The role of intrinsic muscle atrophy in the etiology of claw toe deformity in diabetes may not be as straightforward as widely believed

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Submitted 5 December 2008 and accepted 2 March 2009.
Objective: Clawing of the toes in the diabetic neuropathic foot is believed to be caused by muscle imbalance resulting from intrinsic muscle atrophy. However, experimental data that supports this mechanism is lacking. The aim of this study was to evaluate this hypothesis using magnetic resonance imaging (MRI).

Research Design and Methods: In twenty neuropathic diabetic patients, ten with claw toe deformity and ten with normally aligned toes, multiple plane images of the foot and lower leg were acquired using T1-weighted spin-echo MRI. Atrophy of the intrinsic and extrinsic muscles controlling the toes were assessed using a semi-quantitative 5-point atrophy scale. An intrinsic-to-extrinsic foot muscle imbalance score was derived from these atrophy scores and correlation coefficients were established.

Results: Mean (SD) intrinsic muscle atrophy score was 3.1 (1.1) for the toe deformity group and 2.6 (1.2) for the non-deformity group (not significantly different). Intrinsic muscle atrophy score was not correlated with degree of toe deformity (r = -0.18). Muscle imbalance score was not significantly different between study groups and not correlated with degree of toe deformity (r = -0.14).

Conclusions: Neither intrinsic muscle atrophy nor muscle imbalance discriminated between neuropathic patients with or without claw toe deformity. This suggests that the role of these muscle factors in claw toe development may not be primary or as straightforward as previously believed. These findings shed new light on the etiology of foot deformity in diabetes and suggest a more complex nature of development, potentially involving anatomical and physiological predisposing factors.
Clawing or hammering of the toes is a common foot deformity in patients with diabetes mellitus, with reported prevalence values between 32% and 46% (1,2). Both claw and hammer toes involve hyperextension of the metatarsal-phalangeal (MTP) joint as most important structural abnormality, and will be referred to as ‘claw toes’ in this article. Claw toes in diabetic patients are associated with a distal displacement of the protective sub-metatarsal head fat pads and an increase of plantar foot pressures at these regions (3,4). Furthermore, in prospective analyses, claw toe deformity has been found to be a predictor of diabetic foot ulceration (5), which may lead to infection or amputation. Therefore, a proper understanding of the etiology of claw toe deformity is important if we are to initiate or improve interventions for the prevention or correction of claw toe deformity with which we can reduce the risk for ulceration and further complications in this patient group.

There are several theories that may explain why claw toes develop in diabetic patients. Ill-fitting footwear, in particular the effect of cramped toe boxes in patients that lack protective sensation, may externally force the toes in a clawed position (6). There are some suggestions that rupture of the plantar fascia or ligament contractures at the MTP joints may be involved (7,8). However, the most commonly reported cause of claw toe deformity is intrinsic muscle atrophy and weakness secondary to motor neuropathy, leading to an imbalance between intrinsic and extrinsic muscles across the MTP and interphalangeal (IP) joints (9-11). 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 (6,12). 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, which eventually may result in clawing of the toes.

Despite the existence of numerous anecdotal and observational reports on this mechanical theory of claw toe pathogenesis and despite wide acceptance of this mechanism in the diabetic foot literature, experimental data that supports this theory does not exist. In addition, some reservations to this mechanism were provided by the results from recent studies. Our own group performed quantitative analyses of muscle atrophy and toe deformity using magnetic resonance imaging (MRI) and concluded that intrinsic muscle atrophy does not necessarily imply claw toe deformity in the diabetic neuropathic foot (13). In agreement with these results, Andersen et al. found many of their studied neuropathic patients with normally aligned toes to have significant degrees of atrophy of the intrinsic foot muscles (14). Furthermore, van Schie et al. found no association between semi-quantitative scores of muscle weakness and foot deformity in diabetic male patients (15). Therefore, even though these findings do not suggest that intrinsic muscle atrophy and muscle imbalance are no longer contributing factors in the development of toe deformity, their role may not be as straightforward as widely believed.

A better understanding of the associations between muscle atrophy, imbalance and toe deformity may be achieved with a more quantitative in-vivo examination using MRI of both the foot and lower leg muscles in a group of patients with toe deformity and a matched group with normally aligned toes. Therefore, the purpose of this study was to use MRI to examine the extrinsic and intrinsic foot muscles in patients with claw toe deformity and matched patients with
normally aligned toes in order to explore in a
more objective manner the association
between intrinsic muscle atrophy and claw toe
deformity. Based on the current widespread
beliefs we intended to test the hypothesis that
clear differences in both intrinsic muscle
atrophy and muscle imbalance between
patients with toe deformity and those without
are present.

