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Sonographic features of peripheral nerves at multiple sites in patients with diabetic polyneuropathy

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ABSTRACT

Objective: Diabetic polyneuropathy (DPN) is one of the major complications of diabetes mellitus. Ultrasound has been frequently used for evaluation of peripheral nerves. However, there are few studies that have evaluated multiple peripheral nerves in DPN. In this study, ultrasonographic features of multiple peripheral nerves in upper and lower extremities of DPN patients were investigated and compared with those of healthy controls.

Methods: This study was a case–control study that enrolled 20 patients with confirmed diagnosis of DPN and 20 healthy controls. The ultrasonography was performed on the sural, tibial, fibular, sciatic, median, ulnar, radial, and musculocutaneous nerves. Nerve cross-sectional area (CSA) was measured at multiple points for each peripheral nerve. The CSAs were compared between DPN and control groups, and analyzed in relation to the clinical characteristics and electrophysiologic findings.

Results: The CSAs were significantly larger in the DPN group for sural nerve, fibular nerve at the fibular head level, median nerve at the carpal tunnel and mid-humerus level, ulnar nerve at the cubital tunnel outlet and mid-humerus level, and radial nerve at the spiral groove. The CSAs of sural nerve, tibial nerve and median nerve were significantly correlated with electrophysiologic findings. The sural nerve CSA revealed significant correlation with HbA1c.

Conclusions: These results suggest that the ultrasonography can provide useful information in diagnosis and evaluation of DPN.

1. Introduction

The number of diabetic patients has increased to more than 180 million people worldwide (Wild, Roglic, Green, Sicree, & King, 2004). Diabetic polyneuropathy (DPN) is a major complication of diabetes mellitus, and the prevalence of DPN has been estimated to be from 35% to 45% of all diabetic patients. DPN causes peripheral nerve dysfunction and is associated with foot ulceration, gangrene, and Charcot joint. The neuropathy can be silent and undetected, and thus early diagnosis of DPN is important to prevent related complications. The diagnosis of DPN is based on clinical symptoms and signs, which are confirmed by nerve conduction study (NCS).

Ultrasonography is a painless, noninvasive procedure that allows real-time inspections of abnormal findings, such as space occupying lesions or synovitis (Klauser et al., 2010; Walker, 2004). Peripheral nerve ultrasound has been frequently used for a diagnosis of neuromuscular disorders, such as carpal tunnel syndrome and ulnar neuropathy at the elbow (Beekman & Visser, 2003; Beekman, Visser, & Verhagen, 2011; Smith, O'Neill, Parasu, & Finlay, 2009; Volpe et al., 2009). There are some reports of sonographic evaluation of peripheral nerve in diabetic patients, which examined limited number of nerves. These studies traced nerve cross-sectional area (CSA) at vulnerable sites to the compressive neuropathy, such as median nerve at the carpal tunnel, tibial nerve at the level of posterior medial malleolus, and found that the CSAs of peripheral nerves were larger in patients with DPN than those of controls (Watanabe et al., 2009; Watanabe et al., 2010). In another study, however, ultrasonographic measurements of lower extremity peripheral nerve CSA did not significantly differ between DPN patients and controls (Hobson-Webb, Massey, & Juel, 2013). So far, there are no studies which have performed ultrasonography on multiple nerves and at multiple sites in DPN patients.

The aim of this study is to investigate the ultrasonographic features of multiple peripheral nerves in patients with DPN. Thus, we have performed the ultrasonography on several peripheral nerves at multiple sites in upper and lower extremities and compared the findings between DPN patients and healthy controls.

Conflicts of interest: None.

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2. Materials and methods

2.1. Subjects

This study was designed as a cross-sectional case control study. Twenty diabetic patients who were diagnosed with DPN and 20 healthy volunteers were enrolled in this study. The inclusion criteria for case group were as follows; age ≥ 18 years, type 2 diabetes mellitus and confirmed diagnosis of DPN. The diagnosis of DPN was conducted by a combination of neuropathic symptoms and/or signs plus abnormal electrodiagnostic studies, according to the recommendations of the American Academy of Electrodiagnostic Medicine (AAEM) (England et al., 2005). The neuropathic symptoms are either sensory symptoms (numbness, burning, prickling paresthesias, dysesthesias, and allodynia) or motor symptoms (distal muscle weakness or atrophy), and the neuropathic signs include abnormalities of sensory (distal sensory decrease or absence), motor system (distal weakness and muscle atrophy), or tendon reflexes (absent or decreased ankle deep tendon reflex). The healthy control group was matched to case group on age and sex, and consisted of subjects without diabetes mellitus, and history of peripheral neuropathy. General baseline characteristics of both groups, such as age, height, weight, body mass index (BMI), disease duration, and glycosylated hemoglobin (HbA1c) levels, were recorded.

In both groups, subjects who had any clinical and electrophysiological evidence of entrapment neuropathy (such as carpal tunnel syndrome, ulnar neuropathy), polyneuropathy other than the DPN (such as inflammatory neuropathy, hereditary neuropathy, metabolic neuropathy), or traumatic nerve injury were excluded.

