VALIDITY AND RELIABILITY OF LOWER-LIMB PULSE-WAVE VELOCITY ASSESSMENTS USING AN OSCILLOMETRIC TECHNIQUE

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NEW FINDINGS

• What is the central question of this study?

There is growing interest on the effects of sedentarism on central and peripheral cardiovascular health. To permit further investigation, including in larger epidemiological studies, there is a need to identify arterial health assessment tools that are valid (accurate) and reliable (precise), yet practical.

• What is the main finding and its importance?

Lower-limb vascular health (femoral-ankle pulse-wave velocity) can be determined in a supine position with accuracy and precision using an oscillometric-based device. This technology may help further the understanding of the pathological mechanisms linking cardiovascular disease to sedentarism, including the interaction between peripheral and central vasculature.

ABSTRACT

Background: There is a growing interest in the deleterious effects of sedentary behaviour on lower-limb arterial health. To permit further investigation, including in larger epidemiological studies, there is a need to identify lower-limb arterial health assessment tools that are valid and reliable, yet simple to administer. **Purpose:** This study sought to determine the validity and between-day reliability of femoral-ankle pulse-wave velocity (faPWV) measures obtained using an oscillometric-based device (SphygmocCor XCEL) in supine and seated positions. Doppler ultrasound (US) was used as the criterion. **Methods:** A total of 47 healthy adults were recruited for validity (n=32) and reliability (n=15) analyses. Validity was determined by measuring faPWV in seated and supine positions using the XCEL and US devices, in a randomised order. Between-day reliability was determined by measuring seated and supine faPWV using the XCEL on 3 different mornings, separated by a maximum of 7 days. **Results:** The validity criteria (absolute standard error of estimate [aSEE] <1.0 m/s) was met in the supine (aSEE = 0.8 m/s, 95% CI: 0.4-1.0), but not the seated (aSEE = 1.2 m/s, 95 % CI: 1.1, 1.2) position. Intras-class correlation coefficient estimates revealed the XCEL demonstrated good reliability in the supine position (ICC=0.83, 95% CI: 0.65, 0.93), but poor reliability in the seated position (ICC = 0.29, 95% CI: 0.23, 0.63). **Conclusions:** The oscillometric XCEL device can be used to determine lower-limb PWV with acceptable validity and reliability in the conventionally recommended supine position, but not the seated position.

