Atrophy of Foot Muscles

A measure of diabetic neuropathy

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OBJECTIVE — Diabetic neuropathy is a length-dependent process that leads to reduced muscle strength and atrophy of leg muscles in some patients. We hypothesized that intrinsic foot muscles are atrophied in diabetic neuropathy and that the degree of atrophy is a measure of motor dysfunction closely related to the neuropathic process.

RESEARCH DESIGN AND METHODS — Consecutive cross-sectional magnetic resonance images of the nondominant foot were obtained for stereological determination of the total volume of the intrinsic foot muscles (VFM) in 23 long-term diabetic patients with (n = 15) and without (n = 8) chronic neuropathy and in 23 matched healthy nondiabetic control subjects. Based on clinical examination, nerve conduction studies, and quantitative sensory examination, a neuropathy rank-sum score was calculated for each patient.

RESULTS — Total VFM was 86 ± 52, 165 ± 34, and 168 ± 42 cm³ in neuropathic patients, nonneuropathic patients, and healthy control subjects, respectively (P < 0.001). There was a close inverse relationship between the neuropathy rank-sum score and the VFM (r = −0.75, P < 1 × 10⁻⁵).

CONCLUSIONS — Total volume of the foot muscles is halved in patients with diabetic neuropathy. Atrophy of foot muscles is closely related to the severity of neuropathy and reflects motor dysfunction.

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Abbreviations: MRI, magnetic resonance imaging; VFM, volume of the intrinsic foot muscles.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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A 256 × 256 matrix and two excitations were used. The magnetic resonance images were converted to digital pictures for analysis on a PC (Chameleon; Olympus). The identity of the magnetic resonance images was blinded to the observers. Within the muscle compartments, an upper level of signal intensity for muscle tissues was defined. Signal intensities above this level were comparable with signal intensities of fat tissues, allowing a separation of muscle tissues from “nonmuscle tissues” within the muscle compartments. Muscle fascia, tendons, and blood vessels were excluded. At each image, the cross-sectional area of all muscles was estimated by a single observer using a stereological point-counting method as described previously (3,5). The total volume of striated muscle (in cubic centimeters) was calculated by multiplying the distance between the sections by the total cross-sectional area, the first section being randomly placed within the first interslice 10-mm interval. For further analysis, the volume for each patient was expressed as a percentage of the value of the individually matched control subject.

All patients were evaluated clinically according to a neuropathy symptom score (6) and a neurological impairment score (7). Motor nerve conduction velocity and response amplitudes were determined for the dominant median and nondominant peroneal nerve using an electromyograph (Dantec Counterpoint) and standard methods. Vibratory perception thresholds were evaluated at the dominant index finger pulp and at the nondominant dorsum of the great toe using forced-choice techniques (Case IV; WR Medical Electronics). A neuropathy rank-sum score was calculated for each patient based on the findings of the neuropathy symptom score, neurological impairment score, vibratory perception threshold test, and motor nerve conduction velocity, a high score reflecting severe nerve dysfunction. The minimal criteria for diabetic neuropathy were adopted and

Figure 1—Total volume of all foot muscles in 15 type 1 diabetic patients with neuropathy, in 8 nonneuropathic type 1 diabetic patients, and in 23 nondiabetic healthy control subjects (A). Values are means ± SD. Below is a cross-sectional magnetic resonance image at the metatarsal level of the foot in a neuropathic patient (B), in a nonneuropathic patient (C), and in a nondiabetic control subject (D) showing that the neuropathic diabetic patient has a substantial reduction of muscle tissues. *P < 0.001, neuropathic patients compared with nonneuropathic patients and nondiabetic control subjects.
Atrophy of foot muscles in diabetic neuropathy

Figure 2—The relationship between the neuropathy rank-sum score and the volume of foot muscles in all diabetic patients given as a percentage of their individually matched control values ($r = -0.73, P < 0.0001$).

RESULTS — The diabetic patients had a median neurological impairment score of 7 (range 0–36). According to the minimal criteria for diabetic neuropathy, 15 and 8 patients were defined as neuropathic and nonneuropathic, respectively. Patients with and without neuropathy had a diabetes duration of 30 (range 21–38) and 27 years (range 16–35), respectively ($P = NS$). Thirteen patients had symptoms of peripheral neuropathy. All had sensory complaints, with paresthesia and/or loss of sensation in the lower extremities. In addition, two patients had neurogenic pain, and six men complained of erectile dysfunction. Only three patients had motor symptoms, all of which involved the ankles. Motor nerve conduction velocity of the median and peroneal nerves was 48.2 m/s (range 41.3–61.0) and 37.1 m/s (range 20.8–45.6), respectively. In three patients, no response could be obtained from the extensor digitorum brevis muscle.

