Passive Hallux Adduction Decreases Blood Flow to Plantar Fascia

Julia Lorene Dunbar

*Brigham Young University*

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Passive Hallux Adduction Decreases Blood Flow to Plantar Fascia

Julia Lorene Dunbar

A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of
Master of Science

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ABSTRACT

Passive Hallux Adduction Decreases Blood Flow to Plantar Fascia

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Master of Science

Purpose: Due to the vital role that blood flow plays in maintaining tissue health, compromised blood flow can prevent effective tissue healing. An adducted hallux, as often seen inside a narrow shoe, may put passive tension on the abductor hallucis, consequently compressing the lateral plantar artery (LPA) into the calcaneus and thus restricting blood flow. The purpose of this study was to compare blood flow within the LPA before and after passive hallux adduction (PHA). Methods: Forty-five healthy volunteers (20 female, 25 male; age = 24.8 ± 6.8 yr; height = 1.7 ± 0.1 m; weight = 73.4 ± 13.5 kg) participated in this study. Blood velocity and vessel diameter measurements were obtained using ultrasound imaging (L8-18i transducer, GE Logiq S8). The LPA was imaged deep to abductor hallucis for 120 seconds: 60 seconds at rest followed by 60 seconds of PHA. Maximal PHA was performed by applying pressure to the medial side of the proximal phalanx of the hallux. Blood flow was then calculated in mL/min, and pre-PHA blood flow was compared to blood flow during PHA. Results: Log transformed data was used to run a paired t-test between the preadduction and postadduction blood flow. The volume of blood flow was 22.2% lower after PHA compared to before (−0.250 ± 0.063, \( p < 0.001 \)). Conclusion: Although PHA is only a simulation of what would happen to the hallux inside of a narrow shoe, our preliminary findings of decreased blood flow through PHA suggest blood flow in narrow footwear and its effects on tissues within the foot are worth investigating.

Key Words: plantar fasciitis, narrow shoes, footwear
ACKNOWLEDGMENTS

Having been very new to research at the start of the master’s program, I am incredibly grateful for my thesis committee and other faculty mentors who have patiently taught me about the research process. Their investment in my endeavors has been truly meaningful. I am especially appreciative of my thesis chair, Dr. Wayne Johnson. Dr. Johnson has been a tremendous support to me throughout the master’s program. He introduced me to the world of ultrasound and was instrumental in the development of my thesis project. He was always quick to offer help, and, in spite of setbacks along the way, he didn’t let me get discouraged. It has been a joy to work with him. Additionally, our sonographer, Annie Brewerton, was a tremendous asset to the success of this project. Her input and expertise in both the development and execution of the project were invaluable. I greatly appreciate her help and the assistance of other undergraduate and graduate students. I also can’t express enough gratitude to The Church of Jesus Christ of Latter-day Saints for not only shaping me as a person but blessing me with an opportunity to further my education. Without the tithes of faithful church members and generous donations to Brigham Young University, graduate school may never have been a possibility for me. Lastly, my parents have always been supportive of both my personal and academic pursuits, which means a great deal to me. I likely never would have attended Brigham Young University had I not been striving to follow in their footsteps. I will forever be indebted to them for their exceptional examples and unwavering love.
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Introduction

Plantar fasciitis is a highly prevalent injury and the most common cause of plantar heel pain.\textsuperscript{1,2} The pathology accounts for one million medical visits in the United States each year.\textsuperscript{2} However, in spite of its frequent diagnosis, plantar fasciitis remains poorly understood.\textsuperscript{2} Research suggests that the cause of plantar fasciitis may be multifactorial.\textsuperscript{3,4} These factors may include repetitive strain on the plantar fascia,\textsuperscript{3,5,6,4} intrinsic foot muscle weakness,\textsuperscript{7} calf tightness,\textsuperscript{3} improper shoes,\textsuperscript{3,8} pes planus,\textsuperscript{3,8,5,6,4} pes cavus\textsuperscript{3,6,4} and hyperpronation.\textsuperscript{5,4} It has also been suggested that plantar fasciitis may be accompanied by degenerative changes rather than inflammation.\textsuperscript{9} We hypothesize that this tissue degeneration may be due to a lack of blood flow to the plantar fascia. The relationship between blood flow and healing may help explain the 46% recurrence rate of plantar fasciitis reported in previous research.\textsuperscript{10}

