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Gait Analysis of Foot Compensation After Arthrodesis of the First Metatarsophalangeal Joint

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Abstract

Background: Arthrodesis of the first metatarsophalangeal (MTP1) joint is an intervention often used in patients with severe MTP1 joint osteoarthritis and relieves pain in approximately 80% of these patients. The kinematic effects and compensatory mechanism of the foot for restoring a more normal gait pattern after this intervention are unknown. The aim of this study was to clarify this compensatory mechanism, in which it was hypothesized that the hindfoot and forefoot would be responsible for compensation after an arthrodesis of the MTP1 joint.

Methods: Gait properties were evaluated in 10 feet of 8 patients with MTP1 arthrodesis and were compared with 21 feet of 12 healthy subjects. Plantar pressures and intersegmental range of motion were measured during gait by using the multisegment Oxford Foot Model. Pre- and postoperative X-rays of the foot and ankle were also evaluated.

Results: The MTP1 arthrodesis caused decreased eversion of the hindfoot during midstance, followed by an increased internal rotation of the hindfoot during terminal stance, and ultimately more supination and less adduction of the forefoot during preswing. In addition, MTP1 arthrodesis resulted in a lower pressure time integral beneath the hallux and higher peak pressures beneath the lesser metatarsals. A mean dorsiflexion fusion angle of 30 ± 5.4 degrees was observed in postoperative radiographs.

Conclusion: This study demonstrated that the hindfoot and forefoot compensated for the loss of motion of the MTP1 joint after arthrodesis in order to restore a more normal gait pattern. This resulted in a gait in which the rigid hallux was less loaded while the lesser metatarsals endured higher peak pressures. Further studies are needed to investigate whether this observed transfer of load or a preexistent decreased compensatory mechanism of the foot can possibly explain the disappointing results in the minority of the patients who experience persistent complaints after a MTP1 arthrodesis.

Level of Evidence: Level III, comparative series.

Keywords: MTP1 arthrodesis, hallux, gait analysis, Oxford Foot Model, multisegment foot model, plantar pressure, compensatory mechanism

Introduction

Osteoarthritis (OA) of the first metatarsophalangeal (MTP1) joint is a common disorder of the musculoskeletal system in elderly, which progresses with age.¹⁰ The exact etiology of MTP1 joint OA is unknown, although trauma, overuse, operations, deformations, and the length of the first metatarsal seem to be involved.⁵,³⁴ Patients usually present with pain, stiffness, and swelling of the MTP1 joint. Erythema and a limited range of motion of this joint are observed during physical examination, while conventional radiographs show degenerative changes of the MTP1 joint.⁷,¹⁴

First metatarsophalangeal joint OA severely affects quality of life since patients experience chronic pain and more difficulties while performing physical tasks and daily activities.¹⁴ An arthrodesis of the MTP1 joint is the preferred
intervention to relieve pain when the articular cartilage is extensively damaged and patients have been refractory to conservative treatment. Approximately 80% of the patients were satisfied after this intervention, in which an arthrodesis alleviated pain complaints and increased function. The reason for dissatisfaction in the remaining 20% of the patients is unknown. It is reasonable to assume that adjacent joints in the foot will compensate for the lack of motion in the MTP1 joint after an arthrodesis in order to restore foot function. An impaired ability of these adjacent joints to compensate for the motionless MTP1 joint can possibly explain the disappointing results of some MTP1 arthrodeses. However, it is not known if and how the foot compensates for restoring the gait pattern toward a normal gait pattern after this intervention.

Motion capture analysis, in which the human body is divided in several segments, allows for measurements and analysis of motion between these segments during gait. This method provides an opportunity to clarify which joints are responsible for restoring the gait pattern after a MTP1 arthrodesis. To our knowledge, only 3 studies used motion capture analysis to assess gait properties after a MTP1 arthrodesis and showed a decrease in step length and step width, although no differences in foot kinematics were detected after this intervention. However, these studies were particularly limited by the gait models used, which presented the foot as a single segment instead of multiple segments. This would be more representative since the foot consists of 26 bones. As a result, the compensatory mechanism after a MTP1 arthrodesis remains unknown.

