ORIGINAL RESEARCH

Diagnostic value of ultrasonography versus electrodiagnosis in ulnar neuropathy

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Purpose: Ulnar neuropathy at elbow is the second-most common compression neuropathy. The main aim of this study was to assess the diagnostic value of ultrasonography (US) as an alternative method to electrodiagnosis (EDX), which had traditionally been used as the method of choice.
Methods: This diagnostic study was conducted on 66 participants (32 patients` elbows and 34 normal elbows) referred for EDX. Both groups were reassessed by US to evaluate the consistency of the two tests. The quantitative parameters of US, such as cross-sectional area (CSA) of the ulnar nerve at three different levels around the medial epicondyle (ME) were compared between groups.
Results: Our findings demonstrated that CSA at the ME and 2 cm distal to the ME were significantly larger in the patient group than normal participants. This higher nerve size was more prominent among those who had predominant axonal loss rather than demyelinating lesions ($P<0.01$). Finally, we evaluated US diagnostic value with the best singular feature (2 cm distal to ME) at a cutoff of 9 mm^2, which revealed specificity of 80% and sensitivity 84%.
Conclusion: Based on these results we can conclude that US is a sensitive and specific method in diagnosing ulnar neuropathy at the elbow and can be used as an acceptable complementary method, in particular when EDX is not available.
Keywords: Cubital Tunnel Syndrome, elbow, diagnostic tests, nerve compression syndromes, electromyography

Introduction

Ulnar nerve entrapment at the elbow is the second-most common compression neuropathy, preceded only by carpal tunnel syndrome.[1,3] The annual incidence of ulnar neuropathy at the elbow is 24.7 per 100,000, and incidence in men is nearly double that of women (32.7 vs 17.2 per 100,000).[4,5] Ulnar nerve entrapment can be characterized by such symptoms as paresthesia in the fourth and fifth fingers, weakness of hand grip, and atrophy of intrinsic muscles in advanced stages. These abnormalities can lead to functional impairment, especially in fine-motor tasks.[6] Diagnosis is often based on clinical history and physical examination, and is usually confirmed by electrodiagnosis (EDX). EDX has a sensitivity of about 37%–86% and specificity of 95%.[7] EDX and nerve-conduction study (NCS) can determine the site of entrapment, severity, and type of injury (axonal or demyelinating), as well as disease prognosis. In addition, it should be performed sometimes to rule out other causes of intrinsic muscle atrophy, such as radiculopathy or thoracic outlet syndrome. However, since EDX is a less available, expensive and somewhat painful procedure, ultrasonography (US) as an alternative or adjunct to EDX might be helpful in confirmation of entrapment, as well as in diagnosis

of anomalous innervation.[8] Moreover, US through real-time high-resolution imaging can evaluate cubital zone anatomy and ulnar nerve condition in different positions.[2]

In recent years, the development achieved in high-resolution US has encouraged researchers to investigate its efficacy in diagnosing different musculoskeletal conditions, guiding therapeutic injections, and diagnosing of compression neuropathies.[9–11] There are a lot of studies that have focused on evaluating the median nerve in carpal tunnel syndrome.[12–14] Several have tried to evaluate US for diagnosing ulnar neuropathy and to assess the consistency of US and EDX findings.[3,15,16] Some of these have demonstrated remarkable consistency between the two methods.[3,15,17] Furthermore, in several investigations, a significant relationship has been found between US findings and severity of nerve entrapment based on EDX.[7,18–20] On the other hand, in one study, strong consistency was found in multisite measurement of US values along the entire course of the ulnar nerve.[21]

Despite numerous studies in this field, there is still disagreement concerning the best US location and criteria to better diagnose ulnar neuropathy.[18,20] These controversial results may be due to operator dependency of US, various inclusion criteria in different studies, and heterogeneity in chronicity of symptoms. The aim of this study was to validate further US as an alternative to electromyography (EMG)–nerve conduction study (NCS) in ulnar neuropathy diagnosis, as well as to assess the maximum level of US sensitivity and specificity by measuring at different anatomical locations.

Methods
Study population
This study was conducted in Shohada-e-Tajrish Hospital in Tehran during 2016 among patients who had been referred to the EDX clinic with suspected ulnar neuropathy at the elbow. Exclusion criteria were history of trauma or surgery in the elbow region, cervical radiculopathy, brachial plexopathy, or any underlying systemic diseases with peripheral polyneuropathy, including diabetes mellitus, chronic kidney disease, and hypothyroidism.

