Foot deformity in diabetic neuropathy. A radiobiological and biomechanical analysis

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Chapter 4

The pathogenesis of claw/hammer toe deformity in diabetic neuropathy

No evidence for the role of intrinsic muscle atrophy

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Submitted
Abstract

Clawing/hammering of the toes in the diabetic neuropathic foot is believed by many authors to be caused by an imbalance between the intrinsic and extrinsic toe muscles resulting from atrophy of the deep intrinsic muscles (i.e., interossei and lumbricals). Rupture or degeneration of the plantar aponeurosis and metatarsal-phalangeal joint capsule has also been suggested to play a role. The objective was to examine intrinsic and extrinsic toe muscle status and connective tissue structure in neuropathic patients with toe deformity and neuropathic controls without deformity using magnetic resonance imaging (MRI).

Coronal and sagittal plane images of the foot and transverse plane images of the lower leg were acquired using T1-weighted spin-echo MRI in nine neuropathic diabetic patients with claw/hammer toe deformity (experimental group) and nine matched neuropathic diabetic patients without deformity (control group). Atrophy of the intrinsic and extrinsic muscles and derived measures of muscle imbalance were assessed using a semi-quantitative 5-point atrophy scale. The lower-leg images were assessed for extrinsic muscle fibrosis. The plantar aponeurosis and joint capsule were also assessed from the foot images.

Mean (SD) intrinsic muscle atrophy score was 3.0 (1.1) for the experimental group and 2.6 (1.2) for the control group (not significantly different, \( P = 0.2 \)), and was not associated with deformity. Average atrophy scores for the extensor and flexor digitorum longus muscles were low and, together with the muscle imbalance ratios, not significantly different between groups. Fibrosis was absent in both extrinsic muscles. Plantar aponeurosis rupture was not diagnosed in any of the 18 feet. Joint capsule abnormalities were found in 4 experimental patients and in 2 controls (not significantly different).

Intrinsic and extrinsic muscle atrophy and muscle imbalance do not seem to distinguish neuropathic patients with toe deformity from matched patients without deformity. This suggests that the intrinsic and extrinsic muscles of the toes are not (exclusively) responsible for clawing/hammering of the toes. Abnormalities in plantar aponeurosis or joint capsule do not seem to have discriminative power either. These results challenge the present theories of claw/hammer toe deformity pathogenesis in the diabetic neuropathic foot, and provisionally suggest an idiopathic nature. An alternative hypothesis is presented in this study.
Introduction

Clawing or hammering of the toes is a common foot deformity in the population of patients with diabetes mellitus, with reported prevalence values of 32% and 46%. There are several theories that may explain why claw/hammer toe deformity develops. Ill-fitting footwear, in particular cramped toe boxes in high-heeled shoes, is a commonly reported external cause. Sequential sectioning of soft-tissue components at the metatarsal-phalangeal (MTP) joint in feet with clawing or hammering of the toes demonstrated that the release of the collateral ligaments resulted in the largest improvement towards a normally aligned toe, suggesting that pathology of these connective tissue structures may be responsible for toe deformity. More recently, Taylor et al. found rupture of the plantar aponeurosis (fascia) in diabetic subjects with hyperextended toes, and suggested that non-enzymatic glycosylation of the aponeurosis may render this structure less functional and capable of causing toe deformity.

However, the most commonly reported cause of toe deformity in diabetic patients is intrinsic muscle atrophy secondary to motor neuropathy leading to an imbalance between intrinsic and extrinsic muscles across the MTP and inter-phalangeal (IP) joints. The long extrinsic flexors have a greater mechanical advantage over the extensors at the IP joints and the extensors have a greater mechanical advantage over the flexors at the MTP joint. If the intrinsic muscles (i.e., the lumbricals and interossei) function correctly, they compensate for this by flexing the MTP joint while extending the IP joints. But when the intrinsic muscles are atrophic and overpowered by the extrinsic muscles, this stabilizing action is lost, resulting over time in clawing or hammering of the toes. Within this context, fibrotic contractures of the extrinsic muscles overpowering the intrinsic muscles may play a role, although this mechanism has been described in non-diabetic feet only. Despite numerous anecdotal reports and observational studies, experimental data to support this mechanical theory of claw/hammer toe pathogenesis does not exist. Recently, we found that intrinsic muscle atrophy does not necessarily imply claw/hammer toe deformity in the diabetic neuropathic foot. (Chapter 2) These findings do not, however, exclude the possibility that intrinsic muscle atrophy and abnormal extrinsic muscle status are permissive factors for the development of toe deformity.