ABBREVIATIONS

AIx - augmentation index

AIx@75 - augmentation index normalized to a heart rate of 75 bpm

aSEE - absolute standard error of estimate

cfPWV - carotid-femoral pulse-wave velocity

CO – cardiac output

cSBP – central systolic blood pressure

d – Cohens *d*

DBP - diastolic blood pressure

D – pulse-wave velocity distance

faPWV - femoral-ankle pulse-wave velocity

FMD - flow mediated dilation

HR – heart rate

MAP – mean arterial pressure

Pb - backward aortic pressure

Pf - forward aortic pressure

PTA – posterior tibial artery

PTT - pulse transit time

PWV - pulse wave velocity

RM - reflection magnitude

RSE - relative standard of error

SBP - systolic blood pressure

SFA – superficial femoral artery

sSEE - standardized standard error of estimate

SV – stroke volume

SVR – systemic vascular resistance

US – Doppler ultrasound

XCEL - SphygmoCor XCEL

INTRODUCTION

Epidemiological research supports the association between chronic sedentary behaviour and cardiovascular health (Huynh *et al.*, 2014; Young *et al.*, 2016), but the mechanisms by which acute sedentarism leads to impaired cardiovascular health are not well understood. Sedentary behaviour appears to target the athero- and arterio-sclerotic susceptible vasculature of the lower extremities (Carter *et al.*, 2017). For example, recent evidence indicates that the unique haemodynamic milieu created by prolonged sitting can acutely impair lower-extremity endothelial function, mediated by reductions in conduit artery antegrade blood flow and shear rate (Thosar *et al.*, 2014; Restaino *et al.*, 2015; Thosar *et al.*, 2015; Restaino *et al.*, 2016). Arterial health in the leg is typically assessed using flow mediated dilation (FMD), a measure of endothelial function (Thosar *et al.*, 2014; Restaino *et al.*, 2016). Whilst leg FMD is arguably valid (Kooijman *et al.*, 2008), a highly trained operator is required to ensure precision (reliability) (Stoner & Sabatier, 2012), and in spite of this, reliability may still be poor (McLay *et al.*, 2016).Secondly, leg FMD assessments have only been validated in the supine position (Kooijman *et al.*, 2008; Thijssen *et al.*, 2011) and unavoidable postural manoeuvres may confound study outcomes. Therefore, to assist further investigation of the deleterious effects of sedentary behaviour, there is a pressing need to identify valid (accurate) and reliable (precise), yet simple, techniques for evaluating lower-limb arterial health.

One of the most popular methods for measuring arterial health, and the gold-standard assessment of arterial stiffness, is pulse-wave velocity (PWV) (O'Rourke *et al.*, 2002). Arterial stiffness, and thus PWV, is dependent on arterial structure as well as arterial function. For example, a reduction in the endothelium-derived vasodilator nitric oxide leads to a decrease in arterial elasticity (Kinlay *et al.*, 2001), the reciprocal of arterial stiffness. Whilst lower-limb arterial structure is not expected to change following acute sedentary behaviour, arterial function can become impaired, as indicated by decreased FMD, i.e., impaired endothelial function (Thosar *et al.*, 2014; Restaino *et al.*,

2015; Thosar *et al.*, 2015; Restaino *et al.*, 2016). The relationship between arterial function and arterial stiffness suggests that assessments of PWV may be a viable alternate to FMD. However, any measurement tool must first demonstrate accuracy and precision, and ideally should be user objective and simple to conduct. Measurements of PWV can be undertaken using several methodologies, including ultrasound (Baguet *et al.*, 2003) and applanation tonometry (McEniery *et al.*, 2010). Doppler ultrasound (US) is often used in population-based studies (Sutton-Tyrrell *et al.*, 2005) having been shown to be precise (Baguet *et al.*, 2003) and accurate (Jiang *et al.*, 2008; Calabia *et al.*, 2011). But the most widely used technique is applanation tonometry, where typically a tonometer (a pen-like sensor) is used to obtain electrocardiogram gated proximal and distal arterial pulse waveforms (Townsend *et al.*, 2015). However, the high skill requirements and sequential nature of both ultrasound and tonometry techniques make them unsuitable for large epidemiological studies.

Recently it has been demonstrated that carotid-femoral (aortic) PWV (cfPWV) can be measured simply and quickly when applanation tonometry is combined with oscillometry (Butlin *et al.*, 2013), permitting immediate measurement output. To assess cfPWV, the SphygmoCor XCEL (XCEL) device makes use of a volume displacement cuff placed around the upper leg to acquire the femoral pulse, and a tonometer to simultaneously record the carotid pulse. This simple and largely automated technique makes it an attractive tool for determining arterial health. However, it is currently unknown whether this technique is suitable for investigating arterial health in the legs. If XCEL-derived measurement of femoral-ankle PWV (faPWV) in the leg is shown to be both valid and reliable, in the supine and/or seated position, this would represent a potentially viable tool for a range of larger-scale investigations of the effects of sedentary behaviour on cardiovascular health. Therefore, the primary aim of this study was to determine the validity and between-day reliability of faPWV measures obtained using the XCEL in a supine position, which is conventionally used for vascular assessments. The secondary aim was to determine the validity and between-day reliability

of faPWV measures obtained using the XCEL in a seated position. When comparing against the criterion, US, the accuracy of the XCEL device was considered acceptable if the absolute standard error of estimate was <1.0 m/s (Vlachopoulos *et al.*, 2010) and the standardized standard error of estimate was moderate (0.6 – 1.2) or better (Hopkins, 2000). Although there is no universal criterion, in general, intra-class correlation coefficient (ICC) estimates of < 0.5, 0.5-0.75, 0.75-0.9 and > 0.9 indicate poor, moderate, good and excellent reliability (Koo & Li, 2016).