Few studies have examined blood flow to the plantar fascia with regard to healing. Blood flow is essential following injury as it provides the vital reparative factors for healing.\textsuperscript{11} For example, anatomical structures such as the scaphoid and patella have difficulty healing due to poor vascularization.\textsuperscript{12,13} Previous research has shown that decreased blood flow can also prevent healing in the Achilles tendon.\textsuperscript{14} Due to the continuity of the plantar fascia and Achilles tendon,\textsuperscript{15,16,17,18} it can be assumed that decreased blood flow may be preventing healing not only of the Achilles tendon but of the plantar fascia as well. In the plantar fascia, however, the lack of blood flow may be augmented by footwear.

Modern footwear, which is often tight or narrow,\textsuperscript{19} can laterally deviate the hallux\textsuperscript{20} which may consequently affect blood flow. A laterally deviated hallux may place the posterior tibial artery at risk for partial occlusion from impingement. Prior to supplying blood to the plantar aspect of the foot, the artery passes posterior and inferior to the sustentaculum tali of the
calcaneus and then divides into medial and lateral plantar arteries deep to the abductor hallucis.\textsuperscript{21} There is a possibility of impingement against the calcaneus if the abductor hallucis were to be enlarged, contracted or passively tensed as would be seen during passive hallux adduction (PHA). Eighty-eight percent of women and a large proportion of men have been shown to wear ill-fitting shoes.\textsuperscript{19,20} Due to the narrow toe box featured in modern footwear,\textsuperscript{19} lateral deviation of the hallux may be a common phenomenon, making its effects on blood flow worth investigating.

In addition to adduction of the hallux, this impingement may be influenced by overall foot structure. Pes planus and pes cavus foot structures are associated with higher plantar fasciitis incidence rates.\textsuperscript{3,6,4} This is thought to be due to their effect on foot mechanics.\textsuperscript{22} However, few studies have considered the additional influence these structural deformities may have on blood flow. A pes cavus foot, for example, may have tighter muscles due to the shortened medial longitudinal arch. A tight and shortened abductor hallucis could be more likely to occlude the posterior tibial artery that runs deep to it. Also, pes planus may put excessive stretch or tension on the abductor hallucis, which could theoretically put pressure on the posterior tibial artery.

Thus, the purpose of this study was to 1) examine the effects of PHA on blood flow and 2) determine if changes in blood flow are related to arch height. We theorized that lateral deviation of the hallux would contribute to a decrease in the amount of lateral plantar artery blood flow and that the decrease in blood flow would be greatest in the low-arch and high-arch individuals.

Methods

Forty-five healthy volunteers (20 female, 25 male; age = $24.8 \pm 6.8$ yr; height = $1.7 \pm 0.1$ m; weight = $73.4 \pm 13.5$ kg) participated in the present study. All subjects were free of lower extremity injury or pain at the time of the study and had been for at least 6 months. Subjects were
excluded if they had moderate to severe hallux valgus. Hallux valgus deformity was defined using the grading scale established by Garrow et al (Fig. 1). Individuals interested in participating were sent these photographs electronically and were asked to identify which image their feet most closely resembled. Individuals who identified as between the B and C images or more severe were excluded from the study. Prior to participation, written informed consent was obtained from all subjects, and study procedures were approved by the Institutional Review Board at Brigham Young University.

Participants’ shoes were removed, and seated foot posture measurements of the right foot were obtained using the Arch Height Index Measurement System (Jaktool Engineered Solutions, Cranbury, NJ). Arch height index (AHI) was then calculated by dividing dorsum height by truncated foot length.

Prior to ultrasound imaging, each subject lay supine on a treatment table for 5 minutes in order to allow blood flow to normalize. Each subject was positioned with a pillow under the externally rotated right leg (Fig. 2). Electrocardiogram (ECG) electrodes were adhered to the skin over the right and left chest and lower right abdomen. Ultrasound images were then recorded of the right foot before and after the initiation of maximal PHA. The images were taken by a licensed ultrasound technician with 4 years of vascular sonography experience.