A better understanding of the pathogenesis of claw/hammer toe deformity may be possible if the internal anatomical structures responsible for digital stabilization are examined within the same patient. These are the extrinsic and intrinsic muscles, the plantar aponeurosis, and the MTP joint capsule consisting of plantar plate and collateral ligaments. Magnetic resonance imaging (MRI) has evolved as the method of choice with which pathology in these soft-tissue structures in the foot and lower leg can be studied in-vivo.
(chapter 2) Therefore, the purpose of this study was to use MRI to examine these structures in a group of neuropathic diabetic patients with claw/hammer toe deformity and a matched group of neuropathic patients with normally aligned toes. Based on the above-mentioned prevailing theory of claw/hammer toe deformity pathogenesis, we hypothesized that there would be consistently larger degrees of intrinsic muscle atrophy and muscle imbalance in patients with toe deformity when compared with patients without deformity.

**Methods**

**Subjects**

Nine diabetic patients (5 men, 4 women) with distal symmetric polyneuropathy and claw/hammer toe deformity in, at least, the second or third digit of the foot (experimental group) and nine age- and gender-matched neuropathic diabetic patients with normally aligned toes (control group) participated. The presence of toe deformity was initially assessed clinically for recruitment purposes but eventually based on MRI analysis as described below. Five age-matched healthy subjects (3 men, 2 women) with normally aligned toes were included for reference purposes. One lower extremity per subject was studied to limit data collection time. This was the extremity with the deformed foot if the contralateral foot was not deformed or was randomly assigned, if not excluded by the criteria mentioned below. Distal symmetric polyneuropathy was assessed clinically and confirmed present in all patients by (1) abnormal vibration perception thresholds measured at the dorsal surface of the hallux in both feet using a Biothesiometer (abnormality according to 95% age-adjusted confidence intervals, e.g. >30 Volts for 55-year-old person)$^{2}$, and (2) the inability to sense the pressure of a 10-grams (5.07) Semmes-Weinstein monofilament at, at least, one of eight sites tested (6 plantar foot regions, dorsum of the foot and medial malleolus). Patient characteristics are summarized in Table 1.

In order to exclude congenital or external causes of toe deformity, the patients’ shoes were examined and patients in the experimental group were asked about the onset of their deformity and the fitting of their shoes in the past. Patients were excluded if their shoes were found to be too small in size for their feet, if they reported to have worn ill-fitting shoes in the past or if deformity was present before the onset of diabetes. For the same reason, patients with neuromuscular diseases or neurological problems other than diabetic polyneuropathy were excluded.$^9,^{11,18}$ Other exclusions were 1) age <40 or >65 years, 2) peripheral vascular disease, as determined by absent pedal pulses with an ankle-brachial index <0.75 or toe pressure <50 mmHg, 2) current ulceration, prior ulceration at the metatarsal heads, prior surgery or fracture in the lower extremity studied, 4) rheumatoid
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arthritis, lower-extremity amputation or Charcot neuro-osteoarthropathy, and 6) conditions precluding MRI assessment. None of the five healthy non-diabetic subjects had any known (history of) foot pathology.

