

Diagnosis and Severity Evaluation of Ulnar Neuropathy at the Elbow by Ultrasonography: A Case-control Study

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Abstract

Background: Traditional diagnostic techniques such as clinical examination and electrodiagnosis are less sensitive in diagnosing ulnar neuropathy at the elbow (UNE). Ultrasonography (USG) is increasingly being used to diagnose UNE. However, clinical applicability is limited by the lack of uniformity in the previous studies. Therefore, we aimed to study in the Indian patients the diagnostic utility of the ulnar nerve cross-sectional area (CSA) and a novel parameter-entrapment index (EI) in UNE measured by USG and to find if both these parameters correlate with the electrodiagnostic severity. **Methods:** This retrospective casecontrol study included 28 patients (36 nerves) of UNE and 12 (24 nerves) age- and gender-matched healthy controls. Electrodiagnostic severity was graded using the Padua classification. USG was performed in both groups, and CSA was measured at the medial epicondyle (ME) and 5 cm proximally and distally. EI was calculated by multiplying the ratio of CSA above ME over CSA at ME by 100. Best cutoffs were derived by the receiver operating characteristic curve analysis. **Results:** UNE group had significantly higher CSA at all three locations and lower EI than the control group. CSA at ME ≥ 9.7 mm² and EI ≤ 61.5 has sensitivity and specificity of 88.9%/87.5% and 72.2%/79.2%, respectively. There was no significant difference in CSA and EI between nonsevere and severe UNE groups. **Conclusion:** CSA at ME and EI have good sensitivity and specificity in diagnosing UNE. However, they cannot differentiate nonsevere from severe UNE.

Keywords: Electrophysiology, entrapment index, nerve cross-sectional area, ulnar neuropathy, ultrasonography

INTRODUCTION

Ulnar neuropathy at the elbow (UNE) is the second most common entrapment neuropathy encountered in the clinical practice and electrodiagnostic laboratories.^[1] It is caused by entrapment of the ulnar nerve in the course across the elbow. The clinical features include intermittent pain and paresthesias of the ring and little fingers at an early stage to persistent sensory symptoms and weakness of the ulnar nerve innervated intrinsic muscles of the hand.^[2] Electrodiagnostic evaluation is essential to diagnose UNE and differentiates it from C8 radiculopathy, lower cord brachial plexopathy, and ulnar neuropathy at the axilla and wrist.^[3] The most vital part of the electrodiagnostic evaluation is demonstrating conduction velocity slowing and conduction block across the elbow segment. It is a technically demanding part of electrodiagnostic study even to expert technologists, and the reasons are many. Curvilinear distance measurements across

the elbow, increased temperature sensitivity of the nerve above the elbow, and mismatch between nerve distance and skin distance in subjects with high body mass index are the primary source of error.^[4] Hence, the low sensitivity and specificity of electrodiagnostic studies are in UNE.^[5] Moreover, they are painful, nonlocalizing, and do not provide any anatomical detail of the ulnar nerve and surrounding structures.^[6]

Ultrasonography (USG) is a novel imaging technique that is increasingly being used to evaluate neuromuscular disorders.^[7] It can visualize nerves and their relation to the surrounding structures throughout the nerve with precision and provides dynamic details.^[8] It is easy to do, painless, and convenient and can be repeated multiple times.^[9] The role of the USG

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in the diagnosis of UNE was explored in many studies.^[10] Among the various sonographic parameters, enlarged ulnar nerve cross-sectional area (CSA) and abnormal swelling ratios were consistently associated with UNE in various studies.^[11,12] However, the best cutoff values varied widely in the studies. Nerve CSA could vary with age, gender, weight, body mass index, and coexistent polyneuropathy.^[13] The swelling ratio of CSA at ME and a point at proximal or distal to the elbow can overcome this limitation, and therefore, have broader clinical applicability. Entrapment index (EI) is a rational number obtained multiplying the swelling ratio of nerve CSA at ME and proximal to it by 100. Very few studies compared the sonographic parameters and electrophysiological severity of UNE.^[14-17] Most of these either compared only one electrophysiological parameter or had a small sample size. Moreover, there is a scant literature on this topic in the Indian population. Therefore, in this case-control study, we aimed (1) to study the utility of the nerve CSA and EI as measured by USG in patients with UNE and (2) to find if these sonographic parameters correlate with the electrophysiological severity of UNE.