METHODS

This observation study is reported in accordance with STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines (von Elm *et al.*, 2007).

Ethical Approval

The study conformed to the Declaration of Helsinki, except for registration in a database, and was approved by the University of North Carolina at Chapel Hill Office of Human Research Ethics (17-0745). Participants were informed of the methods and study design verbally and in writing before providing written informed consent.

Participants

To ascertain the upper limit of validity and reliability for XCEL measures of faPWV, a homogenous cohort of young (18 – 40 years), healthy participants were recruited. A total of 32 participants were recruited for validity analyses only, whilst a distinct group of 15 participants were recruited for reliability analyses only. Participants were excluded if they reported any known cardio-metabolic disorders, were taking medications known to effect cardiovascular function or reported cigarette

smoking. To account for potential influences of hormonal status on study outcomes, premenopausal women were studied during the early follicular phase of their menstrual cycle or during placebo phase of oral contraceptive use.

Experimental Design

Following familiarisation, participants were tested in an environmentally controlled room (temperature: 22 ± 1°C, relative humidity: 51 ± 2%). All participants were 12h fasted and were asked to avoid strenuous physical activity, caffeine and alcohol for 24 h prior. Following a 20-min rest period in a supine or seated position, faPWV was determined in the non-dominant leg using the XCEL and the criterion, Doppler ultrasound, devices. The participant was then transferred into the alternate posture, and asked to rest quietly for a further 20-min, after which all assessments were repeated. At each posture oscillometric pressure waveforms were recorded on the left upper arm, from which central haemodynmic measures were derived. Stroke volume, cardiac output and peripheral vascular resistance were also determined. For reliability analyses, the same experimental protocol outlined above was subsequently repeated on three separated occasions, separated by a maximum of 7 days, whereby only faPWV and cfPWV measures were recorded in supine and seated positions using the XCEL. PWV assessment sites were marked and recorded to ensure consistency across test days. Measurement of cfPWV acted as a quality control for identifying the suitability of lower-limb PWV assessments using the XCEL. Positioning was randomised for the determination of validity and reliability, whereby participants were allocated to one of two conditions: i) supine first, or, ii) seated first. All measures were recorded in triplicate, with the average of the closest two recordings being used for analyses.

Experimental Measures

SphygmoCor XCEL Pulse Wave Velocity.

The XCEL device (AtCor Medical, Sydney, New South Wales, Australia) enables simultaneous assessment of proximal and distal arterial waveforms using a tonometer and volume displacement cuff, respectively, to determine arterial pulse transit time (PTT). Femoral-ankle ($faPTT_{XL}$) and carotid-femoral (cfPTT) PTT was measured as the time between diastolic feet of the proximal (tonometer) and distal (cuff) arterial pulse waveforms (Figure 1a). PWV is calculated by dividing PTT by arterial path length, or PWV distance (*D*).

For cfPWV, the tonometer was placed on the left carotid artery and the oscillometric cuff was placed on the left thigh at the level of the femoral artery, following recommended manufacturer guidelines (Butlin *et al.*, 2013). Using custom made callipers; the carotid-femoral *D* (cf*D*) was estimated by measuring the liner distance from the suprasternal notch to the top of the cuff at the centre line of the leg and subtracting the distance from the suprasternal notch to the carotid artery. Accordingly, cfPWV was calculated as: cfPWV = cf*D* / cfPTT..