Table 1. Baseline patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Experimental group (n = 9)</th>
<th>Control group (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.0 (7.3)</td>
<td>57.9 (6.0)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.75 (0.08)</td>
<td>1.73 (0.05)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>85.1 (13.8)</td>
<td>81.3 (10.8)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.6 (3.2)</td>
<td>27.2 (4.0)</td>
</tr>
<tr>
<td>Diabetes type (1/2)</td>
<td>5/4</td>
<td>7/2</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>34.1 (12.6)</td>
<td>30.3 (15.2)</td>
</tr>
<tr>
<td>HbA₁c (%)</td>
<td>7.6 (1.0)</td>
<td>7.9 (1.1)</td>
</tr>
<tr>
<td>Neuropathy duration (years)*</td>
<td>12.1 (5.5)</td>
<td>12.2 (8.9)</td>
</tr>
<tr>
<td>Vibration perception threshold (Volts)</td>
<td>35.6 (12.2)</td>
<td>36.3 (9.9)</td>
</tr>
<tr>
<td>Toe angle (degrees)</td>
<td>-20.3 (5.5)</td>
<td>-2.5 (7.1)*</td>
</tr>
<tr>
<td>Arch angle (degrees)</td>
<td>32.7 (7.4)</td>
<td>28.5 (7.7)</td>
</tr>
<tr>
<td>Arch index (%)</td>
<td>9.4 (7.3)</td>
<td>15.3 (10.8)</td>
</tr>
</tbody>
</table>

Data are means (SD) or numbers (n). *As derived from medical records or, when absent, estimated by the patient based on the first appearance of neuropathic symptoms.

* Significantly different from experimental group (P < 0.001)

All patients in the experimental group, except for one, had flexible toe deformity as opposed to rigid deformity since we believed that its pathogenesis could be best studied at an early stage of deformity where cause-and-effect issues may be less of a problem. In a rigid state, structural changes found in muscle and connective tissue may equally be a result of the deformity (due to disuse or overstrectching) as it may be a cause.

Procedures

A Siemens 1.5-Tesla Magnetom 63SP/4000 imager (Siemens, Erlangen, Germany) was used to acquire T1-weighted spin-echo series of the foot and lower leg. The subject lay supine with the foot or leg inserted into a circular polarized head coil. In a comfortable position at approximately 30 degrees plantar flexion, the foot was immobilized using padding material without affecting the natural configuration of the toes. The foot was imaged in a sagittal and coronal (axial) plane view, the lower leg in a transverse (axial) plane view. Two separate datasets, a distal and proximal, were acquired for the lower leg.
due to the limited field of view (FOV) of the coil used. For all images collected, repetition
time (TR) was 577 msec, echo time (TE) 17 msec, and slice thickness 3 mm. The sagittal
plane dataset of the foot was oriented parallel to the second metatarsal bone and consisted
of 19 slices acquired between the first metatarsal head medially and the fifth metatarsal
head laterally with FOV 256x256 mm, in plane resolution 512x512 pixels, and inter-slice
gap 0.9 mm (Figure 1A). The coronal plane dataset of the foot was oriented perpendicular
to the sagittal plane images and consisted of 20 slices collected between the proximal
phalanges distally and the cuneiform bones proximally with FOV 150x150 mm, resolution
256x256 pixels, and 0.9 mm inter-slice gap (Figure 1B). The lower-leg datasets were
oriented perpendicular to the long axis of the tibial bone in a coronal and sagittal view and
consisted each of 20 slices with FOV 200x200 mm, resolution 256x256 pixels, and inter-
slice gap 5 mm (Figures 1C and 1D). The distal lower-leg dataset included the ankle joint,
and the proximal dataset the knee joint. Total acquisition time was 45 minutes per subject.

Figure 1. Scout views with slice orientation for the acquired sagittal plane foot images (A), coronal plane foot images
(B), transverse plane images of the distal lower leg (C), and transverse plane images of the proximal lower leg (D).

Toe deformity was assessed non-weight bearing from the sagittal plane images using Agfa
IMPAX WEB1000 software (Agfa-Gevaert N.V., Mortsel, Belgium) by measuring the
angle between a line parallel to the sole of the forefoot and the bisector of the proximal
phalanx (named ‘toe angle’, negative values denoting extension); toe angles >13 degrees of
extension indicated deformity based on 95% normal limits from the neuropathic control
group presented in chapter 5.\(^5\) Claw/hammer toe deformity has been associated with the
presence of cavus foot type.\(^{16,27,30}\) Therefore, we measured the arch angle in the first ray,
defined as the angle between the sole of the foot and the bisector of the metatarsal bone,
and used this angle as indicator for arch height. Additionally, we calculated the arch index
from pressure plots obtained from 10 seconds of quiet standing on an EMED pressure
platform (Novel, Munich, Germany).\(^7\) The arch index is defined as the ratio of the contact
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area of the middle third of the footprint to the entire footprint contact area (excluding the toes). The closer to zero this ratio is, the higher the arch is.