MATERIALS AND METHODS

Study design

This study is a retrospective analysis of all consecutive patients with UNE who presented to the neurology outpatient department between May 2015 and July 2019. It was carried out at CARE Hospital, Banjara Hills, Hyderabad, Telangana state, India. Data from healthy controls were collected prospectively. The study was conducted following the declaration of Helsinki Ethical principles and Good Clinical Practices. It was approved by the Institutional Ethics committee (Ref. No-IEC/CARE/20458/2020/IIS). The written informed consent was obtained from all the healthy participants. The Ethics committee approved consent waivers for cases.

Subjects

During the study period, 28 patients with UNE and 8 with bilateral disease were enrolled. In total, data from 36 ulnar nerves comprised the patient group. The diagnosis of UNE was based on the clinical examination and electrodiagnostic findings. Clinical diagnosis was based on paresthesias in the ring and little finger with or without weakness of ulnar innervated intrinsic muscles of the hand. Patients with polyneuropathies, lower trunk and medial cord brachial plexopathies, ulnar neuropathy at the level of axilla and wrist, C8 radiculopathy, UNE with a known cause, and those with a history of surgery or elbow trauma were excluded. Twelve healthy participants comprised the control group. Electrodiagnostic studies were not done in the control group due to ethical reasons.

Clinical and electrophysiological evaluation

All patients were examined clinically by the second author for UNE. Nerve conduction studies were performed in all subjects by a senior qualified neuro-technologist (E. S. S.

Kiran) on the electrodiagnostic machine (Nicolet Synergy, Natus Medical Inc., USA). The electrodiagnostic evaluation was done per the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) guideline.^[5] The ulnar nerve motor conduction study was performed by stimulating the nerve at the wrist, below, and above the elbow, and recording the compound muscle action potential (CMAP) from abductor digiti minimi (ADM). The distance between the below the elbow and above elbow stimulation sites was in the range of 10 cm. The Short segment inching study was done at 2 cm intervals across the elbow. An orthodromic technique of ulnar sensory conduction study was performed by stimulating the digital nerve at the little finger and recording response from the ulnar nerve at the wrist. The electrophysiological severity of UNE was graded as per the Padua classification.^[18] Patients with a normal sensory nerve action potential (SNAP) and slowed motor nerve conduction velocity (MNCV) across the elbow were classified as mild UNE, those with decreased SNAP and slowed MNCV as moderate UNE, those with absent SNAP and slowed MNCV as severe UNE and absent ADM CMAP and SNAP as very severe UNE. The former two categories were designated as nonsevere and the latter two as severe categories for the analysis.

Ultrasonography

USG was performed by the first author on Philips HD15 machine (Massachusetts, USA) using a 3–12 MHz linear array transducer. USG study was performed on the same day as the electrodiagnostic evaluation in all patients. Participants were placed supine with abducted, externally rotated arm and flexed elbow (the angle between the arm and forearm was 70°). The ulnar nerve was examined from the axilla down to Guyon's canal at the wrist. CSA (mm²) was measured circumferentially by the freehand delimitation technique at the inner hyperechoic rim of the nerve with the transducer placed firmly over the skin and perpendicular to the nerve to avoid the measurement errors. CSA measurements were done at three locations: (1) 5 cm proximal to the medial epicondyle (ME), (2) at the ME, and (3) 5 cm below the ME. EI was calculated by multiplying the ratio of CSA above ME over CSA at ME by 100.

Statistical analysis

Statistical analysis was performed using the SPSS software version 21.0. (Armonk, NY, USA: IBM Corp.) Discrete variables were represented as percentages, and continuous variables were represented as mean and standard deviation (SD). Unpaired Student's *t*-test was done to test the significance between the groups for the continuous data. The Chi-square test and Fisher's exact test were done to test the significance between the groups for the qualitative variables. Receiver operating characteristic curve (ROC) analysis was done to identify the best cutoffs for CSA at all three levels, and EI based on the Youden index and the area under the curve (AUC) was calculated. A test result was considered significant if the $P \leq 0.05$. Graphical representations were made using the Tableau Desktop 2020.1 version.

