Diabetic Neuropathy Is Related to Joint Stiffness During Late Stance Phase

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The majority of plantar ulcers in the diabetic population occur in the forefoot. Peripheral neuropathy has been related to the occurrence of ulcers. Long-term diabetes results in the joints becoming passively stiffer. This static stiffness may translate to dynamic joint stiffness in the lower extremities during gait. Therefore, the purpose of this investigation was to demonstrate differences in ankle and knee joint stiffness between diabetic individuals with and without peripheral neuropathy during gait. Diabetic subjects with and without peripheral neuropathy were compared. Subjects were monitored during normal walking with three-dimensional motion analysis and a force plate. Neuropathic subjects had higher ankle stiffness (0.236 N-m/deg) during 65 to 80% of stance when compared with non-neuropathic subjects (−0.113 N-m/deg). Neuropathic subjects showed a different pattern in ankle stiffness compared with non-neuropathic subjects. Neuropathic subjects demonstrated a consistent level of ankle stiffness, whereas non-neuropathic subjects showed varying levels of stiffness. Neuropathic subjects demonstrated lower knee stiffness (0.015 N-m/deg) compared with non-neuropathic subjects (0.075 N-m/deg) during 50 to 65% of stance. The differences in patterns of ankle and knee joint stiffness between groups appear to be related to changes in timing of peak ankle dorsiflexion during stance, with the neuropathic group reaching peak dorsiflexion later than the non-neuropathic subjects. This may partially relate to the changes in plantar pressures beneath the metatarsal heads present in individuals with neuropathy.

Key Words: biomechanics, foot, diabetes

It has been reported that as many as 35% of ulcers in individuals with diabetes occur on the plantar surface of the first metatarsal head (Birke and Sims, 1986; Cavanagh et al., 2000). Increased plantar pressures beneath the metatarsal heads in individuals with diabetes are predictive of ulceration in this region (Veves et al., 1992). Peripheral neuropathy is a serious secondary complication associated with diabetes and has received much attention as a possible predisposing factor in increased plantar pressures and subsequent ulceration in the diabetic population (Cavanagh et al., 1991; Frykberg et al., 1998; Pitei et al., 1999; Stess et al., 1997). Since neuropathy affects both sensory and motor function in the diabetic patient (Boulton, 1996; Reiber et al., 1999; Kwon et al., 2003), neuromuscular compromise likely results in changes in lower extremity biomechanics.
It has been previously reported that persons with diabetic neuropathy have demonstrated alterations in general gait parameters (Katoulis et al., 1997). Specifically, it has been shown that during ambulation, diabetics with peripheral neuropathy demonstrate smaller stride length, slower walking speed, and less time spent in single support. This gait pattern is described as slow and conservative, and it is suggested to be a result of decreased proprioception from the feet (Courtmanche et al., 1996). As a result of this altered gait pattern, it is likely that changes would be present in other biomechanical parameters. In fact, biomechanical changes have been reported in individuals with peripheral neuropathy (Dingwell et al., 1999; Hastings et al., 2000; Mueller et al., 1994; Salsich & Mueller, 2000). Further, a relationship has been demonstrated between lower extremity mechanics and decreased pressures (Mueller et al., 1994b; Brown & Mueller, 1998). Recent studies suggest changes in pressures beneath the metatarsal heads as a result of foot orthotic intervention in individuals with diabetes (Mueller et al., 2006). Because the highest forces and pressures are present beneath the metatarsal heads during the second half of the stance phase of the gait cycle, differences in biomechanics should be evaluated during this time.