For faPWV, the tonometer was placed at the point indicating the top edge of the ultrasound probe at the level of the superficial femoral artery (SFA), whilst the ankle cuff (SC10, Hokanson) was positioned with the bottom edge proximal to the malleoli. Femoral-ankle *D* (faD_{XL}) was estimated by measuring the linear distance from the point of tonometric applanation to the top of the ankle cuff at the centre line of the leg. The XCEL device automatically corrects for sources of difference that exist when using an oscillometric rather than a tonometric only technique to determine its intended outcome measure, cfPWV (Butlin *et al.*, 2013). Of relevance to the present study, the XCEL reduces both *D* and PTT in order to adjust for the inclusion of an extra segment of femoral artery due to the position of the cuff being below the femoral bifurcation. Accordingly, *D* is reduced by an operator-determined measurement, termed 'Femoral to Cuff' distance ($D_{F\text{-}C}$). PTT is reduced by a constant factor multiplied by $D_{F\text{-}C}$ in order to remove the time delay (PTT_{DELAY}) associated with the inclusion

of the additional femoral artery segment. In order to eliminate these in-built adjustments and obtain a true or corrected $faPTT_{XL}$, the following formulas were applied to the PTT reported by the XCEL:

1. $PTT_{DELAY} = (D_{F\text{-}C}) \times 0.08449$ ms†
2. *Corrected* $faPTT_{XL} = PTT_{DELAY} + faPTT_{XL}$

faPWV was then calculated as:

3. $faPWV = faD_{XL}$ / *Corrected* $faPTT_{XL}$

Technical Note: faPWV was measured using the 'Direct PWV Distance method' inherent to the XCEL. An arbitrary distance (e.g. 100 mm) can be entered for $D_{F\text{-}C}$ during data collection and subsequently used during the calculation of PWV. †This value represents an average femoral transit time per unit distance measured in a group of 15 individuals as indicated in the original validation paper (Butlin *et al.*, 2013) and subsequently provided by AtCor.

Doppler Ultrasound Pulse Wave Velocity.

Ultrasound assessments of faPWV were used as the criterion. A LOGIQ P6 ultrasound device equipped with an 11-2 mHz linear array probe (GE Healthcare, Wauwatosa, USA) was used to sequentially scan and obtain ECG gated pulse-wave Doppler waveforms at the SFA and posterior tibial artery (PTA) sites. The SFA was imaged 2cm below the bifurcation from the common femoral artery; the PTA was imaged by placing the ultrasound probe directly over the line indicating the top of the ankle cuff used for XCEL assessments. Three 10s video recordings were obtained at each position. Images were analysed offline using ImageJ (Version 1.51q, National Institutes of Health, Bethesda, USA) (Schneider *et al.*, 2012) by a single blinded operator. The interval between the r-wave of the QRS complex and the foot of the systolic upstroke in the Doppler spectral envelope was measured and averaged over at least five consecutive cardiac cycles for each video (Figure 1b)

(Baguet *et al.*, 2003; Jiang *et al.*, 2008). Ultrasound PTT was defined as the difference between the intervals of time measured at each arterial segment ($faPTT_{US}$). Ultrasound arterial path length was estimated by measuring the linear distance from the mid-point of probe at the SFA to the mid-point of the probe at the PTA (faD_{US}). $faPWV_{US}$ was then calculated as: $faPWV = faD_{US} / faPTT_{US}$.

Pulse Wave Analysis.

To aid in the interpretation of the effects of posture on faPWV, oscillometirc pressure waveforms were recorded on the left upper arm using pulse wave analysis (PWA) inherent to the XCEL device (Stoner *et al.*, 2013). Each single measurement cycle consisted of a 60s brachial blood pressure recording followed by a 10-s sub-systolic recording. A corresponding aortic pressure waveform was then generated using a validated transfer function (Butlin *et al.*, 2012), from which central: systolic blood pressure (cSBP), augmentation index (AIx), augmentation index normalized to heart rate of 75 bpm (AIx@75), forward aortic pressure (Pf), backward aortic pressure (Pb) and reflection magnitude (RM) were derived.

Cardiac Output, Stroke Volume and Peripheral vascular resistance.

Cardiac output (CO), stroke volume (SV) and systemic vascular resistance (SVR) were determined using a commercially available continuous-wave Doppler ultrasound device (USCOM 1A, Uscom, Sydeny, Austrailia). A single operator placed a 3.3MHz continuous-wave probe over the acoustic window at the level of the sternal notch to obtain six consecutive trans-pulmonary Doppler flow profiles.