RESULTS

Comparison between healthy controls and cases

There were no significant differences in the mean (SD) age in years (49.17 ± 15.84 vs. 53.74 ± 15.06 ; P 0.39) and male gender (10 vs. 24; P 0.84) between the healthy controls and cases. The mean (SD) duration of the disease in the UNE group was 10.89 ± 6 months. The subjective sensory symptoms or objective sensory deficits were present in all UNE group nerves. Motor weakness of ulnar innervated hand muscles accompanied sensory abnormalities in 20 nerves. UNE group had significantly higher mean (SD) CSA at all three levels [Table 1]: Above ME (5.48 ± 1.15 vs. 6.66 ± 1.67 ; P 0.004), at ME (8.07 ± 2.16 vs. 13.23 ± 4.42 ; P 0.001) and below ME (5.28 ± 0.87 vs. 6.56 ± 1.41 ; P 0.001). The mean (SD) EI was significantly lower in the UNE than controls (70.53 ± 16.47 vs. 53.04 ± 14.6 ; P 0.001). The ROC analysis showed that the CSA at ME ≥ 9.7 mm² has a sensitivity of 88.9% and specificity of 87.5% in differentiating UNE from controls. CSA below ME ≥ 6.15 mm² has a sensitivity of 66.7% and specificity of 87.5%, while CSA above ME yielded sensitivity and specificity of 63.9% and 75% to diagnose UNE, respectively [Figure 1a and Table 2]. EI ≤ 61.5 has a sensitivity of 72.2% and specificity of 79.2% to diagnose UNE [Figure 1b and Table 2]. Sonographic data of all healthy controls and UNE cases are represented are the bubble diagram [Figure 2].

Comparison between nonsevere and severe groups

UNE was categorized as nonsevere in 17 and severe in 19 hands. Out of the eight patients with bilateral UNE, four patients (8 nerves) had the nonsevere disease, three patients (6 nerves)

had severe disease, and one patient had nonsevere disease on the right side and severe on the left side. There was no significant difference in the mean (SD) CSA of the ulnar nerve at all three locations [Table 3]: Above ME (6.70 ± 1.57 vs. 6.60 ± 1.82 ; P 0.86), at ME (12.81 ± 5.13 vs. 13.69 ± 3.58 ; P 0.56) and below ME (6.66 ± 1.45 vs. 6.46 ± 1.42 ; P 0.68).

Table 1: Comparison of ultrasonography parameters between controls and ulnar neuropathy at the elbow

Parameter	Mean \pm SD		P
	Control (24)	UNE (36)	
CSA above ME	5.48 \pm 1.15	6.66 \pm 1.67	0.004
CSA at ME	8.07 \pm 2.16	13.23 \pm 4.42	0.001
CSA below ME	5.28 \pm 0.87	6.56 \pm 1.41	0.001
EI	70.53 \pm 16.47	53.04 \pm 14.6	0.001

CSA: Cross-sectional area in mm², ME: Medial epicondyle, EI: Entrapment index, UNE: Ulnar neuropathy at the elbow, SD: Standard deviation

Table 2: Receiver operating characteristic curve analysis cutoffs of ultrasonography parameters to differentiate controls and ulnar neuropathy at the elbow

Parameter	Cutoff value	Sensitivity (%)	Specificity (%)
CSA above ME	≥ 5.95	63.9	75
CSA at ME	≥ 9.7	88.9	87.5
CSA below ME	≥ 6.15	66.7	87.5
EI	≤ 61.5	72.2	79.2

