Midfoot and Ankle Movement Dysfunction in People with Diabetes Mellitus and Peripheral Neuropathy

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Midfoot and Ankle Movement Dysfunction in People with Diabetes Mellitus and Peripheral Neuropathy
by
Hyo Jung Jeong

A dissertation presented to
The Graduate School
of Washington University in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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Hyo Jung Jeong

Washington University in St. Louis

January 2021
Dedicated to my family

My husband JuHeon

My daughter Giann
ABSTRACT OF THE DISSERTATION

Midfoot and Ankle Movement Dysfunction in People with Diabetes Mellitus and Peripheral Neuropathy

by

Hyo Jung Jeong

Doctor of Philosophy in Movement Science

Washington University in St. Louis, 2020

Professor Michael J. Mueller, Chair

Professor Mary K. Hastings, Co-Chair

People with diabetes mellitus and peripheral neuropathy (DMPN) have midfoot and ankle musculoskeletal problems, including limited joint mobility and weakness and atrophy of foot intrinsic and calf muscles. Impaired foot structures and function could lead to midfoot and ankle movement dysfunction, measured by a heel rise task. A repeated movement dysfunction during weightbearing tasks (e.g., heel rise, walking) could cause excessive stress on the plantar tissue, which is a leading cause of plantar ulceration in people with DMPN. Understanding heel rise performance and the underlying mechanisms could help prevent the sequence of events associated with plantar ulcer development in people with DMPN.

In Chapter 2, we examined the effects of DMPN, limited midfoot and ankle joint mobility, and weightbearing on midfoot and ankle sagittal movements during heel rise; and characterized the midfoot and ankle position and movement trajectories of heel rise. Our results showed that midfoot and ankle plantarflexion were reduced during heel rise and non-weightbearing
plantarflexion tasks in people with DMPN. Reduced midfoot and ankle plantarflexion in non-weightbearing suggests that people with DMPN had limited joint mobility. However, peak unilateral (i.e., single-limb) and bilateral (i.e., double-limb) heel rise was less than the full available plantarflexion range of motion measured in non-weightbearing, indicating that limited joint mobility did not limit heel rise performance. A higher percentage of people with DMPN were in midfoot and ankle dorsiflexion at peak unilateral heel rise compared to the non-DMPN controls, but the position and movement trajectories were restored with bilateral heel rise, a reduction in weightbearing load. Clinicians should consider appropriate resistance when treating midfoot and ankle movement dysfunctions since midfoot and ankle plantarflexion magnitude, position, and movement trajectory during unilateral heel rise were improved by reducing the amount of weightbearing.

In Chapter 3, we determined the factors associated with midfoot angle at peak heel rise. We found that body mass index and maximum available midfoot plantarflexion range of motion were significant factors that accounted for 41.4% of variance of the midfoot angle at peak heel rise, while age and intrinsic foot muscle volume were not significant predictors. Weight and midfoot plantarflexion range of motion are potentially modifiable, which should be considered when health care professionals prescribe foot exercises to improve midfoot performance during weightbearing tasks in people with DMPN.

In Chapter 4, we examined the relationship of heel rise performance to gait and characterized the trajectory of midfoot and ankle motion of unilateral heel rise and gait in people with DMPN. People with DMPN who failed to plantarflex the midfoot and ankle during heel rise had
difficulty plantarflexing the midfoot and ankle during gait. Clinicians could use the heel rise task to identify midfoot and ankle dysfunction associated with gait in people with DMPN.

The results of this dissertation support the use of plantarflexion tasks of unilateral, bilateral, and non-weightbearing to help identify midfoot and ankle movement dysfunction in people with DMPN. Weight management and increasing joint motion might improve midfoot and ankle movements during weightbearing tasks in people with DMPN. Furthermore, clinicians could also benefit by utilizing a simple heel rise task as a surrogate measure for evaluating midfoot and ankle movement dysfunction during gait.
Chapter 1: Introduction
1.1 Midfoot and ankle movement dysfunction in people with diabetes and peripheral neuropathy

In the United States, it is estimated that 34.1 million people have diagnosed and undiagnosed diabetes mellitus (DM), which is 10.5% of the United States population. Peripheral neuropathy (PN) is a common complication of type 2 DM, with a prevalence of 24% up to 39%. DM and PN could result in midfoot and ankle musculoskeletal problems, including limited ankle joint mobility and weakness and atrophy of the foot and calf muscles. Impairments in structures (i.e., muscle and joint) and function (i.e., strength and mobility) could lead to midfoot and ankle movement dysfunction. Impaired heel rise may be an indicator of impaired midfoot and ankle movements during daily activities, such as walking. It is hypothesized that repetitive movement dysfunction during daily activities contributes to midfoot deformity, increasing the stress on the plantar tissue. Loss of protective sensation and elevated stress on plantar tissue are risk factors associated with plantar ulceration, which could ultimately lead to lower extremity amputation (Figure 1.1). Identifying and understanding the underlying mechanisms of midfoot and ankle movement dysfunction are needed to help prevent the cascade of events associated with ulceration and amputation in people with DMPN.
Figure 1.1 Theoretical framework of developing ulceration and amputation in people with diabetes mellitus and peripheral neuropathy.

1.2 Identifying midfoot and ankle movement dysfunction using the heel rise task

The heel rise task is a common test used to identify midfoot and ankle dysfunction across a variety of pathologies. Muscle structure and function are significantly correlated to heel rise
However, previous studies\textsuperscript{26,31} were unable to discern the role of muscle strength and limited joint mobility on heel rise performance. Midfoot and ankle angular motion occurs simultaneously to reach peak heel rise.\textsuperscript{24} Examining the midfoot and ankle positions and angular trajectories could allow us to identify normal and aberrant movement patterns during the heel rise task. Thus, identifying the midfoot and ankle movement dysfunction utilizing heel rise task could guide clinicians on treatment strategies to improve midfoot function and prevent foot injury, deformity progression, and ultimately foot ulceration and amputation in people with DMPN.

1.3 Contribut ors to midfoot movement dysfunction

Foot and ankle structures and function are significantly related to midfoot movement during the heel rise task.\textsuperscript{31} Personal factors, such as age and body mass index (BMI), may also be associated with midfoot movement. Aging alters foot structures and impairs weightbearing performances.\textsuperscript{25,32,33} Eighty-nine percent of people with type 2 DM are obese,\textsuperscript{1} and a high BMI is associated with increased midfoot pressure and arch flattening during walking.\textsuperscript{34,35} In a previous study,\textsuperscript{31} plantarflexor torque and intrinsic foot fat volume explained 37\% of the variance in midfoot movement. Intrinsic foot muscle is important to maintain arch;\textsuperscript{36} however, people with DMPN have intrinsic foot muscle atrophy and fat infiltration.\textsuperscript{8,37,38} Increased intrinsic fat volume was associated with reduced heel rise performance;\textsuperscript{31} thus, muscle volume is expected to account for midfoot movement dysfunction. Moreover, joint mobility may also account for midfoot movement dysfunction.
People with DMPN have shown reduced mobility at the midfoot during walking.\textsuperscript{39,40} Reduced range of motion in a non-weightbearing task is believed to reduce the ankle range of motion during weightbearing task. Thus, we expect reduced midfoot plantarflexion range of motion, measured by the non-weightbearing task, could reduce the midfoot plantarflexion range of motion available for performing the weightbearing heel rise tasks. Midfoot movement dysfunction is associated with midfoot deformity in people with DMPN,\textsuperscript{26} which elevates plantar pressure,\textsuperscript{41} a known risk factor for developing plantar ulceration.\textsuperscript{18-21} Understanding underlying mechanisms associated with midfoot movement dysfunction may help health professionals identify treatment targets for DM patient care that might prevent the progression of midfoot deformity and development of plantar foot ulceration.

### 1.4 Relationship of midfoot and ankle movements between heel rise and gait

Midfoot and ankle movement dysfunction is frequently observed in people with DMPN during heel rise and gait.\textsuperscript{26,31,39,40,42,43} Heel rise performance and terminal stance phase (push-off) of gait are theoretically similar as both tasks require midfoot and ankle plantarflexion. Thus, people who fail to plantarflex during the heel rise task may also fail to plantarflex during late stance phase of gait. Physical therapists often rely on visual assessment for evaluating midfoot and ankle movements in clinic.\textsuperscript{44} Motion during gait occurs quickly and can be difficult to evaluate visually if unassisted by technology.\textsuperscript{45,46} If midfoot and ankle movements during the heel rise task are similar to what occurs during walking, the heel rise task could be a surrogate tool to assess midfoot and ankle movements during walking.
1.5 Current knowledge gaps

1.5.1 Descriptors of heel rise task

Previous studies have primarily focused on the number of heel rise repetitions to a given height to quantify plantarflexor strength and endurance.\textsuperscript{28-30,47-52} Although kinematic measures of the heel rise task have been reported in various populations,\textsuperscript{24,25,53} there were limited studies in people with DMPN\textsuperscript{26,31} and bilateral heel rise task performance in people with DMPN has not been previously reported. Strength deficits,\textsuperscript{31} muscle deterioration,\textsuperscript{31} tendon dysfunction,\textsuperscript{24,25,28} and deformity\textsuperscript{25,26,31} are the limiting factors of plantarflexion motion during heel rise task previously identified. People with DMPN also have limited joint mobility\textsuperscript{3-7} that might account for poor heel rise performance. However, whether limited joint mobility limits heel rise is not known. Furthermore, midfoot joint mobility has not been investigated as measured by the non-weightbearing ankle plantarflexion task using 3-dimensional motion analysis. In addition, previous investigations of heel rise kinematics\textsuperscript{24-26,31,53} have not classified the heel rise movement patterns. The classification of midfoot and ankle position at peak heel rise is a novel approach for assessing people with midfoot and ankle movement dysfunction and could be useful in future work defining treatment targets and identifying people at risk for DMPN foot complications.

1.5.2 Mechanisms of heel rise task

Plantarflexor peak torque and intrinsic foot fat volume explained 37\% of the variance of the midfoot function.\textsuperscript{31} The majority of variance in midfoot function during heel rise task is still unexplained. Age, BMI, muscle volume, and maximum available midfoot plantarflexion may explain additional variance of midfoot function during heel rise task. The relationship between
weightbearing and non-weightbearing task is unknown. If the association between maximum available midfoot motion and heel rise task is determined, measures of joint mobility during the non-weightbearing task could help explain functional range of motion during weightbearing tasks for activities of daily living.

1.5.3 Significance of heel rise task

Heel rise plantarflexion moment and work are significantly related to plantarflexion moment and work during gait.\textsuperscript{54} Likely, the midfoot and ankle movement measured during heel rise could be a surrogate measure of movement dysfunction during walking. Despite similar midfoot and ankle mechanics during heel rise and push-off of gait,\textsuperscript{55} the midfoot and ankle kinematic relationship between the heel rise task and gait has not been investigated. Understanding the relationship of heel rise and gait kinematics may provide important information that has significant implications for clinical use of heel rise task.

1.6 Specific aims and hypotheses

1.6.1 Specific Aim 1 (Chapter 2)

Examine the effects of DMPN, limited joint mobility, and weightbearing on midfoot and ankle sagittal plane movements. Midfoot and ankle plantarflexion during three tasks (unilateral heel rise, bilateral heel rise, and non-weightbearing ankle plantarflexion) in two groups (DMPN and controls without DMPN) will be compared.

\textit{Hypothesis 1a:} People with DMPN would have less midfoot and ankle movements during the heel rise tasks compared to controls (effect of DMPN).
Hypothesis 1b: People with DMPN would have less midfoot and ankle movement in the non-weightbearing ankle plantarflexion task compared to controls (limited joint mobility associated with DMPN).

Hypothesis 1c: People with DMPN would have greater reductions in midfoot and ankle movements with higher weightbearing compared to controls (unilateral versus bilateral versus non-weightbearing).

Characterize the position of the midfoot and ankle at the peak heel rise height and non-weightbearing ankle plantarflexion tasks. Additionally, the midfoot and ankle movement trajectories during unilateral and bilateral heel rise tasks will be qualitatively compared.

Hypothesis 1d: The percentage of people with a dorsiflexed midfoot and ankle position would be greater in the DMPN group compared to controls.