Statistical Analysis

Statistical analyses were performed using Statistical Package for Social Sciences version 24 (SPSS, Inc., Chicago, Illinois). All data are reported as means and standard deviation (SD) unless otherwise

stated. Statistical significance was defined as $P<0.05$ (two tailed). Two measures of validity were used to determine agreement between test and criterion devices: i) an absolute standard error of estimate (aSEE), and ii) a standardized standard error of estimate (sSEE). aSEE was calculated as: $aSEE = SD \times \sqrt{(1-r^2)}$ (Hopkins, 2000; Fraser, 2001b), whereby SD is the standard deviation of the criterion measure and r is the Pearson product-moment correlation between test and criterion devices. To calculate a 95% confidence interval for the aSEE, Pearson's correlation and associated 95% confidence intervals were derived from regression analysis. sSEE was calculated by dividing aSEE by the standard deviation of the criterion, whereby <0.20 is considered a trivial difference, 0.2-0.6 small, 0.6-1.2 moderate, 1.2-2.0 large and >2.0 very large difference (Hopkins, 2000). Relative standard of error (RSE) was also calculated by dividing the aSEE by the measurement device mean and multiplying it by 100. Bland-Altman plots (Bland & Altman, 1986) were generated to permit visual analysis of the uniformity of error over the range of participant measurement values. To test the effect of posture on faPWV, following verification of the normality of distribution, two-way repeated measures analysis of variance (ANOVA) was used. Effect sizes are reported using partial eta-squared (η^2_p), where 0.0099, 0.0588 and 0.1379 represent a small, medium and large effects, respectively (Cohen, 1969). Lastly, the effect of posture on all other central and peripheral haemodynamic variables was assessed using pair-wise t-tests. Effect sizes are reported using Cohen's *d*, where <0.20 is considered to be a small effect, >0.20 to <0.50 a moderate effect, and >0.60 a large effect.

For between-day reliability of the XCEL test device, intra-class correlation coefficient (ICC) estimates and their 95% confidence intervals were determined using a single-rating, absolute-agreement, 2-way mixed-effects model in SPSS. A mixed model was used as it is unaffected by sample size (Shrout & Fleiss, 1979). Although there is no universal standard for classifying the magnitude of ICC, for criterion-related assessments: values less than 0.50 are indicative of poor

reliability, values between 0.50 and 0.75 indicate moderate reliability, values between 0.75 and 0.90 indicate good reliability, and values greater than 0.90 indicate excellent reliability (Koo & Li, 2016). A standard error or measurement (SEM) was also calculated according to the formula: SD* √(1-ICC) and a reliability coefficient (RC) was calculated according to the formula: 1.96*SEM*√2 (Hopkins, 2000; Fraser, 2001a).

RESULTS

Of the 32 participants recruited for validation, only 31 were included in the final analyses (Table 1). For the excluded participant, PTA ultrasound images could not be analysed. The excluded participant did not differ in terms of demographics or XCEL PWV from the rest of the study population. All 15 participants completed three sessions for reliability analyses (Table 1).

Table 2 indicates that posture had a significant effect on peripheral and central haemodynamic variables. SBP, DBP, MAP, cSBP, HR and SVR all increased (all P <.05) in the seated compared to supine position, whilst AIx, Pb, Pf, and CO decreased (all P < .05). AIx@75 and RM were not altered by posture (P > .05).

In the supine position, the XCEL faPWV demonstrated acceptable accuracy (aSEE <1.0 m/s), being moderately different when compared to the criterion (Table 3). In contrast, in the sitting position, the aSEE was greater than 1.0 m/s; however, the sSEE indicated that the XCEL faPWV was again only moderately different to the criterion. For supine faPWV measures the error was uniform (Figure 3a), but there was a bias for seated faPWV measures with the difference between devices being greater for the higher PWV values (Figure 3b). Values of faPWV obtained by the two devices

were significantly correlated in the supine ($P < 0.001$, Figure 3c) but not the seated ($P = 0.054$, Figure 3d) position. Repeated measures ANOVA analysis revealed that there was no interaction effect ($P < .844$, $\eta^2_p = .001$), but a significant main effect for device ($P < .001$, $\eta^2_p = .892$, mean difference = 1.2, 95% CI [.8, 1.5]) and posture ($P < .001$, $\eta^2_p = .515$ mean difference 3.0, 95% CI [2.6, 3.4]).