The goal of this study was to elucidate where the foot compensates for the loss of motion after an MTP1 arthrodesis in order to restore the gait pattern toward a normal gait pattern. Currently, there is no foot model available describing motion between all individual foot joints. Therefore, the 4-segment Oxford Foot Model (OFM) was used to evaluate foot kinematics. This foot model divided the foot and ankle in a tibial, hindfoot, forefoot, and hallux segment. Plantar peak pressures, which provided information on the maximal pressure in a plantar area at one moment during stance, and pressure-time integrals, which provided information of total loading of a plantar area during the entire stance phase, were measured to investigate the effect of a MTP1 arthrodesis on foot loading.

We hypothesized that the hindfoot and forefoot would compensate for the absence of motion in the MTP1 joint after an arthrodesis by showing less eversion and more supination, respectively, as it would be expected that the rigid hallux would be avoided during roll-off. As a result, decreased loading of the hallux and increased loading of the lesser metatarsals would be expected during the stance phase of gait.

Materials and Methods

Study Population

This cross-sectional study was conducted at the Human Movement Laboratory of our institution. Potential candidates were identified in the patient files of the department of orthopaedics of our institution. Patients who underwent MTP1 arthrodesis for symptomatic OA of the MTP1 joint in the past 5 years, with a clinical and radiographic consolidation of the arthrodesis, and a minimum follow-up of 1 year were eligible for participation. Patients with an arthrodesis of another joint in the same foot, who required assistance when walking, or were unable to walk more than 100 meters barefoot were excluded. In addition, patients with a total knee prosthesis, a total hip prosthesis, diabetes mellitus, inflammatory joint disease, or neurological disease influencing gait were not eligible for participation in this study. Patients were compared to healthy subjects with no medical history resulting in an abnormal gait pattern (ie, fractures or deformities of the lower extremities, neurological brain, or spinal cord injury). Approval for this study was obtained from the local ethics committee, and all patients provided written informed consent.

Overall, 8 patients were included, of which 6 patients underwent a unilateral MTP1 arthrodesis and 2 patients a bilateral MTP1 arthrodesis, resulting in a total of 10 feet with MTP1 arthrodesis. Twelve healthy subjects were included (9 of whom were measured bilaterally), resulting in a total of 21 control feet.

Operative Technique

All patients were operated between December 2010 and May 2014 by 2 orthopaedic surgeons. Briefly, a longitudinal dorsomedical incision was used. Socked and ball reaming of the metatarsal head and base of the proximal phalanx was applied. Fixation was established with the “HALLUX FIX Integra plate” (Integra Life Sciences, Plainsboro, NJ, USA). During the postoperative period, patients were immobilized with a non–weight bearing cast for 4 weeks, followed by a weight-bearing cast for the subsequent 4 weeks. No complications of the primary surgical intervention (ie, infection or revision surgery) were reported.

Radiographic evaluation

Two independent observers, who were blinded to the gait analysis and patient outcome, evaluated preoperative and postoperative radiographs. The following parameters were evaluated on radiographs: intermetatarsal angle (IMA), hallux valgus angle (HVA), and hallux interphalangeal angle. The dorsiflexion fusion angle (DFA) was measured as described by Coughlin. Mean angles of both measurements...
were calculated. Differences between observers greater than 5 degrees were resolved by consensus. Radiographic consolidation of the MTP1 arthrodesis was confirmed in all patients.

**Motion analysis**

Motion capture was conducted using a Vicon system (Vicon Motion Systems, Oxford, UK), consisting of 16 infrared cameras (8 T10, 6 MX3, and 2 T20 running at 200 Hz). One trained researcher placed all 42 markers (Supplement 1 available in the online journal) according to the OFM protocol after careful identification of the bony landmarks. The OFM is a 4-segment model of the foot and divides the foot and ankle in a tibial (tibia and fibula), hindfoot (calcaneus and talus), forefoot (5 metatarsals), and hallux segment and has been validated to measure intersegmental motion in the sagittal, coronal, and transverse planes.9,39,41 A 10-meter runway was equipped with a forceplate (AMTI OR6 Series, Advanced Mechanical Technology Inc, Watertown, NY, USA) running at a frequency of 1000 Hz and was synchronized with the Vicon Nexus 1.8.5 software. Dynamic plantar pressures were measured using a pressure plate (High Speed Advanced Footscan System, RSscan International, Paal, Belgium), which had a sampling frequency of 253 Hz. The pressure plate was mounted on top of the forceplate and was also synchronized with Vicon Nexus 1.8.5.