Hypothesis 1e: Midfoot and ankle movement trajectories will be altered between unilateral and bilateral heel rise tasks in four movement pattern subgroups identified by unilateral heel rise task.

1.6.2 Specific Aim 2 (Chapter 3)

Determine the contributors to the sagittal midfoot angle at peak unilateral heel rise in people with DMPN.

Hypothesis 2a: Age, BMI, intrinsic foot muscle volume, and maximum available midfoot plantarflexion range of motion would explain substantial variance of the midfoot angle at peak unilateral heel rise in people with DMPN.
1.6.3 Specific Aim 3 (Chapter 4)

Determine the relationship of heel rise performance to gait in people with DMPN.

Hypothesis 3a: Measures of heel rise performance (midfoot and ankle plantarflexion angle at peak bilateral and unilateral heel rise) will be positively correlated with measures of gait performance (midfoot and ankle plantarflexion angle at peak ankle power during gait) in people with DMPN.

Characterize the trajectory of midfoot and ankle motion of unilateral heel rise and gait in people with DMPN. Subgroups of individuals who plantarflex the midfoot and ankle will be compared to individuals who dorsiflex the midfoot and ankle.

Hypothesis 3b: Midfoot and ankle plantarflexed subgroup would have greater plantarflexion during unilateral heel rise and less dorsiflexion during gait compared to midfoot and ankle dorsiflexed subgroup.

1.7 Need for study

The heel rise task has been suggested to assess midfoot and ankle function in various population.\textsuperscript{24-26,31,53} However, the heel rise task has been primarily used to evaluate plantarflexor strength and endurance.\textsuperscript{28-30,47-52,56} Despite the usefulness of the heel rise task in observing midfoot and ankle movement dysfunction, the midfoot and ankle kinematic during heel rise task has not been fully investigated. Understanding the aims of this dissertation may promote clinicians’ utilization of the heel rise task for identifying midfoot and ankle movement dysfunction. Moreover, examining the contributors of midfoot dysfunction and relationship between heel rise and gait could guide clinicians to treat modifiable factors associated with movement dysfunctions. Improving heel rise performance could possibly improve midfoot and
ankle movements during gait, which may prevent progression of midfoot deformity, ultimately, ulceration, and amputation in people with DMPN.
Chapter 2: Heel rise and non-weightbearing ankle plantarflexion tasks to assess foot and ankle function in people with diabetes mellitus and peripheral neuropathy

This chapter has been accepted for publication:

2.1 Abstract

Objective: To examine the effects of diabetes mellitus and peripheral neuropathy (DMPN), limited joint mobility, and weightbearing on foot and ankle sagittal movements; and characterize the foot and ankle position during heel rise.

Methods: Sixty people with DMPN and 22 controls participated. Primary outcomes were foot (forefoot on hindfoot) and ankle (hindfoot on shank) plantarflexion/dorsiflexion angle during three tasks: unilateral heel rise, bilateral heel rise and non-weightbearing ankle plantarflexion. A repeated measures of analysis of variance and Fisher’s exact test were used.

Results: Main effects of task and group were significant, but not the interaction in both foot and ankle plantarflexion. Foot and ankle plantarflexion were less in people with DMPN compared to controls in all tasks. Both DMPN and control groups had significant less foot and ankle plantarflexion with greater weightbearing, however, the linear trend across tasks was similar between groups. The DMPN group had a greater percentage of individuals in foot and/or ankle dorsiflexion at peak unilateral heel rise compared to controls, but the foot and ankle position were similar at peak bilateral heel rise between DMPN and control groups.

Conclusions: Foot and ankle plantarflexion is less in people with DMPN. Less plantarflexion in non-weightbearing suggests that people with DMPN have limited joint mobility. However, peak unilateral and bilateral heel rise is less than the available plantarflexion range of motion measured in non-weightbearing indicating that limited joint mobility does not limit heel rise performance. A higher frequency of people with DMPN are in foot and ankle dorsiflexion at peak unilateral heel rise compared to controls, but the position is restored with lower weightbearing.
Impact Statement: Proper resistance should be considered with physical therapy treatments utilizing heel rise since foot and ankle plantarflexion position could be restored by reducing the amount of weightbearing.

2.2 Introduction

Lower extremity musculoskeletal complications are frequently observed in people with diabetes mellitus (DM) and peripheral neuropathy (PN)\textsuperscript{57} and include limited joint mobility, impaired strength, and atrophy and fat infiltration of muscles.\textsuperscript{3,4,9,37,38} Together, these complications contribute to foot and ankle movement dysfunction, operationally defined as deficits in the magnitude and direction of foot and ankle plantarflexion during weightbearing tasks. Cross sectional data supports a relationship between foot and ankle movement dysfunction and midfoot deformity.\textsuperscript{7,31} Although there is currently no longitudinal data to support a causal relationship between aberrant movement and deformity, the physical stress theory proposes injuries develop when the repetitive stresses exceed the tissues’ tolerance.\textsuperscript{17} We hypothesize a theoretical framework in which foot and ankle movement dysfunction during weightbearing tasks, in the presence of loss of protective sensation, contributes to the development and progression of foot deformity, thereby increasing the risk of skin breakdown and amputation in people with DMPN.\textsuperscript{22,23} Understanding foot and ankle movement dysfunction in DMPN would inform treatment strategies to complete safe exercise programs and daily activities, improving foot and ankle function and reducing the risk of developing foot complications.

The heel rise task is a common test that has been used to identify foot and ankle dysfunction across a variety of pathologies.\textsuperscript{24-28,53} Performance of the heel rise task requires foot and ankle
plantarflexion range of motion and strength\textsuperscript{31,47} as well as simultaneous interplay of foot and ankle plantarflexion motions.\textsuperscript{24} In people with DMPN and midfoot deformity, a unilateral heel rise task was performed with an 85% reduction in foot (forefoot relative to hindfoot) and a 65% reduction in ankle (hindfoot relative to shank) plantarflexion excursions compared to non-DMPN controls.\textsuperscript{26} Although a previous study showed a significant association of calf strength and foot muscle deterioration to unilateral heel rise performance in people with DMPN,\textsuperscript{31} the previous study design was unable to discern if limited foot and ankle joint mobility, a common complication of DM,\textsuperscript{3} contributed to the aberrant heel rise performance. Reducing weightbearing, using bilateral heel rise and non-weightbearing ankle plantarflexion tasks will help discern the role of muscle strength and limited joint mobility to impaired unilateral heel rise performance and understand the role of limited joint mobility on heel rise performance.

Failure to plantarflex the foot and ankle by the end of the heel rise task is particularly concerning, as the sustained dorsiflexed position of the midfoot during the heel rise task could indicate a movement dysfunction that is contributing to midfoot deformity.\textsuperscript{26} Investigating the simultaneous interplay between foot and ankle plantarflexion at peak heel rise and examining the trajectories of the joints together could have substantial clinical implications for defining the magnitude and direction of normal and aberrant movement patterns during the heel rise task. However, foot and ankle position and trajectories in the sagittal plane during heel rise have not been characterized in people with DMPN.

Identifying the foot and ankle movement dysfunction during heel rise tasks could guide physical therapists on treatment strategies to improve foot function and prevent foot injury, deformity
progression, and ultimately ulceration and amputation in people with DMPN. Therefore, the primary purpose of this study was to examine the effects of DMPN, limited joint mobility, and weightbearing on foot and ankle sagittal plane movements. We assessed foot and ankle plantarflexion during three tasks (unilateral heel rise, bilateral heel rise, and non-weightbearing ankle plantarflexion) in two groups (DMPN and controls without DMPN). We hypothesized that people with DMPN, compared to controls, would have (1) less foot and ankle movements during the heel rise tasks (effect of DMPN), (2) less foot and ankle movement in the non-weightbearing ankle plantarflexion task (limited joint mobility associated with DMPN), (3) greater reductions in foot and ankle movements with higher weightbearing (unilateral versus bilateral versus non-weightbearing). The secondary purpose of this study was to characterize the position of the foot and ankle at the peak heel rise height and non-weightbearing ankle plantarflexion tasks and qualitatively compare the movement trajectories of the foot and ankle during unilateral and bilateral heel rise tasks. We hypothesized that the (1) percentage of people with a dorsiflexed foot and ankle position would be greater in the DMPN group compared to controls and (2) foot and ankle trajectories will be altered between unilateral and bilateral heel rise tasks in four movement pattern subgroups identified by unilateral heel rise task.

2.3 Methods

2.3.1 Participants

Sixty people comprised the DMPN group and twenty-two people comprised the control group. Inclusion criteria for the DMPN group were 1) type 2 DM diagnosed by the participant’s physician and 2) PN assessed by the research team. Presence of PN was defined as the (1)
inability to sense a 5.07 monofilament on at least one out of six plantar locations, (2) inability to feel vibration perception threshold less than 25 V tested on the plantar surface of the great toe using a Biothesiometer (Biomedical Instrument Co, Newbury, OH, USA), or (3) Michigan Neuropathy Screening Instrument score greater than or equal to two. PN from causes other than DM were excluded (e.g., chemo toxic, alcoholic, lumbar radiculopathy). Inclusion criteria for the control group was no DM or PN and match for age and body mass index with the DMPN group. Exclusion criteria for both DMPN and control groups were: inability to complete the testing for the study, age greater than 75 years old and, pregnant, on dialysis, severe arterial disease (ankle-brachial index > 1.3 or < 0.9), rigid metatarsophalangeal deformity, presence of a foot ulceration, lower extremity amputation, weight greater than 180 kg, and metal implants and/or pacemaker. All participants read and signed the consent form prior to participating in the study. The protocol was approved by the Washington University Institutional Review Board.

2.3.2 Kinematic and kinetic measurements

A modified Oxford multi-segmental foot model (3 segments: forefoot, hindfoot, and shank) was used to assess foot motion (forefoot relative to hindfoot) and ankle motion (hindfoot relative to shank). Reflective markers (10 mm) were attached to participant’s anatomical landmarks as defined previously and provided in the 2.8 Appendix. Kinematic data were acquired using a 10-camera Vicon motion analysis system (Vicon MX, Los Angeles, California, USA; 100 Hz). Kinematic data was computed using a Cardan x-y-z sequence rotations. The marker located at the posteroinferior aspect of the heel was used to estimate heel height during the heel rise tasks. Kinetic data were collected with Bertec force plates (FP4060-10 model, Bertec Corporation, Columbus, OH, USA; 1000 Hz). After data collection, kinematic data were low-pass filtered
using a Butterworth filter with a 6 Hz cut-off frequency in Visual3D software (C-Motion Inc. Germantown, MD, USA). The zero position of the foot was defined as the position of the forefoot relative to the hindfoot segment using the static standing trial and ankle was defined as the position of the shank relative to the hindfoot segment.

The present study is a secondary analysis of the baseline time point of a longitudinal, parent study (ClinicalTrials.gov, NCT02616263). The target limb of the DMPN group was selected based on the criteria of the parent study that measured toe extension movement pattern associated with metatarsophalangeal joint deformity. The examiner chose the foot that was observed to have the most consistent pattern of toe extension movement during active ankle dorsiflexion, the foot with the least number of foot complications (i.e., history of surgery or traumatic injury), and the metatarsophalangeal joint hyperextension angle needed to match the parent study treatment groups. The target limb of the control groups was randomly selected prior to the data collection. The percentage of right and left were matched between DMPN and control groups.

2.3.3 Tasks

Heel rise tasks: For the unilateral heel rise, participants placed the target limb on the force plate and the non-target limb was flexed at the knee so the foot did not touch the force plate. For the bilateral heel rise, the participants placed the target limb on the force plate and non-target limb on another force plate. For both heel rise tasks, participants placed their hands on the examiner’s outstretched forearm for balance. Participants were asked to raise the heel as high as possible without bending the knee of the stance leg. Participants performed five repetitions of each heel
rise task. We aimed to examine the trials that represented the participant’s best performance, therefore we selected the three trials that had the highest ankle plantarflexion power for analysis. The foot and ankle sagittal dorsiflexion (+)/plantarflexion (-) angles, ankle frontal inversion (+)/ eversion (-) angles, and heel height at the peak heel rise height were averaged and analyzed. A normalized peak heel height was calculated to minimize the influence of different foot lengths in individuals [peak heel height/ truncated foot length X 100 (%)]. The truncated foot length was defined as the distance between the first metatarsal head to the heel.

