Author's response to reviews

Title: The reliability of toe systolic pressure and the toe brachial index in patients with diabetes

Authors:

Mary T Romanos (mary_romanos@hotmail.com)
Anita Raspovic (a.raspovic@latrobe.edu.au)
Byron M Perrin (b.perrin@latrobe.edu.au)

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Author's response to reviews: see over
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The Journal of Foot and Ankle Research
Dr Alan Borthwick
Deputy Editor (UK)

Dear Dr. Borthwick,

Please find enclosed a revised manuscript entitled “The Reliability of Toe Systolic Pressures and Toe Brachial Indices in Patients with Diabetes” and a point-by-point response to the comments outlined in each of the reviewer’s report.

Anna Spencer

Major Compulsory Revisions:

1) Rater A (1 year experience) and B (6 months experience) were routinely using this measurement in their clinical setting on patients with diabetes. Rater A and B have many years of experience with managing and assessing the lower limb of patients with diabetes including Doppler and blood pressure measurements. Raters A and B routinely took toe pressure measurements multiple times per week (average 10 measurements) in their clinical setting. The nature of experience with the measurement is limited reflects the current experience of clinicians with this measurement in general practice in Australia. Rater C (a 4th year student with limited experience) was not routinely using this measurement and this is explicitly stated in the paper to provide an indication of the reliability of the measurement in podiatrists who are new to clinical practice. Please refer to page 7, paragraph 3 of the manuscript.

The sixty minute training session one week prior to commencement was focused on mastering the protocol of the study for standardisation measurements. The protocol was outlined and emailed to all raters a few weeks prior to the training session for their familiarisation. All raters had used a manual sphygmomanometer and PPG previously on a number of occasions (particularly rater A and B), the focus of the training session was to outline the specific research measurement protocol which is modelled on current clinical practice.

The aim of the study was evaluate the reliability of the clinical measurement of Toe Systolic Pressures and Toe Brachial Indices, which includes the technology but also the human element. The manual PPG method was selected as to the author’s knowledge at the time of data collection; it had not been investigated. The manual method is more affordable and accessible in general practice when compared to the automatic system and is preferred by some clinicians given the increased degree of control available. From this perspective, the methods selected are arguably suitable to the purpose and of use and relevance to people who prefer to use the manual system clinically.

2) Sample size. A sample size was difficult to perform given limited data to inform a power calculation. Moore (2000) pg 312 indicates when n≥15, the confidence level is not greatly distributed by non-normal populations unless extreme outliers or quite strong skewness are present. Data for toe systolic pressures and toe brachial indices visually appeared to follow a normal distribution. The author’s suggest that the sample size of 30 was suitable given the intra-class correlations (ICCs) presented reached statistical significance.

Portney and Watkins (2009) do mention “when very small samples are used … power is substantially reduced”. The authors could not locate the statement that n <30 is very small in the 2009 reference. Based on the literature there is some controversy around the exact sample size for such reliability studies however we believe the results show statistically and clinically important and robust findings.
3) Time between sessions. The study investigated the reliability of the technology, namely a manual sphygmomanometer and PPG. Portney and Watkins (2009) indicate “intra-rater reliability is usually assessed using trials that follow each other with short intervals.” The time intervals between tests were considered carefully. An interval of 1 week was considered far enough to avoid fatigue, learning or memory effects but close enough to avoid genuine changes in the measured variable.

4) Environment. Normal room temperature ranges between 20-25 degrees celcius. The room temperature was measured at an average of 20 degrees celcius with the temperature ranging from 20 to 22 degrees celcius across all rooms. As measurements were taken in a private environment similar to a general practice setting, this is more likely to reflect the temperature in such settings. Room temperature was measured constantly throughout the testing period. While participants were lying supine and during the duration of all tests a blanket was placed on the lower limb. Once the rater took the measurement the blanket was placed on the lower limb to avoid measurement variability. Socks were not removed until testing commenced.

Minor Essential Revisions:

1) Background (page 7, paragraph 1): “…a manual sphygmomanometer and PPG” has been added.

2) Statistical Analysis (page 10, paragraph 1): “Data from the right side only of the patient’s hallux…” has been added.

3) Conclusion (page 22, last paragraph): “This potentially clinically significant margin of error (95% LOA) raises questions about the reliability of using a manual sphygmomanometer and PPG to measure toe systolic pressure and toe brachial index. When assessing patients with PAOD, it is important to consider all other non-invasive vascular assessment options. The context of toe systolic pressures as a non-invasive investigation that may determine intervention as the gold standard could be magnetic resonance imaging (MRI) angiography”.

Neil Baker

1&2) Background (page 5, last paragraph and continues onto page 6).
A statement has been added to the paper that identifies PPG has not widely been available or used in general practice.
A statement has been added to the paper that explains what PPG is and how it works together with its advantages and limitations.

“Toe systolic pressures has been available since the early 1930s and recommended in patients with PAOD and an ABI greater than 1.3 [8]. Although, the toe systolic pressure can be measured in the clinical setting using a PPG, it has not been widely available or routinely performed in general clinical practice as it can be expensive and there is limited research investigating the reliability and validity of this measurement [11]. In recent years, portable continuous wave Doppler units have been used to measure toe systolic pressures when the ABI is elevated. However when the toes are cold, Doppler-derived toe systolic pressure are unreliable due to vasoconstriction of digital arteries. This effect persists even when attempts are made to control the temperature of the testing environment [15]. Therefore a low toe systolic pressure may be associated with PAOD or vasoconstriction of the arteries [15]. Toe systolic pressures obtained via PPG are yet to be proven to be reliable at the lower end of the systolic pressure of less than 40mmHg which is particularly relevant in patients with severe POAD”.