Vessel diameter and blood velocity measurements were obtained from the lateral plantar artery (LPA) deep to the abductor hallucis using a Logiq S8 ultrasound system (Fig. 3; General Electric Company, Fairfield, CT). Real-time ultrasound images were recorded using an L8-18i linear transducer. Transverse images were taken of the vessel in brightness mode (B-mode) before and after the initiation of PHA. Longitudinal images were also taken of the vessel before and during PHA but were taken in triplex mode: color flow, pulse-wave, and B-mode.
The same imaging protocol was used for each subject (Fig. 4). Following the initial 5-minute rest period, the LPA was imaged from a transverse view at rest for 30 seconds. Immediately following the transverse video, the transducer was turned 90 degrees, and the LPA was imaged longitudinally in triplex mode for 120 seconds. The first 60 seconds of the longitudinal video was taken at rest while the subsequent 60 seconds of the video was taken during sustained PHA. At the completion of the 120-second video, the hallux was released, and the subject lay at rest for another 5 minutes. The LPA was then imaged transversely for 30 seconds during sustained PHA.

Maximal PHA was applied to each subject by the same investigator. PHA was performed by applying pressure to the medial side of the proximal phalanx of the hallux enough to achieve full frontal plane range of motion at the first metatarsophalangeal (MTP) joint without causing discomfort to the subject. The lateral toes were slightly passively extended when necessary in order to allow unobstructed lateral movement of the hallux. Photographs were taken of the hallux at rest and during each PHA condition in order to measure the amount of PHA in each subject (Fig. 5).

Following data collection, Dartfish Video Software (Fribourg, Switzerland) was used to measure the adduction angle of the hallux before PHA and during both PHA trials. The angle of adduction was measured at the first MTP joint. The origin of the angle was placed over the MTP joint, and the ends were aligned with the first metatarsal proximally, and distally bisected the toenail (Fig. 5). The difference between each subject’s resting angle and the average of the two maximally adducted angles was then calculated to determine the amount of angle change.

Blood velocities were automatically computed from the longitudinal ultrasound videos. In pulse-wave mode, the ultrasound system uses Doppler technology to measure blood velocity.
Due to the natural ebb and flow of blood within a vessel between heartbeats, the ultrasound system outputs an average blood velocity for each cardiac cycle. Average blood velocity was recorded for each cardiac cycle throughout the 120-second longitudinal video.

The B-mode, transverse videos were used to obtain the LPA diameter. This was not done in the longitudinal videos due to the difficulty of imaging such a small vessel. We used the transverse view to ensure the true diameter was measured. The measurement calipers within the ultrasound software were used to measure the vessel diameter manually. The measurement was taken at the widest part of the artery from one tunica intima to the other (Fig. 6). The integrated ECG data was used in order to allow for consistent measurement of vessel diameter throughout each cardiac cycle. Diameter was measured at end-diastole as represented by the peak of the R wave. Vessel diameter was measured and recorded for each cardiac cycle throughout the 30-second resting and 30-second adducted videos.

Due to the variability between average blood velocity measurements, a 3-second rolling average was used to smooth the velocity data over the resting and PHA conditions within each subject. Vessel diameter was averaged over the 30-second resting trial to obtain a preadduction diameter. The postadduction diameter was obtained by averaging the vessel diameters over the 30-second PHA trial. The following equation was then used with the average blood velocity measurement for each heartbeat in order to calculate blood flow in milliliters per minute:

\[
\text{Blood Flow} = \text{Velocity}_{\text{mean}} \cdot \pi \cdot \left(\frac{\text{vessel diameter}}{2}\right)^2 \cdot 60
\]

Preadduction or baseline blood flow (BLBF) was calculated for each subject by averaging blood flow over the entire 60-second resting condition. Postadduction blood flow (PABF\text{Total}) was calculated by averaging blood flow over the 60-second PHA condition. To further examine the difference between BLBF and PABF, blood flow was averaged over 5 cardiac cycles.
immediately following adduction (PABF_{Immediate}) and the final 5 cardiac cycles of the PHA trial (PABF_{Delayed}) (Fig. 7).

Blood pressure was measured at rest and during PHA in a pilot study using photoplethysmography. It was determined that there was no significant change in blood pressure, thus blood pressure was not measured in the present study.