The vertical ground reaction force at peak heel rise was analyzed to assess offloading that could occur through the balance support provided. The participant’s force from bodyweight was measured from the static calibration trial and was equal to the summed left and right vertical ground reaction force. For unilateral heel rise, peak heel rise vertical ground reaction force on the target limb was recorded. For bilateral heel rise, peak heel rise left and right vertical ground reaction forces were summed. Then, the peak heel rise vertical ground reaction force was normalized to the participant’s static calibration ground reaction force, and multiplied by 100. On average, the normalized vertical ground reaction force at peak unilateral heel rise for the DMPN and controls groups were 91% (SD: 6) and 91% (7), respectively, and at peak bilateral heel rise for the DMPN and control groups were 95 % (3) and 96% (2), respectively. There were no group differences in vertical ground reaction force for the heel rise tasks (an independent t-test: unilateral heel rise p=1.00, bilateral heel rise p=0.18), which indicates that the influence of balance support during heel rise was similar across groups.
Non-weightbearing ankle plantarflexion task: Participants were asked to sit on a plinth with the knee extended and the ankle and foot in a relaxed position. They were asked to actively move their foot into maximal plantar flexion followed by maximal dorsiflexion for five consecutive repetitions. The two highest values of foot and ankle plantarflexion angle were analyzed and averaged.

2.3.4 Position of foot and ankle at peak

The position of foot and ankle at peak heel rise height for heel rise tasks and at peak foot and ankle plantarflexion for non-weightbearing ankle plantarflexion task were classified in four subgroups (Figure. 2.1): the plantarflexed position was foot and ankle plantarflexed (foot PF & ankle PF); the dorsiflexed positions were: foot plantarflexed and ankle dorsiflexed (foot PF & ankle DF), foot dorsiflexed and ankle plantarflexed (foot DF & ankle PF), and foot and ankle dorsiflexed (foot DF & ankle DF).
Figure 2.1 Position of foot and ankle at peak heel rise. (A) Foot PF & Ankle PF. (B) Foot PF & Ankle DF. (C) Foot DF & Ankle PF. (D) Foot DF & Ankle DF. Black arrows indicate PF motion and red arrows indicate DF motion in foot and ankle joints. Figure (A) depicts the plantarflexed position, whereas (B), (C), and (D) depict dorsiflexed position of the foot and/or ankle. Abbreviation: PF, plantarflexion; DF, dorsiflexion.

2.3.5 Trajectory analysis

The trajectory of the mean foot and ankle angles during the unilateral and bilateral heel rise were graphed for each of the subgroups identified from the foot and ankle position at the end of unilateral heel rise. We qualitatively compared the foot and ankle movement trajectories between the four subgroups.

2.3.6 Statistical analysis

All statistical analyses were done using SAS 9.4 (SAS Institute, Cary, NC). An alpha level of 0.05 was set for all statistical analyses. An independent t-test and a Fisher’s exact test were used to assess differences in participant characteristics.
**Effect of DMPN, limited joint mobility, and greater weightbearing:** Age was significantly different between the DMPN and control groups (p=0.003). However, the results between the groups did not change after adjusting for age. Shapiro-Wilk test was conducted to test the assumptions for data normality and the dependent variables were normally distributed. Thus, statistical analysis did not require modification. Repeated measures of analysis of variance were used to analyze the association of three dependent variables (unilateral heel rise, bilateral heel rise, non-weightbearing) with group (DMPN and controls) to determine the effect of DMPN, limited joint mobility, and higher weightbearing on foot and ankle sagittal movements. The within-subjects factor was three tasks (unilateral heel rise, bilateral heel rise, and non-weightbearing task) and the between-subjects factor was two groups (DMPN and controls). Due to multiple comparisons, Bonferroni correction was used to adjust the alpha level (α/3 = 0.017).

An independent t-test was used to compare the unilateral and bilateral heel rise ankle inversion, peak heel height, and normalized peak heel height between the DMPN and control groups to support the findings of this study, thus, the analyses were not conducted with a priori hypothesis. An alpha level was adjusted (α/2 = 0.025) using the Bonferroni correction.

**Position of foot and ankle:** A Fisher’s exact test was used to examine the percentage differences between plantarflexed (foot PF & ankle PF) and dorsiflexed position (including foot PF & ankle DF, foot DF & ankle PF, and foot DF & ankle DF) of foot and ankle between DMPN and controls within each task (unilateral heel rise, bilateral heel rise, and non-weightbearing ankle plantarflexion).
2.3.7 Role of the funding source

This study was supported by grants from the National Institute of Diabetes and Digestive and Kidney Diseases (R01 DK107809, F32 DK123916) and the Research Division of the Program in Physical Therapy, Washington University School of Medicine, Saint Louis, Missouri. The funders played no role in the design, conduct, or reporting of this study.

2.4 Results

The participant characteristics between DMPN and controls are provided in Table 2.1.

Table 2.1 Participant characteristics.\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>DMPN</th>
<th>Control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>60</td>
<td>22</td>
<td>-</td>
</tr>
<tr>
<td>Gender (Female/Male)</td>
<td>34/26</td>
<td>14/8</td>
<td>0.621</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>67 (6) [46, 75]</td>
<td>62 (8) [46, 74]</td>
<td>0.003*</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>35 (7) [22, 49]</td>
<td>32 (6) [21, 45]</td>
<td>0.088</td>
</tr>
<tr>
<td>DM duration (yrs)</td>
<td>14 (10) [0.2, 49]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td>7.1 (1.3) [5.1, 11.4]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Foot length (cm)</td>
<td>27.7 (1.7) [24.2, 31.9]</td>
<td>27.3 (1.9) [24.7, 32.2]</td>
<td>0.381</td>
</tr>
<tr>
<td>Truncated foot length (cm)</td>
<td>20.0 (1.2) [17.6, 22.9]</td>
<td>19.9 (1.5) [17.6, 23.2]</td>
<td>0.663</td>
</tr>
</tbody>
</table>

\(^a\)Values are mean (standard deviation) [range].

*Statistically significant (p<0.05)

Abbreviation: DMPN, diabetes mellitus and peripheral neuropathy.
Repeated measures of analysis of variance performed on sagittal foot and ankle motion showed significant overall main effects of within-factor (task) and between-factor (group), but no significant interaction of task x group.

Effect of DMPN: In our post hoc analysis, the DMPN group exhibited significantly less foot and ankle PF in the unilateral heel rise task (foot PF: p<0.001 and ankle PF: p<0.001) and bilateral heel rise task (foot PF: p<0.001 and ankle PF: p=0.001) compared to control group (Table 2.2).

Effect of higher weightbearing: Foot and ankle PF significantly lower with weightbearing change from non-weightbearing, bilateral heel rise, to unilateral heel rise (main effect of task, foot PF: p<0.001 and ankle PF: p<0.001). The difference in the linear trend of foot and ankle PF across tasks between DMPN and control groups was not statistically significant (interaction of task x group, foot PF: p=0.052 and ankle PF: p=0.092).

Limited joint mobility associated with DMPN: A post hoc analysis showed that the DMPN group had significantly less foot and ankle PF during the non-weightbearing task compared to the control group (foot PF: p=0.001 and ankle PF: p=0.004; Table 2.2).

Ankle inversion was not significantly different between DMPN and control group in both unilateral and bilateral heel rise (p=0.079 and p=0.298, respectively; Table 2.2). Peak heel height and normalized peak heel height were significantly lower in the DMPN group compared to the control group in the unilateral and bilateral heel rise task (see Table 2.2).
Table 2.2 Kinematic data.a

<table>
<thead>
<tr>
<th>Variables</th>
<th>Tasks</th>
<th>DMPN</th>
<th>Control</th>
<th>Mean difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot plantarflexion (degrees)b</td>
<td>Unilateral heel rise</td>
<td>1 (6)</td>
<td>-7 (9)</td>
<td>8</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td></td>
<td>Bilateral heel rise</td>
<td>-10 (7)</td>
<td>-17 (8)</td>
<td>7</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td></td>
<td>Non-weightbearing</td>
<td>-22 (7)</td>
<td>-26 (5)</td>
<td>4</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>Ankle plantarflexion (degrees)b</td>
<td>Unilateral heel rise</td>
<td>0 (7)</td>
<td>-6 (6)</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Bilateral heel rise</td>
<td>-10 (6)</td>
<td>-15 (4)</td>
<td>5</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>Non-weightbearing</td>
<td>-18 (5)</td>
<td>-23 (7)</td>
<td>5</td>
<td>0.004*</td>
</tr>
<tr>
<td></td>
<td>Ankle inversion (degrees)c</td>
<td>Unilateral heel rise</td>
<td>5 (7)</td>
<td>7 (5)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Bilateral heel rise</td>
<td>12 (7)</td>
<td>14 (6)</td>
<td>2</td>
<td>0.298</td>
</tr>
<tr>
<td></td>
<td>Peak heel height (cm)</td>
<td>Unilateral heel rise</td>
<td>6.5 (2.0)</td>
<td>9.1 (2.2)</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>Bilateral heel rise</td>
<td>9.0 (1.8)</td>
<td>10.8 (1.6)</td>
<td>1.8</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td></td>
<td>Normalized peak heel height (%)d</td>
<td>Unilateral heel rise</td>
<td>32.3 (9.8)</td>
<td>46.0 (10.8)</td>
<td>13.7</td>
</tr>
<tr>
<td></td>
<td>Bilateral heel rise</td>
<td>45.1 (9.1)</td>
<td>54.6 (7.5)</td>
<td>9.5</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

aValues are mean (standard deviation).

bPositive value indicates dorsiflexion and negative value indicates plantarflexion motion.

cPositive value indicates inversion motion.

dPeak heel height (cm)/ truncated foot length (cm) X 100 (%)

*Statistically significant (p<0.017 for foot and ankle plantarflexion and p<0.025 for ankle inversion, peak heel height, and normalized peak heel height).

Abbreviation: DMPN, diabetes mellitus and peripheral neuropathy.
Position of foot and ankle: The percentage of foot and/or ankle plantarflexed and dorsiflexed position in DMPN and control groups is reported in Figure. 2.2A. In the unilateral heel rise, the DMPN group had a significantly greater percentage of people with foot and/or ankle dorsiflexed position (40 out of 60, 67%) compared to controls (7 out of 22, 32%; p=0.01). In the bilateral heel rise, there were no group differences in percentage of people in the plantarflexed and dorsiflexed position between DMPN and controls (8 out of 60, 13% vs 1 out of 22, 5%, respectively; p=0.43). For the non-weightbearing task all participants in both groups demonstrated plantarflexed foot and ankle position (foot PF and ankle PF; Figure 2.2B).
Figure 2.2 (A) The percentage of subjects in the four foot and ankle positions in the DMPN and control groups. Foot PF & Ankle PF (green) is the plantarflexed position of foot and ankle. Foot PF & Ankle DF (bronze), Foot DF & Ankle PF (brown), and Foot DF & Ankle DF (red) indicates foot and/or ankle are in the opposite position of the plantarflexion. (B) Scatter plot data of peak foot and ankle position (degrees). Quadrant description (starting at upper-right, clockwise): Foot DF & Ankle DF, Foot DF & Ankle PF, Foot PF & Ankle PF, Foot PF & Ankle DF. Red circles represent performance of the unilateral heel rise, yellow diamonds represent performance of the bilateral heel rise, and blue squares represent performance of the non-weight bearing task. Shift toward the lower left quadrant indicates greater foot and ankle plantarflexion at each tasks.