The final sample size was calculated as 66 subjects (32 patients and 34 controls). Subjects were identified based on the patient interviews at the EDX clinic, then were assessed for exclusion criteria. Demographic and other important variables — age, sex, body-mass index, hand dominance, and side of complaint — were recorded for patient and control groups. Selected patients were approached and informed about the procedure and study. Informed written consent was obtained from all participants. Our study was in accordance with the Declaration of Helsinki, and was approved by the Medical Ethical Committee of Shahid Beheshti University of Medical Sciences.

Measurement tools
Electrodiagnosis
EDX was performed for both patient and control groups by an experienced physiatrist (SMR) using EMG (Medelec Synergy; Viasys Healthcare, Conshohocken, PA, USA), based on standard techniques.[22] The control group was selected from asymptomatic participants who were patients' companions (relatives). Exclusion criteria for the control group were any relevant signs and symptoms or any abnormality in ulnar nerve EDX or any subject with abnormal EDX. To obtain ulnar nerve compound muscle action potential (CMAP), the patient's position was lying down with the elbow flexed at 135°, shoulder slightly externally rotated in right-angle abduction, and wrist at neutral position. The E_1 electrode was secured to the motor point of abductor digiti minimi. The E_2 electrode was positioned distally to the metacarpophalangeal joint. The ground electrode was placed on the dorsum of the hand. Markers for electrical stimulation were placed at 8 cm proximal to E_1 along the ulnar nerve at the wrist. The second site of stimulation was 4 cm distal to the medial epicondyle (ME). The third stimulation point was at least 10 cm proximal to the below-elbow stimulation area along the course of the ulnar nerve. EDX parameters assessed were ulnar antidromic sensory nerve action potential with 14 cm distance from wrist to fifth digit, dorsal ulnar cutaneous sensory nerve action-potential peak latency and amplitude, ulnar orthodromic CMAP with stimulation at 8 cm from wrist to hypothenar muscles, and two other stimulation sites at 4 cm above and 8 cm below the ME, across-elbow nerve-conduction velocity (NCV), and ulnar F-wave. EMG was performed utilizing a concentric needle from the biceps brachii, pronator teres, flexor carpi ulnaris, flexor pollicis longus, abductor digiti minimi, and the first dorsal interosseous muscles.

Although NCS is the diagnostic mainstay, there is no true gold standard for the diagnosis of ulnar neuropathy at the elbow. According to EDX findings, we would be able to confirm diagnosis in suspected patients and determine the type of lesion (axonal or demyelinating lesion and conduction block). If there was no more proximal consistent lesion, such as plexopathy or radiculopathy, then a diagnosis of ulnar neuropathy at the elbow would be confirmed based on the criteria in Table 1. Since there were no unique criteria to classify the severity of ulnar neuropathy, patients were

divided into four groups for statistical analysis, based on a local classification system: very mild, mild, moderate, and severe (Table 2).

Ultrasonography

After completion of EDX, all participants were evaluated using US performed in a supine position with the elbow at 90° flexion, wrist in neutral position, and shoulder at 90° abduction and slight external rotation. US was performed by another physiatrist (SAR) experienced in the musculoskeletal US field, using a 5–12 MHz linear array transducer (Philips HD6). Markers were placed at the ME and 2 cm proximal and 2 cm distal to it (Figure 1). In this study, the US operator was blinded regarding the subjects (patients or control group) or severity of participants. To detect the nerve, the US probe was placed behind the epicondyle perpendicularly to the ulnar nerve without any pressure to see the honeycomb appearance of the nerve cross section behind the ME. The ulnar nerve's cross-sectional area (CSA) was measured directly by placing electronic calipers around the margin of the nerve just inside the hyperechoic line (nerve sheath). The CSA of the ulnar nerve was evaluated at three levels: behind the ME (Figure 2A), at 2 cm above it (Figure 2B), and at 2 cm below it (Figure 2C), designated CSA_{med}, CSA_{prox}, and CSA_{dist}, respectively. Each size measurement was repeated three times, the mean value of them was documented as final data of CSA at three levels, and ratios of $CSA_{med:prox}$, $CSA_{med:dist}$, and $CSA_{prox:dist}$ recorded for data analysis.