Intrinsic muscle atrophy in the forefoot (i.e., the interossei and lumbrical muscles) was assessed from the coronal plane foot images. On these images, muscle is represented by a low-intensity (dark gray) signal whereas fatty infiltration (atrophy) of the muscle shows as high-intensity (light gray) signal. Because atrophy is diffusely distributed throughout the muscle, one representative anatomically referenced image cutting through the fifth metatarsal head was selected to score degree of intrinsic muscle atrophy. For this purpose, we used a five-point atrophy scale, with zero representing healthy muscle tissue (no atrophy); one, mild atrophy; two, moderate atrophy; three, severe atrophy; and four, almost complete or complete loss of muscle tissue (Figure 2). Intra-observer agreement in assessing atrophy using this five-point scale was high, with weighted kappa of 0.94 (chapter 3).

**Figure 2.** Five-point intrinsic muscle atrophy score for interossei and lumbrical muscles shown for a representative cross-sectional image through the fifth metatarsal head from five different subjects, with zero score representing healthy muscle tissue from a healthy subject; score one, mild atrophy; score two, moderate atrophy; score three, severe atrophy; and score four, almost complete or complete loss of muscle tissue.

Extrinsic muscle status was assessed using both sets of lower-leg images. The extensor digitorum longus (EDL) and flexor digitorum longus (FDL) muscles were evaluated on all proximal to distal images from the knee to the ankle on which these muscles could be identified (Figure 3A,B). Atrophy was scored using a similar five-point atrophy scale as used for the intrinsic muscles. Proximal and distal portions of the muscle were scored separately (division at mid-tibia). An imbalance between the extrinsic muscles was calculated by dividing the amount of muscle tissue (= score 4 minus atrophy score) in the FDL by the amount in the EDL; values >1 indicate FDL dominance, values <1 indicate EDL dominance. An imbalance between the intrinsic and extrinsic muscles was defined by dividing the amount of muscle tissue of the intrinsic muscles by the amount in the EDL and FDL combined; the closer the value to zero the larger the extrinsic muscle dominance. The
presence of intramuscular fibrosis indicating pathologic muscle contracture, showing as hypo-intense (black) signal on T1-weighted spin-echo images\textsuperscript{22;8;10} was also scored.

The plantar aponeurosis was assessed from its origin at the calcaneus to its insertion in the MTP joint capsule using the sagittal and coronal plane foot images (Figure 4A). All consecutive MRI slices showing plantar aponeurosis were examined for discontinuities representing rupture and for signal intensity change and substantial thickening compatible with plantar fasciitis.\textsuperscript{28;29} The coronal plane foot images and the sagittal plane images cutting through the second or third digit were used to examine the MTP joint capsule for signal intensity increases representing degenerative changes or presence of rupture in the plantar plate or collateral ligaments (Figure 4B).\textsuperscript{31;33}

Two investigators (SB, MM) performed all MRI assessments and reached consensus regarding outcome. All MR images were blinded for patient identity and characteristics. Differences between groups for all dependent variables were tested statistically using SPSS (SPSS, Chicago, IL). Independent t-tests and Mann-Whitney non-parametric tests were used for normally distributed and skewed data, respectively. Spearman rank correlation coefficients were computed between selected variables of interest in both patient groups and in the pooled group of patients (n = 18). For all analyses, significance levels of $P < 0.05$ were used.
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Results

No significant differences were present between subject groups for baseline data, except for toe angle, which was larger in the experimental group ($P < 0.001$). Arch angle was larger and arch index smaller in the experimental group, but not significantly different compared with the control group (Table 1).

