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Intrinsic foot muscle deterioration is associated with metatarsophalangeal joint angle in people with diabetes and neuropathy

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ABSTRACT

Background: Metatarsophalangeal joint deformity is associated with skin breakdown and amputation. The aims of this study were to compare intrinsic foot muscle deterioration ratios (ratio of adipose to muscle volume), and physical performance in subjects with diabetic neuropathy to controls, and determine their associations with 1) metatarsophalangeal joint angle and 2) history of foot ulcer.

Methods: 23 diabetic, neuropathic subjects [59 (SD 10) years] and 12 age-matched controls [57 (SD 14) years] were studied. Radiographs and MRI were used to measure metatarsophalangeal joint angle and intrinsic foot muscle deterioration through tissue segmentation by image signal intensity. The Foot and Ankle Ability Measure evaluated physical performance.

Findings: The diabetic, neuropathic group had a higher muscle deterioration ratio [1.6 (SD 1.2) vs. 0.3 (SD 0.2), $P < 0.001$], and lower Foot and Ankle Ability Measure scores [65.1 (SD 24.4) vs. 98.3 (SD 3.3) %, $P < 0.01$]. The correlation between muscle deterioration ratio and metatarsophalangeal joint angle was $r = -0.51$ ($P = 0.01$) for all diabetic, neuropathic subjects, but increased to $r = -0.81$ ($P < 0.01$) when only subjects with muscle deterioration ratios >1.0 were included. Muscle deterioration ratios in individuals with diabetic neuropathy were higher for those with a history of ulcers.

Interpretation: Individuals with diabetic neuropathy had increased intrinsic foot muscle deterioration, which was associated with second metatarsophalangeal joint angle and history of ulceration. Additional research is required to understand how foot muscle deterioration interacts with other impairments leading to forefoot deformity and skin breakdown.

1. Introduction

In the United States, over 60% of non-traumatic lower extremity amputations occur in individuals with diabetes, totaling over 65,000 amputations annually (CDC, 2011). A major risk factor is neuropathic plantar ulceration, which precedes amputation over 80% of the time (Lavery, 2012). Previous studies have shown that foot deformities, and the resulting changes in plantar pressure distribution, are major factors leading to ulceration (Boyko et al., 1999; Reiber et al., 1999; Robertson et al., 2002; Van Schie et al., 2004). A common forefoot deformity associated with high plantar pressures and skin breakdown is metatarsophalangeal joint (MTPJ) deformity (Boulton et al., 2008; Boyko et al., 1999; Robertson et al., 2002; Van Schie et al., 2004). The high plantar pressures are associated with a prominent metatarsal head that becomes exposed to plantar forces because of MTPJ hyperextension (Ahroni et al., 1999; Bus et al., 2005). Unfortunately, the causal factors of this deformity are not fully understood. Understanding the etiology of foot deformities would help improve interventions and develop preventative measures to affect change in the impairment cascade of deformity, ulceration, and amputation.

Potential risk factors for acquired MTPJ deformity in people with diabetes mellitus and peripheral neuropathy (DMPN) include intrinsic foot muscle (IFM) deterioration, poor fitting footwear, ruptures in the plantar fascia or the plantar plates of the MTPJ, and decreased ankle range of motion (Boulton, 1996; Bus et al., 2009; Kwon et al., 2009). IFM deterioration is commonly believed to be a factor in the development of MTPJ hyperextension deformities because without the flexion force of the IFMs as an antagonist to the extensor digitorum longus, there would be a muscular imbalance that would destabilize these joints. Specifically, the proximal phalanx will hyperextend as tendon and ligament deformation occurs on the plantar surface of the MTPJ, resulting in a prominent metatarsal head (Fortin and Myerson, 1995; Mizel and Yodlowski, 1995). The few studies that have investigated

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the relationship between IFM deterioration and deformity have shown conflicting results on the association, or lack thereof, between IFM deterioration and MTPJ hyperextension (Bus et al., 2002, 2009; Robertson et al., 2002; Van Schie et al., 2004). None of the studies have used a quantitative volumetric measure of intermuscular adipose tissue (IMAT) to calculate IFM deterioration; a measure that would allow researchers to better understand how IFM deterioration contributes to joint deformity.

The aims of this study were to 1) compare IFM deterioration and physical performance in participants with DMPN to control participants, 2) determine the associations between measures of IFM deterioration, second MTPJ hyperextension, and physical performance, and 3) determine how these associations differ between individuals with and without a history of ulceration. Our hypotheses are that 1) the DMPN group will have increased IFM ratios (ratio of IMAT to lean muscle volume) compared to controls; 2) IFM ratios will be correlated with the severity of the measure of MTPJ hyperextension and inversely correlated with the measure of physical performance; and 3) those with a history of ulcers will have larger IFM ratios, and more severe MTPJ hyperextension and physical performance impairment.