Mechanically, joint stiffness can be represented as angular resistance to a torque. Although lower extremity and joint stiffness can be described using this method, it is in no way inclusive of all the individual stiffnesses that contribute in the body. Each tissue has its own stiffness values and, depending on the tissue, could have several stiffnesses. For example, muscle can generate active stiffness due to its contractile properties, passive stiffness due to its anatomic structure, and reflex stiffness due to its innervation. In the diabetic population, measures of individual stiffness can become more complex as a result of physiological changes that occur over time in collagen. General stiffness is common, especially in the feet, in the diabetic population and has been evaluated statically (Glasoe et al., 2004; Nube et al., 2006; Orendurff et al., 2006; Salsich et al., 2000; Trevino et al., 2004). Because the foot is the interface with the ground during gait, changes in plantar sensation may result in differences in mechanics of the foot and perhaps the entire lower extremity. Recent studies suggest that the knee may be stiffer as a result of more co-contraction in individuals with diabetic neuropathy (Kwon et al., 2003). Further, it has been previously shown that changes in surface stiffness result in changes in total lower extremity stiffness in healthy individuals (Ferris et al., 1999). Because joint stiffness is a contributor to total lower extremity stiffness, it is possible that individuals with peripheral neuropathy would have an impaired sense of the surface stiffness and therefore have increased joint stiffness during gait. As a result, loading rates and plantar pressures could be elevated.

As diabetes and neuropathy progress, so does the stiffness of the joints based partly on glycosylation of collagen (Podwall and Gooch, 2004). However, this stiffness can be variable throughout the body and could result in either minor or devastating changes in joint structure. Several studies have evaluated static stiffness in individuals with Charcot’s foot or equinus deformity, finding changes in collagen structure, collagen mechanics, and joint mechanics (Grant et al., 2005; Grant et al., 1997; Lavery et al., 2002). It is possible that the changes seen in individuals with extreme foot deformities (Charcot’s arthropathy or equinus foot) may present earlier in the disease in individuals without these deformities. Measurement of individuals with diabetes and compromised sensation and no extreme structural deformity may provide some insight into these earlier changes.

It also has been shown that healthy individuals with stiff feet exhibit decreased mobility at other joints in the body, displaying increased total lower extremity stiffness (Williams et al., 2004). As a result of this increased stiffness, loading rates and vertical ground reaction forces have also been elevated. These elevated kinetic parameters have potentially damaging consequences in the diabetic individual with compromised sensation. However, because high pressures under the foot are present only during weight-bearing activities, it is important to evaluate stiffness in the foot and lower extremity during walking. If changes occur in the foot and ankle as a result of these changes in sensation, compensations are likely to occur in other joints, such as the knee or midfoot. To date, no data exist on the changes in joint stiffness during gait in individuals with diabetes and peripheral neuropathy.

Therefore, the purpose of this investigation was to demonstrate differences in ankle and knee joint stiffness between type 2 diabetic individuals with and without peripheral neuropathy.
Methods

Subjects were recruited from a local physician who was aware of all the inclusion and exclusion criteria. Only subjects who fit the inclusion and exclusion criteria were referred to the Human Movement Research Laboratory for participation. Prior to participation in the study, all subjects signed informed consent forms. All subjects were between the ages of 32 and 70 years and had a current diagnosis of type 2 diabetes. The subjects were able to comfortably ambulate 60 feet approximately 20 times with intermittent rest. Subjects were excluded if they had severe orthopedic abnormality, severe neurological compromise (other than peripheral neuropathy), previous cerebrovascular accident, previous or current plantar ulceration, or previous lower extremity amputation. These criteria were designed to exclude individuals who may demonstrate gait deviations related to pathologies other than peripheral neuropathy.

Sensation on the plantar surface of the feet was determined using the method described by Birke and Sims (1986). Nine sites were tested (1st toe, 3rd toe, 5th toe, 1st metatarsal head, 3rd metatarsal head, 5th metatarsal head, base of 5th metatarsal, base of 1st metatarsal, and the heel). Subjects (N = 22) were tested and placed in two groups. The non-neuropathic group consisted of 12 subjects who had been diagnosed with type 2 diabetes and had the ability to feel the 5.07 Semmes-Weinstein monofilament and vibration potential with a biothesiometer at <25 V (Bio-medical Instrument Company, Newbury, OH) on all trials. The neuropathic group comprised 10 subjects who had type 2 diabetes and the inability to feel the 5.07 Semmes-Weinstein monofilament at at least one site and vibration potential >25 V on all trials.

Retroreflective markers (at least three per segment) were placed on the rear foot, shank, and thigh of the right lower extremity by the same investigator (Figure 1). Kinematic data were collected using a five-camera motion analysis system. A standing calibration trial was collected. Each subject was asked to walk barefoot along a 60-ft walkway at a speed of 1.25 m/s (±5%). Speed was monitored with photocells. A force plate mounted in the center of the walkway recorded ground reaction forces. Kinematic data was sampled at 120 Hz, and force data was collected at 960 Hz. Ten foot strikes were collected and averaged for each subject. Kinematic and kinetic data were time-synchronized so that joint moments could be calculated.

