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Purpose Imaging criteria for diagnosing compressive ulnar neuropathy at the elbow (UNE) have recently been established as the maximum ulnar nerve cross-sectional area (UNCSA) upon magnetic resonance imaging (MRI) and/or ultrasonography (US). However, the levels of maximum UNCSA and diagnostic cutoff values have not yet been established. We therefore analyzed UNCSA by MRI and US in patients with UNE and in controls.

Methods We measured UNCSA at 7 levels in 30 patients with UNE and 28 controls by MRI and at 15 levels in 12 patients with UNE and 24 controls by US. We compared UNCSA as determined by MRI or US and determined optimal diagnostic cutoff values based on receiver operating characteristic curve analysis.

Results The UNCSA was significantly larger in the UNE group than in controls at 3, 2, 1, and 0 cm proximal and 1, 2, and 3 cm distal to the medial epicondyle for both modalities. The UNCSA was maximal at 1 cm proximal to the medial epicondyle for MRI (16.1 ± 3.5 mm^2) as well as for US (17 ± 7 mm^2). A cutoff value of 11.0 mm^2 for MRI and US was found to be optimal for differentiating between patients with UNE and controls, with an area under the receiver operating characteristic curve of 0.95 for MRI and 0.96 for US. The UNCSA measured by MRI was not significantly different from that by US. Intra-rater and interrater reliabilities for UNCSA were all greater than 0.77. The UNCSA in the severe nerve dysfunction group of 18 patients was significantly larger than that in the mild nerve dysfunction group of 12 patients.

Conclusions By measuring UNCSA with MRI or US at 1 cm proximal to the ME, patients with and without UNE could be discriminated at a cutoff threshold of 11.0 mm^2 with high sensitivity, specificity, and reliability. *(J Hand Surg Am. 2018;43(6):529–536.*

Type of study/level of evidence Diagnostic III.

Key words Elbow, MRI, ulnar nerve, ulnar neuropathy, ultrasonography.

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Ulnar neuropathy at the elbow (UNE) is a common entrapment neuropathy in the upper extremities that is characterized by paresthesia and numbness in the little and ring fingers. Patients with UNE may demonstrate abnormal 2-point discrimination or intrinsic muscle weakness in the later stages, whereas in the early stages, provocation testing may be the only positive sign. In patients who have positive cervical cord or root compression[1–3] upon magnetic resonance imaging (MRI) or similar symptoms from other neuromuscular disease, it is may be difficult to discriminate UNE fully from these conditions.[1,2]

To date, there are no reference standards for objective diagnostic criteria for UNE. The diagnosis of UNE can best be made using clinical provocation testing along with reduced ulnar nerve motor nerve conduction velocity (MCV) across the elbow.[1,2] However, electrodiagnostic study is not universally employed for UNE because these studies are frequently negative in the early stages[4] and often compound motor action potential cannot be detected in the later stages.[5] Recently, high-resolution[6,7] or diffusion-weighted[8,9] magnetic resonance neurography, which qualitatively evaluates pathological changes in the nerve, has been found to be useful for the diagnosis and measurement of enlarged ulnar nerve cross-sectional area (UNCSA) by MRI[10] and ultrasonography (US)[11–20] and has also become a part of modern quantitative diagnostic criteria for this condition. However, studies evaluating UNCSA obtained measurements at either a single site[13,15,19] or only a few of them.[11,12,16,17,20] Consequently, in cases in which the diagnosis of UNE is uncertain and imaging tests are used as a diagnostic modality, clarification of the optimal measurement site, differences in UNCSA between MRI and US, the diagnostic cutoff value, and measurement reliability are all important considerations.

The purpose of this study was to determine the segment level of maximum UNCSA and the cutoff threshold for diagnosing between patients with UNE and those without it by MRI and US.