RESEARCH DESIGN AND METHODS

Subjects: Twenty diabetic patients
with distal symmetric polyneuropathy
participated in this cross-sectional study. Ten
of these patients (5 men, 5 women) had claw
toe deformity involving hyperextension of the
MTP joint (experimental group). The other 10
patients were matched on age (+ 5 years) and
gender and had normally aligned toes (control
group). Five age-matched healthy subjects (3
men, 2 women) with normally aligned toes
were included for reference purposes in MRI
assessments. The presence of toe deformity
was initially assessed clinically for
recruitment purposes but eventually based on
MRI analysis as described below. One lower
extremity per subject was examined due to the
limited time available per patient on the MRI
scanner. This was the extremity with toe
deformity if the toes of the contra-lateral foot
were 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 abnormal vibration perception
thresholds measured at the dorsal surface of
the hallux in both feet using a Biothesiometer
(Bio-Medical Instrument Company, Newbury,
OH)) (16) and 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).
Written informed consent was obtained from
each subject prior to the start of the study,
which was approved by the local medical
ethics committee. Patient characteristics are
summarized in Table 1.

Maximal effort was done to exclude
congenital or external causes of claw toe
deformity in the experimental group. For this
purpose, the patients’ shoes were examined
and patients 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. Other
exclusion criteria 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, 3) a current foot ulcer, a prior
ulcer at the metatarsal heads, or prior lower
extremity surgery or fracture, 4) rheumatoid
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.

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 (17). 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. 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. 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. The distal lower-leg dataset included the ankle joint, and the proximal dataset the knee joint. Total data acquisition time was 45 minutes per subject.

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 of the second or third toe (named ‘toe angle’, negative values denoting extension). Toe angles smaller than -13 degrees indicated deformity based on 95% normal limits (3).

Atrophy of the intrinsic muscles in the forefoot (i.e., the interossei and lumbricals) 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 was 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 semi-quantitative 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. Intra-observer agreement in assessing atrophy using this five-point scale was high, with weighted kappa of 0.94 (18).

Extrinsic foot muscle status was assessed using both sets of lower-leg images. The extensor digitorum longus (EDL) and flexor digitorum longus (FDL) muscles were evaluated using all proximal to distal images from the knee to the ankle on which these muscles could be identified (Figure 1A, B). Extrinsic foot muscle atrophy was scored using a similar semi-quantitative five-point atrophy scale as used for the intrinsic foot muscles. Proximal and distal portions of the muscle were scored separately (division at mid-tibia). A muscle imbalance score between the intrinsic and extrinsic muscles which act at the level of the MTP joint was defined by subtracting the intrinsic muscle atrophy score with the average proximal and distal EDL muscle atrophy score. The possible range of muscle imbalance scores was between zero and four, with zero representing no muscle imbalance and four representing maximal muscle imbalance. Only the atrophy scores of the EDL muscle were entered in the equation since, according to the theory, this muscle acts in overpowering the intrinsic muscles at the MTP joint, which is the primary joint in claw toe deformity. The presence of intramuscular fibrosis indicating muscle contractures, which may additionally play a role in overpowering the intrinsic muscles (19,20), was scored as hypo-intense (black) signal on the transverse plane T1-weighted spin-echo images of the lower leg (21).
Two observers, blinded for patient identity and study group, independently performed assessments of muscle atrophy and reached consensus regarding outcome when discrepancies in observations were found.

**Statistical Methods:** SPSS version 16.0 was used for statistical analysis. For all continuous data, independent t-tests (normally distributed data) and Mann-Whitney non-parametric tests (skewed data) were used to compare study groups. Fisher’s exact test was used to compare groups for dichotomous data. Spearman rank correlation coefficients were computed for associations between selected variables in the pooled group of patients (n = 20). For all tests, significance levels of \( P < 0.05 \) were used.

**RESULTS**

Except for toe angle, no significant differences were present between subject groups for baseline data (Table 1).