The three-dimensional (3-D) coordinates of each marker were reconstructed using a direct linear transformation method. The 3-D coordinates were filtered using a second-order recursive Butterworth filter with an 8-Hz cutoff frequency. These data were used to calculate relative 3-D knee and ankle angles in an anatomical reference frame. Joint moments were calculated employing a standard inverse-dynamic calculation method.

Ankle and knee joint stiffnesses were calculated using the method described by Stefanyshyn and Nigg (1998) during running and more recently by Hansen et al. (2004) during walking. Specifically, ankle joint moment was plotted against ankle joint angle in the sagittal plane during the stance phase of gait. The same plot was created at the knee. The slope between successive points was determined,

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Figure 1 — Unilateral marker placement for dynamic trials. Additional standing calibration markers were placed on the medial and lateral forefoot, medial and lateral malleolus, medial and lateral knee, and bilateral greater trochanters. These markers were removed for dynamic trials.
averaged over the periods of 50 to 65% and 65 to 80% of stance, and compared between groups. This calculation was focused on the second half of the stance phase of normal walking because this is the time when pressures are highest beneath the metatarsal heads and forefoot. The time for reversal of motion in the ankle and knee in the normal population is represented by 65% of stance, and 80% is consistent with the propulsive peak of the vertical ground reaction force. For the purposes of this investigation, stiffness will be given a positive (+) value for a line progressing from left to right on the graph and a negative (−) value for a line progressing from right to left (Figure 2). Comparisons between neuropathic and non-neuropathic subjects were made using Student’s one-tailed t test (p ≤ 0.05). Dependent measures were ankle and knee joint stiffnesses during 50 to 65% of stance and during 65 to 80% of stance. These intervals were chosen based on the nearly linear portions of both the ankle and knee stiffness curves during the second half of stance.

### Results

Subjects in each group were similar in age, height, mass, and years with diabetes (Table 1). There was no difference in walking velocity between groups. Table 2 shows mean and variability data for ankle and knee stiffness at the selected intervals of stance. Ankle joint stiffness for both neuropathic and non-neuropathic subjects is shown in Figure 3. The slope of the line on the position by torque graph provides the estimate of total ankle joint stiffness. From 50 to 65% of the gait cycle, there is no significant difference in ankle stiffness between the groups (p = 0.13). However, during the period of 65 to 80%, the stiffness in the neuropathic group is significantly higher and in the direction opposite that of the non-neuropathic subjects (p < 0.01). Unlike the ankle, knee stiffness (Figure 4) was different between groups from 50 to 65% of stance (p < 0.01). However, there was no difference in knee stiffness between groups during the time of 65 to 80% of stance (p = 0.22).

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**Figure 2** — The slope of the motion vs. moment graph defines the stiffnesses described in the current study. As the line progresses from left to right, the stiffness value will be positive, whereas a line progressing from right to left will be defined as negative.
Diabetic Neuropathy and Joint Stiffness

Table 1  Subject Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Neuropathic</th>
<th>Non-neuropathic</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Sex</td>
<td>6 females, 4 males</td>
<td>7 females, 5 males</td>
</tr>
<tr>
<td>Height</td>
<td>1.73 m (0.08)</td>
<td>1.72 m (0.09)</td>
</tr>
<tr>
<td>Mass</td>
<td>97.8 kg (21.1)</td>
<td>95.4 kg (25.6)</td>
</tr>
<tr>
<td>Age</td>
<td>49.5 yr (3.7)</td>
<td>51.1 yr (10.9)</td>
</tr>
<tr>
<td>Years with diabetes</td>
<td>11.0 yr (8.6)</td>
<td>10.6 yr (11.5)</td>
</tr>
<tr>
<td>Forward velocity</td>
<td>1.24 m/s (0.11)</td>
<td>1.22 m/s (0.10)</td>
</tr>
</tbody>
</table>

Note. Values are presented as mean (SD).