Data analyses

Demographic and clinical data were imported to SPSS version 22 for both patient and control groups. Normal distribution of data was evaluated using the Shapiro–Wilk method. Finally, statistical analyses were done using t-tests and χ^2 for quantitative and qualitative variables, respectively. Independent-sample t-tests were used for comparing means between two groups. Afterward, we compared CSA means in categorical variables like duration of symptoms using ANOVA. $P<0.05$ was considered statistically significant. To evaluate US diagnostic value accuracy, sensitivity, and specificity and to find out the best cutoff points, the area under the receiver-operating characteristic (AUROC) curve was used.

Results

In the current study, we evaluated 66 elbows of 32 patients with ulnar neuropathy and 34 normal elbows as control group.

Table 1 Electrodiagnostic findings of patients

EDX findings	Criteria	Frequency (%)
Demyelination	Across-elbow NCV <49 m/second or difference between across-elbow NCV and forearm NCV >10 m/second	6 (18.8)
Conduction block	> 20% decrement in across-elbow CMAP amplitude	2 (6.3)
Axonal loss	Absence of ulnar SNAPs (fifth finger/DUC) or low-amplitude SNAP/CMAP or presence of denervation potentials (positive sharp wave and fibrillation) or chronic neurogenic motor-unit action potentials on EMG in ulnar innervated muscles	15 (46.7)
Demyelination + conduction block	Criteria of both categories	2 (6.3)
All above criteria	Criteria of all categories	7 (21.9)
Total		32 (100)

Abbreviations: CMAP, compound muscle action potential; DUC, dorsal ulnar cutaneous; EDX, electrodiagnosis; EMG, electromyography. NCV, nerve-conduction velocity; SNAPs, sensory nerve action potentials.

Table 2 Severity-grading classification of ulnar neuropathy based on electrodiagnostic findings

Severity	Criteria	Frequency (%)
Very mild	Only conduction block at elbow	3 (9.0)
Mild	Conduction block + demyelination	4 (12.2)
Moderate	Low amplitude in ulnar SNAPs + demyelination	1 (3.0)
Severe	Low-amplitude ulnar CMAP or absence of ulnar SNAPs (fifth finger/DUC) or presence of denervation potentials (PSW, fibrillation) or chronic neurogenic MUAPs in EMG in ulnar innervated muscles	24 (75.8)

Abbreviations: CMAP, compound muscle action potential; DUC, dorsal ulnar cutaneous; EMG, electromyography; MUAPs, motor-unit action potentials; PSW, positive sharp wave; SNAPs, sensory nerve action potentials.

Figure 1 Position of elbow in ultrasonography (from left to right) at level of medial epicondyle, 2 cm above it, and 2 cm below it, respectively.

In the patient group, the female:male ratio was 65:35 and in the control group 58:42. Neither this ratio nor other demographic data showed significant differences between the two groups (Table 3). EDX findings are summarized in Table 1.

Measurement of nerve CSA at three different levels was performed using US and the mean value for each level is shown in Table 4. There were significant differences between the patient and control groups in ulnar nerve CSA at two levels: CSA_{med} and CSA_{dist} ($P<0.001$ and <0.05, respectively). CSA-ratio measurements between different levels are presented in Table 4. Mean $CSA_{med:prox}$ and $CSA_{med:dist}$ were significantly different between the patient and control groups ($P<0.001$).

We also evaluated correlations between severity of neuropathy and CSA at three levels: CSA_{med} was significantly higher in those with more severe grades ($P=0.006$). Additionally, it should be noted that CSA_{med} in patients who had axonal lesions (denervation on EMG or low-amplitude CMAP) was significantly higher than in those without these findings. We then assessed the relationship between duration of symptoms and CSA. Chronic lesions had larger values on CSA_{med} measurements using US ($P=0.0001$). Eventually, on the ROC curve, optimum specificity and sensitivity in ulnar neuropathy diagnosis were determined for each sonographic feature as different parameters and ratios. AUROC for CSA_{med} (0.871) was almost equal to that of the best ratio, ie, $CSA_{med:dist}$ ratio (AUROC 0.872; Table

4). Therefore, we could state that these ratios did not add any further benefit to CSA_{med} regarding their diagnostic value based on the ROC curve. As the final evaluation, CSA_{med} provided specificity and sensitivity of 80% and 84%, respectively (at cutoff of $CSA_{med}=9$ mm^2); whereas these amounts were 80% and 87% for the more difficult $CSA_{med:dist}$ ratio, respectively.