CSA: Cross-sectional area in mm², ME: Medial epicondyle, EI: Entrapment index

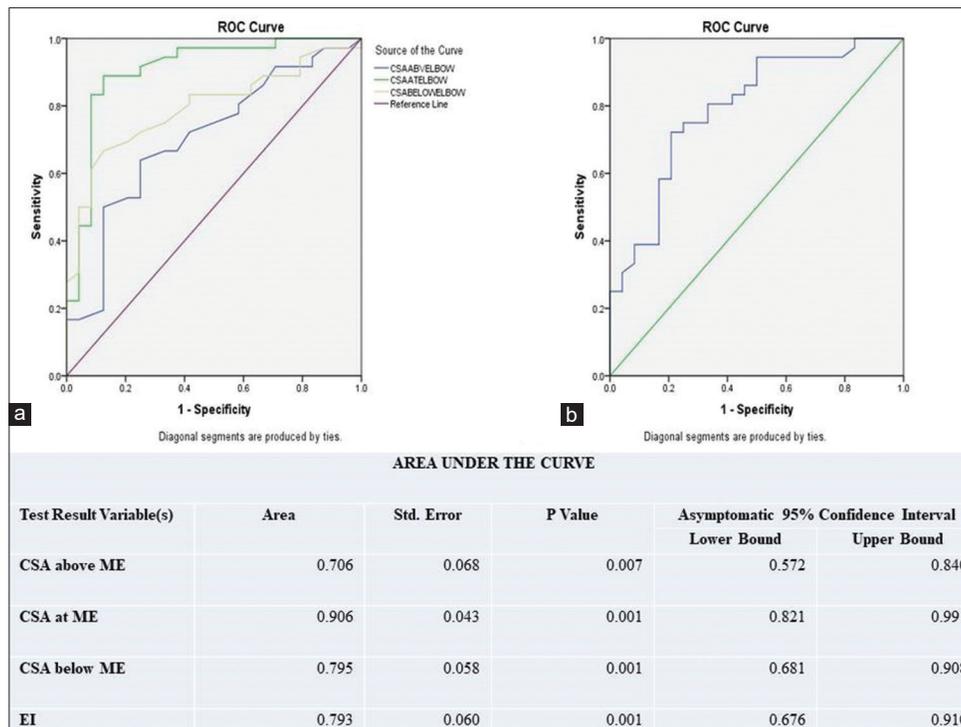


Figure 1: (a and b) Receiver operating characteristic curve analysis of cross-sectional area at three levels and entrapment index