MATERIALS AND METHODS

The ethics committee of the senior author's hospital approved the study protocol. Subjects were enrolled between 2010 and 2013. Ulnar neuropathy at the elbow was diagnosed by sensory and motor symptoms with clinical provocation testing. Thirty patients with UNE were enrolled in the MRI study and 12 patients with UNE were enrolled in the US study. In addition, 12 patients in the US study were included in the MRI study. Table 1 describes the demographic characteristics of the patients with UNE and controls. Associated elbow lesions in the UNE group consisted of elbow osteoarthritis (OA) in 19 patients and cubitus valgus in 2. Elbows with Kellgren–Lawrence grade 2, 3, or 4 OA,[21,22] as determined using plain anteroposterior and lateral radiographs, were considered to have OA. Motor nerve conduction velocity of the ulnar nerve across the elbow was 50 m/s[1] or more in 10 patients and less than 50 m/s in 17 patients. In the remaining 3 patients, compound muscle action potential from the abductor digiti minimi could not be evoked. The senior author treated patients with UNE surgically by subcutaneous transposition of the ulnar nerve in 27 patients and simple decompression of the ulnar nerve in 3. Patients with UNE associated with acute fracture or dislocation around the elbow, ganglion, or tumor at the cubital tunnel, or recurrence after surgery were excluded. All patients were observed for at least 1 year after surgery and were confirmed to have achieved improvement in symptoms.

Magnetic resonance imaging and determination of UNCSA

We obtained the results of 58 MRI examinations from 30 patients with UNE and 28 control subjects without it (Table 1). Control subjects in the MRI measurement study were patients diagnosed as having lateral epicondylitis of the humerus or soft tissue tumor at the lateral or anterior side of the elbow during the same period, and who had no complications or findings related to UNE.

Imaging examinations were performed with 1 of 2 1.5-T systems (Symphony and Avanto, Siemens Healthcare, Erlangen, Germany). Participants were placed in a supine position with arms at their side, elbows at maximum extension, and forearms supinated. The elbows were placed in a single- or 4-channel, phased-array, receive-only extremity coil. For the measurements described subsequently, transverse T2-weighted, fast spin-echo images without fat suppression were obtained in a plane perpendicular to the bone axis with the following pulse sequences: repetition time was 3,500 to 5,500 ms, echo time was 70 to 95 ms, section thickness was 3 or 4 mm, section interval was 5 mm, field-of-view was 150 × 150 mm, and acquisition matrix was 256 × 320.

The first author, who had 11 years of clinical experience in hand surgery, was blinded to the diagnosis in the UNE and control groups; manually drawn regions of interest on a computer workstation

TABLE 1. Demographic Characteristics of Patients and Controls in MRI and US Measurements

Imaging Examination	MRI		US	
	UNE	Control	UNE	Control
Subjects, n	30	28	12	24
Measured elbows, n	30	28	12	48
Mean age, y	67.5	63.0	68.0	64.0
(25th through 75th percentile)	(59.0–74.8)	(57.8–69.3)	(61.8–75.3)	(59.8–67.3)
Mean height, cm	164.5	161.0	166.0	167.0
(25th through 75th percentile)	(157.3–168.8)	(154.8–167.3)	(163.5–167.3)	(155.0–170.0)
Mean body weight, kg	65.0	63.0	63.5	59.5
(25th through 75th percentile)	(58.5–73.0)	(60.0–68.5)	(59.7–70.8)	(53.5–65.5)
Mean body mass index, kg/m^2	25.0	24.8	23.6	22.7
(25th through 75th percentile)	(22.8–26.5)	(23.3–25.7)	(22.1–25.1)	(20.7–23.4)
Female/male	7/23	12/16	0/12	12/12
Right/left	19/11	18/10	8/4	24/24
Elbows with OA, n	19		8	
Kellgren–Lawrence classification* (2/3/4)	4/9/6		2/3/3	
Ulnar nerve palsy by McGowan classification† (1/2/3)	6/6/18		0/4/8	
Measured levels, n	7	7	15	15
MCV of ulnar nerve, m/s (≥50/<50/could not be evoked)	10/17/3		2/9/1	

*Kellgren–Lawrence classification: 2 = possible narrowing of joint space with definite osteophyte formation; 3 = definite narrowing of joint space with moderate osteophyte formation; and 4 = large osteophyte formation, severe narrowing of joint space with marked sclerosis, and definite deformity of bone contour.

†Mild dysfunction is defined as grade 1 or 2 of McGowan classification.[23] Severe dysfunction is defined as grade 3.

(EV Insite, PSP Corp, Tokyo, Japan) (Fig. 1A) were used to determine UNCSA. Upon MRI, the ulnar nerve appeared as several mild-high or iso-signal intensity fascicles surrounded by a hypointense margin. We plotted just outside this hypointense margin on the display and defined it as a region of interest. The UNCSA values within regions of interest were recorded in square millimeters to the first decimal place at 7 segment levels: 3, 2, and 1 cm proximal to the medial epicondyle (ME), at the ME (0 cm; station ME), and 1, 2, and 3 cm distal to the ME.