The following patient characteristics were measured for running the OFM: height, weight, knee and ankle width (distance between the lateral and medial condyle of the knee and the distance between the lateral and medial malleolus of the ankle, respectively), and leg length (distance between the anterior iliac spine and the medial malleolus). One trained researcher performed all measurements. Markers were calibrated, and subject-specific axes were calculated during 1 static trial, with the patients standing in an anatomically neutral position. After this static trial, 3 markers were removed according to the OFM protocol, and patients were asked to walk at a comfortable speed with their eyes focused on the wall in front of them. After the practice trials, at least 15 proper recordings with the subject cleanly striking the pressure plate were obtained while walking barefoot.

**Data processing**

Markers were tracked and labeled using Vicon Nexus 1.8.5. Intersegmental range of motion and spatio-temporal parameters of interest were calculated with MATLAB software (version R2012A, The MathWorks Inc, Natick, MA, USA). All trials with a gait velocity ranging between 2 standard deviations of the subjects’ own average speed were used for further analysis. The pelvic segment center of mass, which was estimated based on the pelvic markers, was used to define gait velocity. Stance time was defined as the time between heel strike and toe off of the foot of interest. Step length was calculated as the distance between both heel markers in the direction of gait, while step width was the distance between these markers in the plane perpendicular to the direction of gait. Intersegmental range of motion (ROM) was calculated for the hindfoot-tibia and forefoot-hindfoot segment in the frontal plane (ie, inversion/eversion and pronation/supination, respectively), sagittal plane (ie, dorsiflexion/plantarflexion), and transverse plane (ie, external/internal rotation and abduction/adduction, respectively) and for the hallux-forefoot segment in the sagittal plane (ie, dorsiflexion/plantarflexion). The ROM was calculated for the 4 phases of stance as defined by Perry32 after time normalization of the gait cycle. These phases were the loading response (0%-17% of stance phase), midstance (18%-50%), terminal stance (51%-83%), and preswing (84%-100%). The ROM was defined as the difference between the minimum and maximum joint angle during each phase. Initial contact was identified as the onset of a vertical ground reaction force exceeding 20 Newtons (N), and toe off was identified as the first moment after initial contact with the vertical ground reaction force below 20 N. The ROM was averaged for at least 6 trials per subject, which has proven to be a sufficient number of trials to achieve high intraclass correlation coefficients for the OFM.39

Since it is known that bilateral disease can influence compensatory mechanisms, motion patterns of the segments of interest and the pelvis, hip, and knee of bilateral and unilateral treated patients were compared to assess this influence. In addition, left and right feet of healthy subjects were compared to assess if analysis of both feet influences outcome.

For analysis of dynamic plantar pressure, the foot was automatically divided in 10 anatomical areas (ie, the hallux [Toe1], lesser toes [Toe2-5], metatarsal heads [Meta1-Meta5], midfoot, medial heel, and lateral heel) by the Footscan 7.0 Gait 2nd Generation software. Trials with inconsistencies in the automatic masking procedure were manually adjusted. An ASCII output was generated in which peak pressures (PP), force-time integrals, and contact areas were obtained. Peak pressure was defined as the highest magnitude measured by any sensor in an area and reflects the highest value in a peak pressure-time curve of a particular area. The force-time integral and contact area were used for calculating the pressure-time integral (PTI) as described by Melai et al.31 This alternative calculation of the PTI described the cumulative effect of pressure on a plantar area over time (ie, area under the peak pressure-time curve) instead of summing the PP per timeframe for an entire trial. It thereby provided a more representative value of the total load exposure of a plantar area during stance. Both PP and PTI were calculated for the 10 described areas.
Statistical analysis

Statistical analyses were performed with SPSS software (version 23; IBM, Armonk, NY, USA). The Shapiro-Wilk test was performed to assess whether gait parameters were normally distributed. Log linear transformations were used for not normally distributed data. The unpaired Student t test was used to detect differences in patient characteristics, spatio-temporal parameters, intersegmental ROM, and plantar pressure data between patients and healthy subjects. Differences in radiographic angles between pre- and postoperative radiographs and differences in intersegmental ROM in both feet of bilateral evaluated healthy controls were tested with the paired t test. A P value less than .05 was considered to be statistically significant for patient characteristics, spatio-temporal parameters, and plantar pressure data. To adjust for multiple tests over the 4 phases of stance, a Bonferroni correction was applied to achieve an overall error rate of 5%. Therefore, a P value less than .0125 was considered to be statistically significant for differences in intersegmental ROM.