Some degree of intrinsic muscle atrophy was present in each of the 18 neuropathic patients; the whole range of atrophy scores (1-4) was represented in both groups. Ten patients had atrophy score 3 or 4. Mean (SD) atrophy score was 3.0 (1.1) for the experimental group and 2.6 (1.2) for the control group, which was not significantly different ($P = 0.2$, Table 2). Correlation coefficients between intrinsic muscle atrophy score and toe angle were 0.09 and
0.11 for the experimental and control groups, respectively, and -0.10 for the pooled group of neuropathic subjects; none were statistically significant. Figure 5 shows two examples, one of an experimental patient with severe deformity (toe angle -26.3 degrees) but with only mild degrees of intrinsic muscle atrophy (score 1) and a control patient with almost no intrinsic muscle left (score 4) but with perfectly aligned toes. None of the five healthy, non-diabetic, subjects showed any degree of intrinsic muscle atrophy (all score 0).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Experimental group (n = 9)</th>
<th>Control group (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrinsic muscle atrophy score</td>
<td>3.0 (1.1)</td>
<td>2.6 (1.2)</td>
</tr>
<tr>
<td>EDL atrophy score (proximal)</td>
<td>0.6 (0.5)</td>
<td>0.4 (0.7)</td>
</tr>
<tr>
<td>EDL atrophy score (distal)</td>
<td>1.2 (1.1)</td>
<td>0.9 (1.4)</td>
</tr>
<tr>
<td>FDL atrophy score (proximal)</td>
<td>0.1 (0.3)</td>
<td>0.2 (0.7)</td>
</tr>
<tr>
<td>FDL atrophy score (distal)</td>
<td>0.2 (0.4)</td>
<td>0.8 (1.1)</td>
</tr>
<tr>
<td>Extrinsic muscle imbalance</td>
<td>1.3 (0.3)</td>
<td>1.1 (0.2)</td>
</tr>
<tr>
<td>Intrinsic/extrinsic muscle imbalance</td>
<td>0.3 (0.3)</td>
<td>0.4 (0.3)</td>
</tr>
<tr>
<td>Extrinsic muscle fibrosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Plantar aponeurosis abnormalities, of which:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plantar fascitis</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Rupture</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thickening</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Joint capsule abnormalities*</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

Data are means (SD) or n. *Degeneration or rupture of plantar plate or collateral ligaments.

Neither the FDL nor the EDL muscle showed any hypo-intense signal on the lower-leg images representing fibrosis. The EDL was atrophic in six experimental and four control subjects with more atrophy present distally (Table 2, Figure 3B). The FDL muscle was atrophic in three experimental patients and in four control patients. In those experimental patients showing FDL atrophy, a score higher than one (i.e., mild atrophy) was not found. No significant differences were found between experimental and control groups in any of the extrinsic muscle atrophy scores. The EDL was slightly more atrophic compared to the FDL in both patient groups, with imbalance values >1. The intrinsic muscles were more atrophic than the extrinsic muscles, with imbalance factors of 0.3 and 0.4 for the experimental group and control group, respectively; the difference between groups was not significant. Correlation coefficients between imbalance measures and toe angle varied from -0.31 to 0.10 and were not significant.
Four patients in the experimental group and four in the control group showed plantar aponeurosis abnormalities (Table 2). Three patients in each group had abnormalities close to the insertion of the aponeurosis at the calcaneus compatible with plantar fasciitis (Figure 4C) and one patient in each group showed substantial thickening of the proximal part of the aponeurosis. More distally in the foot, no disturbances were seen on sagittal and coronal plane images. None of the patients showed any evidence of partial or complete rupture of the plantar aponeurosis.

![Figure 5](image-url)

**Figure 5.** Two cases illustrating the lack of association between intrinsic muscle atrophy and toe deformity. Sagittal and coronal plane foot images of an experimental patient with severe deformity but only mild atrophy (left side plane), and a control patient with perfectly aligned toes but almost no intrinsic muscle left in the foot (right side plane).