Table 2  Joint Stiffness (newton-meters per kilogram per degree) During Late Stance Phase of Gait (50 to 80%)

<table>
<thead>
<tr>
<th>Stiffness</th>
<th>Neuropathic (n = 10)</th>
<th>Non-neuropathic (n = 12)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K_{\text{ankle}}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–65%</td>
<td>0.146 (0.039)</td>
<td>0.209 (0.561)</td>
<td>0.131</td>
</tr>
<tr>
<td>65–80%</td>
<td>0.236 (0.054)</td>
<td>–0.113 (0.193)</td>
<td>0.000</td>
</tr>
<tr>
<td>$K_{\text{knee}}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–65%</td>
<td>0.015 (0.035)</td>
<td>0.075 (0.064)</td>
<td>0.009</td>
</tr>
<tr>
<td>65–80%</td>
<td>–0.026 (0.017)</td>
<td>–0.007 (0.122)</td>
<td>0.215</td>
</tr>
</tbody>
</table>

Discussion

The purpose of this study was to compare dynamic lower extremity joint stiffness between neuropathic and non-neuropathic individuals with diabetes. None of the subjects in the current study had any extreme deformities in the feet or lower extremities. Therefore, no inferences can be made regarding stiffness during gait in individuals with severe foot deformity. Joint stiffness is a function of joint moment and motion, where an increase in moment and/or a decrease in motion equate to increased stiffness. It is important to note that this general measure of stiffness does not fully explain the individual responses or mechanics of the tissue that surround the ankle and knee joints. Further study of tissue mechanics in individuals with diabetic neuropathy is necessary to fully explain these differences. The current study showed differences in joint stiffness in the ankle and knee between individuals with and without diabetic neuropathy. Although changes in gait are often multifactorial, there were changes in joint function as a result of loss of sensation. Because peripheral neuropathy in the diabetic individual is not completely understood, there may be other physiological factors contributing to these differences. The findings in the current study are similar to recent findings with diabetic subjects having greater stiffness during late stance (Rao et al., 2006). Although not evaluated statistically, slight differences exist in peak dorsiflexion values in the current study when compared with previous studies (Rao et al., 2006). These differences may be related to the fact that all subjects in the current study had diabetes, and there may be some changes in range of motion related to the presence of diabetes. There may also be an offset in the data, but if this is the case, the offset would be consistent across all subjects. A single investigator placed all the markers from day to day, data (other than peaks) can be considered reliable (Ferber et al., 2002).

The current study shows that the timing, amplitude, and direction of motion at the ankle and knee are different, which therefore affected the magnitude and patterns of the stiffness. At the ankle during 50 to 65% of stance, the slopes of the plots are not significantly different and the change in plantar flexion torque and joint position were therefore similar between groups. As the neuropathic group continued to dorsiflex, the non-neuropathic group demonstrated a period of limited motion slightly toward plantar flexion and, therefore, a significant increase in stiffness. Stiffness then decreased as motion continued into plantar flexion. For the non-neuropathic group, this pattern of stiffness reflects a change from an eccentric to a concentric load (Figure 3). The neuropathic subjects demonstrated delayed time to peak dorsiflexion. In addition, peak knee extension occurred earlier than peak dorsiflexion for the neuropathic subjects. In the non-neuropathic group, timing and joint angle data at the ankle and knee are similar to previous data for normal individuals during walking (Mann & Hagy, 1980; Mueller et al., 1994a; Wu et al., 2005). It is reasonable to assume, therefore, that the differences in stiffness observed between the groups are partially due to level of neuropathy. We believe that there is a necessary coupling of stiffness between the knee and the ankle in the sagittal plane that may partially manage pressures in the forefoot. Based on these data, it appears that the position of the joint is
Figure 3 — Ankle joint motion, moment, and stiffness. Note the bimodal nature of the ankle stiffness in the non-neuropathic group. Peak ankle dorsiflexion occurs at approximately 65% in the non-neuropathic group.
Figure 4 — Knee joint motion, moment, and stiffness. There was no difference in stiffness between groups when calculated across the entire range of 50 to 80%. Note the similarities in stiffness patterns between groups.
not maintained properly (i.e., poor proprioception) and the stiffness in the joint changes too early at the knee and not at all at the ankle.