Results

Patient characteristics

Baseline patient characteristics are presented in Table 1 and depict differences between both groups. Healthy subjects were significantly younger (P = .003), had a greater height (P = .002) and lower body mass index (P = .05), and contained more male participants compared to the MTP1 arthrodesis group. Radiographic angles are presented in Table 2, showing a significant decrease in IMA and HVA (P = .02 and P = .03, respectively) after MTP1 arthrodesis. The mean postoperative DFA was 30.0 ± 5.4 degrees (range, 21-35 degrees).

Gait analysis

Gait analysis took place at a median follow-up of 27 months (range, 18-60 months) postoperatively. With the numbers available, no significant differences in gait velocity, stance time, and step length were detected between both groups, as is shown in Table 3. Step width was significantly smaller in the MTP1 arthrodesis group compared to the healthy control group (P < .05).

Kinematic results are presented in Figure 1 and Figure 2. The MTP1 arthrodesis group showed a significantly increased ROM in the terminal stance phase in the transverse plane in the hindfoot-tibia segment (P = .002, Figure 1A), which was the result of a more internally rotated hindfoot (Figure 2A). A significantly decreased ROM was observed after a MTP1 arthrodesis in the frontal plane during midstance in this
segment \( (P = .001, \text{Figure 1C}) \), due to diminished eversion of the hindfoot (Figure 2C). No significant differences could be detected in sagittal plane motion in the hindfoot-tibia segment (Figure 1B and Figure 2B).

Transverse plane motion showed a significantly reduced ROM after a MTP1 arthrodesis in the forefoot-hindfoot segment during preswing \( (P = .003, \text{Figure 1D}) \), due to diminished adduction of the forefoot in this phase (Figure 2D). In addition, significantly less plantarflexion was observed during midstance \( (P < .001, \text{Figure 2E}) \) and terminal stance \( (P = .001, \text{Figure 2E}) \) in this segment, which resulted in a significantly reduced ROM in the sagittal plane in the MTP1 arthrodesis group (Figure 1E). A significant increase in ROM after a MTP1 arthrodesis, as a result of increased supination of the forefoot \( (P < .001, \text{Figure 1F and Figure 2F}) \), was detected in the frontal plane during preswing in the forefoot-hindfoot segment.

Decreased ROM of the hallux was observed in the loading response \( (P < .001, \text{Figure 1G}) \) and terminal stance phase \( (P = .001, \text{Figure 1G}) \) in the MTP1 arthrodesis group,
which was the result of less plantarflexion of the hallux during loading response and less dorsiflexion of the hallux during terminal stance (Figure 2G).

Evaluation of motion patterns of the segments of interest (Figure 3) and proximal joints (Supplement 2 in the online journal) showed no major differences between unilateral and bilateral treated patients. Differences in joint angles were below 5 degrees for all joints, except sagittal hip and knee joint motion, showing a maximum difference in joint angle of 7 degrees between those patients. Evaluation of healthy controls showed no significant differences in ROM and joint motion patterns between left and right feet (Supplement 3 in the online journal), which justified the usage of both left and right feet in this study.
Figure 3. Average absolute joint angles in the (A-C) hindfoot-tibia segment, (D-F) forefoot-hindfoot segment, and (G) hallux-forefoot segment in the transverse, sagittal, and frontal planes during stance for patients with a unilateral and bilateral first metatarsophalangeal joint arthrodesis.
Plantar pressure

Significantly higher PPs were observed beneath the lesser toes (Toe 2-5, $P = .013$); second, third, fourth, and fifth metatarsal head areas ($P = .025$, $P = .038$, $P = .003$, and $P = .05$, respectively); and midfoot ($P = .017$) in the MTP1 arthrodesis group, as is shown in Figure 4. Evaluation of the PTI showed a significantly lower PTI in the hallux area (Toe 1, $P < .001$), while a higher PTI was observed in the fourth metatarsal ($P = .03$) and midfoot area ($P = .003$) in the MTP1 arthrodesis group.