Signal intensity increases in the plantar plate and collateral ligaments were seen in five experimental patients and two control patients, but one abnormality in the experimental group was present in a toe that was not deformed. The remaining difference in prevalence of two cases was not statistically significant ($P = 0.3$). Figure 4D shows the plantar plate and collateral ligaments of the patient with the most substantial disturbance of these hypo-intense structures representing degeneration or rupture. This was the only patient in the study with rigid toe deformity and dislocated MTP joints.
Discussion

No significant difference in degree of intrinsic muscle atrophy was found between neuropathic patients with claw/hammer toe deformity and neuropathic patients without deformity. Furthermore, correlation coefficients between intrinsic muscle atrophy score and degree of toe deformity (toe angle) were low, showing no association between these two variables. This is clearly illustrated by the two cases shown in Figure 5. These results imply that intrinsic muscle atrophy does not discriminate the patients with toe deformity from the patients without deformity. The present data confirms previous findings from our groups that intrinsic muscle atrophy does not necessarily imply toe deformity\(^6\) (chapter 2) by showing substantial degrees of atrophy in feet with normally aligned toes. In support of these findings, previous studies on clawed toes, albeit in non-diabetic subjects, showed no abnormalities of the intrinsic muscles by gross inspection, stimulation, or microscopic examination of biopsy material\(^27\), and no abnormality in motor nerve conduction velocity.\(^17\) In further support of our findings, van Schie et al.\(^32\) found that muscle weakness is not associated with foot deformity in diabetic patients. The present results suggest that the intrinsic muscles are not (exclusively) responsible for the development of claw/hammer toes in the diabetic foot, although it may still be a permissive factor since we found all patients with toe deformity to have at least a mild degree of intrinsic muscle atrophy.

The extrinsic muscles, whether or not being in a state of contracture\(^11:23\), are thought to overpower the decidedly weaker intrinsic muscles across the MTP and IP joints, leading to a characteristic ‘cocked-up’ position of the toes.\(^3:12:14\) In this study we found no signs of fibrosis in either neuropathic group that may indicate the presence of pathologic muscle contracture\(^8:19:22\) nor did we find significant differences in extrinsic muscle atrophy score between the neuropathic groups. Furthermore, the extrinsic muscle imbalance and the intrinsic/extrinsic muscle imbalance ratios were not different between groups and not associated with toe angle. This suggests that an imbalance between the extrinsic and intrinsic muscles is not likely to be responsible for claw/hammer toe deformity and challenges the prevailing theory of toe deformity pathogenesis. Alternatively, predisposing anatomical factors should explain why an imbalance between the intrinsic and extrinsic muscles leads to deformity in some, but not all patients with neuropathy. Although foot type may be such a factor, our analyses showed only a trend towards a higher arch in the group with toe deformity.

The use of high-resolution T1-weighted spin-echo MRI allowed us to examine the plantar aponeurosis in detail over its entire length and width.\(^28\) None of the 18 neuropathic subjects showed any evidence of discontinuity in plantar aponeurosis indicating rupture. Three patients in each group showed abnormalities compatible with plantar fasciitis and one
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The pathogenesis of claw/hammer toe deformity in each group showed abnormal thickening. As for the muscle data, these findings imply that plantar aponeurosis abnormalities do not distinguish the neuropathic feet with toe deformity from the feet without deformity. This lack of discriminative power does not correspond with data from Taylor et al.\textsuperscript{26} who consistently showed plantar aponeurosis discontinuity in diabetic feet with hyperextended toes and not in patients with normally aligned toes. The difference with our data is striking. However, an in-depth comparison between these two studies was not possible, as the results from Taylor have been reported in abstract form only; MR sequences, degree of deformity, and location and type of signal intensity changes may have been different. Therefore, it remains unclear what the exact role of the plantar aponeurosis is in the development of toe deformity in the diabetic foot.