Some degree of intrinsic muscle atrophy (minimum score 1) was present in each of the 20 neuropathic feet examined and the whole range of atrophy scores (1 to 4) was represented in both groups. Twelve patients had severe degrees of atrophy (score 3 or 4), seven in the experimental group and five in the control group. Mean (SD) atrophy score was 3.1 (1.1) for the experimental group and 2.6 (1.2) for the control group, which was not significantly different \( (P = 0.34, \text{Table 1}) \). The correlation coefficient between intrinsic muscle atrophy score and toe angle was -0.18 (not significant, \( P = 0.44 \)). Figure 2 shows two examples, one of an experimental group patient with severe deformity (toe angle -26.3 degrees) but with only a mild degree of intrinsic muscle atrophy (score 1) and a control group patient with almost no intrinsic muscle left (score 4) but with normally aligned toes. None of the five healthy non-diabetic subjects showed any degree of intrinsic muscle atrophy (all subjects had score 0).

Neither the FDL nor the EDL muscle showed any hypo-intense signal indicating fibrosis on the lower-leg MR images. The EDL muscle was atrophic in six experimental and four control group subjects with more atrophy present distally (Table 1 and Figure 1B). The FDL muscle was atrophic in three experimental and four control group patients. In those experimental group patients showing FDL muscle atrophy, a score higher than one (i.e., mild atrophy) was not found. The EDL muscle was slightly more atrophic than the FDL muscle. No significant differences were found between experimental and control groups in any of the extrinsic muscle atrophy scores. The intrinsic muscles were more atrophic than the extrinsic muscles, with muscle imbalance scores of 2.2 and 2.0 for the experimental group and control group, respectively. The difference in muscle imbalance score between the two groups was not significant \( (P = 0.60) \). The correlation coefficient between muscle imbalance score and toe angle was -0.14 (not significant, \( P = 0.56 \)).

**CONCLUSIONS**

The results of this study showed no significant difference in degree of intrinsic muscle atrophy between patients with claw toe deformity and patients with normally aligned toes. Furthermore, no association was found between intrinsic muscle atrophy score and degree of deformity (toe angle) in the group of 20 tested patients. This is clearly illustrated by the two cases shown in Figure 2. In the extrinsic foot muscles, we found no signs of fibrosis in either group that may indicate the presence of muscle contractures nor did we find significant differences in extrinsic muscle atrophy scores between the groups. Furthermore, intrinsic-to-extrinsic muscle imbalance score was not different between groups and not associated with toe...
angle. This means that neither intrinsic muscle atrophy nor muscle imbalance was able to discriminate between neuropathic patients with claw toe deformity and those without. To the best knowledge of the authors, this is the first study that measures intrinsic-to-extrinsic foot muscle imbalance in the diabetic foot and attempts to associate intrinsic muscle atrophy and muscle imbalance with claw toe deformity in an objective manner.

The present data confirm previous MRI reports on intrinsic muscle status in diabetes from Bus et al.(13) and Andersen et al.(14), who also showed substantial degrees of intrinsic muscle atrophy in neuropathic diabetic feet. Regarding the association between muscle status and foot deformity, our findings are in agreement with data from van Schie et al. (15) who showed that muscle weakness in the foot, assessed using manual muscle testing, was not associated with foot deformity in diabetic patients. Based on the lack of associations found between muscle atrophy or muscle imbalance and claw toe deformity, the present results suggest that the widely reported theory that intrinsic muscle atrophy and loss of muscle balance are causative of claw toes in the diabetic foot should be treated with caution. This does not mean, however, that we suggest that muscle atrophy and imbalance are no longer permissive factors in claw toe etiology. All patients with toe deformity in our study had at least some degree of intrinsic muscle atrophy (score 1 or higher) and because intrinsic muscle atrophy can precede toe deformity (14), it may still be a contributing factor. Nevertheless, this relationship may not be as straightforward in the diabetic foot. Other factors may be (more) important with the likelihood that multiple factors conspire to explain the presence of claw toe deformity in diabetic patients.