To determine differences between BLBF and PABF_{Total}, a paired t-test was used. However, physiological differences in blood flow suggested the need for a natural log transformation in order to account for the skewness in flow across subjects. A second paired t-test was then used to compare lnBLBF and lnPABF_{Total}.

In order to address the question of whether or not AHI had an influence on the change in blood flow ($\Delta BF$), a log transformation was again used. The $\Delta BF$ can be represented as the natural log of the ratio of PABF_{Total} over BLBF. Stepwise multiple regressions (forward and backward) were then used to determine if there were any variables which significantly influenced $\Delta BF$. Subject height, weight, age, foot length, AHI, heart rate, resting toe angle, adducted toe angle, average toe angle change between resting and adducted positions, and BLBF were all used as variables in the stepwise regression analysis.

To better understand the change in blood flow, a repeated measures analysis of 3 time points was used. The analysis was run using BLBF, PABF_{Immediate} and PABF_{Delayed}. To test whether there was a difference in vessel diameter before and after PHA or a difference in the adducted toe angle between transverse and longitudinal ultrasound trials, paired t-tests were used. Means and standard deviations were calculated for all variables. Statistical tests were run in SAS (SAS Institute, Inc, Cary, NC) with alpha set to 0.05 for significance.
Results

Prior to using a log transformation, there was no significant difference found between BLBF and PABF<sub>Total</sub> (BLBF = 3.53 ± 8.93 mL/min, PABF<sub>Total</sub> = 2.16 ± 4.49 mL/min, \( p = 0.079 \)). There was, however, a significant difference found between lnBLBF and lnPABF<sub>Total</sub> (−0.250 ± 0.063, \( p < 0.001 \)). This difference in the log transformed blood flow can be represented by a 22.2% decrease in overall blood flow before and after PHA.

Two variables in the regression were found to have a significant influence on ∆BF: AHI (\( p = 0.04 \)) and BLBF (\( p = 0.023 \)). As AHI decreased, there was a greater negative ∆BF. As BLBF increased, there was also a greater negative ∆BF.

When comparing additional time points to further examine the blood flow curve (Fig. 7), BLBF was found to be significantly different from both PABF<sub>Immediate</sub> (BLBF = 3.53 ± 8.93 mL/min, PABF<sub>Immediate</sub> = 1.36 ± 2.06 mL/min, \( p < 0.001 \)) and PABF<sub>Delayed</sub> (PABF<sub>Delayed</sub> = 2.42 ± 5.48 mL/min, \( p = 0.008 \)). An immediate 60% decrease in blood flow was found between BLBF and PABF<sub>Immediate</sub>, while a 29% decrease in blood flow was found between BLBF and PABF<sub>Delayed</sub>. A significant difference was also found between PABF<sub>Immediate</sub> and PABF<sub>Delayed</sub> (\( p = 0.014 \)). This difference can be represented by a 31% increase in blood flow from PABF<sub>Immediate</sub> to PABF<sub>Delayed</sub>.

There was a significant difference in vessel diameter between pre-PHA and post-PHA (pre = 0.129 ± 0.05 cm, post = 0.120 ± 0.05 cm, \( p < 0.001 \)). However, adducted toe angles were not significantly different between transverse and longitudinal ultrasound trials (transverse = 29.1 ± 4.7°, longitudinal = 28.6 ± 4.2°, \( p = 0.08 \)). The means and standard deviations of participants’ age, height, weight, foot length, AHI, resting toe angle, adducted toe angle, toe angle change, and heart rate are represented in Table 1.
Discussion

The purpose of this study was to 1) examine the effects of PHA on blood flow and 2) determine if changes in blood flow were related to arch height. We found that due to the skewness in blood flow among our subjects, it was necessary to use a natural log transformation to account for the skewed data. After implementing the log transformation, standard error throughout the trial reduced considerably (Fig. 8), and we noted a significant decrease in overall blood flow after PHA compared to before.

The significant decrease in both blood flow and vessel diameter shown in our results suggest that passive adduction of the hallux influenced a change in blood flow volume. This was to be expected as the posterior tibial artery, which feeds the LPA, runs deep to the abductor hallucis.\textsuperscript{21} Passive adduction of the hallux results in an elongation or tensing of the abductor hallucis. This tension in the muscle may have compressed the artery into the calcaneus contributing to a decrease in vessel diameter, consequently decreasing blood flow.