Discussion

In this study, biomechanical gait properties, plantar pressures, and radiographs were evaluated in patients who underwent an arthrodesis of the MTP1 joint for symptomatic OA of this joint. This was the first study investigating the compensatory mechanism of the foot after this intervention in order to restore the gait pattern. We hypothesized that the hindfoot and forefoot would compensate due to less eversion of the hindfoot, followed by increased supination of the forefoot. This compensatory mechanism subsequently results in decreased loading of the hallux and increased loading of the lesser metatarsals during stance.

As expected, our findings demonstrated an altered motion pattern in the forefoot and hindfoot after MTP1 arthrodesis. This motion pattern consisted of decreased eversion of the hindfoot during midstance, followed by increased internal rotation of the hindfoot in terminal stance, and ultimately increased supination and decreased adduction of the forefoot during preswing. In addition, decreased PTI beneath the hallux together with higher PTIs and PPs beneath the lesser metatarsals were observed. This consecutive altered motion pattern served as a compensatory mechanism in which the rigid hallux was avoided during roll-off. This was confirmed by the plantar pressure results showing a load transfer from the first ray toward the lesser toes. 

*Figure 4. (A) Plantar peak pressure and (B) pressure time integrals for the 10 anatomical areas of the foot for the first metatarsophalangeal joint arthrodesis group and healthy controls. *Indicates a significant difference between both groups ($P < .05$).
metatarsals. These findings support our hypothesis that the hindfoot and forefoot are responsible for restoring the gait pattern after MTP1 arthrodesis.

To our knowledge, this was the first study evaluating foot and ankle kinematics after MTP1 arthrodesis with a multisegment foot model. The validated OFM was used to assess foot and ankle kinematics in our study.12,13,16,25,30 This foot model has been progressively used to gain more insight into the biomechanical consequences of foot and ankle pathologies on gait.18,38 The high reliability of the OFM for measuring joint kinematics during gait has been proved in several studies. The highest repeatability was reported in the sagittal plane, followed by the frontal and transverse planes.9,15,39,41 Previous studies evaluating gait properties after MTP1 arthrodesis are scarce and show a decrease in step length and step width.5,16,22 A decrease in step width was observed in this study, which is consistent with a previous study of Brodsky et al.,5 who suggested that this resulted in increased stability during gait. However, we suggest that this is due to the higher number of women in the MTP1 arthrodesis group since it is known that step width is smaller in women.17,27 As described before, none of these previous studies were able to evaluate the effects of MTP1 arthrodesis on foot and ankle kinematics as the models used in these studies were not suitable for assessing foot and ankle kinematics. Therefore, the compensatory mechanism remained unclear.

From a kinematic point of view, the compensatory mechanism of the foot and ankle as shown in our study suggests decreased loading of the hallux with subsequently increased loading of the lateral plantar areas of the foot. As stated, the results support our hypothesis as a decreased PTI beneath the hallux with higher PPs beneath the second, third, fourth, and fifth metatarsal heads and a higher PTI beneath the fourth metatarsal head were observed. This is contradictory to previous studies, which showed an increased PP beneath the hallux. Therefore, it was concluded that fusion of the MTP1 joint restored the weight-bearing function of the first ray due to pain relief and mechanical stabilization of the medial column.12,13,16,25,30

A possible explanation for the differences in results between our study and previous pressure studies is the nature of measuring plantar pressures, which was performed dynamically in this study while assessed statically in most previously studies.12,13,25,30 In addition, previous studies were limited since they only reported PP, which gives information about the maximal pressure in an area during one timeframe but provides no information concerning the pressure load during the rest of the stance phase.16,23,36 Our results perfectly demonstrate the additive value of assessing the PTI since this value showed that the hallux was less loaded during stance after MTP1 arthrodesis. If PP was used as our single pressure measurement outcome, this would have resulted in the incorrect conclusion that MTP1 arthrodesis restores the weight-bearing function of the hallux as no differences in PP beneath the hallux were observed between the groups.

Based on the observed compensatory mechanism, we expected to observe unloading of the first metatarsal head. This effect of MTP1 arthrodesis was not observed. It is known from the literature that the optimal DFA of the hallux ranges between 20 degrees and 25 degrees, with higher Dfas causing higher pressures beneath the first metatarsal.1,3 In our opinion, decreased PP or PTI beneath the first metatarsal head was not observed since patients included in this study had an average DFA of 30 degrees.