To evaluate intra-rater reliability, the first author reassessed the UNCSA in the same 30 patients with UNE within 1 to 8 weeks and in the 28 control subjects after 24 months. Measurements were obtained at all 7 segment levels for every patient. Intra-rater reliability was calculated by comparing the 2 UNCSA measurements at each level. Afterward, the 58 subjects, including 30 patients with UNE and 28 control subjects, were assigned numbers from 1 to 58 according to the order of their MRI screening date, and the 29 subjects with odd numbers were selected to evaluate inter-rater reliability. For these subjects, the fourth author, who had 12 years of clinical experience, measured the UNCSA at the 7 segment levels using the same method. Inter-rater reliability was calculated by comparing the respective UNCSA measurements.

Ultrasound and determination of UNCSA

We obtained the results of 60 US examinations performed on 12 elbows in 12 patients with UNE and 48 bilateral elbows in 24 control subjects without it. The 24 control subjects in this US measurement study were healthy volunteers with no problems or findings related to UNE, elbow disease, or elbow trauma (Table 1).

A 15-MHz probe in B-mode (Preirus, Hitachi, Tokyo, Japan) was used for US-based analysis of UNCSA. Subjects were placed in a supine position with the shoulder at 60° abduction and 45° external rotation, the elbow joint at 30° flexion, and the forearm in the supinated position. The examiner held the probe perpendicular to the skin and adjusted the

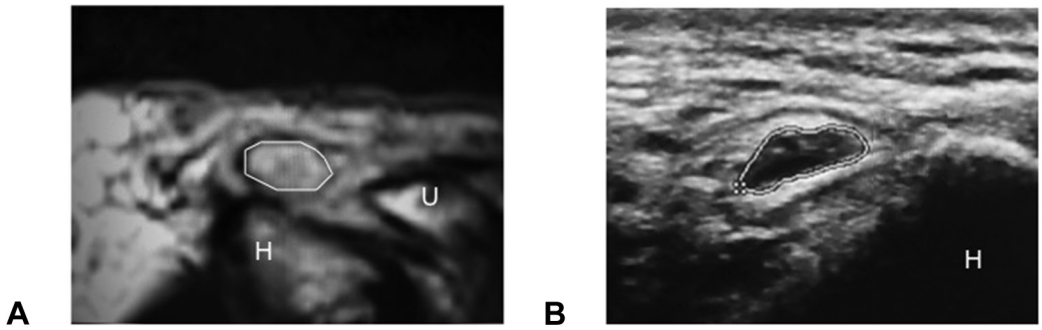

FIGURE 1: Cross-section of the ulnar nerve at the ME level by **A** T2-weighted axial MRI and **B** US imaging. H, humerus; U, ulna. Both images are oriented with the superficial layer at the top and the deep layer at the bottom (magnifications × 4.00).

angle to obtain short-axis views of the ulnar nerve. The probe was placed on the skin with minimum pressure.

The first author determined UNCSA in the UNE and control groups unblinded to the diagnosis. The nerve was traced proximally to distally over the medial skin around the elbow and the ME segment level was established by identifying the top of the humeral ME. Then, 15 levels were defined from 8 cm proximal to 6 cm distal to the ME at 1-cm intervals to obtain measurements at positions 8 to 1 cm proximal to the ME, at the ME, and 1 to 6 cm distal to the ME. The UNCSA was calculated by US workstation software to the nearest whole number and expressed in square millimeters. Based on short-axis US views of the ulnar nerve, manually traced areas along the outside edge of the hypoechoic rims of the fascicles of the ulnar nerve were defined as the UNCSA[14] (Fig. 1B). Distal to the ME, short-axis US views of branches of the flexor carpi ulnaris or flexor digitorum profundus were not included in UNCSA calculations when they were apparently separated from the main ulnar nerve trunk (Fig. 2I, L).

To evaluate intra-rater reliability in US measurements, the first author reassessed the UNCSA of the 12 patients within 1 to 8 weeks and of 24 elbows in 12 control subjects after 24 months using the same method. To assess interrater reliability, the senior author, who had 35 years of clinical experience, also evaluated the UNCSA of all 12 elbows in the 12 patients with UNE and 48 elbows in the 24 control subjects by US using identical methods. Interrater reliability was calculated by comparing the UNCSA measurements for respective segment levels in each patient.