Although PHA was only a simulation of what would happen to the foot inside of a narrow shoe, the results of this study are suggestive that tight or narrow footwear could theoretically have an influence on blood flow within the foot. Narrow footwear is known to laterally deviate the hallux.\textsuperscript{20} Thus, a decrease in blood flow through PHA, due to footwear or otherwise, could have a negative impact on blood flow and therefore tissue healing.

Blood flow is essential in maintaining tissue health.\textsuperscript{11} Consequently, a lack of blood flow over time could have negative effects on tissue healing as has been seen with the Achilles tendon,\textsuperscript{14} scaphoid\textsuperscript{12} and patella.\textsuperscript{13} Similarly, decreased blood supply to the plantar fascia could prevent full recovery from an injury such as plantar fasciitis. Thus, a decrease in the amount of LPA blood flow to the plantar fascia and the resultant lack of healing may help account for the
46% recurrence rate seen in patients with plantar fasciitis. Although the results of our study did indicate an overall decrease in blood flow to the plantar fascia, the blood flow response can be better understood after taking a closer look at the blood flow response curve (Fig. 7).

Our findings indicated an overall decrease in blood flow from before PHA to after PHA; however, the blood flow response varied throughout the PHA trial. The overall 22.2% decrease in blood flow (PABF_total) was not as drastic as the initial 60% drop in flow immediately following adduction of the hallux (PABF_immediate). This suggests that the body was able to adapt to the change in flow, hence the 31% increase in blood flow from PABF_immediate to PABF_delayed. However, the amount of adaptation following the immediate response varied greatly between individuals.

Although the overall blood flow across subjects significantly decreased after PHA, approximately one-third of the individuals actually had an overall increase in blood flow. Upon further examination of these individuals’ blood flow curves, it was determined that they collectively still had an initial decrease in blood flow but appeared to overcompensate by the end of the PHA trial, resulting in an overall increase in blood flow (Fig. 9). This suggests that some individuals’ posterior tibial arteries responded to and were ultimately affected by PHA while others compensated quickly. For those whose vessels compensate quickly, PHA may not have a noticeable effect on blood flow. These findings suggest the two-thirds of the subject population which decreased in flow without returning to normal blood flow are perhaps at a higher risk of suffering from a lack of blood flow and consequently tissue healing. Future research should aim to investigate the effects of prolonged PHA on blood flow to the plantar fascia in order to determine whether or not decreased blood flow will remain decreased.
Several factors contribute to the development of plantar fasciitis, two of which are pes planus and pes cavus feet.\textsuperscript{3,4} Although pes planus and pes cavus have typically been described to have a mechanical influence on the development of plantar fasciitis,\textsuperscript{4} we theorized that foot structure may also affect the pathology through blood flow. Thus, we hypothesized a greater decrease in blood flow would be seen in both the high-arch individuals and low-arch individuals. Our results, however, indicated a greater decrease in blood flow in only the low-arch feet. This suggests that the abductor hallucis may already be lengthened to accommodate the flatter foot. Further lengthening of the abductor hallucis through PHA would tense the muscle even more, potentially contributing to compression and partial occlusion of the posterior tibial artery. With so many other factors contributing to the development of plantar fasciitis,\textsuperscript{3,4} it seems likely that a high-arch foot may be more susceptible to the injury for reasons other than restricted blood flow.

An additional finding was the significant influence of BLBF on the blood flow change. Normal blood flow varies between individuals. Our results indicated the greater BLBF, the greater the decrease in blood flow following PHA. This suggests that the more blood there is flowing through a vessel, the greater the potential blood flow has to drop. If blood flow is already low, then the magnitude of the change in flow is lessened.