This was the first study investigating the compensatory mechanism of the foot with a multisegment foot model and assessing PTIs of plantar areas in patients with MTP1 arthrodesis. Despite the described findings, we acknowledge that this study had some limitations. Selection of a gender- and age-matched control group would have been more appropriate as significant differences in gender and age distribution were detected between the groups. Besides, a significant difference in height was detected between both groups. The number of studies evaluating the effect of age, height, and gender on gait parameters is limited. It is known that age and height mainly affects gait velocity and gait velocity subsequently strongly influences foot kinematics.2,8,11,20,27,28 Since gait velocity was comparable between both groups, the difference in age was deemed not to have influenced our results. In addition, the effect of gender on foot and ankle kinematics has not been defined yet, although some studies suggest a true gender effect in ankle motion in the sagittal plane.26,27,33 Therefore, the effect of gender cannot be completely ruled out. In addition, it is known that a bilateral intervention or disease can influence gait characteristics since the limbs do not act independently during gait. Kinematics of unilateral and bilateral treated patients were compared to assess this potential effect. Kinematics at the knee, hip, and pelvic levels were visually compared in order to elucidate whether compensation appeared at a distal level (ie, the foot) or at a more proximal level as well. Our data showed no major differences in segmental motion patterns, and maximum differences in joint angles were below 5 degrees for all motions (except sagittal hip and knee motion) at these proximal levels, resulting in the conclusion that compensation mainly occurred in the foot. Subsequently, foot kinematics of these patients were visually compared, showing small differences in joint angles (ranging between 2 degrees and 5 degrees) between those patients. Therefore, it was concluded that inclusion of bilaterally treated patients did not significantly influence our data. However, we were only able to assess this visually as the number of feet that were unilaterally and bilaterally treated was too small for statistical evaluation. Although both limbs do not act independently during gait, inclusion of both left and right feet of bilaterally evaluated healthy subjects was justified since no significant differences in ROM and joint
motion patterns were observed between left and right feet. Furthermore, small errors in marker placement could result in variability despite the acceptable to good reproducibility of the OFM.\textsuperscript{10,39,41} To minimize this effect, one experienced researcher placed all markers. In addition, as this was the first study evaluating foot and ankle kinematics after MTP1 arthrodesis, sample size was not calculated before the start of the study. This study was therefore limited due to the number of patients. As a result, inclusion of a patient with a more deviated gait pattern had a major influence on the results, as can be seen in the large variability in the joint motion patterns. Although variation in ROM and joint motion patterns existed between individuals, no major inconsistencies (ie, phase shifts) were detected between subjects.

Conclusion
This was the first study demonstrating that the hindfoot and forefoot compensate for the loss of motion after MTP1 arthrodesis, thereby resulting in a gait pattern in which the lesser metatarsals endured higher peak pressures while the hallux was less loaded during the stance phase of gait. These results indicate that the foot had the intrinsic capacity to compensate for the loss of motion of the hallux after MTP1 arthrodesis. We suggest that a preexisting reduced compensatory mechanism of the forefoot or hindfoot or the transfer of load from the first ray to the lesser metatarsals could result in persistence of symptoms in the minority of the patients who were dissatisfied after MTP1 arthrodesis. Prospective studies are necessary to demonstrate which of these explanations are the cause of the persistent complaints in the minority of the patients treated with an arthrodesis of the MTP1 joint.

Authors’ Note
Since gait analysis studies were performed multidisciplinary in the Maastricht University Medical Centre, more than 6 authors were involved in this study. Jasper Stevens, MD, Mathijs C.H.W. Fuchs, MD, Lodewijk W. van Rhijn, Prof, MD, Joris P.S. Hermus, MD, and Adhiambo M. Witlox, MD, PhD, were involved in collecting eligible participants, the surgical intervention, and evaluation of clinical functioning. Jasper Stevens, MD, Kenneth Meijer, PhD, Wouter Bijnens, BScEng, Mathijs C.H.W. Fuchs, MD, Sander van Hoeve, MD, Martijn Poeze, MD, PhD, and Adhiambo M. Witlox, MD, PhD, performed gait analysis and were involved in data collection. All authors were involved in analyzing kinematic data and plantar pressure data and participated in writing and revising the manuscript.

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Supplemental Material
Supplementary material is available online with this article.

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