To the best knowledge of the authors, the plantar plate and collateral ligaments have not been studied before \textit{in-vivo} in the diabetic foot, although several authors have associated plantar plate rupture or degeneration with MTP joint instability and toe deformity.\textsuperscript{11,31} The lack of significant difference in abnormalities between groups and the mixed results obtained per group shows that changes in joint capsule structure do not clearly distinguish the patients with claw/hammer toe deformity from the patients with normally aligned toes. The fact that the most widespread signal intensity increases in these structures were found in the only patient with rigid deformity and dislocated joints, suggests that connective tissue pathology at the MTP region may equally be a result as a cause of the deformity. Due to the limited time available per patient for MRI data collection and the additional use of the coronal plane foot images for assessment of intrinsic muscle atrophy, a relatively large FOV and single MR sequence were chosen to study the MTP region. As a result, we could not examine this region in great detail and may have missed smaller-scale pathologies present.\textsuperscript{31,33} Therefore, the conclusions drawn from this analysis should be considered with some caution.

Overall, the results suggest that there is no single factor that can explain the presence of claw/hammer toe deformity in the diabetic neuropathic foot. This is supported by data from Myerson and Sheriff\textsuperscript{21}, who sequentially sectioned claw toes and hammer toes in non-diabetic cadaver feet and concluded that there are multiple components to the hyperextended position of the MTP joint, which included the long toe extensors and the collateral ligaments. However, a subjective analysis of our data suggested that even combined factors cannot explain why some patients have toe deformity and others not, which leaves us with the question how claw/hammer toes develop in the diabetic foot? Analogous to how finger deformity can develop in the hands\textsuperscript{4}, the repetitive application of abnormally high loads at the toes in combination with intrinsic muscle atrophy may produce joint moments at the IP and MTP joints that cannot be sufficiently opposed by the weakened intrinsic muscles, which overtime may lead to claw/hammer toe deformity.
Plantar pressure measurements in the toes and long-term follow-up of patients should lead to acceptance or rejection of this alternative hypothesis. It should further be stressed that anatomical predisposing factors may vary extensively between individuals and may prevent the clear identification of a single factor causing toe deformity.10,13

Several limitations apply to this study. First, the cross-sectional design did not allow the establishment of cause-and-effect relationships, despite the focus on flexible toe deformity as a pre-stage of rigid toe deformity. Long-term follow-up of patients with flexible toe deformity may improve our understanding of toe deformity pathogenesis. However, intrinsic and extrinsic muscle atrophy are not likely a result of claw/hammer toe deformity, but are probably merely a result of the (long-lasting) presence of peripheral neuropathy, as evidenced by the significant degrees of muscle atrophy found in neuropathic patients with normally aligned toes. Secondly, using MRI, we were unable to assess the stiffening of connective tissue structures in the foot that may have occurred as a result of non-enzymatic glycosylation of proteins in patients with long-term diabetes and that has been suggested to play a role in toe deformity.26 MR spectroscopy can be used to assess glycosylation of connective tissue and may therefore be used in future studies for assessing soft-tissue architecture in deformed feet. Thirdly, we did not measure motor nerve conduction velocities as a measure of peripheral motor nerve dysfunction, which prevented us from determining the associations between motor nerve impairment and structural outcomes.32 However, because muscle atrophy results from motor nerve impairment12,25 and is the factor believed to be associated with toe deformity, we considered muscle atrophy indicative of motor impairment and therefore used only this variable. Finally, this was an explorative study. Considering the limitations and the small number of subjects used, we by no means claim to be fully comprehensive in our analysis. We expected to find consistent differences between the two groups of patients primarily in intrinsic and/or extrinsic muscle atrophy, muscle imbalance or, alternatively, in connective tissue abnormalities. If present, they would suggest the importance of this (these) variable(s) in the pathogenesis of claw/hammer toe deformity.

Conclusions

In conclusion, our results suggest that the intrinsic and extrinsic muscles are not, or at least not exclusively, responsible for the development of claw/hammer toe deformity in the diabetic foot as is widely believed. Abnormalities in the plantar aponeurosis and joint capsule seem to have no discriminatory power either. Currently unknown (predisposing) factors are presumably influential. Abnormal loading of the toes in combination with intrinsic muscle atrophy may be such a factor. While awaiting further longitudinal (biomechanical) studies or in-depth analyses using MRI in combination with techniques
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such as MR spectroscopy or histochemical examination of muscle and other soft-tissue structures, we provisionally conclude that the pathogenesis of claw/hammer toe deformity is idiopathic in nature.
References


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