Abbreviation: DMPN, diabetes mellitus and peripheral neuropathy; PF, plantarflexion; DF, dorsiflexion.
Trajectory Analysis: The foot and ankle trajectory of the DMPN group during the unilateral and bilateral heel rise tasks are in Figure 2.3. During unilateral heel rise, subgroups with foot PF pattern (Foot PF & Ankle PF and Foot PF & Ankle DF) had foot plantarflexion movement trajectories, whereas subgroups with foot DF pattern (Foot DF & Ankle PF and Foot DF & Ankle DF) had foot dorsiflexion movement trajectories. All four subgroups during unilateral heel rise had ankle plantarflexion movement trajectories (Figure. 2.3A). During bilateral heel rise, all four subgroups had both foot and ankle plantarflexion movement trajectories (Figure. 2.3B).
**Figure 2.3** Foot and ankle movement trajectory depicting (A) unilateral heel rise and (B) bilateral heel rise in DMPN group. Subgroup allocations were based on foot and ankle position at peak unilateral heel rise and maintained for the bilateral heel rise. (A) The unilateral trajectories showed that all subgroups plantarflexed the ankle (moving down the y-axis) during the unilateral task. Subgroups with the foot DF pattern, dorsiflexed the foot during unilateral heel rise (moving to the right on the x-axis). Changes in the trajectories from (A) to (B) show that all subgroups had increased excursions and restoration of foot and ankle plantarflexion when weightbearing was reduced from unilateral to bilateral heel rise. Each dot is a normalized time point of heel rise from 0% to 100%.

Abbreviation: DMPN, diabetes mellitus and peripheral neuropathy. PF, plantarflexion; DF, dorsiflexion
2.5 Discussion

The results of this study determined that (1) people with DMPN have less foot and ankle movements during heel rise tasks, (2) people with DMPN have limited foot and ankle plantarflexion mobility measured during the non-weightbearing task; (3) the increased weightbearing reduces foot and ankle movements, however, the reduction across tasks is similar between people with DMPN and controls, and (4) people with DMPN have dorsiflexed foot and ankle position and aberrant trajectory which is most apparent in the unilateral heel rise, but reducing weightbearing helps restore foot and ankle plantarflexion motion.

Presence of DMPN was associated with less unilateral and bilateral heel rise performance. In a previous study, the mean difference of foot and ankle plantarflexion during unilateral heel rise was greater (21° and 11°, respectively) than what was measured in this study. The difference between studies likely reflects progression of foot and ankle movement dysfunction as foot pathology worsens, as the previous study examined a cohort with established medial column foot deformity. Deficits in both unilateral and bilateral heel rise tasks in the DMPN group suggest that people with DMPN have substantial loss of muscle strength that may lead to aberrant foot and ankle biomechanics during daily activities. Examination of muscle capacity as well as foot and ankle performance of patients with DM utilizing the heel rise task could assist physical therapists in prescribing appropriately dosed weightbearing exercise programs. Foot and ankle movements should be observed to prescribe effective and safe exercise programs. For example, bicycling or swimming would be recommended if abnormal foot mechanics are observed and cannot be corrected, resulting in less stress to the foot, but promoting physical activity to help glycemic control.
We observed limited ankle and foot plantarflexion mobility in people with DMPN compared to controls during the non-weightbearing task (reduction of 22% at ankle and 15% at foot plantarflexion). Our ankle findings are similar to Abate and colleagues who found a 24% reduction in ankle plantarflexion range of motion compared to age-matched healthy controls. To our knowledge, limited foot plantarflexion mobility has not been previously reported in people with DMPN. Multiple factors can contribute to reduced range of motion, including aging and glycemic control. In general, DM is known to cause an increased formation of advanced glycation end-products that results in increased collagen cross-links, associated with joint stiffness and decreased range of motion. Interventions to address foot and ankle plantarflexion range of motion could improve foot and ankle function and minimize risks associated with movement dysfunction.

The plantarflexion reduction from non-weightbearing to bilateral to unilateral heel rise implies that the impaired heel rise performance in DMPN and control groups appears to be caused primarily by calf and intrinsic foot muscle weakness. All of the participants were not able to plantarflex through their available full range of motion measured during the non-weightbearing task. Aging and obesity have been reported to be associated with reducing plantarflexor strength that may explain less plantarflexion with increased weightbearing in both DMPN and control groups. A previous study of Flanagan et al. (2005) demonstrated an aging-associated response to body weight during heel rise that showed significant ankle (foot relative to shank) plantarflexion reduction in older adults during unilateral heel rise compared to that of bilateral heel rise task. From the results of our study, we speculate that improving the strength of
foot intrinsic and calf muscles might increase the plantarflexion of weightbearing task performance and should be examined in future research.

A trend of greater foot plantarflexion reduction with increased weightbearing in people with DMPN compared to controls suggests that the foot is more vulnerable to deform with increased weightbearing in people with DMPN. PN in people with DM accelerates the muscle degenerative process, which results in greater impairments in muscle strength and atrophy. Up to a 38% decreased plantarflexion force, 37% increased intrinsic muscle adipose tissue volume in gastrocnemius-soleus muscle, and 49% decreased muscle volume in intrinsic foot have been measured in people with DMPN compared to controls. We believe assessing foot capacity using different weightbearing conditions has potential to identify people with foot movement dysfunction early in their disease process and provide important targets for interventions aimed at reducing risk of foot complications.

Sixty-seven percent of people with DMPN did not end the unilateral heel rise task with the foot and/or ankle in plantarflexion. Fifty-three percent of people with DMPN were unable to complete the unilateral task with the foot plantarflexed and the foot DF pattern subgroups (foot DF & ankle PF and foot DF & ankle DF) moved their foot into dorsiflexion during the unilateral heel rise (Fig. 3A). Importantly, when weightbearing was reduced with the bilateral heel rise task, the majority of people with DMPN were able to restore the final foot and ankle position and trajectory to plantarflexion (Fig. 2A and 2B and Fig 3B). Thus, with decreased weightbearing, the magnitude, direction, and end position of the foot and ankle were improved. This finding implies the importance of examining foot and ankle movements of unilateral and bilateral heel
rise to understand how loading influences foot and ankle movements and informs exercise prescription.

It is interesting to note that controls also had a substantial percentage of people who were unable to reach a foot and ankle plantarflexed position at peak unilateral (32%) and bilateral (5%) heel rise. A previous study\textsuperscript{24} has shown that 100% of controls achieved foot plantarflexion (first metatarsal relative to hindfoot) during bilateral heel rise. Our control group was slightly older and heavier (age=62 years old, body mass index=32.1 kg/m\textsuperscript{2}) compared to the previous reported controls\textsuperscript{24} (age=56 years old, body mass index=30.6 kg/m\textsuperscript{2}). A combination of aging and obesity may have contributed to aberrant foot and ankle position at peak heel rise. Future study is needed to investigate the contribution of age and body mass index on altering foot and ankle function during heel rise.

\textbf{2.5.1 Limitations}

There are several limitations to our study. People with DMPN may have leaned forward or slightly bent their knees to raise their heels. Future kinematic examination of the heel rise task could include trunk and femur segments to allow tracking of compensatory strategies. Although practice trials and balance support were given during unilateral and bilateral heel rise, people with DMPN may have balance deficits, that were not measured, that could contribute to difficulty completing the tasks. The foot mechanics during non-weightbearing do not fully replicate foot motion during a heel rise and under load. The loaded heel rise task includes components of shear and compressive stress at the joint that may inherently change joint motion. Lastly, this study was designed as a cross-sectional study that does not explain causal
relationships of heel rise task and development of lower extremity musculoskeletal problems. Future study is needed to determine the relationship of foot deformity progression to heel rise performance.

2.6 Conclusions

The presence of DMPN and increased weightbearing was associated with less foot and ankle movements. People with DMPN have limited joint mobility, but that does not appear to be the primary factor limiting foot and ankle kinematics during a heel rise task. People with DMPN not only performed less foot and ankle movements during heel rise task, but also had foot and/or ankle dorsiflexion during the unilateral heel rise task. However, reducing the weightbearing helped restore foot and ankle plantarflexion magnitude, joint position, and movement trajectories. These findings provide useful information in the utilization of the heel rise task to quickly identify foot and ankle movement dysfunction and to provide guidance for the appropriate weightbearing during exercise prescription.

2.7 Acknowledgments

The authors acknowledge Kathryn Bohnert, Darrah Snozek, and Christopher Sorensen who assisted with subject recruitment and data collection and Jessica Stumpf, Kaitlyn Winter, Jadean Hoff, Hana Bernhardson, Haley Brogan, Nick Youmans, Mary Ellis, Whitney Korgan, and Nick Schroeder who assisted with data processing.
**2.8 Appendix**

Marker placement for multi-segment model

<table>
<thead>
<tr>
<th>Segment</th>
<th>Marker location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forefoot</td>
<td>1(^{st}) and 5(^{th}) metatarsal heads</td>
</tr>
<tr>
<td></td>
<td>1(^{st}) and 5(^{th}) metatarsal base</td>
</tr>
<tr>
<td></td>
<td>Between the 2(^{nd}) and 3(^{rd}) metatarsal head</td>
</tr>
<tr>
<td>Hindfoot</td>
<td>Sustentaculum tali</td>
</tr>
<tr>
<td></td>
<td>Peroneal trochlea</td>
</tr>
<tr>
<td></td>
<td>Bisection of the posterior calcaneus (two markers</td>
</tr>
<tr>
<td></td>
<td>aligned in a thermoplastic plate)</td>
</tr>
<tr>
<td>Shank</td>
<td>Tibial tuberosity</td>
</tr>
<tr>
<td></td>
<td>Head of the fibula</td>
</tr>
<tr>
<td></td>
<td>Medial and lateral malleoli</td>
</tr>
<tr>
<td></td>
<td>Four markers mounted on a thermoplastic plate</td>
</tr>
<tr>
<td></td>
<td>(secured at lateral-distal part of the shank)</td>
</tr>
</tbody>
</table>
Chapter 3: Body mass index and maximum available midfoot motion are associated with midfoot angle at peak heel rise in people with diabetes

This chapter has been submitted for review:

Jeong H, Mueller MJ, Zellers JA, Commean PK, Chen L, Hastings MK. Body mass index and maximum available midfoot motion are associated with midfoot angle at peak heel rise in people with diabetes.
3.1 Abstract

Background: Midfoot movement dysfunction, as measured by heel rise performance, is associated with midfoot deformity in people with diabetes and peripheral neuropathy. Understanding contributors of midfoot movement dysfunction may help clinicians understand deformity progression. The purpose of this study was to determine the factors associated with midfoot angle at peak unilateral heel rise.

Methods: Midfoot (forefoot on hindfoot) sagittal kinematics of 58 participants with diabetes and peripheral neuropathy during unilateral heel rise task were measured using 3-dimensional motion analysis. A multivariate linear regression model was used to predict midfoot sagittal movements at peak heel rise. Independent variables that were entered in the model were (in order of entry): age, body mass index, intrinsic foot muscle volume, and maximum available midfoot plantarflexion range of motion. Intrinsic foot muscle volume was obtained from magnetic resonance imaging and maximum available midfoot motion was measured during non-weightbearing plantarflexion using 3-dimensional motion analysis.

Findings: Body mass index ($R^2=30.5\%, r=0.56$) and maximum available midfoot plantarflexion range of motion ($R^2=10.9\%, r=0.26$) were significant factors that accounted for 41.4% of variance of midfoot angle at peak unilateral heel rise, while age and intrinsic foot muscle volume were not significant predictors.

Interpretation: Weight and midfoot plantarflexion range of motion are important predictors of midfoot movement dysfunction, which are potentially modifiable. Health care professionals should consider patient’s weight and joint motion when prescribing foot exercise(s) to prevent excessive midfoot collapse during weightbearing tasks.
3.2 Introduction

People with diabetes mellitus (DM) and peripheral neuropathy (PN) have been found to have midfoot movement dysfunction. Greater midfoot movement dysfunction is associated with severe midfoot deformity. Midfoot deformity elevates peak plantar pressure and increases the risk of developing an ulcer. Identifying underlying mechanisms associated with midfoot movement dysfunction may help healthcare professionals understand the progression of midfoot deformity and ultimately prevent the cascade of events associated with ulcer development and amputation in people with DMPN.

Heel rise is a common task that is clinically useful for evaluating dynamic midfoot function. In individuals with DMPN, midfoot movement dysfunction has been assessed utilizing the heel rise task as measured by the sagittal midfoot angle. Heel rise performance is an activity that could be impacted by multiple factors. A previous study focused on the muscular function and structure of the ankle and foot (i.e., ankle plantarflexor strength and intrinsic foot fat volume) when investigating the underlying mechanisms associated with heel rise, which explained 37% of the variance in sagittal midfoot excursion during the unilateral heel rise task in people with DMPN. However, this focus left a majority of variance in heel rise performance unexplained.