“Commonly, toe systolic pressures and TBIs are measured in vascular or research laboratories by trained technicians using nonportable PPG equipment [32]. PPG assesses blood flow by emitting an infrared light that is reflected by the red blood cells in superficial vessels and detected by the transducer. The amount of reflected light corresponds to pulsatile changes and tissue blood volume [32]. PPG does not measure absolute blood flow, but it does provide a functional assessment of perfusion status”.

3) Methods (page 7, paragraph 2).
A statement has been added to the paper qualifying the study population and how they selected.
“A convenience sample of thirty participants with diabetes was recruited from a university podiatry clinic [37]. Most of the patients who attend this clinic do so to have their foot health status screened and to receive basic foot care. Participants were eligible for inclusion if they were 21 years of age and older and available during the planned time for tests”.

The study population is also qualified in the results section (page 11).

4) Reworded throughout the manuscript, digital vessels are “less affected by medical wall calcification”.

5) Background (page 3, paragraph 1 and continues onto page 4).
Stated that medial wall calcification is also present in other conditions.

“In addition Mönckeberg’s sclerosis is highly prevalent in autonomic neuropathy and chronic renal insufficiency [19]”

6) Background (page 3, paragraph 1). The prevalence of PAOD in diabetes is stated.

“The prevalence of diabetes is increasing with peripheral arterial collusive disease (PAOD) being a common condition in this population [1-4]. PAOD is a progressive disorder that affects approximately twenty five per cent of adults in Australia who are over 55 years of age or have diabetes [5]”

7) Background (page 3, paragraph 1): “severe” replaced with “aggressive”.
Background (page 3, paragraph 1): PAOD “particular targets the distal popliteal and trifurcation vessels”.

8) Background (page 3, last paragraph): qualified “hardening”.
“The hardening of the artery is due to the stiffening of the elastic layer of the arterial wall, but in contrast to intimal artery calcification, it does not obstruct the arterial lumen”.

9) Reworded throughout the manuscript, “TBI’s are less affected by medial wall calcification”. See page 4, paragraph 1, line 2 and 6.

10) Information regarding the ABI for the study subjects has been included on page 11 in table 2.

11) Table 3. Mean ± standard deviation (SD) for the measurement of Toe Systolic Pressures and Toe Brachial Indices according to rater and session has been moved from the manuscript and placed as a supplementary/additional file. The authors think this information is not essential but rather more informative if the reader wishes to know the raw values of the data.

12) Discussion (page 20, paragraph 3): the effect of vasospacity and post occlusion hyperaemia by repeated inflation of digital cuffs.

“The interval between each rater after taking the toe systolic pressure and brachial systolic pressure was short. After measurements were completed, the participant was allowed to rest for 5 minutes in the same position (supine) before the next rater took the measurements. As measurements on each participant within the same session were performed within a short interval this could have caused vasospacity and post occlusion hyperaemia of the digital vessels. The repeated inflation of the digital cuffs could have affected the measurements and contributed to the large range of error”.

Alistair A McInnes

1) Background (page 3, last paragraph and continues onto page 4): Additions have been made to the paper which identifies Mönckeberg’s sclerosis and the associated aetiology of autonomic neuropathy.
“In addition Mönckeberg’s sclerosis is highly prevalent in autonomic neuropathy and chronic renal insufficiency [19]”.
2) Background (page 5): paragraph that immediately follows Table 1, a reference to the unpublished work is provided in the reference list.

3) Discussion (page 21, paragraph 2).
Severe peripheral neuropathy may have been associated with quite irregular patters in blood flow that could have caused differences in measurements. The authors do agree that a comparison/control group could be useful in a future study to investigate the variability of the measurement in patients with diabetes and various vascular complications. Information regarding the vascular status of the participants and the recorded values has been included on page 11 in table 2 of the manuscript.

The time period between the raters tests was approximately 5 minutes (refer to page 8, paragraph 2). There is a statement in the discussion (page 20, paragraph 3) mentioning the effect of vasospacity and post occlusion hyperaemia by repeated inflation of digital cuffs.

“The interval between each rater after taking the toe systolic pressure and brachial systolic pressure was short. After measurements were completed, the participant was allowed to rest for 5 minutes in the same position (supine) before the next rater took the measurements. As measurements on each participant within the same session were performed within a short interval this could have caused vasospacity and post occlusion hyperaemia of the digital vessels. The repeated inflation of the digital cuffs could have affected the measurements and contributed to the large range of error”.

Participants with possible severe neuropathy were not excluded from the study; however this was not assessed for during data collection. As a convenience sample of participants were recruited, namely those attending the diabetes clinic at the university, it was difficult to recruit those with severe PAOD as most participants who attend this clinic are not high risk.

5) Conclusion (page 21, last paragraph): “This potentially clinically significant margin of error (95% LOA) raises questions about the reliability of using a manual sphygmomanometer and PPG to measure toe systolic pressure and toe brachial index. When assessing patients with PAOD, it is important to consider all other non-invasive vascular assessment options. The context of toe systolic pressures as a non-invasive investigation that may determine intervention as the gold standard could be magnetic resonance imaging (MRI) angiography”.

I look forward to hearing from you.

Yours Sincerely,
Mary Romanos