Discussion

As mentioned, ulnar neuropathy is the second-most common compression neuropathy and occurs often due to compression of the ulnar nerve at the elbow.[1,2] Several studies have investigated various criteria, including nerve CSA in several regions, longitudinal and axial diameter of nerve, and echogenicity changes, to confirm ulnar neuropathy diagnosis using US.[3,16,17,23–25] In a large study, the authors stated that US accuracy was lower than NCS. In fact, they considered two categories of ulnar neuropathy patients: those with conduction block and demyelination pattern vs axonal degeneration. According to their findings, US proved to be particularly helpful in subjects of ulnar axonal degeneration, while NCS was rather useful in diagnosis of nerve demyelination or conduction block.[20] This issue might happen due to larger CSA of axonal degenerated nerves, rather that demyelinating ones, as our results proved, too.

In the present study, ulnar nerve CSA was measured at three levels: behind the ME and 2 cm proximal and 2 cm
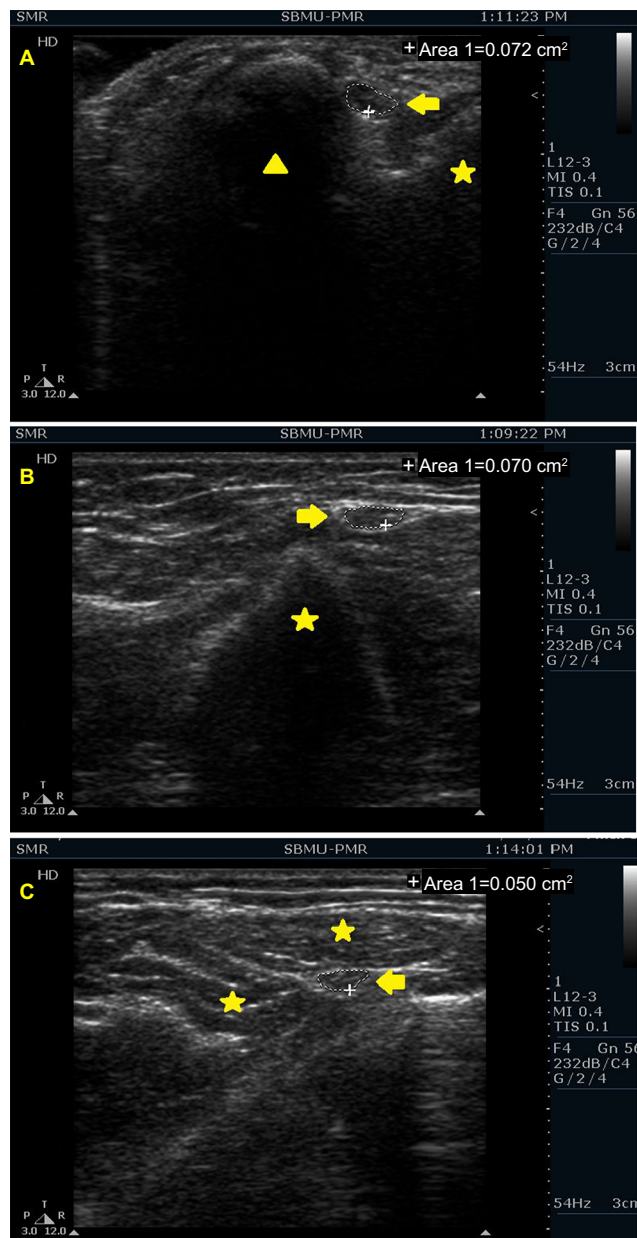
Figure 2 Ulnar nerve cross-section area on ultrasonography.
Note: (**A**) At level of medial epicondyle (arrow, ulnar nerve; arrowhead, medial epicondyle; star, olecranon); (**B**) 2 cm above medial epicondyle (arrow, ulnar nerve; star, medial epicondyle); (**C**) 2 cm below medial epicondyle (arrow, ulnar nerve; stars, two heads of flexor carpi ulnaris muscle).

distal to it. The maximum nerve CSA in patients with ulnar neuropathy was observed at the level of the epicondyle (CSA_{med}=12.68±3.96 mm²), which was almost similar to previous studies.[18,26] In addition to nerve CSA, several studies have evaluated different area ratios, eg, the ratio of maximum nerve CSA at the elbow to its size at the Guyon's canal[26] or at the mid-forearm,[18,26] some of which revealed significant differences between case and control groups.

