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The feasibility of using high frequency ultrasound to assess nerve ending neuropathy in patients with diabetic foot

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ABSTRACT

Objectives: The nerve ending problem is one of the major causes for diabetic feet. In this work, we explored the feasibilities of using high frequency ultrasound (US) in nerve ending problem evaluation for patients with diabetic foot.
Methods: The endings of the medial branch of deep peroneal nerves (mbDPN) were interrogated by US, and the nerve conduction characters were studied in a cohort of 19 clinically diagnosed diabetic feet patients and a control group of healthy volunteers.
Results: Distinct echoic appearances were consistently detected between the mbDPN nerves of diabetic feet patients and healthy volunteers. In healthy volunteers, hypoechoic bands were readily observed at the anatomical locations of mbDPNs. However, these hypoechoic bands of the mbDPNs were not clear in the diabetic feet patients, and the surfaces of the mbDPNs appeared obscure and irregular in these patients relative to those of healthy volunteers. In addition, the US echoes of mbDPN in patients with diabetic feet were more heterogeneous than those in healthy volunteers. The mean diameters of mbDPNs were 1.3 ± 0.4 mm in patients with diabetic foot and 0.8 ± 0.2 mm in the control group ($P < 0.05$). Finally, results from the nerve conduction studies (NCS) showed abnormalities in patients with diabetic feet syndrome.
Conclusion: High frequency US can be a useful modality for evaluating nerve ending problems in diabetic feet patient; and the mbDPN enlargement, obscurity, surface irregularity and heterogeneity in echo can serve as the markers indicating nerve ending problems in the diabetic feet patients under ultrasound interrogation.

1. Introduction

Diabetic foot ulcers affect 5–15% of the patients with diabetes [1] and cause the patients enormous physical, emotional, and financial burdens. Reports showed that almost 80% of amputations in patients with diabetes were preceded by foot ulcers [2]. Simple tests such as monofilament, tuning fork, vibration perception threshold determination, ankle reflexes, and pinprick sensation alone or in combination have been studied and shown useful for identification of patients at risk [3]. The diagnostic principle of conventional method for detecting diabetic neuropathy is based primarily on characteristic symptoms and is confirmed with nerve conduction studies (NCS), which are time-consuming, relatively invasive. Particularly, repeated evaluations, in these cases, have been correlated to poor patient tolerance. When it comes to the nerve conduction studies, albeit well standardized, they are large limited to the evaluation of the largest nerve fibers and cause too much discomforts to patients that, sometimes, they dissuade patients from serial evaluations.

Other than the before mentioned diagnostic techniques, the state-of-the-art imaging modalities were also been explored in the diagnosis of diabetic neuropathy. It has been shown that under

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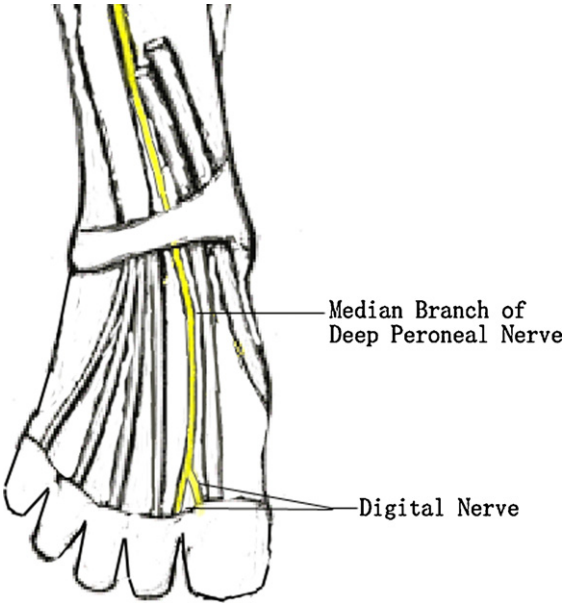

Fig. 1. Cartoon shows that the anatomy of the mbDPN is relatively straight.

magnetic resonance imaging (MRI), an elevated intraneural T2-weighted signal of the median nerve (MN) [4], possibly related to intranervous edema, was found in symptomatic patients. In recent years, US were also investigated to study several disorders, including carpal tunnel syndrome, of the peripheral nerves and has been shown to reduce the discomforts in patients.

