Ultrasonographic Evaluation of Ulnar Neuropathy Around the Elbow in Diabetes Mellitus

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Objective: We evaluated the usefulness of ultrasonography for subclinical ulnar neuropathy at the elbow (UNE) in patients with diabetes.

Methods: Ultrasonography of the ulnar nerve was performed on 140 limbs in 73 patients with diabetes mellitus at 8 standardized sites proximal and distal to the medial epicondyle (1-cm intervals). The ulnar nerve cross-sectional area (CSA) at each site was analysed according to the presence of electrophysiological diabetic polyneuropathy (DPN) or UNE (UNE_e).

Results: Fifty-nine limbs were electrophysiologically normal, 22 limbs had UNE, 39 limbs had DPN, and 20 limbs had DPN and UNE_e. In patients without DPN, the maximal CSA, swelling ratio, and CSAs were greater in the UNE_e group than in the normal group (p < 0.01). No significant differences were noted between the DPN and DPN+UNE_e groups regarding the CSAs, maximal CSA, and swelling ratio.

Conclusion: Ultrasonography of ulnar nerve swelling is helpful for diagnosing subclinical UNE in patients with diabetes.

Keywords: Ulnar neuropathies; Diabetes mellitus; Ultrasonography; Electrodiagnosis; Polyneuropathies

Introduction

Ulnar neuropathy at the elbow (UNE) is the second most common focal entrapment neuropathy in patients with diabetes following carpal tunnel syndrome. Standard 10-cm nerve conduction studies revealing reduced conduction velocity (less than 50 m/s) or conduction block in the elbow segment are commonly used to diagnose UNE [1]. However, it is difficult to diagnose UNE based on the motor conduction velocity (MCV) in patients with diabetic polyneuropathy (DPN) [2]. In particular, it can be extremely challenging to establish diagnostic criteria for UNE in patients with diabetes who have a forearm segment MCV less than 50 m/s. In these patients, decreased conduction velocity in the elbow segment can result from UNE or DPN.

Short-segment nerve conduction studies are also used to diagnose UNE with higher diagnostic accuracy [3–5].

High-resolution ultrasonography is widely applied to investigate peripheral nerve lesions. Ultrasonography has also been recommended as a useful and reliable secondary approach for diagnosing UNE [6]. In many ultrasonography studies [7–9], UNE was diagnosed based on the maximum cross-sectional area of the ulnar nerve around the elbow (CSAmax); the cut-off values of the ulnar nerve cross-sectional areas (CSAs) varied marginally from 8.3 to 11.0 mm². In patients with diabetes, however, the cut-off values of the ulnar nerve CSAs for diagnosing UNE are unknown.

Subclinical UNE (UNE_sc) is frequently encountered in patients with diabetes during electrodiagnostic studies. Jang et al.

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examined 105 patients with diabetes and diagnosed UNE_sc using the ulnar MCV and inching techniques with a 1-cm interval of stimulation around the elbow for increased detection of ulnar nerve lesion. The authors suggest that diagnosing UNE_sc early is important because it can exacerbate ulnar neuropathy through external compression or continuous elbow flexion. However, the morphologic change of the ulnar nerve at the elbow in patients with diabetes with UNE and/or DPN remains unknown. In the present study, we identify the changes in ulnar nerve CSA that occur around the elbow in patients with diabetes according to the presence of electrophysiological DPN or UNE to evaluate the diagnostic utility of ultrasonography for UNE_sc in patients with diabetes.

Materials and Methods

1) Patients

Patients with type-2 diabetes mellitus diagnosed according to the criteria of the American Diabetes Association with no symptoms of ulnar neuropathy were enrolled in the present study prospectively. Patients were excluded if they had a history of previous elbow surgery or trauma, cervical radiculopathy, any inflammatory disorder, any malignancy, and/or a medical disease associated with polyneuropathy other than diabetes mellitus. Patients who had brachial plexopathy or who chronically consumed alcohol were also excluded. The study protocol was approved by the Institutional Review Board of Korea University Ansan Hospital (AS13033) and all patients provided written informed consent before participating in the study.