In the current study, nerve $CSA_{med:prox}$ and $CSA_{med:dist}$ ratios were significantly higher in the patient group (P=0.001). Also, in another study, it was demonstrated that the CSA ratio can improve the US diagnostic value, especially in very slim or very obese people, but our findings did not achieve the same result.[26] We evaluated the relationship between types of lesion based on EDX and nerve CSA measurement. In axonal nerve lesions, CSA_{med} was larger, which could be explained by inflammation around nerve tissue. This relationship was statistically significant, especially in the axonal type, but there was no significant change in nerve size for the demyelination type. In some other studies, nerve CSA in axonal lesions was significantly different from demyelinating entrapment.[16,18,24,25]

The association between severity of ulnar neuropathy on EDX and nerve CSA was also evaluated using ANOVA, and revealed a strong consistency between severity and CSA_{med} (P=0.006). In a similar study, significant correlations were found in regard to all three CSAs.[15] Moreover, in one study a significant correlation was found between NCV at the elbow region and nerve CSA.[19] Similarly, we found that CSA_{med} was significantly correlated with NCV in the elbow region (P<0.01). In previous studies, the relationship between nerve CSA and duration of symptoms was not investigated; therefore, we evaluated this relationship. Based on the duration of symptoms, patients were divided into three groups (<6 weeks, 6–12 weeks, and >12 weeks). Eventually a significant relationship was observed between chronicity and CSA_{med} (P=0.001).

Table 3 Demographic characteristics of control and patient groups

Variables	Patient group (n=32)	Control group (n=34)	*P*-value
Mean age (95% CI), years	45.5 (35.16–55.96)	44.5 (34.13–54.93)	0.673
Sex (M:F)	20 (65%):12 (35%)	18 (58%):14(42%)	0.619
BMI (95% CI), kg/m²	25.5 (22.1–28.9)	26.5 (23.1–29.9)	0.204
Hand dominance (R:L)	28 (87%): 4 (13%)	28 (88%): 4 (12%)	0.610
Side of complaint (R:L)	18 (56.3%):14 (43.7%)	—	—
Chronicity <6 weeks	8 (25%)	NA	NA
6–12 weeks	11 (35%)		
>12 weeks	13 (40%)		

Abbreviations: BMI, body-mass index; F, female; L, left; M, male; NA, not applicable; R, right.

Table 4 Distribution of ulnar nerve sonographic parameters between control and patient groups

Parameters	Patients, mean ± SD	Controls, mean ± SD	P-value	AUROC curve	Cutoff	Sen	Spe
CSA$_{prox}$ (mm^2)	7.47±1.43	7.52±1.55	0.913	0.492	NS	—	—
CSA$_{dist}$ (mm^2)	8.37±1.89	7.57±1.34	0.81	0.625	NS	—	—
CSA$_{med}$ (mm^2)	12.68±3.96	8.27±1.74	<0.001	0.871	9 mm^2	84.4%	80.6%
CSA$_{med:prox}$	1.7±0.86	1.1±0.17	<0.001	0.870	1.312	75.0%	85.3%
CSA$_{med:dist}$	1.5±0.37	1.1±0.19	<0.001	0.872	1.185	87.5%	80.6%
CSA$_{prox:dist}$	0.9±0.21	1±0.19	0.094	0.380	NS	—	—