Many of the available literatures focuses on the median nerve neuropathy at the carpal tunnel level [5] or the tibial nerve neuropathy at the tarsal tunnel level [6], and the median nerve (MN) and the tibial nerve (TN) are relatively bigger among the peripheral nerves. Inevitably, most of the non-invasive imaging studies of peripheral nervous systems has been biased focusing on the MN [7] or the TN [8] of the diabetic patients. Recent evidences have shown that the enlargement of MN [7] or TN [8] found in diabetic patients was related to the progress of diabetes; and the nerve ending [9] and microcirculation [10] problems were thought to be the causes for diabetic feet. However, to the best of our knowledge, no attention has been given in the literature to the non-invasive imaging evaluation of the nerve ending damages of the diabetic feet patients.

With the rapid development of high frequency ultrasound, the very small nerves close to the nerve endings, such as digital nerve [11] and palmar cutaneous nerve [12], could be clearly observed by high-resolution ultrasound.

The goals of this study were to (1) explore the potential value of high-resolution ultrasound for evaluation of the medial branch of deep peroneal nerve (mbDPN) of diabetic feet patients, and (2) determine whether the abnormalities of the nerve branch close to the nerve ending can serve as the diagnostic signatures for nerve ending problems in patients with diabetic foot. Our deep interest in imaging the mbDPN was prompted by two rationales. First, it is the simple anatomy of mbDPN, which is relatively straight, and allows the easy tracking by US. This rationale is supported by our preliminary results (Fig. 1). Second, in one study involving 169 patients with diabetes, common peroneal motor nerve conduction velocity was found to be the best and the only independent predictor for new foot ulceration within a period of 6 years compared with monofilament testing, vibration perception threshold (VPT) measurement, and temperature perception threshold measurement [13].

2. Materials and methods

2.1. Patients

One experienced sonographer (Dr. Ping Zhang) examined a cohort of 19 clinically diagnosed diabetic feet patients [12 females and 7 males; age range, 56–79 years; height, 150–170 cm; disease duration range, 18–35 years] and a control group of healthy volunteers matched for sex, age and height [12 females and 7 males; age range, 56–83 years; height, 155–175 cm]. There were not any diabetes history or other clinically diagnosed nerve problems among these healthy volunteers. There were no significant differences in age, sex and height between the two groups ($P > 0.05$).

The diagnosis of diabetic feet was based on established criteria [2]. All patients had skin ulcer on the feet and sensory disturbances (numbness) or weakness in their feet. The study protocol was approved by the ethical committee of Second Affiliated Hospital of Chongqing Medical University, and written informed consent was obtained from all patients and controls subjects.

2.2. US studies

US examination of the medial branch of deep peroneal nerve (mbDPN) was performed with a digital scanner equipped with a broadband high-frequency (14–6 MHz) linear transducer (L14-6s, Mindray Co., Shenzhen, China). The imaging depth was 1.8 cm, the Dynamic range (DR) was 90 dB and Mechanic Index (MI) was 0.2. The diameters of the mbDPNs (D_mbDPN) acquired on longitudinal-sectional US images instead of the nerve cross-sectional areas (CSA) acquired on transverse-sectional US images were used to make the diagnosis since the edge of the longitudinal section of the nerve was relatively clear enough for diameter measurement, while the obscurity of the edge of the transverse section of the nerve in patients with diabetic foot prohibited the acquirement of CSA measurement. The echo shape, surface and inner fascicular bundles of the nerves were depicted. In each study, the mbDPN was evaluated at the zones 1 cm proximal to where the nerves divide into the two digital branches. The diameters of 38 mbDPN nerves (two per subject) were imaged in the diabetic feet patients and same numbers were imaged in the healthy volunteers. To prevent the introduction of interpersonal variability, all US studies were performed by the same radiologist (Dr. Ping Zhang) who is very experienced in musculoskeletal US, and the recorded images were blindly analyzed by two experienced radiologists (Dr. Zhigang Wang and Dr. Haitao Ran) independently. The mean value for the associated values were calculated and included in the results.

2.3. Neurophysiologic examination

Electrophysiologic Examinations Routine NCS were performed with conventional procedures with a standard electromyography system (NDI-92X, Chengdu Senchuan Technical Co., Chendu, China). All electrophysiological NCS of motor and sensory function of the peroneal nerve were performed bilaterally in all diabetic feet patients. Values of the distal motor and sensory latencies, motor and sensory nerve conduction velocities, and amplitude of evoked potentials were adjusted according to the patients' ages[14,15], and the nerve was examined as described elsewhere[16].

2.4. Statistical analysis

Statistical analysis was performed using the Mann–Whitney U test for unpaired data to compare patients and controls, as well as between patient groups. Values were expressed as mean ± SD (standard deviation). $P < 0.05$ is considered statistically significant.