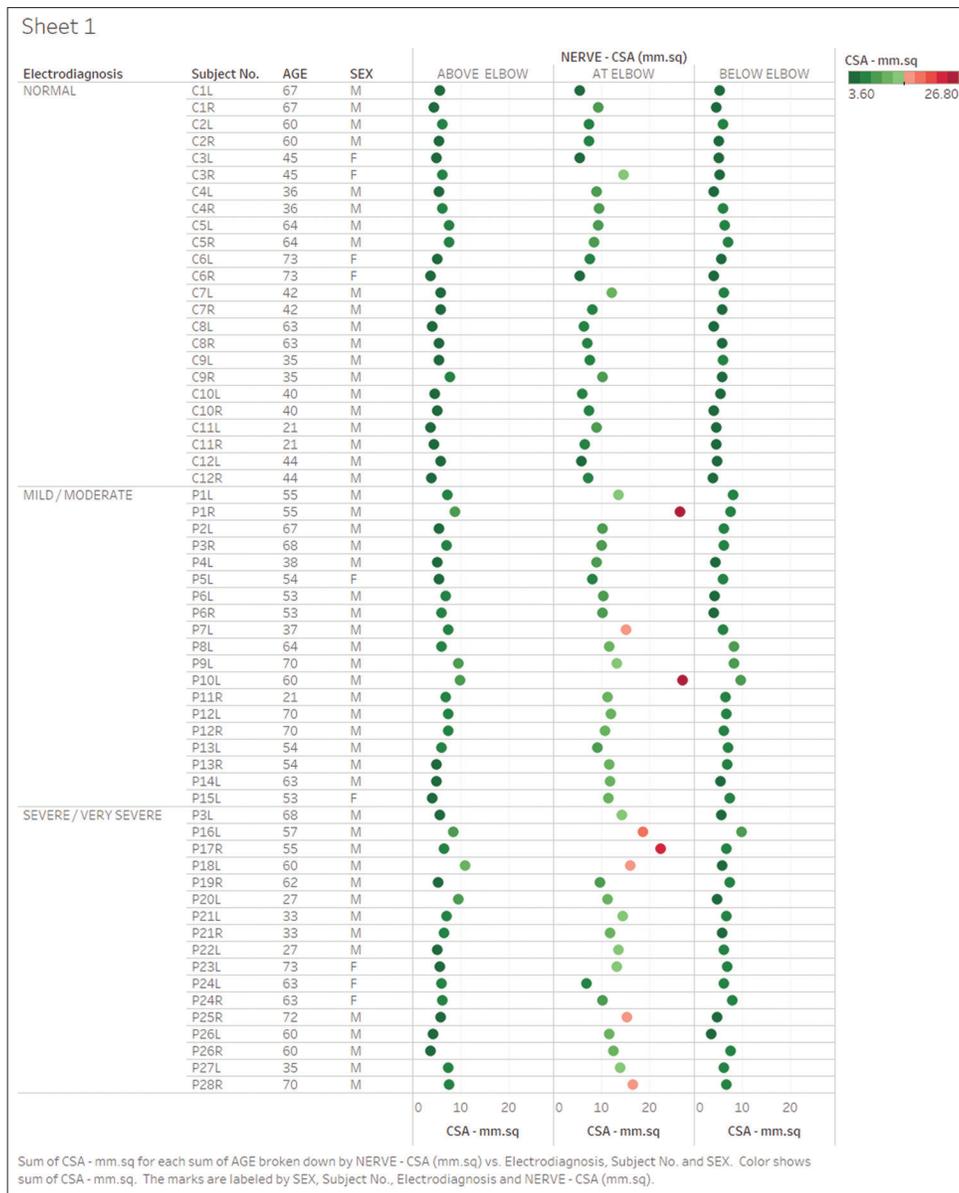


Figure 2: Bubble diagram representing the ultrasonography data of whole cohort

Table 3: Comparison of ultrasonography parameters between nonsevere and severe ulnar neuropathy at the elbow

Parameter	Mean±SD		P
	Nonsevere UNE (19)	Severe UNE (17)	
CSA above ME	6.70±1.57	6.60±1.82	0.86
CSA at ME	12.81±5.13	13.69±3.58	0.56
CSA below ME	6.66±1.45	6.46±1.42	0.68
EI	55.24±12.32	50.58±16.83	0.34

CSA: Cross-sectional area in mm², ME: Medial epicondyle, EI: Entrapment index, UNE: Ulnar neuropathy at the elbow, SD: Standard deviation

The mean (SD) EI was also not significantly different between the two severity groups (55.24 ± 12.32 vs. 50.58 ± 16.83; P 0.34). ROC analysis to derive the best cutoffs did not show

good predictive value for all four parameters. USG images of a moderate (P9 L) and a severe case (P17R) of UNE are shown in Figures 3 and 4.

DISCUSSION

Our study has four main findings: (1) CSA of the ulnar nerve at all three predefined locations was significantly higher in the UNE group than in healthy controls, (2) CSA at the ME ≥9.7 mm² had the best accuracy in diagnosing UNE, whereas CSA values of the nerve above and below the ME did not achieve similar accuracy, (3) EI is lower in patients with UNE, and a value ≤61.5 had the best accuracy in differentiating UNE patient from healthy control and (4) there was no significant difference in CSA and EI between the nonsevere and severe UNE groups.

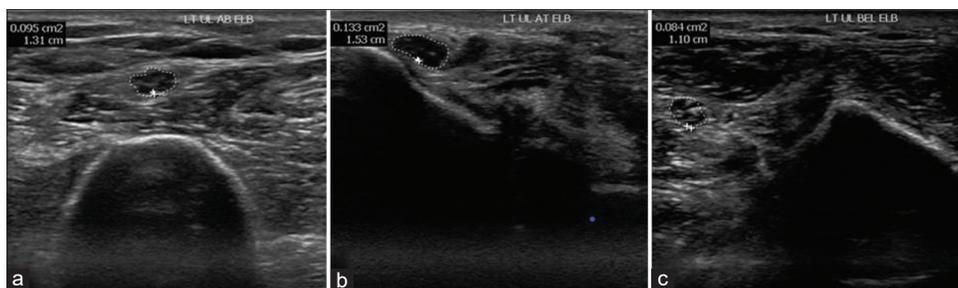


Figure 3: (a-c) Sonographic images showing cross-sectional area above, at and below the medial epicondyle in a patient of moderate ulnar neuropathy at the elbow