Abbreviations: AUROC, area under receiver-operating characteristic; CSA, cross-sectional area; dist, distal to medial epicondyle; med, at the level of medial epicondyle; NS, not significant; prox, proximal to medial epicondyle; Sen, sensitivity; Spe, specificity.
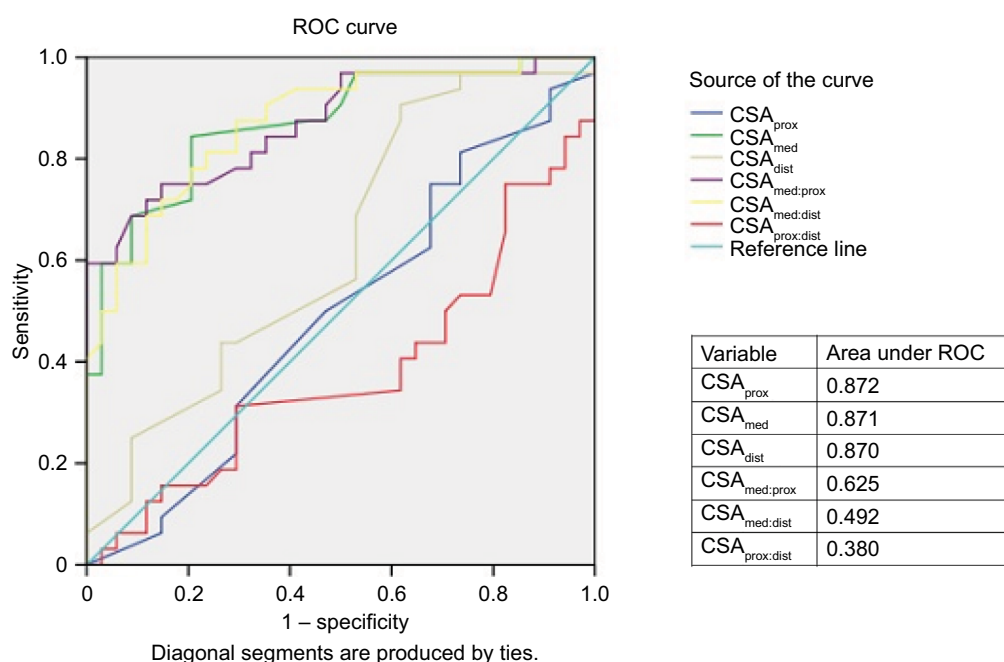
Another study discussed US performance in prediction of surgical decompression outcomes. They measured pre- and postoperative CSA values of the ulnar nerve among 38 severe cases of ulnar neuropathy that were candidates for surgery, and finally concluded that CSA at both the level of the ME (P=0.001) and proximal to the ME (P=0.005) were primarily correlated with motor-fiber NCV.[27] The latter correlation was almost consistent with the present findings. These differences are probably because of different criteria for patient-selection: they included more severe subjects who were candidates for surgery.

As we know, the performance of a new diagnostic tool is quantified by calculation of the AUROC curve (a plot of sensitivity against 1 – specificity on the x- and y-axes). A new diagnostic method is accepted as good by an AUROC >0.8 and strong by an AUROC >0.9.[25] In this study, as shown in Table 4 and Figure 3, we determined an AUROC of 0.871, which means US could be an acceptable measure to diagnose ulnar neuropathy patients. In a prior study,[16] specificity and sensitivity were calculated at about 88% for US as an alternative diagnostic test, with a cutoff of CSA$_{med}$=10 mm^2. In another study,[28] investigators calculated specificity and sensitivity of about 88.3% and 93.8%, respectively, with a cutoff of CSA$_{med}$=8.95 mm^2. Our cutoff point (CSA$_{med}$=9 mm^2) was slightly smaller than and close to threshold points.[16,28] As mentioned earlier, this point in the present research revealed specificity and sensitivity of 80% and 84%, respectively.

Limitations

One of the main limitations of our study was the relatively small sample size. Therefore, it is recommended to design larger studies along with evaluation of inter-observer bias in two or more US operators. According to existing evidence, chronic nerve entrapment may lead to a shrinkage phenomenon in nerve tissue. However, in the current study, which has discussed subacute cases, this phenomenon was not

Variable	Area under ROC
CSA$_{prox}$	0.872
CSA$_{med}$	0.871
CSA$_{dist}$	0.870
CSA$_{med:prox}$	0.625
CSA$_{med:dist}$	0.492
CSA$_{prox:dist}$	0.380

Figure 3 Receiver-operating characteristic (ROC) curve for diagnostic value of ultrasonographic parameters in ulnar neuropathy.
Abbreviations: CSA, cross-sectional area; dist, distal to medial epicondyle; med, at the level of medial epicondyle; prox, proximal to medial epicondyle.

detected. It is also suggested to evaluate other US parameters like nerve subluxation, echogenicity and hypervascularity. Findings from this study were obtained based on primary ulnar neuropathy, and cannot be generalized to secondary ones; therefore, it is recommended to evaluate US diagnostic value in cases of ulnar neuropathy secondary to diabetes, hypothyroidism, and collagen vascular diseases in future. Furthermore, it is necessary to do some comprehensive studies on the cost-effectiveness of US in the diagnosis of ulnar neuropathy.

Conclusion

To summarize, US could be an acceptable method for the diagnosis of ulnar neuropathy, especially by means of measuring nerve CSA at the ME level (CSA_{med}) as the best singular feature. According to the findings, it seems that US is a sensitive (84%) and specific (80%) method, and could be utilized as a complementary but not definite alternative method for EDX.

Acknowledgments

Disclosure

The authors report no conflicts of interest in this work.

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