2) Electrodiagnostic study

Nerve conduction studies were performed in the bilateral ulnar motor and sensory nerves, unilateral median motor and sensory nerves, peroneal, tibial motor nerves and sural, superficial peroneal sensory nerves using the Viking Select EMG NCS Machine (Nicolet Viasys; Nicolet Viasys Healthcare, Madison, WI, USA). H-reflex and the ulnar, median, peroneal, and tibial F-waves were also obtained. Prior to the nerve conduction studies, the skin temperature was maintained above 32°C. The inching test of the ulnar nerve was performed with bilateral abductor digiti minimi recording to detect abnormal focal slowing of the nerve using the TenElectrodes stimulator [11]. Although there is no gold standard for the electrodiagnosis of DPN, in this study, patients were diagnosed with DPN if the electrophysiological criteria from the Diabetes Control and Complication Trial, with some modifications, were met [12,13]. Specifically, electrophysiological DPN was diagnosed when the sural sensory amplitude was less than or equal to 5 μV and 2 or more of the median sensory, peroneal motor, peroneal F-wave, H-reflex, and fibrillations in the lower extremity muscles were abnormal.

Electrophysiological UNE (UNE_e) in patients with diabetes was established using the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) guidelines and the results of the inching test [14]. The AANEM guidelines for diagnosing UNE_e were as follows: (1) absolute ulnar MCV of the elbow segment less than 50 m/s or (2) the elbow segment was more than 10 m/s slower than the forearm segment. In the inching test, the ulnar nerve is stimulated at intervals of 1 cm beginning 4 cm distal to the medial epicondyle (ME) and ending 3 cm proximal to the ME. We diagnosed a patient with UNE_e when the latency difference per 1-cm segment was greater than 0.4 ms. If the absolute MCV of the forearm segment was less than 50 m/s, which could result from DPN, then a diagnosis of UNE_e was made when the MCV of the elbow segment was slower than that of the forearm segment by 10 m/s or more or based on the results of the inching test. Patients were classified into the following 4 groups according to the electrophysiological diagnosis: normal, UNE_e, DPN, or DPN with UNE_e (DPN+UNE_e).

3) Ultrasonographic study

Ultrasonography was performed using the ACCUVIX V20 system (Samsung Medison, Seoul, Korea) interfaced with a 6 to 13 MHz linear array transducer by a physiatrist with more than 8 years of experience in ultrasonography of peripheral nerves. Sonographic examinations were conducted with the patient in a supine position and the elbows flexed at 10 degrees with the forearms supinated. Initially, marks were made on the skin overlying the ulnar nerve at the level of the ME; 3, 2, and 1 cm proximal to the ME; and 4, 3, 2, and 1 cm distal to the ME (proximal to dis-

Fig. 1. Sites of nerve stimulation and cross-sectional area measurements of the ulnar nerve. Stimulation was performed at the medial epicondyle (ME); 1, 2, and 3 cm proximal (P1, P2, and P3, respectively) to the ME; and 1, 2, 3, and 4 cm distal (D1, D2, D3, and D4, respectively) to the ME.
tial: P3, P2, P1, ME, D1, D2, D3, and D4 in Fig. 1). The probe was placed in the transverse plane on the proximal arm to verify the ulnar nerve and then moved distally. The probe was held perpendicular to the skin. Minimal pressure was applied to avoid extrinsic nerve compression. At each of the 8 standardized and marked sites, the CSA of the ulnar nerve was measured within the hyperechoic rim of the nerve using the “AreaTrace” function of the ultrasonography system. The ulnar nerve-swelling ratio was calculated by dividing the CSAmax by the CSA measured from D4.