Comparison of UNCSA determined by MRI and US

The UNCSAs measured by MRI and US in 12 patients with UNE who underwent both imaging modalities were compared for 7 common segment levels: 3, 2, and 1 cm proximal to the ME, at the ME, and 1, 2, and 3 cm distal to the ME.

Cutoff value and receiver operating characteristic curve analysis for diagnosis of UNE

The area under the receiver operating characteristic curve (AUC) was calculated for UNCSA values obtained using MRI at 1 cm proximal to the ME for discrimination between the UNE and control groups. In the same way, the AUC was created for UNCSA values obtained using US. Cutoff values with maximized sensitivity and specificity were also determined separately for both MRI and US.

Relationship between UNCSA measured by MRI and severity of ulnar nerve dysfunction

To evaluate the severity of ulnar nerve dysfunction, grades 1 and 2 of the McGowan classification system were defined as mild dysfunction and grade 3 was considered to represent severe dysfunction.[23] We compared UNCSA values between the mild and severe groups among the 30 patients who underwent MRI.

Statistical analysis

After setting the clinically significant difference of UNCSA between patients with UNE and controls as 6 mm^2, the statistical power (1 — s) as 0.8, and the significance level (α) as .05, we calculated the necessary number of patients with UNE and control subjects based on the SD for the UNCSA to be 1.0 cm proximal to the ME. The required numbers were 7 for the MRI measurement and 23 for the US measurement. Welch's *t* test was adopted for comparisons of the UNCSA measured by MRI and US at each segment level between the UNE and control groups. We used Ebel's intraclass correlation coefficients to calculate intra-rater and interrater reliability for