Figure 4: (a-c) Sonographic images showing cross-sectional area above, at and below the medial epicondyle in a patient of severe ulnar neuropathy at the elbow

Compression sites and pathological changes in ulnar neuropathy at the elbow

The ulnar nerve is prone to entrapment at one of the following four locations within 10 cm around the elbow (1) between the medial intermuscular septum and medial head of triceps called as arcade of struthers, (2) behind the ME in the ulnar groove, (3) at the dense aponeurosis between tendinous origins of humeral and ulnar heads of Flexor carpi ulnaris (FCU) called humeroulnar arcade, and (4) at the point where the nerve exits FCU.^[19] Higher CSA at all the three predefined locations in the present study is attributable to wide-ranging entrapment sites. Nerve entrapment leads to pathological changes such as endoneurial oedema, demyelination and remyelination, inflammation, distal axonal degeneration and regeneration, and thickening of the perineurium and endothelium.^[20] These pathological changes are likely to be responsible for the increased CSA on USG in our study.

Nerve cross-sectional area

Ulnar nerve CSA and diameter were the most consistently abnormal sonographic parameters in UNE across various previous studies.^[21] We chose nerve CSA in our study as the nerve diameter may vary depending on the shape of the nerve at various locations.^[22] Most previous studies used either maximal CSA (CSA_{max}) of the nerve around the elbow or CSA at the ME in discriminating patients with UNE from healthy controls. We opted for the latter in our study as it is an easily identifiable landmark. Moreover, CSA_{max} lies within 0.5 cm of the ME in more than 85% of UNE patients.^[23] We chose to do all USG studies with the elbow flexed to 70° as this happens to be also the position

recommended by AANEM for performing electrodiagnostic studies across the elbow.^[5]

Chiou *et al.* were the first to show a higher CSA at ME in UNE than controls ($13.9 \pm 6 \text{ mm}^2$ vs. $6.8 \pm 1.9 \text{ mm}^2$), and they also concluded that a CSA at ME larger than 7.5 mm^2 is suggestive of UNE. However, the study was underpowered due to the small sample size.^[24] Later, Wiesler *et al.* showed a significantly higher CSA_{max} in UNE than healthy controls ($19 \pm 8 \text{ mm}^2$ vs. $6.5 \pm 1 \text{ mm}^2$), and they proposed a cutoff value of more than 10 mm^2 can identify UNE with a sensitivity and specificity of 93% and 98%, respectively. However, the small sample size in each group, unmatched patient and control groups for age and gender, and multiple sonographers involved limited the interpretation of the results.^[25] Another study by Mondelli *et al.* showed higher CSA at the ME ($9.6 \pm 8.5 \text{ mm}^2$ vs. $5.7 \pm 2.3 \text{ mm}^2$) and 2 cm above the ME ($9.3 \pm 5.6 \text{ mm}^2$ vs. $5.7 \pm 2.3 \text{ mm}^2$) in UNE compared to controls. They measured nerve CSA with the elbow in full extension. However, CSA at the ME showed very low sensitivity of 24.5% due to the inclusion of milder cases and the exclusion of cases with only sensory abnormalities.^[15] A similar study by Yoon *et al.* showed higher CSA at the ME in UNE ($18.5 \pm 7.3 \text{ mm}^2$ vs. $6.6 \pm 1.1 \text{ mm}^2$), and the sensitivity and specificity were 100% and 93.3%, respectively. Sonography was done at 90° elbow flexion.^[23] Bayrak *et al.* showed a sensitivity and specificity of 83% and 81%, respectively, and AUC of 0.89 for CSA cutoff of $\geq 10 \text{ mm}^2$ at ME. The CSA_{max} $\geq 11 \text{ mm}^2$ showed sensitivity and specificity of 95% and 71%, respectively.^[22] Volpe *et al.* showed significantly increased CSA at all three levels of measurement at the ME and proximal and distal to ME. They also noted that CSA_{max} $\geq 10 \text{ mm}^2$ showed both sensitivity and

specificity of 88%.^[26] Our results were similar to those done by Bayrak *et al.* and Volpe *et al.* A meta-analysis showed that a CSA at ME ≥ 10 mm² showed a sensitivity of 85%, specificity of 91%, and odds ratio of 53.96 in diagnosing UNE.^[11]

Swelling ratio and entrapment index

The swelling ratios are unaffected by the factors as described earlier, and therefore, can be more helpful.^[13] We calculated EI, similar to the swelling ratio using CSA measurements of ulnar nerve CSA at ME and proximal site. Proximal CSA was chosen because distal CSA measurement can be difficult in occasional cases of hyperechoic FCU due to denervation. We multiplied the ratio by 100 to derive a rational number that is easy to remember.