4) Statistical analyses

Statistical analyses were performed with IBM SPSS ver. 20.0 for Windows (IBM Corp., Armonk, NY, USA). Independent t-tests were used to evaluate differences in the demographic data between patients with and without DPN. Categorical values (gender and presence of DPN symptoms) were analysed using $\chi^2$ tests. To compare the ultrasonographic nerve CSAs among the 4 patient groups, analyses of variance were employed. Fisher Least Significant Difference tests were used for the post hoc analyses. The cut-off values of the CSA at the ME, CSAmax, and swelling ratio for diagnosing UNE_sc were calculated using receiver operating characteristic (ROC) curves and the resultant specificity and sensitivity were obtained. Differences were considered statistically significant at $p < 0.05$.

Results

From the 73 patients with diabetes mellitus in this study, 140 upper limbs (59 normal, 22 UNE_e, 39 DPN, and 20 DPN +UNE_e) were included in the analysis. Demographic data are presented in Table 1. Differences in the age, diabetes duration, DPN symptoms, and glycosylated hemoglobin were noted between patients with and without DPN.

In patients without DPN (normal and UNE_e groups), significant increases in the ulnar nerve CSAs were identified in the UNE_e group (Fig. 2) when compared with the electrophysiologically normal group at all sites except D4 and D3 ($p < 0.01$). The CSAmax and swelling ratio were also significantly greater in the UNE_e group than in the normal group ($p < 0.001$). Conversely, no significant differences in the ulnar nerve CSAs, CSAmax, and swelling ratio were identified between the DPN and

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Without DPN (n = 38)</th>
<th>With DPN (n = 35)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female: male)</td>
<td>12:26</td>
<td>13:22</td>
<td>0.617</td>
</tr>
<tr>
<td>Age (y)</td>
<td>52.4 ± 10.3</td>
<td>60.2 ± 11.0</td>
<td>0.003</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.5 ± 6.7</td>
<td>163.8 ± 9.6</td>
<td>0.384</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.0 ± 11.2</td>
<td>65.3 ± 12.4</td>
<td>0.327</td>
</tr>
<tr>
<td>Diabetes mellitus duration (mo)</td>
<td>64.9 (1-300)</td>
<td>138.0 (1-480)</td>
<td>0.003</td>
</tr>
<tr>
<td>DPN symptoms*</td>
<td>12</td>
<td>28</td>
<td>0.001</td>
</tr>
<tr>
<td>Symptom duration (mo)*</td>
<td>11.3 (1-120)</td>
<td>24.5 (1.5-120)</td>
<td>0.081</td>
</tr>
<tr>
<td>Glycosylated hemoglobin</td>
<td>7.5 ± 1.5</td>
<td>9.0 ± 2.5</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation or mean (range).

*DPN symptoms include unsteady walking and numbness, burning pain, and a prickling sensation in the distal legs and feet. †Diabetes mellitus duration refers to the time interval between the diagnosis of diabetes mellitus and recruitment.

Fig. 2. Ultrasound image of the ulnar nerve in a patient without diabetic polyneuropathy, but with subclinical ulnar neuopathy at the elbow (UNE_e group) at 8 stimulation sites, including 3 sites proximal (P3, P2, and P1) to the medial epicondyle (ME), ME, and 4 sites distal (D1, D2, D3, and D4) to the ME. The maximum cross-sectional area (CSA) was observed 1 cm distal (D1) to the ME.
Table 2. Mean CSAs of the Ulnar Nerve around the Elbow