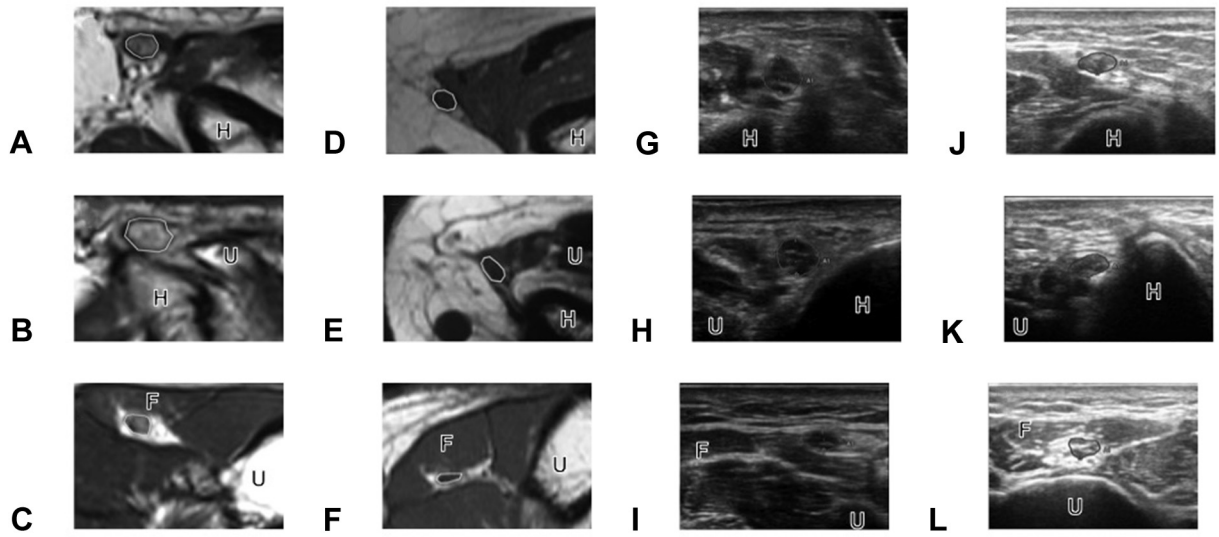

FIGURE 2: Cross-section of the ulnar nerve at different segment levels by **A–F** T2-weighted axial MRI and **G–L** US imaging in patients with UNE (A–C and G–I) and control subjects (D–F and J–L). Images A, D, G, and J were taken at 3 cm proximal to the ME (P3 level). Images B, E, H, and K were taken 1 cm proximal to the ME (P1 level). Images C, F, I, and L were taken 3 cm distal to the ME (D3 level). The UNCSAs in patients with UNE were larger than those in controls at all levels. Images A through C were taken from one patient with UNE, whereas images G through I were obtained from another patient. Images D through F were taken from one control subject, whereas images J through L were obtained from another control subject. H, humerus; U, ulna; F, flexor carpi ulnaris. Measured UNCSAs were 12.6 mm^2 (A), 18.8 mm^2 (B), 11.6 mm^2 (C), 7.3 mm^2 (D), 8.3 mm^2 (E), 3.8 mm^2 (F), 12 mm^2 (G), 15 mm^2 (H), 7 mm^2 (I), 6 mm^2 (J), 7 mm^2 (K), and 5 mm^2 (L) (magnifications × 4.00).

UNCSA measurements. Paired *t* tests were employed for comparisons of UNCSA from patients and controls. We employed the Mann–Whitney *U* test to examine the relationship between UNCSA and the severity of nerve dysfunction. In all analyses, $P < .05$ was defined to be statistically significant.

RESULTS

Ulnar nerve cross-sectional area measured by MRI

The UNCSA was significantly larger in the UNE group than in controls at 3 to 1 cm proximal to the ME, at the ME, and at 1 to 3 cm distal to the ME. The maximum mean ± SD UNCSA was 16.1 ± 3.5 mm^2, which was observed at 1 cm proximal to the ME (Fig. 3). Intra-rater and interrater reliability for UNCSA measurements obtained by MRI was 0.88 and 0.77, respectively.

Ulnar nerve cross-sectional area measured by US

The UNCSA was significantly larger in the UNE group than in controls at 4 to 1 cm proximal to the ME, at the ME, and at 1 to 5 cm distal to the ME. The maximum mean ± SD UNCSA was 17 ± 7 mm^2 in the UNE group, which was observed at 1 cm proximal to the ME (Fig. 4). Intra-rater and interrater reliability for UNCSA measurements obtained by US was 0.86 and 0.81, respectively.

Ulnar nerve cross-sectional area between MRI and US

Mean UNCSA calculations measured by MRI were not significantly different from those determined by US at any of the 7 common levels (Table 2).

Ulnar nerve cross-sectional area cutoff values and receiver operating characteristic curve analysis

In UNCSA measurements of the ulnar nerve by MRI, we found a cutoff value of 11.0 mm^2 to discriminate optimally between patients with and without UNE. Sensitivity and specificity at this threshold were 0.97 and 0.93, respectively, and the AUC was 0.95. In UNCSA calculations measured by US, a similar cutoff value of 11 mm^2 differentiated best between patients with UNE and those without it. Sensitivity and specificity were 0.92 and 0.90, respectively, and the AUC was 0.96.

Relationship between severity of ulnar nerve dysfunction and UNCSA

The UNCSA in the group of 18 patients with severe ulnar nerve dysfunction was significantly larger than that in the group of 12 patients with mild dysfunction at 1 cm proximal to the ME, at the ME, and at 1 to 3 cm distal to the ME (Table 3).

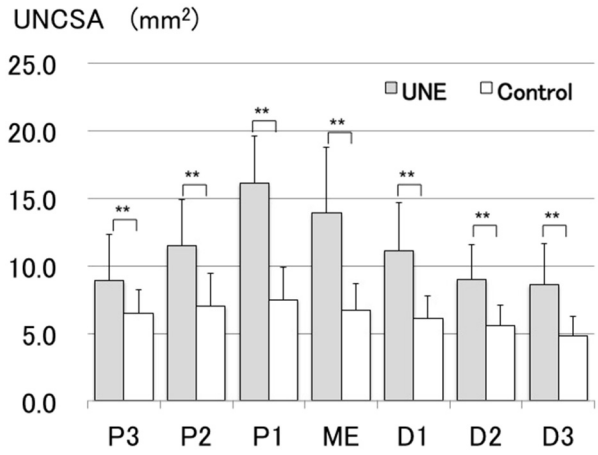

FIGURE 3: Ulnar nerve cross-sectional area measured by T2-weighted MRI at different segment levels (UNE: n = 30; control: n = 28). ME, medial epicondyle; P3, P2, and P1, 3, 2, and 1 cm proximal to the ME; D1, D2, and D3, 1, 2, and 3 cm distal to the ME. *$P < .05$, **$P < .01$. Error bars represent 1 SD.