Limitations

As can be expected with any research project, there were a few limitations in our study. Although the same investigator maximally passively adducted the hallux of each subject, the adduction between trials was not identical. We did measure the angle of adduction and determined those measurements were not significantly different from one another, but there were minor differences in the amount of hallux adduction. Also, we obtained average blood velocity readings and measured vessel diameter from two separate PHA trials. We assumed that the blood
flow response to PHA would be the same between the two trials. Even though we cannot
guarantee that there was an identical response, we do feel this was the most accurate way to
measure the diameter of this relatively small artery. Additionally, there was a substantial amount
of variation in BLBF potentially due to the small vessel size. Variation between subjects was
accounted for using the natural log transformation, but BLBF varied greatly within individuals as
well. We feel as though this variation was accounted for by averaging blood flow over the entire
60-second preadduction trial in order to obtain one baseline reading. In future studies, we may
try to assess BLBF independently to better understand within-subject variation. Variation was
also observed between subjects’ blood flow responses to hallux adduction. We averaged the
blood flow responses between subjects in order to analyze the overall response. However, it
should be noted that the total blood flow response shown in Figure 8 may not be an accurate
depiction of the variety of responses as demonstrated by the relatively large error bars in the
figure. The LPA was imaged deep to the abductor hallucis and just distal to the bifurcation of the
posterior tibial artery, but the exact location of the image on the artery was determined based on
image quality in order to obtain accurate diameter measurements. The location of the image
between trials may have varied slightly; although the possible location difference would have
been less than half a centimeter based on the size of the artery and size of the ultrasound
transducer. Lastly, image quality varied greatly between individuals, which made vessel diameter
difficult to obtain for some subjects. As with BLBF, however, we felt that any error between
diameter measurements was accounted for by averaging over the entire trial.

Conclusion

In conclusion, PHA has been shown to have a negative effect on blood flow within the
foot. This decrease in blood flow was greatest in the low-arch individuals. Although future
research is needed to determine the effects of PHA in a weight-bearing position and the effects of actual footwear on blood flow, our preliminary findings of decreased blood flow through PHA suggest blood flow in narrow footwear and its effects on the plantar fascia are worth investigating.
References


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Figure 1. Hallux valgus grading scale. A) Grade 1 (no deformity), B) Grade 2 (mild deformity), C) Grade 3 (moderate deformity), D) Grade 4 (severe deformity).
Figure 2. Subjects lay in supine position with the externally rotated right leg resting on a pillow.
Figure 3. Lateral plantar artery images taken deep to abductor hallucis. L8-18i transducer; longitudinal image of vessel.
Figure 4. Ultrasound imaging protocol. Longitudinal images were taken in triplex mode (B-mode, color flow and pulse-wave modes) to obtain blood velocity. Transverse images were taken in B-mode to obtain vessel diameter measurements.
Figure 5. Photographs of each subject’s foot were taken at rest (left photo) and during both of the adducted hallux phases (center and right photos) of the ultrasound protocol. First metatarsophalangeal joint angles were then measured using Dartfish software.
Figure 6. The lateral plantar artery diameter was measured at the widest part of the artery from one tunica intima to the other as indicated by the white walls of the vessel.
Figure 7. Baseline blood flow (BLBF), overall postadduction blood flow (PABF_{Total}), average blood flow over the 5 cardiac cycles immediately following PHA (PABF_{Immediate}), and average blood flow over the 5 cardiac cycles at the end of PHA (PABF_{Delayed}).
Figure 8. Blood flow before and after passive hallux adduction (top). Log transformed blood flow before and after passive hallux adduction (bottom). Red line indicates initial adduction of the hallux. Error bars show standard error and represent a relatively large amount of variance.
Figure 9. There were 29 subjects with an overall decrease in blood flow after PHA (green line); 16 subjects had an overall increase in blood flow after PHA (blue line). Blood flow is represented by the 42 cardiac cycles before PHA and 46 cardiac cycles during PHA. Red line indicates the start of PHA.
Table 1

Demographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>24.8 (6.8)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.73 (0.10)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.4 (13.46)</td>
</tr>
<tr>
<td>Foot Length (cm)</td>
<td>25.2 (1.78)</td>
</tr>
<tr>
<td>AHI</td>
<td>0.372 (0.34)</td>
</tr>
<tr>
<td>Resting Toe Angle</td>
<td>16.1° (4.8)</td>
</tr>
<tr>
<td>Adducted Toe Angle</td>
<td>28.7° (4.4)</td>
</tr>
<tr>
<td>Toe Angle Change</td>
<td>12.7° (3.7)</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>62.8 (8.8)</td>
</tr>
</tbody>
</table>

Data presented as mean (standard deviation)