While foot and ankle muscular components appear to be important contributors to heel rise performance, personal factors may also be important mechanisms associated with heel rise performance. Personal factors such as age and body mass index (BMI) can contribute to reduced midfoot range of motion during weightbearing tasks. Aging has been reported to alter foot
structures and function (i.e., plantar soft tissue, joint range of motion and strength), which impairs foot performance during weightbearing tasks. In studies that measured multi-segment foot kinematics, older adults have shown smaller sagittal midfoot range of motion during walking and significantly less first metatarsal sagittal plane excursions during unilateral heel rise compared to younger adults. Aging as well as increased BMI were significantly associated with a dynamic arch index measured during walking in postmenopausal women. BMI directly increased the stress to the midfoot and midfoot plantar loading during walking in obese adults (BMI average 36.5 kg/m²) compared to non-obese adults (BMI average 24.0 kg/m²). From previous publications, both age and BMI could potentially play a role in midfoot motion during the heel rise task.

Midfoot movement dysfunction could also be related to changes in foot structure associated with DM (i.e., decreased muscle volume and increased joint stiffness). Intrinsic foot muscles generate force to counter longitudinal arch deformation when the foot is loaded. People with DMPN have intrinsic muscle atrophy and deterioration. Intrinsic foot fat volume accounted for 18% of the variance in midfoot excursion during unilateral heel rise in people with DMPN. People with DMPN have significantly reduced mobility at the midfoot, which could be an offset affecting heel rise performance. Midfoot range of motion along with intrinsic muscle volume may account for significant variance of heel rise performance which has yet to be investigated.

Given that midfoot movement dysfunction is problematic for midfoot deformity progression, understanding the contributors to midfoot motion during heel rise could help identify specific treatment targets for patient care. The aim of this study was to determine the contributors that
affect the sagittal midfoot angle at peak unilateral heel rise in people with DMPN. We hypothesized that age, BMI, intrinsic foot muscle volume, and maximum available midfoot plantarflexion range of motion would explain substantial variance of the midfoot angle at peak unilateral heel rise in people with DMPN.

3.3 Methods

3.3.1 Participants

Age was self-reported at the time of participation. Height (cm) and weight (kg) were measured and BMI was calculated as weight (kg)/ height$^2$ (m$^2$). The inclusion criteria were type 2 DM, confirmed by the participant’s physician and PN, considered present if the participant (1) could not feel a 5.07 Semmes-Weinstein monofilament on the tested plantar surfaces (six locations), (2) had Michigan Neuropathy Screening Instrument lower extremity screening exam scores higher than or equal to two, or (3) could not sense the vibration perception threshold of 25 V on the tested plantar surface of the great toe measured by biothesiometry. Participants were excluded if they did not meet the requirements for magnetic resonance imaging (MRI) (i.e., had metal implants, pacemaker, or weighed greater than 180 kg as a weight limit for the scanner), had PN not associated with DM (e.g., alcoholic, chemotoxic, or lumbar radiculopathy), had severe arterial diseases (ankle-brachial index less than 0.9 or higher than 1.3), current ulceration or amputation, on dialysis, pregnant, rigid metatarsophalangeal joint deformity, or age greater than 75 years old (minimize extreme aging-associated changes on joint or muscle).
The foot selected for MRI and kinematic data analysis was based on the parent study criteria focused on forefoot deformity (Clinicaltrials.gov, NCT02616263). The foot selected was the one with: (1) resting metatarsophalangeal joint extension required to match intervention groups, (2) a consistent toe extension movement pattern with active ankle dorsiflexion observed by the examiner, and (3) the fewest non-DM associated complications (e.g., history of surgery, edema). All participants read and signed the provided written informed consent approved by Washington University Institutional Review Board (Washington University School of Medicine, Saint Louis, USA; #201511090).

### 3.3.2 Kinematic and kinetic data acquisition

Three-dimensional kinematic data from a 2-segment foot (forefoot and hindfoot) and shank model were analyzed. Reflective markers were placed on the following anatomical landmarks: 1) Forefoot markers: first and fifth metatarsal bases and heads and between the second and third metatarsal heads, 2) Hindfoot markers: sustentaculum tali, peroneal trochlea, and a thermoplastic plate with two markers at the bisection of the posterior calcaneus, and 3) Shank: tibial tuberosity, fibular head, medial and lateral malleolus, and a thermoplastic plate with four markers at the lateral distal shank. The reflective markers were captured using a 10-camera Vicon motion analysis system (Vicon MX, Los Angeles, CA, USA) at a sampling rate of 100 Hz. Kinetic data were obtained for trial selection as described below (2.3). Force data were acquired using one force plate (FP4060-10 model, Bertec Corporation, Columbus, OH, USA) at a sampling rate of 1000 Hz. Vicon Nexus software (Vicon MX, Los Angeles, CA, USA) and Visual 3D software (C-motion Inc, Germantown, MD, USA) were used for post-processing the kinematic and kinetic data.
3.3.3 Heel rise task

The unilateral heel rise task was completed with the selected extremity, knee extended, on the force plate. The knee of the non-selected side was bent to avoid the non-selected foot touching the force plate. Participants were instructed to raise the heel as high as possible and were provided verbal cues for pacing. Balance support was given by having the participant place their hands on the examiner’s outstretched forearm. Participants performed five repetitions of the unilateral heel rise. The three repetitions with the highest plantarflexor power were selected for data analysis. The midfoot (forefoot relative to hindfoot) angle at peak heel height from the three selected repetitions were analyzed and averaged.

3.3.4 Non-weight bearing ankle plantarflexion task

Participants sat on a plinth with the knee of the selected side extended and the foot relaxed. Participants were instructed to move their foot into maximal plantarflexion and then into maximal dorsiflexion consecutively for five repetitions. Among the five repetitions of plantarflexion, the two highest midfoot plantarflexion angles were averaged and used for statistical analysis.

3.3.5 Intrinsic foot muscle volume

Foot intrinsic muscle volume was measured using MRI (Siemens Prisma Fit 3T, Siemens Medical Systems, Malvern, PA, USA). Participants laid in a supine position with the selected foot placed in a neutral position on the table. An extremity coil was wrapped around the foot to achieve the best signal-to-noise ratio. The MRI sequence parameters were previously described.
using Dixon acquisition. The estimated muscle volume was then divided by the number of slices to normalize the muscle volume by the length of the foot.

We had a priori hypothesis that midfoot plantarflexion during heel rise would be predicted by intrinsic foot muscle deterioration, calculated by intrinsic fat volume to muscle volume ratio. To increase the predictability of midfoot plantarflexion at peak heel rise, all the variables (i.e., muscle and fat volume, normalized muscle and fat volume, fat to muscle volume ratio) related to muscle deterioration were considered and the variable that accounted for the greatest variance was entered into the model. As a result, intrinsic foot muscle volume was selected as the independent variable for the full multiple regression model.

### 3.3.6 Statistical analysis

The dependent variable was midfoot angle at the peak unilateral heel rise height. Age, BMI, intrinsic foot muscle volume, and maximal available midfoot plantarflexion motion (listed in order of entry) were the independent variables entered into a multivariate regression model. The entry order of independent variables was decided a priori as personal factors (age and BMI) and then foot structure (muscle and joint). A forward selection procedure was chosen adding independent variables one at a time, in order to estimate the variance in midfoot angle at peak heel rise explained by each independent variable. A series of multivariate linear regression analyses were performed, each with an additional variable than its former model. The independent variable was left in the model if (1) the $P$-value for the F-statistic (analysis of variance with the overall model) was significant ($P<0.05$); (2) the individual $P$-value for the t-statistic was significant ($P<0.05$); and (3) the added variable contributed at least 5% additional r-
squared value beyond the former model. If one of the criteria was not met, the variable was removed from the model, and the next variable was entered. Correlation analyses were completed between dependent and independent variables to help interpret the results. Since age was not normally distributed, Spearman correlation (ρ) analysis was used. For the remaining independent variables, Pearson correlation (r) analysis was used. All the statistical analyses were conducted with R statistical package software version 3.6.0. (R Foundation for Statistical Computing, Vienna, Austria; www.r-project.org).

3.4 Results

3.4.1 Participants

Sixty people were enrolled in the study; however, two participants were excluded because they did not have MRI measures. As a result, data from 58 participants were analyzed. Descriptive statistics of gender, age, BMI, hemoglobin A1c, and duration of DM are reported in Table 3.1.

Table 3.1 Participant demographics.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: female/male</td>
<td>58</td>
<td>34/24</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58</td>
<td>67 (6) [46, 75]a</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>58</td>
<td>35 (7) [22, 49]a</td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td>57</td>
<td>7.0 (1.3) [5.1, 11.4]a</td>
</tr>
<tr>
<td>Diagnosed diabetes duration (years)</td>
<td>58</td>
<td>14 (10) [0.2, 49]a</td>
</tr>
</tbody>
</table>

a mean (standard deviation) [range]
3.4.2 Predictors of the midfoot angle at peak heel rise

Age was not a significant independent predictor of midfoot angle at peak heel rise (Table 3.2. Model 1; \( P=0.286 \)) and, therefore, it was not considered in a multivariate linear regression model. BMI was a significant independent predictor that accounted for 30.5\% of the variance in midfoot angle at peak unilateral heel rise (Table 3.2. Model 2; \( P<0.001 \)). Intrinsic foot muscle volume was a significant predictor after adjusting for BMI (Table 3.2. Model 3; \( P=0.044 \)). However, muscle volume only added 3.8\% to the r-squared value beyond model 2. Thus, intrinsic foot muscle volume was not retained in the next model. The maximum available midfoot plantarflexion motion was a significant predictor that explained 10.9\% of the unique variance of midfoot angle at peak unilateral heel rise after adjusting for BMI (Table 3.2. Model 4; \( P=0.001 \)). The final model with BMI and maximum available midfoot plantarflexion motion accounted for 41.4\% of variance in midfoot angle during peak unilateral heel rise.

BMI was moderately correlated with midfoot angle at the peak unilateral heel rise (\( r=0.56, P<0.001 \); Figure. 3.1B). Maximum available midfoot plantarflexion motion was weakly correlated with midfoot angle at peak unilateral heel rise (\( r=0.26, P=0.045 \); Figure. 3.1D). Age and muscle volume did not show a significant linear correlation with midfoot angle at peak unilateral heel rise (age: \( \rho=-0.23, P=0.087 \); intrinsic foot muscle volume: \( r=-0.07, P=0.608 \); Figure. 3.1A and 3.1C).
Table 3.2 Prediction of the midfoot angle at the peak unilateral heel rise (n=58).

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$B^a$</td>
<td>$P^b$</td>
<td>$B^a$</td>
<td>$P^b$</td>
</tr>
<tr>
<td>Age</td>
<td>-0.137</td>
<td>0.286</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.468</td>
<td>&lt;0.001*</td>
<td>0.517</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Intrinsic foot muscle volume</td>
<td>-0.002</td>
<td>0.044*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Maximum available midfoot plantarflexion motion</td>
<td>0.308</td>
<td>0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted $R^2$</td>
<td>0.003</td>
<td>0.305</td>
<td>0.343</td>
<td>0.414</td>
</tr>
<tr>
<td>$P^c$</td>
<td>0.29</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Age and intrinsic foot muscle volume were not retained since these variables did not meet the criteria for remaining in the model.

Dependent variable: the midfoot angle at the peak unilateral heel rise.

$^a$ Unstandardized beta coefficient.

$^b$ $P$-value of two-tailed t-test.

$^c$ $P$-value of F-statistics (analysis of variance with the overall model).

*significant $P$-value.
Figure 3.1 Scatter plot of midfoot angle at peak unilateral heel rise vs age, body mass index, and maximum available midfoot plantarflexion range of motion (n=58).

(A) Spearman correlation (\(\rho\)) was used for age vs heel rise.

(B), (C), and (D) Pearson correlation (\(r\)) was used for body mass index, intrinsic foot muscle volume, and maximum available midfoot plantarflexion vs heel rise.