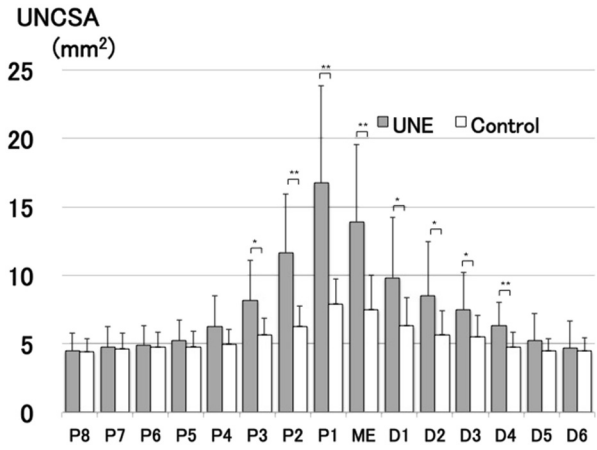

FIGURE 4: Ulnar nerve cross-sectional area measured by US at different segment levels (UNE: n = 12; control: n = 48). ME, medial epicondyle; P8, P7, P6, P5, P4, P3, P2, and P1, 8, 7, 6, 5, 4, 3, 2, and 1 cm proximal to the ME; D1, D2, D3, D4, D5, and D6, 1, 2, 3, 4, 5, and 6 cm distal to the ME. *$P < .05$, **$P < .01$. Error bars represent 1 SD.

TABLE 2. Comparison of UNCSA as Measured by MRI or US in 12 Patients With UNE

Level*	MRI	US	*P* Value
P3	9.6 (6.7)	8 (3)	.51
P2	15.7 (7.2)	11 (4)	.11
P1	20.2 (6.0)	17 (7)	.21
ME	16.8 (4.8)	14 (6)	.19
D1	11.5 (4.3)	10 (4)	.35
D2	9.9 (2.7)	9 (4)	.34
D3	9.8 (3.7)	8 (3)	.10

Data are expressed as mean (SD) in mm^2. Measured UNCSA values are comparable between imaging modalities ($P < .05$, paired *t* test).
*P1, 2, and 3: 1, 2, and 3 cm proximal to ME; D 1, 2, and 3: 1, 2, and 3 cm distal to the ME.

TABLE 3. Comparison of UNCSA as Measured by MRI Between Mild and Severe Ulnar Nerve Dysfunction Groups

Level	Mild (n = 12)	Severe (n = 18)	*P* Value
P3	7.7 (3.3)	9.7 (3.4)	.14
P2	10.2 (3.3)	12.3 (3.4)	.10
P1	13.9 (2.9)	17.6 (3.6)	<.01*
ME	11.6 (3.9)	15.4 (4.9)	<.05*
D1	9.4 (2.9)	12.3 (3.6)	<.05*
D2	7.7 (1.3)	9.8 (2.9)	<.05*
D3	6.9 (1.5)	9.7 (3.3)	<.05*

Data are expressed as mean (SD) in mm^2. P1, 2, and 3 were 1, 2, and 3 cm proximal to the ME, respectively; D1, 2, and 3 were 1, 2, and 3 cm distal to the ME, respectively. Mild dysfunction is equivalent to grade 1 or 2 of the McGowan's classification system and severe dysfunction is equivalent to grade 3.
*The UNCSAs in the severe nerve dysfunction group were significantly larger than those in the mild nerve dysfunction group (P <.05, Mann-Whitney U test).

DISCUSSION

The current study demonstrated that UNCSA in patients with UNE significantly increased over that in control subjects from 3 cm proximal to 3 cm distal to the ME as measured by MRI, and from 5 cm proximal to 4 cm distal to the ME as measured by US. No significant differences in UNCSA were noted between MRI and US at any of 7 common segment levels. The UNCSA was maximal at 1 cm proximal to the ME in both MRI and US evaluations, which showed high intra-rater and interrater reliabilities. By measuring UNCSA using MRI or US at 1 cm proximal to the ME, patients with and without UNE could be discriminated with high sensitivity and specificity at a cutoff threshold of 11.0 mm^2.