This study was approved by the institutional review board at Korea University Guro Hospital (Seoul, Korea), and written informed consent was obtained from all participants.

2.2. Electrodiagnostic examinations

NCS was performed for all patients with diabetes using a Nicolet Viking Select System (Nicolet Biomedical Inc. Madison, USA) on both lower and upper extremities with skin surface temperatures of ≥ 30 °C (legs) and ≥32 °C (arms). Each sensory NCS was performed for the sural nerve, median nerve, and ulnar nerve. Motor NCS was performed for the fibular nerve, tibial nerve, median nerve, and ulnar nerve. The F-wave latencies were measured in all examined motor nerves, and the H-reflex study was performed in both sides of the leg. The AAEM definition criterion for electrodiagnostic confirmation of distal symmetric polyneuropathy is an abnormality of any attribute of nerve conduction in two separate nerves, one of which must be the sural nerve (England et al., 2005).

2.3. Sonographic examinations

Sonographic examinations were performed with an HD15 ultrasound system (Philips Ultrasound Inc., Bothell, Washington, USA) using a 7–12 MHz linear array transducer by a single examiner who had experience of more than 10 years in musculoskeletal ultrasonography. Cross-sectional areas (CSAs) of peripheral nerves were measured by direct tracing just inside the hyperechoic rim of each nerve. At each site, the nerve CSA was measured three times to increase reproducibility and the mean value was used for analysis. To prevent overestimation of the nerve CSA by inclusion of blood vessels, the color Doppler mode was used before nerve tracing.

The transducer was placed on skin with minimal pressure perpendicularly to the nerve being measured to minimize anisotropy. Most of peripheral nerves were traced from distal to proximal directions. The measuring points were defined by anatomic landmarks or clinically important points: for the sural nerve at calf (just before the point which split from small saphenous vein, Fig. 1.A); for the tibial nerve at posterior knee (1 cm distal to branching from sciatic nerve), mid-tibia (midpoint between the medial condyle of the tibia and the tip of medial malleolus), ankle (at the level of medial malleolus); for the fibular nerve at popliteal fossa (1 cm distal to branching from sciatic nerve) and fibular head (Fig. 1.B); for the superficial fibular nerve, at lower third of the leg (point at which the nerve pierces the deep fascia); for the sciatic nerve at proximal thigh (10 cm proximal from branching point to the common fibular nerve and tibial nerve) and mid-thigh (1 cm proximal from branching point of the sciatic nerve); for the median nerve at carpal tunnel inlet (at the scaphoid–pisiform level, Fig. 2A), midpoint of the forearm (between the flexor digitorum superficialis and flexor digitorum profundus muscle), antecubital fossa (beside the brachial artery to be just proximal to the pronator teres), and mid-humerus (runs with the brachial artery, Fig. 2B); for the ulnar nerve at wrist (at the scaphoid–pisiform level), forearm (just before the point which split from ulnar artery), cubital tunnel outlet (between the two heads of the flexor carpi ulnaris muscle, Fig. 2C), inlet (just proximal to the medial epicondyle), and mid-humerus (Fig. 2D); for the radial nerve at spiral groove (courses with the deep brachial artery and vein between the triceps brachii and humerus) and antecubital fossa (just before branching to the superficial radial nerve and posterior interosseous nerve); and, for the musculocutaneous nerve at proximal humerus (between the long and short heads of the biceps brachii and coracobrachialis).

2.4. Statistical analysis

Data were analyzed by using SPSS (version 20.0) software. The Kolmogorov–Smirnov distance method was used for analysis of normal distribution. The independent t-test was performed to

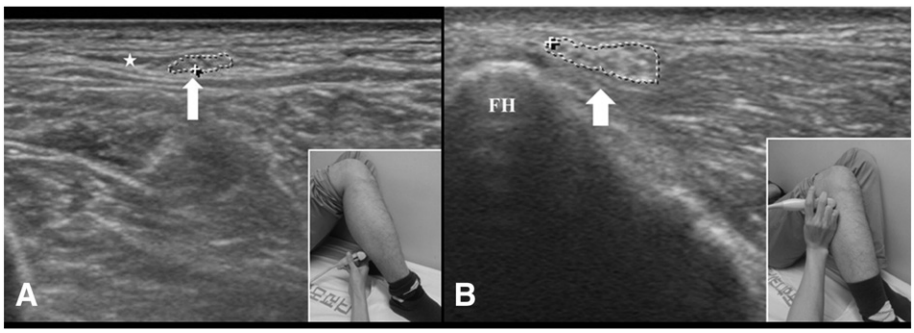

Fig. 1. Sonographic findings of the lower extremity nerves in a patient with DPN. (A) The sural nerve (arrow) at the calf is observed lateral to the small saphenous vein (star). (B) The common fibular nerve (arrow) is observed at the fibular head. FH; fibular head.