*significant correlation. Values are correlation coefficients (\(\rho\) or \(r\)).
3.5 Discussion

In this study, the contributors of midfoot function during unilateral heel rise were examined using multiple linear regression analysis. BMI and maximum available midfoot plantarflexion motion explained 41.4% of the variance in peak heel height in people with DMPN. Higher BMI and lower midfoot plantarflexion motion were associated with a reduction in midfoot angle at peak heel rise. Weight and limited midfoot mobility are both potentially modifiable factors related to midfoot movement dysfunction and provide treatment targets aimed at reducing the risk of midfoot deformity and preventing skin breakdown in people with DMPN.

BMI was the most important predictor, accounting for 30.5% of the variance in midfoot motion during the unilateral heel rise task. Increased BMI results in increased load during weightbearing tasks that could collapse the longitudinal arch and elevate midfoot pressure. Increased peak pressure is a risk factor for ulceration in people with DMPN. Since weight is a potentially modifiable factor, people with DMPN should be provided with resources for weight management not only for DM management but also to potentially improve foot mechanics and reduce the risk of foot complications.

Maximum available midfoot plantarflexion motion was a significant predictor ($R^2=10.9\%$) and correlated with midfoot motion during unilateral heel rise ($r=0.26$). A linear trend of available midfoot plantarflexion range of motion and heel rise performance indicates that mobility in non-weightbearing task could be an offset to midfoot motion during unilateral heel rise. Increasing midfoot plantarflexion range of motion may improve midfoot performance during weightbearing activities and reduce plantar loading. However, current evidence suggests that limited joint
mobility (ankle dorsiflexion) in individuals with diabetes may not be modifiable with a stretching intervention, perhaps as a result of the systemic nature of limited joint mobility in diabetes. Future research is needed to assess the benefits of a stretching program to address plantarflexion range of motion and its association with loading during weightbearing tasks.

Intrinsic foot muscle volume was a significant factor, explaining 3.8% of the variance in midfoot motion during unilateral heel rise; however, it did not meet the criteria to remain in the model. Considering the insignificant correlation between the muscle volume and the heel rise task (r= -0.07), it is not surprising that the intrinsic foot muscle volume was excluded in the final model. We hypothesize that the insignificant finding is due to the preserved muscle quality of the current cohort of study participants. In a study by Cheuy et al., the inverse correlation between the deterioration ratio and forefoot deformity became greater when intrinsic foot muscle was severely deteriorated (threshold ratio greater than 1). Our findings, combined with those of Cheuy et al., suggests that intrinsic muscle deterioration becomes an important factor as diabetes related foot deterioration progresses.

3.5.1 Limitations

Eighty-six percent of the current study participants were greater than 60 years old (50 out of 58). Although the age of our study sample represents the age of the DMPN population, the unequal distribution of age might have resulted in insignificant findings in aging. Prevalence of type 2 DM is growing in younger population, thus, future work is needed to address the changes in foot function over the lifespan including younger to middle-age participants. A large amount of variance in midfoot motion during heel rise still remains unexplained. Current study measured a
static muscle structure (i.e., intrinsic foot muscle volume); however, dynamic muscle function (i.e., activation and contractility) could potentially have a greater relationship to dynamic performances. Thus, we believe future work in this area should include additional factors such as muscle function (i.e., muscle activity, contractility, strength), plantar fascia stiffness, neural drive, extrinsic muscles (i.e., calf), and balance in order to more fully understand midfoot movement dysfunction during unilateral heel rise. Finally, a prospective longitudinal study is needed to explore the relationship of reduced midfoot motion of heel rise to midfoot deformity progression and occurrence of ulceration in this population with DMPN.

3.5.2 Clinical implications

Possible modifiable factors, such as weight and range of motion, were significant predictors of midfoot plantarflexion motion during unilateral heel rise. By controlling weight and improving range of motion, people with DMPN may improve midfoot function. Improving midfoot motion during heel rise has the potential to improve other functional weightbearing activities such as walking. Health care professionals would need to consider weight and midfoot range of motion when prescribing foot exercise. By addressing potential modifiers with an appropriate foot exercise program, patients with DMPN might reduce excessive midfoot collapse on weightbearing tasks and ultimately prevent developing risk factors associated with ulceration.

3.6 Conclusion

Midfoot motion during unilateral heel rise is associated with BMI and maximum available midfoot motion in people with DMPN. Weight and range of motion are potentially modifiable factors that could be addressed to improve midfoot function during unilateral heel rise. Increased
weight and reduced maximum midfoot motion would need to be considered when prescribing foot exercise program for people with DMPN.

### 3.7 Acknowledgments

We would like to acknowledge Kathryn Bohnert, Darrah Snozek, and Christopher Sorensen for their contributions to the subject recruitment and data collection. Also, Haley Brogan, Jessica Stumpf, Jadean Hoff, Hana Bernhardson, Nick Youmans, Mary Ellis, and Nick Schroeder for their assistance with data post-processing. This study was supported by National Institute of Diabetes and Digestive and Kidney Diseases (R01 DK107809, F32 DK123916) and the Research Division of the Program in Physical Therapy, Washington University School of Medicine, St. Louis, Missouri.
Chapter 4: Midfoot and ankle motion during heel rise and gait are related in people with diabetes and peripheral neuropathy

This chapter has been published:
4.1 Abstract

**Background:** Midfoot and ankle movement dysfunction in people with diabetes mellitus and peripheral neuropathy (DMPN) is associated with midfoot deformity and increased plantar pressures during gait. If midfoot and ankle motion during heel rise and push-off of gait have similar mechanics, heel rise performance could be a clinically feasible way to identify abnormal midfoot and ankle function during gait.

**Research question:** Is midfoot and ankle joint motion during a heel rise associated with midfoot and ankle motion at push-off during gait in people with DMPN?

**Methods:** Sixty adults with DMPN completed double-limb heel rise, single-limb heel rise, and walking. A modified Oxford multi-segment foot model (forefoot, hindfoot, shank) was used to analyze midfoot (forefoot on hindfoot) and ankle (hindfoot on shank) sagittal angle during heel rise and gait. Pearson correlation was used to test the relationship between heel rise and gait kinematic variables (n=60). Additionally, we classified 60 participants into two subgroups based on midfoot and ankle position at peak heel rise: midfoot and ankle dorsiflexed (dorsiflexed; n=23) and midfoot and ankle plantarflexed (plantarflexed; n=20). Movement trajectories of midfoot and ankle motion during single-limb heel rise and gait of the subgroups were examined.

**Results:** Peak double-limb heel rise and gait midfoot and ankle angles were significantly correlated (r=0.49 and r=0.40, respectively). Peak single-limb heel rise and gait midfoot and ankle angles were significantly correlated (r=0.63 and r=0.54, respectively). The dorsiflexed subgroup, identified by heel rise performance showed greater midfoot and ankle dorsiflexion during gait compared to the plantarflexed subgroup (mean difference between subgroups: midfoot 3°, ankle 3°).
**Significance:** People with DMPN who fail to plantarflex the midfoot and ankle during heel rise have less midfoot and ankle plantarflexion during gait. Utilizing a heel rise task may help identify midfoot and ankle dysfunction associated with gait in people with DMPN.

### 4.2 Introduction

Midfoot and ankle movement dysfunction is often observed in people with diabetes mellitus and peripheral neuropathy (DMPN)\(^{26,31,39,40,42,43}\) and is associated with medial column deformity and elevated plantar loading.\(^{26,39}\) The repetition of increased plantar pressure during walking accompanied with loss of sensation and deformity is a pathway to developing ulceration and amputation.\(^{18,19,23,68}\) Identification of midfoot and ankle movement dysfunction during gait and provision of appropriate interventions (e.g. foot and ankle strengthening, off-loading footwear) to address the movement dysfunction is an important component in preventing the cascade of events in which abnormal plantar loading contributes to plantar ulceration and amputation in people with DMPN.\(^{80}\)

Midfoot and ankle plantarflexion during late stance phase of gait is a critical component of normal foot mechanics in which the foot becomes more rigid and allows efficient and safe transfer of plantarflexor force through the foot.\(^{81}\) Previous studies have reported altered midfoot and ankle sagittal plane motions during gait in individuals with DMPN.\(^{39,40}\) DiLiberto et al.\(^{40}\) observed a reduced sagittal excursion of the forefoot and hindfoot during stance phase of gait in people with DMPN compared to healthy matched-controls. Rao et al.\(^{39}\) identified the relationship of reduced sagittal plane excursion of the first metatarsal and lateral forefoot and increased plantar loading during gait. Clinical assessment of gait often relies on visual assessment.\(^{44}\)
However, use of visual assessment to identify ankle and particularly midfoot movement dysfunction during gait is difficult because movements occur at the small joints, i.e. foot and ankle, within a short period of time.\textsuperscript{45,46}

Heel rise performance is likely similar to the terminal stance phase of gait where the largest generation of the ankle plantarflexor power occurs at the timing of single-limb to double-limb transition between 40\% and 60\% of gait cycle.\textsuperscript{55} Clinically, the heel rise task could be used to easily assess plantarflexion motion of midfoot and ankle, acting as a surrogate of midfoot and ankle motion during gait. Despite theoretical similarities of heel rise and gait midfoot and ankle mechanics, the relationships of the heel rise task to gait in people with DMPN have not been examined.

People with DMPN have shown reduced midfoot and ankle plantarflexion during double and single-limb heel rise compared to non-DMPN controls.\textsuperscript{26} Dorsiflexion of the midfoot or/and ankle during single-limb heel rise was observed in 67\% of people with DMPN, whereas plantarflexion of the midfoot and ankle was consistently observed in non-DMPN controls.\textsuperscript{82} If movement patterns of midfoot and ankle during heel rise and gait are related, individuals who fail to plantarflex during heel rise may also fail to plantarflex during late stance phase of gait.

By evaluating the association of midfoot and ankle motion between heel rise and gait, clinicians can benefit from using a simple heel rise task to aid the identification and clinical management of foot problems driven by poor midfoot and ankle mechanics during gait. The primary purpose of this study was to determine the relationship of heel rise performance to gait in people with
DMPN. We hypothesized that measures of heel rise performance (midfoot and ankle plantarflexion angle at peak double- and single-limb heel rise) will be positively correlated with measures of gait performance (midfoot and ankle plantarflexion angle at peak ankle power during gait) in people with DMPN. The secondary purpose of this study was to characterize the trajectory of midfoot and ankle motion of single-limb heel rise and gait in people with DMPN by comparing subgroups of individuals who plantarflex the midfoot/ankle compared to individuals who dorsiflex the midfoot/ankle.

### 4.3 Methods

This study is a secondary analysis that used data at the baseline time point of a longitudinal study (Clinicaltrials.gov, NCT02616263). Thus, inclusion and exclusion criteria, sample size calculation, and selection of the foot for measurements were based on the parent study.

#### 4.3.1 Participants

Sixty people with DMPN participated in this study. Inclusion criteria for this study were the presence of type 2 DM and PN. DM was diagnosed by the participant’s physician. At least one out of three positive findings on the following clinical tests verified PN: (1) inability to sense Semmes Weinstein 10 g monofilament on at least one of six plantar foot locations, (2) inability to sense vibration perception threshold of 25 Volts applied to the plantar surface of the great toe, and (3) Michigan Neuropathy Screening Instrument lower extremity screening exam score equal to or greater than two. Exclusion criteria were: people who were greater than 75 years old, on dialysis, pregnant, or had severe arterial disease (i.e., ankle-brachial index greater than 1.3 or less than 0.9), great toe extension less than 30°, had a current ulcer or lower extremity amputation,
and unable to complete the testing for this study. The parent study included magnetic resonance imaging with the associated exclusion criteria of weight greater than 180 kg, metal or pacemaker implant. Data from 47 individuals without DMPN (non-DMPN) were retrospectively added to provide a reference of the linear relationship between heel rise and gait. The exclusion criteria for non-DMPN were: type 1 or type 2 DM, PN, current plantar ulcer, vascular disease, rheumatoid arthritis, on dialysis, pregnant, history of foot or ankle fracture or surgery, current injury that changes walking behavior, current foot and ankle pain, needed assistance during walking, or wearing prescribed shoes to accommodate foot problems. The study was approved by the Washington University Institutional Review Board (#201511090). All the participants read and signed a consent form to participate the study.