2. Methods

2.1. Subjects

Thirty-five adult subjects participated in this study [22 male, 13 female; age 59 (SD 11) years], who were recruited from an ongoing study and from whom informed consent was obtained. The complete demographic summary is shown in Table 1. Twenty-three of the subjects had DMPN [age 59 (SD 10) years], meeting the inclusion criteria of having type 1 or 2 DM and the inability to sense a 5.07 Semmes-Weinstein monofilament on at least one location on the plantar foot (Diamond et al., 1989). Severity of peripheral neuropathy also was assessed using vibration perception threshold assessment with a biothesiometer at the plantar great toe and first metatarsal head; a 128 Hz tuning fork on the first metatarsal head; and joint position sense tested at the interphalangeal joint of the great toe and at the ankle joint. Taken together, these measures indicate that the DMPN subjects had a relatively severe sensory neuropathy (Table 1). Eleven DMPN subjects had medial column deformity, assessed by meeting 2 of the following criteria: calcaneal eversion $\geq 5°$, medial longitudinal arch angle $<130°$, navicular height ≤ 24 mm, and medial column peak plantar pressure >29 N/cm^2 (Jonson and Gross, 1997; Menz and Munteanu, 2005). These subjects were selected to provide a spectrum of foot alignment angles. The remaining 12 control subjects [age 57 (SD 14) years] did not have a history of DM or PN, were able to sense the monofilament everywhere on the plantar foot, and were matched to the DMPN subjects by age, height, and weight. Exclusion criteria for all subjects were metal implants or pacemakers present, amputations to the lower extremity, and a weight greater than 181 kg (due to the weight limit on the MRI scanning table).

Table 1
Subject characteristics.

	Control (n = 12)	DMPN (n = 23)
Age (yrs)	57 (14)	59 (10)
Sex (male/female)	8/4	14/9
Type 1/type 2 DM	–	3/20
Duration of DM (yrs)	–	18 (10)
Vibration perception threshold — biothesiometer (L/R)		
Plantar great toe (V)	18 (12)/22 (15)	43 (13)/41 (13)
1st metatarsal head (V)	15 (9)/21 (15)	40 (14)/40 (13)
Vibration sense present — tuning fork (L/R)		
1st metatarsal head	12/12	6/7
Joint position sense present (L/R)		
Great toe	12/12	14/14
Ankle joint	12/12	20/23
History of ulceration	–	8
Medial column deformity	–	11
Target foot (L/R)	5/7	11/12
Height (cm)	174 (12)	173 (9)
Weight (kg)	108 (30)	109 (27)
BMI (kg/m^2)	35 (8)	36 (8)
HbA1c (%)	5.7 (0.3)	8.0 (2.1)

2.2. Image acquisition and data collection

Weight bearing foot and ankle lateral radiographs were taken of all subjects (Fig. 1A). The target foot for all subjects was the right foot unless the medial column deformity was present in the left. DMPN subjects with a left foot scan were then matched with a left foot scan in the control group. The radiographs were imported into iSite PACS software (Philips Healthcare Informatics, Foster City, CA), and the static foot alignment of second MTPJ angle was made to the nearest degree (Fig. 1A). Second MTPJ angle is defined as the angle between the longitudinal axis of the second proximal phalanx and the longitudinal axis of the second metatarsal parallel to the dorsal cortex.

The coronal plane MR images of all subjects were collected using a Siemens Magnetom Trio 3T scanner (Siemens Medical Systems, Malvern, PA). The subjects were positioned supine with the target foot perpendicular to the table. The foot was placed in a head coil to achieve the best signal to noise ratio (Commean et al., 2011). The following MR parameters were used for all 35 subjects: spin echo pulse sequence, TR/TE = 5360/38 ms, field of view = 140 mm, bandwidth = 181 Hz/pixel, 35 slices, coronal orientation, signal averages = 1, flip angle = 141°, matrix = 384 × 384, echo train length = 9, acquisition time ≈12 min, and voxel size 0.365 × 0.365 × 3.5 mm.

The region of interest for each subject was defined as the talonavicular joint to the tarsometatarsal joint. The talonavicular joint was defined as the most distal portion of the talus on the navicular, and the tarsometatarsal joint was defined as the articulation between the intermediate cuneiform and the second metatarsal bones. This region was selected because each subject had usable data in this region from an ongoing study focused on the midfoot and hindfoot; therefore the forefoot region was not included.

Methods to segment muscle and IMAT volumes from the IFMs in these images have been previously reported (Cheuy et al., 2013). IMAT is defined as the visible adipose tissue beneath the muscle fascia, between muscles, and within the muscle (Commean et al., 2011). Briefly, a program developed using MatLab (Mathworks, Natick, MA) produces a histogram of all voxel intensities from the inputted MR slice (Fig. 1B). In order to categorize the voxels into muscle and IMAT, an intensity threshold is calculated using a multiple Gaussian function fitting algorithm. The threshold corresponds to the minimum point between the maximum peaks of the two tissue types, as determined from the best-fit curve (Fig. 1C, red line). This is calculated on an individual subject basis, unique to each MR image. An edge detection algorithm allows for the segmentation of subcutaneous fat from the IFMs, where the second derivative of intensities determines the border between the subcutaneous fat and the IFMs (Cheuy et al., 2013; Commean et al., 2011). The same edge detection methods are used to define the IFM compartment as the region of interest, which is then separated into muscle and IMAT volumes as determined by the threshold calculated earlier (Fig. 1D,E). On an individual subject basis, the IFM deterioration (ratio of IMAT volume to lean muscle volume) of each MR slice was calculated and averaged over the region between the talonavicular and tarsometatarsal joints. The IFM ratio is a measure of muscle deterioration over the region of interest, and does not depend on the size of the IFM compartment. Total lean muscle and IMAT volume measures, however are dependent on foot size.

Physical performance was evaluated in each of the 35 subjects using the Activities of Daily Living (ADL) subscale of the Foot and Ankle Ability (FAAM) questionnaire. The FAAM is a reliable and validated self-report