One of these factors may be pathology of the plantar aponeurosis, an important connective tissue structure which contributes to MTP joint stability by providing plantar flexion at this joint during weight-bearing. On MRI, Taylor et al. (8) consistently found plantar aponeurosis discontinuity, indicating rupture, in diabetic patients with claw toes and normal aponeurosis appearance in patients with aligned toes. With rupture, the aponeurosis would lose its stabilizing properties which may draw the MTP joint in a hyper-extended position. However, robust studies that support these preliminary data have not been found. Another factor may be pathology of the MTP joint capsule including the plantar plate and collateral ligaments. Some authors studying non-diabetic subjects have associated rupture or degeneration in these structures with MTP joint instability and toe deformity (19,22). In diabetes, these soft-tissue abnormalities in the foot may be fueled by the process of non-enzymatic glycosylation which renders fascia and ligaments less functional in their capacity to control joint configuration in the forefoot. Finally, externally applied forces through the effect of ill-fitting footwear may play a role, in particular when the intrinsic foot muscles are no longer able to contribute to MTP and IP joint stabilization due to atrophy and weakness. Clearly, prospective follow-up studies are needed to show the validity of these alternative mechanisms in contributing to claw toe deformity in the diabetic patient.

Our findings may have implications if surgical corrective interventions are the choice of treatment for claw toes in diabetic patients. Extensor tenotomies may not have the desired outcome and a multi-tissue approach may be warranted, an observation which is supported by the work from Myerson and Shereff in non-diabetic feet (7), who suggested that the correction of claw toes may require more extensive sectioning than formerly believed. This includes the sectioning of the MTP joint collateral ligaments. Whether this also accounts for the
Intrinsic muscle atrophy and claw toe deformity remains to be investigated.

This study was limited in that the cross-sectional design did not allow the establishment of cause-and-effect relationships. Long-term follow-up of patients with variable degrees of toe deformity may further improve our understanding of toe deformity pathogenesis. Secondly, we did not assess the physiological effects of diabetes and neuropathy on muscle tissue properties which may influence muscle function and the associations sought between foot structure parameters. $^3$P MR spectroscopy can be used for this purpose, including the measurement of non-enzymatic glycosylation and metabolite concentrations (23,24), and may be found valuable in future studies on claw toe pathogenesis. Finally, this study should be considered as a first attempt to obtain objective data on the association between muscle atrophy, imbalance, and toe deformity with the goal to increase awareness on the possibly more complex relationship between these parameters than previously thought. We expected to find clear and consistent differences between the two study groups for the muscle factors evaluated, which, if present, would indicate their importance in the etiology of claw toe deformity.

In conclusion, our results suggest that the role of intrinsic muscle atrophy and muscle imbalance in explaining the presence of claw toe deformity in the diabetic foot may not be as straightforward as widely believed. These muscle factors may not be primary or solely responsible for the development of claw toe deformity in diabetes. Other (predisposing) internal or external factors may be (more) important contributors, either in causing toe deformity or in preventing the establishment of a clear relationship between muscle atrophy and toe deformity. All these factors may also act together in a multi-component fashion. Prospective follow-up studies are required to test these hypotheses. Hopefully, the findings from this study will provoke further research that eventually may lead to the acceptance or rejection of the ‘muscle atrophy and imbalance’ theory in the development of claw toe deformity in the diabetic foot.

Disclosure: None of the authors have a relevant conflict of interest
REFERENCES

**Table 1.** Baseline patient characteristics and experimental results. Data are means (SD) or numbers (n).

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<th>Variable</th>
<th>Experimental group Claw toe deformity</th>
<th>Control group Aligned toes</th>
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<td>Number of subjects</td>
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<td>10</td>
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<td>Gender (male/female)</td>
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<td>27.4 (3.8)</td>
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<td>8/2</td>
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<td>Diabetes duration (years)</td>
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<td>11.9 (8.5)</td>
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<td>Vibration perception threshold (V)</td>
<td>32.6 (13.9)</td>
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<td>Intrinsic-to-extrinsic muscle imbalance score</td>
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*As derived from medical records or, when absent, estimated by the patient based on the first appearance of neuropathic symptoms. EDL: extensor digitorum longus muscle; FDL: flexor digitorum longus muscle. ² P < 0.001 between groups
**Figure 1.** Cross-sectional images of the distal lower leg in a healthy non-diabetic subject (A) and a neuropathic patient with severe atrophy of the extensor digitorum longus muscle (EDL) and mild atrophy of the flexor digitorum longus muscle (FDL) (B). The EDL and FDL muscles were scored proximally and distally by sequentially examining all cross-sectional images that included these extrinsic foot muscles.

**Figure 2.** Two cases illustrating the lack of association between intrinsic muscle atrophy and claw toe deformity. Sagittal and coronal plane foot images of a patient with severe deformity but only mild atrophy (left side pane), and a patient with perfectly aligned toes but almost no intrinsic muscle left in the foot (right side pane).