4.3.2 Sample size

The sample size of 60 participants was powered to evaluate the effects of foot interventions on intrinsic foot muscle deterioration in people with DMPN. Thus, a power analysis for this secondary analysis was not conducted a priori.

4.3.3 Kinematic and kinetic data acquisition

The foot measured for double-limb heel rise, single-limb heel rise, and gait was selected based on the criteria from the parent study which selected the foot with: (1) the fewest complications (i.e., history of surgery or traumatic injury); (2) metatarsophalangeal joint hyperextension angles needed to balance group assignment; and (3) the most consistent pattern of toe extension during active dorsiflexion, hypothesized to be a contributing factor to toe deformity in people with DMPN.
Kinematic data were collected from a 10-camera 100Hz Vicon motion analysis system (Vicon MX, Los Angeles, California, USA). A modified Oxford multi-segmental foot model was used to measure midfoot and ankle motion that showed good accuracy of between-trial variability.\textsuperscript{58} Experienced examiners (HJJ, MKH, KLB) mounted twenty four reflective markers on the skin or thermoplastic plates for forefoot, hindfoot, and shank segments according to previously reported methods.\textsuperscript{26,58} Kinetic data were obtained using a Bertec force plate at a sampling rate at 1000 Hz (FP4060-10 model, Bertec Corporation, Columbus, OH, USA).\textsuperscript{83} Kinematic and kinetic data were analyzed from Visual3D software (C-Motion Inc. Germantown, MD, USA). Kinematic data was smoothed using a Butterworth filter with a cut-off frequency of 6 Hz. Kinetic data was filtered at a cut-off frequency of 25 Hz.\textsuperscript{84} The kinetic data were used to select the trials analyzed for the heel rise and to set the event marker for extraction of gait variables. The neutral (0) position of the forefoot and hindfoot segments (midfoot) was set during the calibration trial in a relaxed standing position. The ankle position reflected the position of the shank segment relative to the neutral position of the hindfoot in relaxed standing. The kinematic variables of interest were: sagittal plane midfoot angle, defined as forefoot relative to hindfoot, and sagittal plane ankle angle, defined as hindfoot relative to shank, at peak heel rise and peak ankle power during gait.

Each participant performed five repetitions of both a double- and single-limb heel rise, going as high as possible. All the participants placed their hands on the extended forearm of the tester for balance. Among the five repetitions of the heel rise, the three trials that had the greatest plantarflexor power were selected and the kinematic variables of interest were averaged across the three trials.\textsuperscript{26}
All participants were instructed to walk barefoot at their self-selected speed (see Table 1 for average gait velocity) contacting two force plates with the involved-limb. Self-selected gait speed was chosen to capture the midfoot and ankle kinematics during the participants’ habitual walking pattern. Six individuals with DMPN (10% of DMPN group) walked with hand support of the tester for safety. None of the participants in non-DMPN group required hand support during walking. Two strides of the involved-limb were recorded during one walking trial. Trials were excluded if the participant’s foot did not completely step on a single force plate. Three valid walking trials were obtained for analysis. A total of six steps of midfoot and ankle angle at peak ankle power during gait were averaged.

4.3.4 Subgroups of midfoot and ankle motion

The classification of subgroups by midfoot and ankle motion during heel rise was implemented in this study to illustrate two distinct heel rise performance patterns and its effect on the gait trajectory in individuals with DMPN. We defined subgroups based on the position of the midfoot and ankle at peak single-limb heel rise: (1) dorsiflexed subgroup: the midfoot and ankle were dorsiflexed and (2) plantarflexed subgroup: the midfoot and ankle plantarflexed. The midfoot and ankle angles of the two subgroups throughout a single-limb heel rise and stance phase of the gait were examined. Timing of heel rise and gait cycles was normalized to time of the entire task, and is reported as the percent of total task.

4.3.5 Statistical analysis

The data acquired from the participants were analyzed with R statistical package software version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria; www.r-project.org). The
Shapiro-Wilk normality test and Q-Q plots were used to test the assumptions for a Pearson correlation. Since assumptions for parametric testing were met, two-tailed Pearson correlations were used to determine the relationship of double-limb heel rise and single-limb heel rise to gait in people with DMPN (n=60) and non-DMPN individuals (n=47, for a reference line). An independent t-test was conducted to compare the characteristics and kinematic variables between dorsiflexed and plantarflexed subgroups. Significance level was set at p < 0.05.

4.4 Results

4.4.1 Participant characteristics

The characteristics of the DMPN and non-DMPN groups are provided in Table 4.1. The characteristics of dorsiflexed and plantarflexed subgroups are provided in Table 4.2.

Table 4.1 Participant characteristics.a

<table>
<thead>
<tr>
<th></th>
<th>DMPN</th>
<th>Non-DMPN</th>
</tr>
</thead>
<tbody>
<tr>
<td>N, Sex (F/M)</td>
<td>60 (34/26)</td>
<td>47 (28/19)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>67 ± 6 [46, 75]</td>
<td>43 ± 19 [22, 74]</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>35 ± 7 [22, 49]</td>
<td>33 ± 7 [21, 54]</td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td>7.1 ± 1.3 [5.1, 11.4]</td>
<td>-</td>
</tr>
<tr>
<td>Duration of DM (years)</td>
<td>14 ± 10 [0.2, 49]</td>
<td>-</td>
</tr>
<tr>
<td>Gait velocity (m/s)</td>
<td>0.81 ± 0.16 [0.30, 1.23]</td>
<td>1.01 ± 0.15 [0.74, 1.38]</td>
</tr>
</tbody>
</table>

aValues are given as mean ± standard deviation [range], except for sex. Abbreviation: DMPN, Diabetes mellitus and peripheral neuropathy.
Table 4.2 Characteristics of subgroups.\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>Dorsiflexed subgroup</th>
<th>Plantarflexed subgroup</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N, Gender (F/M)</td>
<td>23 (15/8)</td>
<td>20 (8/12)</td>
<td>0.10(^b)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65 ± 7 [46, 74]</td>
<td>69 ± 5 [58, 75]</td>
<td>0.05(^{*,c})</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>40 ± 5 [30, 49]</td>
<td>30 ± 6 [22, 43]</td>
<td>&lt;0.001(^{*,c})</td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td>7.2 ± 1.6 [5.1, 11.4]</td>
<td>6.8 ± 1.0 [5.3, 9.1]</td>
<td>0.35(^c)</td>
</tr>
<tr>
<td>Duration of DM (years)</td>
<td>16 ± 8 [5, 30]</td>
<td>13 ± 9 [0.5, 33]</td>
<td>0.29(^c)</td>
</tr>
<tr>
<td>Gait velocity (m/s)</td>
<td>0.76 ± 0.15 [0.30, 1.06]</td>
<td>0.81 ± 0.19 [0.45, 1.10]</td>
<td>0.41(^c)</td>
</tr>
</tbody>
</table>

\(^a\)Values are given as mean ± standard deviation [range], except for gender.

\(^b\)Significance of chi-square test between dorsiflexed and plantarflexed subgroups.

\(^c\)Significance of an independent t-test between dorsiflexed and plantarflexed subgroups.

\(^*\)Significant p-value.

Abbreviation: DMPN, Diabetes mellitus and peripheral neuropathy.
4.4.2 Midfoot and ankle angles of double-limb heel rise, single-limb heel rise, and gait in individuals with DMPN

The midfoot was plantarflexed at peak double-limb heel rise [mean (SD); -10° (7°)]. The midfoot was dorsiflexed at peak single-limb heel rise [1° (6°)] and at peak ankle power during gait [2° (4°); Figure. 4.1A]. The ankle was plantarflexed at peak double-limb heel rise [-10° (7°)]. The ankle was dorsiflexed at peak single-limb heel rise [0° (7°)] and at peak ankle power during gait [12° (4°); Figure. 4.1B].
**Figure 4.1** Violin and box plots of (A) midfoot and (B) ankle plantarflexion angles at peak double-limb heel rise, peak single-limb heel rise, and peak ankle power during gait. The width of the colored regions indicates the number of individuals with the measurement. A black line at the center of box plot is the median and the red dot is the mean of the group within the task. The box indicates the interquartile range. The vertical black lines from the box are third quartile + 1.5 interquartile range (upper bound) and first quartile - 1.5 interquartile range (lower bound). Black dot outside the vertical line is an outlier. A dashed line in the center indicates neutral position, defined as the midfoot or ankle at 0 degree.
4.4.3 Correlations of double-limb heel rise and single-limb heel rise to gait

In this group of individuals with DMPN, midfoot and ankle angles at peak double-limb heel rise were both significantly correlated with midfoot \( r=0.49, p<0.001 \) and ankle \( r=0.40, p=0.002 \) angles at peak ankle power during walking (Figure. 4.2A and 4.2B). Midfoot and ankle angles at peak single-limb heel rise were both significantly correlated with midfoot \( r=0.63, p<0.001 \) and ankle \( r=0.54, p<0.001 \) angles at peak ankle power during walking (Figure. 4.2C and 4.2D).

Figure 4.2 Relationship of the double-limb heel rise (A and B) and single-limb heel rise (C and D) to gait, of the midfoot and ankle sagittal angle in groups of DMPN (blue solid line) and non-DMPN (black dashed line). Shaded area represents 95% confidence interval for non-DMPN group. *significant Pearson correlation coefficient \( p<0.05 \).

Abbreviation: DMPN, diabetes mellitus and peripheral neuropathy.
4.4.4 Subgroup analysis of midfoot and ankle during the complete single-limb heel rise and gait cycle

As defined by subgroup assignment, the dorsiflexed subgroup’s midfoot dorsiflexed throughout single-limb heel rise, whereas the plantarflexed subgroup’s midfoot plantarflexed (Figure. 4.3C). Both subgroups plantarflexed the ankle throughout single-limb heel rise, although the dorsiflexed subgroup showed consistently less plantarflexion compared to the plantarflexed subgroup (Figure. 4.3D). Similar to single-limb heel rise performance, the dorsiflexed subgroup performed greater midfoot and ankle dorsiflexion throughout the stance phase of gait compared to the plantarflexed subgroup (Figure. 4.3E and 4.3F).

The dorsiflexed subgroup showed significantly less plantarflexion of midfoot and ankle at peak single-limb heel rise compared to plantarflexed subgroup (mean difference between subgroups in single-limb heel rise: midfoot 11°, p<0.001 and ankle 11°, p<0.001). The dorsiflexed subgroup showed significantly greater midfoot and ankle dorsiflexion at peak ankle power during gait compared to plantarflexed subgroup (mean difference between subgroups in gait: midfoot 3°, p=0.01 and ankle 3°, p=0.03; Table 4.2).
Figure 4.3 Images of midfoot and ankle position at peak single-limb heel rise and gait in the (A) dorsiflexed and (B) plantarflexed subgroups. The participant in (A) show greater midfoot and ankle dorsiflexion at both single-limb heel rise and gait compared to that of the participant in (B). Midfoot and ankle motions (degrees) during single-limb heel rise (C and D) and stance phase of gait (E and F). The dorsiflexed subgroup is in red and the plantarflexed subgroup is in blue. Error bars represent standard deviation. The vertical line (gray) in (E) and (F) is the timing of peak ankle power during the stance phase of gait. In (E), note the dorsiflexed subgroup is in greater midfoot dorsiflexion throughout stance phase of gait and does not cross into plantarflexion until 94% of stance phase.
4.5 Discussion

The key findings of our study indicate individuals demonstrating greater midfoot and ankle plantarflexion at peak double and single-limb heel rise also have greater midfoot and ankle plantarflexion at peak ankle power during gait. In addition, people with DMPN who dorsiflex their midfoot and ankle at peak single-limb heel rise have increased midfoot and ankle dorsiflexion through the entire stance phase of gait compared to people who plantarflexed midfoot and ankle. To our knowledge, this is the first study to report the midfoot and ankle kinematic relationship between heel rise and gait in individuals with DMPN. The stronger correlation of single-limb heel rise compared to double-limb heel rise suggests single-limb heel rise as the better surrogate for assessing midfoot and ankle movements during gait. These findings underscore the potential benefit of the heel rise as a simple, foot and ankle specific, clinically applicable test to screen for midfoot and ankle movement dysfunction that may be present during gait.