Yoon *et al.* reported a proximal swelling ratio (CSA at ME/proximal CSA) of 2.8:1 in the UNE group and 1.1:1 in the control group. However, it did not improve the accuracy when compared with CSA at ME alone.^[23] Gruber *et al.* found a highly significant difference in the proximal swelling ratio (CSA at ME/CSA at mid-arm) between patients with UNE and controls (1.7 vs. 1.13). However, the swelling ratio as a singular parameter was not helpful in milder cases. They proposed that combination of fascicular effacement and a swelling ratio >1.4 could improve the accuracy of diagnosis in milder UNE.^[27] Kim *et al.* showed significant differences in CSA_{max}, CSA_{max}/CSA at Guyon's (CSA_{max}/G), CSA_{max}/CSA at mid-forearm (CSA_{max}/F) between the control and patient groups. The cutoff value for diagnosing UNE was 8.95 mm² for the CSA_{max} (sensitivity 93.8% and specificity 88.3%), 1.99 for the CSA_{max}/G (sensitivity 75.0% and specificity 73.3%), and 1.48 for the CSA_{max}/F (sensitivity 93.8% and specificity 95.0%).^[28] A meta-analysis by Chen *et al.* showed a sensitivity and specificity of 67% and 81%, respectively, for proximal swelling ratio and 62% and 86% for distal swelling ratio in diagnosing UNE.^[12] Our results show that the specificity of EI was not superior to CSA at ME.

Correlation between sonographic parameters and electrodiagnostic severity

The published correlation studies attempted to correlate sonographic parameters with either a single electrophysiological parameter or the composite electrodiagnostic severity grade. Beekman *et al.* found thicker ulnar nerve in UNE with axonal pathology compared to demyelinating pathology. The axonal group was further analyzed in a separate study, which showed a negative correlation between nerve thickness and CMAP amplitude.^[29] Simon *et al.* found that both increased CSA_{max} and loss of fascicular architecture correlated with MNCV.^[14] Mondelli *et al.* and Bayrak *et al.* used a composite electrophysiological severity scale score and showed a positive correlation with nerve CSA.^[15,22] Volpe *et al.* have proposed found three cutoff points that may define the severity of UNE: mild ≥ 10 mm², moderate ≥ 15 mm², and severe ≥ 20 mm².^[26] We did not use these scoring systems as they did not account for the CMAP amplitude. However, we could not find this correlation in our study, and the reasons are two-fold. First, the number of

nerves in severe and nonsevere groups was small. Second, in the nonsevere group, only two nerves had the milder disease, and the rest showed moderate severity.

Limitations and future directions

Our study has few limitations: (1) our study is a retrospective analysis of USG and electrodiagnostic data of patients with UNE. Clinical data were obtained mainly from the medical record forms, especially data on anthropometric measures, modalities of sensory deficits, grade of motor weakness, and clinical severity was lacking. (2) We had very few milder cases in the nonsevere group. This could have underpowered the analysis to differentiate nonsevere and severe groups by USG, (3) only two sonographic parameters were studied. Other sonographic findings like nerve mobility and cubital tunnel measurements in flexion and extension, independent pathogenic attributes to UNE, were not studied, and (4) unblinded assessment of the nerve on USG could have led to some bias. Multicentric, prospective, and blinded studies involving a large number of patients, many sonographic variables, and assessment in various degrees of elbow flexion can give additional insight and define the role of USG in evaluating UNE more decisively.

CONCLUSIONS

In conclusion, USG can be used as an alternative method to diagnose UNE. Ulnar nerve CSA at elbow ≥ 9.7 mm² and EI ≤ 61.5 has good sensitivity and specificity to diagnose UNE. However, USG cannot differentiate nonsevere from severe patients of UNE.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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