<table>
<thead>
<tr>
<th>CSA</th>
<th>Normal (n = 59)</th>
<th>UNE_e (n = 22)</th>
<th>DPN (n = 39)</th>
<th>DPN + UNE_e (n = 20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSA_D4</td>
<td>6.9 ± 1.8</td>
<td>7.3 ± 1.5</td>
<td>7.6 ± 1.9</td>
<td>7.6 ± 1.5</td>
<td>0.140</td>
</tr>
<tr>
<td>CSA_D3</td>
<td>7.2 ± 1.8</td>
<td>8.1 ± 1.9</td>
<td>7.9 ± 1.8</td>
<td>7.7 ± 1.4</td>
<td>0.089</td>
</tr>
<tr>
<td>CSA_D2</td>
<td>6.9 ± 1.8</td>
<td>8.3 ± 1.9*</td>
<td>7.8 ± 2.2</td>
<td>7.8 ± 1.6</td>
<td>0.014</td>
</tr>
<tr>
<td>CSA_D1</td>
<td>7.2 ± 2.1</td>
<td>9.8 ± 3.0**</td>
<td>8.4 ± 2.0</td>
<td>9.4 ± 3.6*</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CSA_ME</td>
<td>7.9 ± 2.1</td>
<td>11.3 ± 3.5**</td>
<td>9.6 ± 2.1†</td>
<td>9.8 ± 3.3†</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CSA_P1</td>
<td>8.2 ± 2.4</td>
<td>11.0 ± 3.9**</td>
<td>9.3 ± 2.3</td>
<td>10.4 ± 3.9†</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CSA_P2</td>
<td>7.6 ± 2.3</td>
<td>9.2 ± 2.4*</td>
<td>8.6 ± 2.3</td>
<td>9.0 ± 2.4</td>
<td>0.011</td>
</tr>
<tr>
<td>CSA_P3</td>
<td>6.9 ± 2.1</td>
<td>8.4 ± 2.1*</td>
<td>7.8 ± 2.0</td>
<td>7.5 ± 1.7</td>
<td>0.016</td>
</tr>
<tr>
<td>CSAmax</td>
<td>9.0 ± 2.4</td>
<td>12.6 ± 3.8**</td>
<td>10.5 ± 2.5†</td>
<td>12.0 ± 4.1**</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CSA_SR</td>
<td>1.3 ± 0.3</td>
<td>1.7 ± 0.5**‡‡</td>
<td>1.4 ± 0.3</td>
<td>1.6 ± 0.3</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

CSA, cross-sectional area; UNE_e, electrophysiological ulnar neuropathy at elbow; DPN, diabetic polyneuropathy; ME, medial epicondyle; D4, D3, D2, and D1, 4, 3, 2, and 1 cm distal to the ME, respectively; P1, P2, and P3, 1, 2, and 3 cm proximal to the ME, respectively; CSAmax, maximum CSA; SR, swelling ratio (CSAmax/CSA_D4).

Post hoc analyses using the Fisher least significant difference tests: *p < 0.01 and **p < 0.001 for UNE_e vs. normal; †p < 0.01 for DPN vs. normal; ‡‡p < 0.01 and ‡‡‡p < 0.001 for DPN + UNE_e vs. normal; ††p < 0.001 for UNE_e vs. DPN.

Table 3. Cut-Off Values of the Ulnar Nerve CSA for Diagnosing Subclinical Ulnar Neuropathy at the Elbow in Patients with Diabetes

<table>
<thead>
<tr>
<th>CSA</th>
<th>Without DPN</th>
<th>With DPN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cut-off value</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>CSA_ME</td>
<td>9.85</td>
<td>72.7</td>
</tr>
<tr>
<td>CSAmax</td>
<td>9.85</td>
<td>77.3</td>
</tr>
<tr>
<td>CSA_SR</td>
<td>1.43</td>
<td>72.7</td>
</tr>
</tbody>
</table>

CSA, cross-sectional area; DPN, diabetic polyneuropathy; ME, medial epicondyle; CSAmax, maximum CSA; SR, swelling ratio (CSAmax/CSA_D4).