As indicated in Table 2, ankle stiffness is significantly greater for the neuropathic group when calculated from 65 to 80% of stance. This difference in calculated stiffness is due to a relatively small amount of dorsiflexion motion in the neuropathic group compared with the plantar flexion motion of the non-neuropathic group. Second, averaging of the data from 65 to 80% does not fully describe the stiffness at the ankle in the non-neuropathic group that occurs between 60 and 70% of stance (Figure 3). This is the transition between eccentric and concentric plantar flexor activity at the ankle. During this time, there is little motion in the ankle, whereas the plantar flexor torque continues to increase. This makes for a very stiff ankle (−29.3 N·m/deg) at this transition period, but the ankle is compliant before and after, thus affecting the overall stiffness at the joint. In the neuropathic group, the ankle continues to dorsiflex with an increase in plantar flexion moment. The rapid increase in stiffness, noted in the non-neuropathic group, is avoided. It is possible that these changes in ankle stiffness around the push-off phase of gait are not present in the neuropathic group as a result of proprioceptive loss. The change from ankle dorsiflexion to plantar flexion occurring later in the neuropathic group may create greater passive stiffness over the period of 65 to 75% of stance. This passive stiffness may result in the increased plantar pressures seen in neuropathic individuals. Further investigation of the components of stiffness in the joints of the ankle and foot is necessary.

At the knee, the neuropathic subjects demonstrated lower stiffness during 50 to 65% of stance, whereas there was no difference during 65 to 80%. Also interesting is the pattern of the knee stiffness. The non-neuropathic subjects make an abrupt change in stiffness at the knee, whereas the neuropathic subjects have a longer period of transition. This is opposite of what happens at the ankle. It is possible that this earlier shift in stiffness away from the knee is related to the maintenance of stiffness at the ankle from 65 to 80%. Interestingly, peak knee extension (58% of stance) occurred earlier than peak dorsiflexion (77% of stance) in the neuropathic group, whereas they occurred simultaneously in the non-neuropathic group (Figure 4). Unlike the ankle, there appear to be changes in both the position and moment at the knee that contribute to the earlier decrease in stiffness in the neuropathic group.

The results of this study demonstrate that non-neuropathic subjects have a period of high stiffness from 65 to 75% of stance, which is a short transition between two periods of low stiffness during the second half of stance phase. This is the period of transition between dorsiflexion and plantar flexion and eccentric and concentric plantar flexor activity. Those with neuropathy maintained a consistent increase in stiffness toward dorsiflexion. The difference in gait may be due to the neuropathy, but it is unclear how these changes influence plantar pressures and subsequent plantar ulcers. It is reasonable to assume that the change in ankle and knee motion may be to avoid the period of high stiffness during the change from dorsiflexion to plantar flexion. Although peak pressures may decrease, the time of pressure on the metatarsal heads may increase. That is, the increased time to peak dorsiflexion likely allows the metatarsal heads to remain in contact with the surface for a longer time, which may result in a higher pressure–time integral. Previous relationships between high pressure–time integrals and ulceration have been suggested (Lin et al., 1996; Maluf et al., 2004; Maluf & Mueller, 2003).

The current paper has shown that there are clear differences in knee and ankle stiffnesses between subjects with and without peripheral neuropathy related to type 2 diabetes. Joint moments at the ankle were not different between the groups, suggesting that ankle muscle strength during a simple task may not be a contributing factor to increased plantar pressures and, therefore, ulcers. However, slight differences in knee moments and stiffness may suggest that knee muscle activation contributes to differences in shock absorption in the neuropathic population. In general, the different patterns in joint motion dictated differences in joint stiffness at the knee and ankle. Simultaneously with a large increase in ankle stiffness, those without neuropathy showed a transition between dorsiflexion and plantar flexion. Whereas the non-neuropathic group demonstrated a pattern of motion expected with normal gait, the neuropathic subjects continued into dorsiflexion with a constant level of stiffness. It is important to note that there is no clear association at this time between these differences in stiffness and plantar tensions.
pressures. However, it is likely that there is an association between the differences in lower extremity kinematics and increased plantar pressures in diabetic individuals with neuropathy. Future studies are needed to relate these differences in stiffness and motion to plantar pressures and, if necessary, to develop intervention strategies.

References