The significant relationship between midfoot motion during double and single-limb heel rise and gait indicates that people who have difficulty plantarflexing their midfoot during the heel rise tasks also have difficulty plantarflexing their midfoot during walking. When we examined the kinematic trajectories of midfoot motion during gait between dorsiflexed and plantarflexed subgroups, two primary differences are evident. First, at peak ankle power during gait, the dorsiflexed subgroup was in a more midfoot dorsiflexed position. Second, the dorsiflexed subgroup did not cross into midfoot plantarflexion at the instant of the peak ankle power during gait. The last portion of the stance phase of gait is a critical time during which midfoot
plantarflexion, combined with inversion, assist the foot in becoming a more rigid lever allowing transfer of extremely high forces through the foot joints to avoid midfoot collapse.81

Increased midfoot dorsiflexion into terminal stance (midfoot collapse), likely results in abnormal stress through the midfoot joints with every step. A repetitive, moderate stress is the most common cause of ulceration in people with DMPN.85 People with DMPN take an average of 4909 to 8818 steps a day.86-88 Given that midfoot collapse can occur with every step, the cumulative stress could be substantial. The heel rise task is a clinical test that could help identify individuals who may have midfoot collapse during walking and guide treatment programs aimed at reducing midfoot movement dysfunction and minimizing the risk of increasing mechanical plantar loading in people with DMPN.

People who perform less ankle plantarflexion during heel rise tasks also had reduced ankle plantarflexion at push-off during gait, in other words, they stayed in greater dorsiflexion throughout gait. Heel rise is a measure of plantarflexor strength56 and a strengthening exercise for plantarflexor muscles.89 The positive relationship between ankle motion during the heel rise task and gait suggests strengthening the plantarflexor muscles may improve gait performance. Further research is needed to test the effects of plantarflexor strengthening on heel rise and gait mechanics and plantar pressure in people with DMPN.

The difference between the dorsiflexed and plantarflexed subgroups for midfoot and ankle motion were larger during heel rise compared to gait. Small magnitude change of in midfoot and ankle motion during gait is difficult to observe for clinicians and results in unreliable
The heel rise task is completed more slowly and magnifies the dysfunction making it easier to visually assess motion and suggests it could be a useful clinical examination item.

The plantarflexed subgroup had a lower body mass index and older age compared to dorsiflexed subgroup. Overweight, a modifiable factor, is known to directly increase midfoot pressure during walking\textsuperscript{35} and increases the weight that must be lifted during daily tasks. Future work should examine the contribution of body mass index to foot function, so that we know targets and limits to improving foot function in patients with DMPN.

This study has a few limitations. First, the cause and effect relationship of movement dysfunction to deformity cannot be determined due to the cross-sectional study design. Future work should consider a longitudinal study design to understand the relationship of midfoot and ankle movement dysfunction to the development of midfoot deformity and ulceration in people with DMPN, and if heel rise tasks could be used to identify and treat movement dysfunction during gait. Second, the midfoot and ankle kinematic relationships between heel rise and walking may be uniquely altered by disease (e.g., DMPN) or pathology (e.g., foot and ankle tendon dysfunction, osteoarthritis, etc.). Further study is needed to expand our observations to confirm if the relationship of heel rise to gait is maintained in other people with foot and ankle pathology. Finally, gait kinematics were collected at a self-selected speed, thus, the results cannot be generalized to other walking speed. Despite these limitations, this study provides evidence of associations of midfoot and ankle movement dysfunction across tasks that may provide helpful information to clinical assessment of individuals with DMPN.
4.6 Conclusions

Our study showed a significant relationship of midfoot and ankle sagittal angles between heel rise and gait. In addition, those individuals with dorsiflexed midfoot and ankle at peak single-limb heel rise had greater dorsiflexion of the midfoot and ankle throughout the stance phase of gait compared to individuals with plantarflexed midfoot and ankle during heel rise. These results provide support for using the heel rise task to help identify movement dysfunction of midfoot and ankle during gait. Additional research is needed to clarify the proposed progression of midfoot movements to midfoot injury or deformity.

4.7 Acknowledgments

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Chapter 5: Summary and significance
5.1 Summary

The primary objectives of this dissertation were to (1) understand midfoot and ankle movement dysfunction utilizing the heel rise task; (2) examine factors associated with midfoot motion during the heel rise task; and (3) determine the relationship of midfoot and ankle motion between the heel rise task and gait performance in people with DMPN.

5.1.1 Chapter 2

The purpose of chapter 2 was to (1) examine the effects of DMPN, limited joint mobility associated with DMPN, and weightbearing on midfoot and ankle movements utilizing heel rise task and non-weightbearing ankle plantarflexion task and (2) characterize the peak midfoot and ankle position during heel rise and non-weightbearing tasks, and (3) explore heel rise movement trajectories utilizing a novel classification based on midfoot and ankle position at peak unilateral heel rise task.

People with DMPN had reduced midfoot and ankle plantarflexion motion during non-weightbearing and heel rise tasks compared to those without DMPN (hypotheses 1a and 1b supported). However, contrary to the hypothesis 1c, people with and without DMPN had a similar linear trend of progressive reduction in midfoot and ankle motion across non-weightbearing, bilateral, and unilateral heel rise tasks. The effect of increasing weightbearing was similar between groups. Thus, the available midfoot and ankle plantarflexion range of motion during non-weightbearing is not the limiting factor as weightbearing increases from bilateral to unilateral, but acts as the foundation or the “offset” for heel rise performance.
People with DMPN not only show reduced plantarflexion motion in both unilateral and bilateral heel rise tasks, but also had a greater percentage of people with a peak heel rise midfoot and/or ankle dorsiflexed position compared to non-DMPN controls (*hypothesis 1d* supported). Midfoot and ankle movement trajectories between the four movement pattern subgroups showed midfoot dorsiflexion or plantarflexion and ankle plantarflexion during unilateral heel rise task, reducing weightbearing from unilateral heel rise to bilateral heel rise restored the movement trajectories into midfoot and ankle plantarflexion motion (*hypothesis 1e* supported). Proper weightbearing should be considered when treating patients with foot and ankle exercise program since midfoot and ankle plantarflexion magnitude, position, and movement trajectories can be restored by reducing weightbearing.

### 5.1.2 Chapter 3

The purpose of chapter 3 was to determine the predictors of midfoot motion during heel rise task in people with DMPN. BMI and available maximum midfoot plantarflexion motion explained 41.4% of the variance in midfoot motion during the heel rise task. However, age and intrinsic foot muscle volume were not significant predictors of heel rise performance; thus, *hypothesis 2a* was partially supported. Reducing body weight and improving midfoot range of motion have potential to improve midfoot movements when prescribing safe foot exercise programs to prevent midfoot collapse in people with DM.

### 5.1.3 Chapter 4

The purpose of chapter 4 was to (1) determine the relationship of midfoot and ankle movement dysfunction between heel rise and gait and (2) characterize movement trajectories of unilateral
heel rise and gait in individuals who plantarflexed and dorsiflexed the midfoot and ankle. Midfoot and ankle sagittal kinematics of heel rise and push-off of gait are correlated (hypotheses 3a and 3b supported). Additionally, individuals who were in a dorsiflexed midfoot and ankle position at peak unilateral heel rise showed a greater midfoot and ankle dorsiflexion throughout stance phase of gait compared to individuals who plantarflexed midfoot and ankle at peak unilateral heel rise. From these results, the heel rise task could be utilized to help identify midfoot and ankle movement dysfunction during gait.

5.2 Significance of Key Findings

There were several significant findings from the studies included in this dissertation. People with DMPN showed limited midfoot joint mobility. This study was the first to measure midfoot joint mobility using non-weightbearing ankle plantarflexion task with a 3-dimensional motion analysis system. This finding suggests that the non-weightbearing ankle plantarflexion task could be used as an indicator of joint mobility in people with and without DMPN.

The observed limited midfoot and ankle joint mobility in people with DMPN did not limit heel rise performance. However, a linear trend of plantarflexion motion across non-weightbearing, bilateral, and unilateral heel rise tasks suggests that joint mobility in non-weightbearing task could be an offset to midfoot motion during heel rise task. This result was also supported in the relationship between maximal available midfoot motion and unilateral heel rise task, which explained 10.9% of variance to the midfoot motion at peak heel rise.
A novel classification system based on the midfoot and ankle position of the peak heel rise was developed in this dissertation. From this classification system, we found that people with DMPN had a greater percentage of individuals whose midfoot and ankle were dorsiflexed at peak unilateral heel rise compared to the non-DMPN controls. Utilizing peak heel rise to identify midfoot and ankle position has implications for physical therapists in the evaluation of those with a higher risk of midfoot collapse, a risk factor for increasing plantar pressure associated with plantar ulceration in people with DMPN.  

Body mass index and available maximum midfoot plantarflexion motion were associated with midfoot motion at peak heel rise. Identified predictors (i.e., weight and midfoot plantarflexion motion) are potentially modifiable intervention targets for improving midfoot and ankle movements.

Midfoot and ankle motion during heel rise and push-off of gait showed a significant association. Specifically, individuals with less midfoot and ankle plantarflexion during heel rise task were in more dorsiflexion at push-off of gait. This finding implies that the novel classification assessed at peak heel rise translates to evaluating movement patterns during gait. This finding suggests that the heel rise task could be a surrogate measure of midfoot and ankle movement dysfunction during gait.

Together, current results emphasize utilizing the heel rise task to identify movement midfoot and ankle movement dysfunction. Understanding midfoot and ankle dysfunction during the heel rise
task might help clinicians design interventions to target movement dysfunction that could potentially translate to improvements in walking in people with DMPN.

5.3 Future directions

The findings of this dissertation suggest that heel rise task performance is reduced by the amount of weight lifted as part of the task, modified by the task itself (bilateral/unilateral) and by the weight of the individual. Although reduced joint mobility did not limit performance, it did provide an offset that reduced bilateral and unilateral heel rise in people with DMPN. Future studies should examine the effects of foot intrinsic and calf muscle strengthening and/or midfoot and ankle plantarflexion stretching interventions on improving heel rise performance. Weight loss could potentially increase midfoot and ankle movements during weightbearing performance. Strategies to effectively improve midfoot and ankle movements should be considered when prescribing foot and ankle interventions in people with DMPN.

Future studies should include multiple factors associated with midfoot movements to understand the remaining unexplained variance in midfoot plantarflexion during the heel rise task. Adding younger and middle-aged population with DMPN might help understand the association of aging and foot function that diminishes over a lifespan. Dynamic performance (i.e., heel rise task) may be affected by dynamic muscle function, such as muscle activation, contractility, and strength. Additional factors (e.g., plantar fascia stiffness, neural drive, calf muscles, and balance), as well as dynamic muscle function, should be considered for understanding the contributors of midfoot motion during heel rise.
The proposed progression of midfoot and ankle movement dysfunction to midfoot deformity and ulceration in people with DMPN is unknown. Although cross-sectional studies\textsuperscript{7,26} suggest a significant relationship between movement dysfunction and midfoot deformity, the problems associated with midfoot and ankle movement dysfunction are empirically derived from Kinesiopathology Model\textsuperscript{16} and Physical Stress Theory.\textsuperscript{17} A longitudinal study might help understand the role of movement dysfunction during heel rise task in predicting midfoot deformity progression and ulceration development in people with DMPN.

\textbf{5.4 Conclusion}

Current data shows that people with DMPN have limited midfoot and ankle mobility and reduced heel rise performance compared to non-DMPN controls. Reducing weightbearing load helps restore midfoot and ankle magnitude of motion, joint position, and movement trajectories during heel rise. Additionally, reducing body weight and increasing the available midfoot plantarflexion range of motion may increase midfoot motion at peak heel rise. Since midfoot and ankle movements during heel rise and gait are related, improving heel rise tasks has a potential to improve midfoot and ankle dysfunction during gait. However, the effects of strengthening, stretching, or weight management program on midfoot and ankle movements during heel rise task have yet to be examined. Future studies should consider suggested factors associated with heel rise task to target foot interventions and seek the longitudinal effect of midfoot and ankle movement dysfunction on midfoot deformity progression to better understand the development of plantar ulceration in people with DMPN.
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