Discussion

In the present study, ultrasonographic evaluations performed at 1-cm intervals were conducted to investigate the changes in the CSA of the ulnar nerve around the elbow with the aim of identifying UNE_sc in patients with diabetes. In the absence of electrophysiologic DPN, the UNE_e group demonstrated greater swelling than the electrophysiologically normal group without UNE_e, especially near to the ME (P1, ME, and D1). Conversely, in the presence of DPN, no significant swelling differences were identified between the DPN and DPN+UNE_e groups. These results reflect that ulnar nerve swelling can be induced by the UNE_e and DPN simultaneously. They also suggest that DPN-induced ulnar nerve swelling can limit further enlargement of the ulnar nerve from UNE_e, although the exact pathophysiology remains unclear. Although the examined nerve was different, the results of the present study resemble those of a prior study reporting that the distal median nerve CSA did not differ significantly between those with and without superimposed carpal tunnel syndrome in patients with DPN [15]. These findings imply that a nerve swelling at a common entrapment region in a patient with DPN can be a consequence of DPN, not just entrapment neuropathy.

The present study also revealed that, in the absence of UNE_e, patients with DPN (DPN group) had more swelling at the ME level than did patients without DPN (normal group). These findings are similar to those of a previous study on the upper extremity nerves in patients with diabetes, which reported that the CSAs of the ulnar nerve were larger at the ME level in patients...
with DPN than in those with diabetes without DPN [16]. This implies that peripheral nerve swelling progresses more in the entrapment region of the nerve when DPN is present and reflects the increased susceptibility of patients with DPN to entrapment neuropathy development [17]. Moreover, the ulnar nerve-swelling ratio was significantly greater in the UNE_e group than in the DPN group. This finding is because DPN influences nerve swelling at non-compressive sites (e.g., D4) than UNE_e does.

Although the precise pathophysiological implications of nerve enlargement in DPN have not been fully elucidated, it has been suggested that increased sorbitol levels in patients with diabetes may contribute to increased intracellular hydration, which subsequently affects swelling of the nerves [18]. Furthermore, the ulnar nerve may become enlarged owing to repetitive undetected trauma and external compression, which can increase endoneurial edema, perineural thickening, and vascular changes in the vasa nervorum, causing nerve ischemia [19,20]. Simon et al. [21] reported that even in healthy individuals, the ulnar nerve was larger at the ME level than at more proximal and distal sites of the nerve. This pattern of sonographic change was also observed in the present study, although the extent of nerve swelling at the ME was different among the groups. The authors of the previous study hypothesized that the precipitation of symptomatic UNE can reflect an exacerbation of an existing asymptomatic ulnar nerve lesion [21]. Moreover, diabetes can increase the susceptibility of the ulnar nerve to injury [22,23]. Therefore, early detection of UNE_sc in patients with diabetes can be important for preventing symptomatic UNE. For diagnosing UNE_sc in the present study, the cut-off value of the CSAm of patients without DPN was 9.85 mm². This value was within the range of previously published cut-off values of CSAm (8.3 to 11.0 mm²) for diagnosing symptomatic UNE from ultrasonographic studies [7–9]. This suggests that CSAm in patients with diabetes without DPN is mainly influenced by UNE that is similar in healthy controls [16].

This study has several limitations. First, a healthy control group was not included. Moreover, because the presence of DPN was determined by electrophysiological criteria, it is likely that patients with neuropathic symptoms such as small fiber neuropathy were not included in the DPN group. However, because electrophysiological diagnosis is an objective indicator of neurologic morbidity, it can serve as a reference. Finally, there is a lack of definite diagnostic criteria for UNE in patients with DPN; thus, subsequent electrodiagnostic and ultrasonographic studies that include patients with definite UNE symptoms of DPN are required.

**Conclusion**

Ultrasoundographic evaluations of ulnar nerve swelling are useful for diagnosing UNE_sc in patients with diabetes, although the ability to diagnose UNE based on ultrasonographic abnormalities such as nerve swelling appears to be limited in patients with DPN. Our data supported that a patient with diabetes should be diagnosed with UNE_sc when the CSAm of the ulnar nerve is greater than 9.8 mm² around the ME or when the swelling ratio is greater than 1.4. In such cases, education and treatment to prevent progression to symptomatic UNE is recommended.

**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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