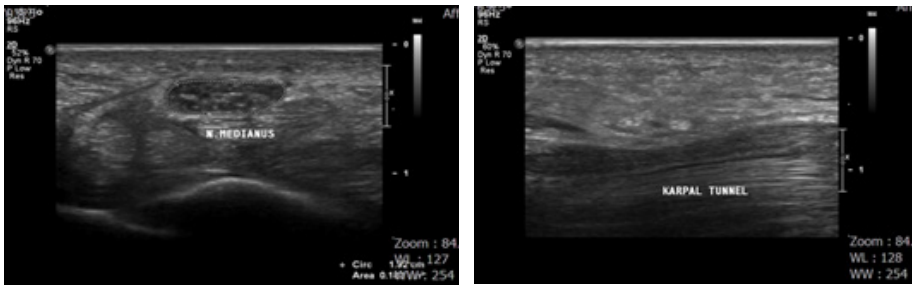

Figure 3. Median nerve ultrasound of CTS patient. (a) Transverse section of median nerve cross-sectional area of 18.3 mm2 with reduced nerve echogenicity although some hyperechoic structure of fascicle is still visible. (b) The longitudinal section of the median nerve shows shrinking nerve size at the level of carpal tunnel (notch sign).

the notch sign standard. If less ratio was used based on the other study, the more notch sign would likely be detected.

Vascularization was not found in any subject group. Mallouhi, et al[12] obtained 95% sensitivity, 71% specificity, and 91% accuracy of the increment of median nerve vascularization using Color Doppler Ultrasound (CDUS) which was confirmed by Power Doppler Ultrasound (PDUS) examination. Increased intraneural vascularization of the median nerve happens in the acute phase of CTS, while no vascularization is increment seen in the chronic phase.[16] In this study, 20 subjects had felt symptoms of CTS for more than six months which was classified into the chronic phase, explaining why no vascularization was detected by the CDUS technique. The literature stated that the PDUS examination has a higher sensitivity to detect the small and slow streams. Evans[17] stated that CDUS was not sensitive to detecting small and slow streams, which made PDUS the recommended one. The absence of intraneural bloodstream of the median nerve in both subject groups, particularly normal subjects, was thought to the account for the low sensitivity of CDUS to detect vascularization of the small stream.

Limitations

Based on Bland Criteria, most CTS subjects in this study had a moderate degree of severity, which led to a very significant difference in median nerve CSA between normal and CTS subject groups. The measurement of the CSA was performed only at the level of the tunnel inlet, so there was a chance of undetected nerve entrapment at the distal carpal tunnel.

Conclusion

The mean of median nerve CSA at the level of carpal tunnel inlet in normal subjects was 8.3 ± 1.4 mm2 and it was 15.4 ± 4.4 mm2 in CTS subjects. The cut-off point of the median nerve CSA at the level of the tunnel inlet was 10.6 mm2 with 95% sensitivity and 95% specificity to predict CTS. Further study is needed to measure CSA at the level of the tunnel outlet, and to find the relationship between the median nerve CSA and the severity of CTS in the Indonesian population.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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References

1. Pecina MM, Krmpotic-Nemanic J, Markiewitz AD. Tunnel syndromes, peripheral nerve compression syndromes: Carpal tunnel syndrome. 3rd ed. CRC Press LLC, Washington DC; 2001. p. 126-44.
2. Demircay E, Civelek E, Cansever T, Kabatas S, Yilmaz C. Anatomic variations of the median nerve in the carpal tunnel: a brief review of the literature. Turk Neurosurg. 2011;21(3):388-396. https://doi.org/10.5137/1019-5149.JTN.3073-10.1
3. Aboong MS. Review Article: Pathophysiology of carpal tunnel syndrome. Neuroscience. 2015; 20(1): 4-9.
4. Tana L, Halim FXS, Delima, Ryadina W. Carpal Tunnel Syndrome pada Pekerja Garmen di Jakarta. Bul Penel Kesehatan. 2004; 32(2): 73-82.
5. Fu T, Cao M, Liu F, Zhu J, Ye D, et al. Carpal Tunnel Syndrome Assessment with Ultrasonography: Value of Inlet-to-Outlet Median Nerve Area Ratio in Patients versus Healthy Volunteers. PLOS ONE 10(1): e0116777. https://doi.org/10.1371/journal.pone.0116777
6. Hobson-Webb LD, Massey JM, Juel VC, Sanders DB. The ultrasonographic wrist-to-forearm median nerve area ratio in carpal tunnel syndrome. Clin Neurophysiol. 2008;119(6):1353-1357. https://doi.org/10.1016/j.clinph.2008.01.101
7. Burg EW, Bathala L, Visser LH. Difference in normal values of median nerve cross-sectional area between Dutch and Indian subjects. Muscle

Nerve. 2014;50(1):129-132. https://doi.org/10.1002/mus.24124
8. Chan KY, George J, Goh KJ, Ahmad TS. Ultrasonography in the evaluation of carpal tunnel syndrome: Diagnostic criteria and a comparison with nerve conduction studies. Neurology Asia. 2011; 16(1): 57-64.
9. Shim JH, Doh JW, Lee KS, Shim JJ, Yoon SM, Bae HG. The diagnostic value of ultrasonography in Korean carpal tunnel syndrome patients. Korean J Neurotrauma. 2013; 9: 1-5.
10. Hobson-Webb LD, Massey JM, Juel VC, Sanders DB. The ultrasonographic wrist-to-forearm median nerve area ratio in carpal tunnel syndrome. Clin Neurophysiol. 2008;119(6):1353-1357. https://doi.org/10.1016/j.clinph.2008.01.101
11. Burg EW, Bathala L, Visser LH. Difference in normal values of median nerve cross-sectional area between Dutch and Indian subjects. Muscle Nerve. 2014;50(1):129-132. https://doi.org/10.1002/mus.24124
12. Mallouhi A, Pülzl P, Trieb T, Piza H, Bodner G. Predictors of carpal tunnel syndrome: accuracy of gray-scale and color Doppler sonography [published correction appears in AJR Am J Roentgenol. 2006 Aug;187(2):266. Pültzl, Petra [corrected to Pülzl, Petra]]. AJR Am J Roentgenol. 2006;186(5):1240-1245. . https://doi.org/10.2214/AJR.04.1715
13. Lawande AD, Warrier SS, Joshi MS. Role of ultrasound in evaluation of peripheral nerves. Indian J Radiol Imaging. 2014;24(3):254-258. https://doi.org/10.4103/0971-3026.137037
14. Vögelin E, Mészàros T, Schöni F, Constantinescu MA. Sonographic wrist measurements and detection of anatomical features in carpal tunnel syndrome. ScientificWorldJournal. 2014;2014:657906. https://doi.org/10.1155/2014/657906
15. Osbourne A. Peripheral nerve injury and repair. TSMJ. 2007; 8(1): 29-33.
16. Keleş I, Karagülle Kendi AT, Aydin G, Zöğ SG, Orkun S. Diagnostic precision of ultrasonography in patients with carpal tunnel syndrome. Am J Phys Med Rehabil. 2005;84(6):443-450. https://doi.org/10.1097/01.phm.0000163715.11645.96
17. Evans DH. Colour flow and motion imaging. Proc Inst Mech Eng H. 2010;224(2):241-253. https://doi.org/10.1243/09544119JEIM599