In Fig. 1, volume of the intrinsic foot muscles (VFM), together with an illustrative example of a cross-section of the foot, is shown for each of the three groups. It appears that the VFM of diabetic patients with neuropathy is one-half that of control subjects and also one-half that of diabetic patients without neuropathy. Expressed relative to their individually matched control subjects, the median VFMs were 49% (range 11–95) and 106% (range 70–130), respectively ($P < 0.01$). In the combined group of diabetic patients with and without neuropathy, there was a close relationship between the neuropathy rank-sum score and the VFM (Fig. 2). Furthermore, the VFM was closely related to the amplitude of the compound muscle action potential of the peroneal nerve ($r = 0.71, P < 0.001$), whereas no statistically significant relation was found between the VFM and the motor nerve conduction velocity of the peroneal nerve ($r = 0.42, P = 0.06$). No relationship was found between the VFM and duration of diabetes ($r = 0.19, P = 0.39$).

CONCLUSIONS — Applying MRI and a stereological point-counting method, we found that total VFM is halved in diabetic patients with chronic neuropathy as compared with that of nonneuropathic diabetic patients and nondiabetic control subjects. In the most advanced cases of neuropathy, volume was <20% of that of individual control values. Our hypothesis that atrophy of intrinsic foot muscles is a measure closely reflecting motor dysfunction in diabetic neuropathy is supported by the close relationship between degree of atrophy and degree of neuropathy based on clinical, electrophysiological, and quantitative sensory examinations.

Loss of sensation, toe abnormalities, and foot ulcers are easily recognized at the clinical examination of a diabetic foot. In contrast, evaluation of the motor system is hampered by the inability to evaluate the strength of foot muscles and difficulties estimating muscle mass. In a previous study of diabetic patients, we have found a very close relationship between the volume of muscles and strength of ankle dorsal and plantar flexors ($r$ values >0.8) (3). This clearly indicates that determination of muscle mass reflects motor function. In healthy subjects, $r$ values between muscle strength and total muscle volume exceeded 0.85, a slightly closer relation than the one between muscle cross-sectional area and muscle strength (4).

Volume of striated muscles in the foot was determined using a stereological point-counting method (8). This method provides an unbiased estimation of the volume of any structure of interest within an object pending unequivocal definition of the structure, irrespective of the form of the object. In this study, none of the patients had any significant foot or toe deformity. Therefore, a similar orientation of the cross-sectional scans is obtained in the two groups, thereby providing representative views of the striated muscles in both patients and control subjects.

Recently, using MRI in a group of neuropathic patients, Bus et al. (9) observed considerable loss of small foot muscles compared with nondiabetic control subjects. Their study did not include a group of nonneuropathic diabetic patients. We found completely preserved muscle volume in long-term diabetic patients without neuropathy. Despite differences in patient selection and techniques for quantification of muscle mass, the finding of Bus et al. is in accordance with the present observation, emphasizing that diabetic patients with chronic neuropathy have considerable loss of striated muscle in the feet. Atrophy of foot muscles is believed to result in altered architecture of the foot and can thereby cause toe abnormalities (clawing, hammering) (10). Together with sensory loss, this will lead to callus formation and ultimately to foot ulcers. Interestingly, in the study by Buss et al. some patients had atrophy without toe deformities, whereas the opposite was
not the case. In our study, no patient had any significant foot or toe deformity. This supports the notion that loss of foot muscles precedes development of toe abnormalities.

Ultrasoundography has been applied more frequently than MRI in studies of the diabetic foot. An inverse relationship has been found between the plantar fascia thickness and the dynamic foot pressure (11), and changes in the structure of the plantar fascia seem to influence the joint mobility of the first metatarsophalangeal joint (12). No ultrasonographic study has been performed to quantify the amount of striated muscles in the diabetic foot. An inverse relationship between the plantar fascia thickness and the dynamic foot pressure (11), and changes in the structure of the plantar fascia seem to influence the joint mobility of the first metatarsophalangeal joint (12). No ultrasonographic study has been performed to quantify the amount of striated muscles in the diabetic foot.

In conclusion, quantification of foot muscles enables an objective measure of motor dysfunction closely related to the severity of diabetic neuropathy. Monitoring of VFM may be helpful in treatment trials. However, larger-scaled prospective studies are needed to elucidate the relevance of quantitating foot muscle atrophy in relation to other neuropathic manifestations. Because MRI is a relatively time-consuming and expensive technique, an easier-to-perform evaluation of muscle volume is needed.

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References