Ultrasound imaging was frequently employed in previous studies of the UNCSA in patients with UNE. However, reports of mean UNCSA varied widely, at 9.0,[20] 9.6,[14] 13.9,[11] 18.5,[15] and 19.0[12] mm^2. The location of the measurements also differed by study, such as at the ME,[13,19] at the maximum UNCSA segment level,[15] and at only few levels including the ME.[11,12,16,17,20] Magnetic resonance imaging investigations of the UNCSA in UNE are scarce; only Bäumer et al[10] stated the mean UNCSA to be 15.4 mm^2. Apart from their study, the

UNCSA has not been measured in multiple consecutive sections over a wide range of proximal to distal levels across the ME by MRI or US, which makes it difficult to identify the levels at which the UNCSA is maximal in UNE. In addition, whether either modality is a more reliable method for UNCSA measurement in the diagnosis of UNE remains undetermined.

Cross-sectional area cutoff values at the ME measured by US were reported to be 8.3,[15] 10.0,[20] and 11.0[16] mm^2. In the current study, the cutoff threshold was 11.0 mm^2 according to MRI and US assessments. In the previous reports, UNCSA was measured at different points, such as at the ME or at the site of maximal swelling. Here, it was analyzed at 1 cm proximal to the ME, where UNCSA was maximal. Consequently, the sensitivity and specificity for UNE were high using either MRI or US.

Neuropathological changes in patients or animal models with entrapment neuropathy have been reported as perineurial thickness; interfascicular, epineurial, and endoneurial fibrosis; and swelling proximal and distal to the compressed segment.[24–26] In clinical cases of UNE, it is assumed that these pathological alterations occur along the ulnar nerve proximal and distal to the cubital tunnel, thus to increase UNCSA. In experimental studies in which the nerve was compressed at a local level, it was demonstrated that even low pressure could interfere with both anterograde and retrograde axonal transport.[27,28] However, it is unclear how this affects UNCSA in patients with UNE because animal models of conditions such as clinical entrapment neuropathy have not yet been established.

As mentioned earlier, there was considerable variation in mean UNCSA among patients with UNE in previous studies. This discrepancy may primarily have been caused by differences in the severity of ulnar nerve dysfunction among reports. The current investigation revealed that UNCSA became progressively larger with the degree of ulnar nerve dysfunction. In an US examination assessing morphological changes in the ulnar nerve in patients with UNE, Okamoto et al[29] revealed a correlation between the stage of ulnar nerve palsy and the diameter of the major axis of the ulnar nerve. Indeed, in earlier reports showing relatively smaller UNCSA measurements of 9.6 ± 8.5 mm^2, the incidence of UNE with sensory loss and muscle weakness that correlated with McGowan grade 2 or 3 was only 12%.[14] In a cohort study by Yoon et al,[15] with a mean UNCSA of 18.5 ± 7.3 mm^2, 46% of patients with UNE had sensory loss and muscle weakness. This study uncovered a mean UNCSA of 17 ± 7 mm^2 in a cohort containing 80% McGowan grade 2 or 3 patients. Moreover, technical factors affecting US examination, such as elbow positioning, pressure from the probe on the skin, and level of measurement, were different or mentioned imprecisely in earlier studies and might have contributed further to discrepancies in mean UNCSA.

This study had several limitations. The number of UNCSA segments that were tested was 7 for MRI compared with 15 for US, because of the prohibitive resource requirements for MRI. The first and the senior authors could not be blinded to the status of UNE or control conditions during US measurements because they had to face the patients while testing, which might have introduced observer-expectancy bias. Nineteen of the 30 patients with UNE had elbow OA. In Japan, UNE is highly associated with elbow OA.[30,31] In elbows with OA, osteophytes may develop in the medial humeroulnar joint to narrow the bony floor of the cubital tunnel.[32,33] Therefore, UNCSA may differ in patients with UNE with elbow OA. Moreover, in this study, patients with UNE measured by US were all male. Shoulder and elbow positions were slightly different between MRI and US measurements to obtain optimal results for each imaging technique. Magnetic resonance neurography[6,7] and diffusion-weighted imaging MRI[8,9] were not performed. Finally, the shortest interval for intra-rater reliability testing in patients with UNE was 1 week, which may have spuriously increased agreement.

Despite these limitations, this study demonstrated that patients with and without UNE could be discriminated at a cutoff threshold of 11.0 mm^2 by measuring UNCSA with MRI or US at 1 cm proximal to the ME with high sensitivity, specificity, and reliability.

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