Estimates for reliability of measures of faPWV and cfPWV are presented in table 4. The XCEL demonstrated good between-day reliability (ICC: 0.83, 95% CI: 0.65 – 0.93) when measuring faPWV in the supine position, but only moderate (ICC: 0.67, 95% CI: 0.40 – 0.86) reliability when measuring cfPWV. In the supine position, faPWV (ICC: 0.29, 95% CI: 0.23, 0.63) and cfPWV (ICC: 0.57, 95% CI: 0.25, 0.81) measures demonstrated poor and moderate reliability, respectively.

DISCUSSION

Given the growing interest in the effects of sedentary behaviour, particularly prolonged sitting, on cardiovascular health, there is a pressing need to identify tools capable of accurately and precisely measuring the athero- and arterio-sclerotic susceptible vasculature of the lower extremities. The primary finding of the current study is that in the supine position XCEL measures of faPWV demonstrate acceptable validity, when compared against the criterion, and good between-day reliability The secondary finding is that XCEL faPWV measures did not achieve the validity criteria and demonstrated poor reliability in the seated position. It is therefore recommended that, as per conventional practice for many vascular assessments, XCEL-based lower-limb arterial health assessments be conducted in the supine position.

Study Limitations

In order to better contextualize the present findings, several limitations should first be addressed. A relatively homogenous group of young healthy participants were recruited in order to ascertain the upper-limit of validity and reliability for XCEL-based leg PWV assessments. Prior to clinical use it is of high importance to determine whether any error, bias or variability inherent to a health test is caused by the technique itself and not a consequence of the presence of cardiovascular pathology. Further studies are therefore required in order to generalize any findings of the present study in clinical populations of varying age and health states. Second, whilst every effort was made to match PWV distance (arterial path length) between test and criterion techniques, due to variance in participant anatomy this was not always possible. Mean arterial path length (PWV distance) was 672 ± 46.5 mm for XCEL and 662 ± 51.9 mm for US. Consequently, this resulted in small differences in PTT between PWV assessment techniques (Table 3). Although PWV was calculated relative to an independent path length, this may have resulted in the introduction of small measurement error.

Supine Pulse Wave Velocity

The current study found that there was acceptable agreement (aSEE: 0.8 m/s, 95% CI: 0.4, 1.0) between the XCEL device and a criterion, US, for measuring faPWV in the supine position. Relatively few studies have compared electro-mechanical (pressure) and US techniques when determining PWV, and existing research has naturally focused on the assessment of cfPWV as a primary measure. Calabia and colleagues (2011) reported very good agreement (mean difference [MD] = 0.13±0.19 m/s) between US and the tonometer-like mechano-transducer based Complior system, when determining cfPWV in the supine position. Similarly, Jiang et al. (2008) compared US and the standard tonometer only SphygmoCor device for measuring cfPWV and reported good correlation and agreement (MD = 0.3 m/s). Whilst these findings indicate agreement between mechanical (pressure) and US techniques, neither methods employed by Calabia (Calabia *et al.*, 2011) and Jiang

(Jiang *et al.*, 2008) incorporated the use of a volume displacement cuff to detect the femoral or distal arterial waveform. Therefore, prior to this study it was unclear whether a device which combines applanation tonometry and oscillometric arterial waveform detection technologies could be used to accurately measure leg PWV.

It is recognised that although the validity criteria were met, a significant main effect of device was observed. This difference may originate from; i) continued difference in waveform detection between mechanical and acoustic techniques, or, ii) the use of a standard assumed constant when applying the femoral segment correction. The in-built XCEL correction assumes the same PTT when calculating the PTT delay associated with the inclusion of the additional femoral artery segment. The PTT of 0.08449 ms for every 10 mm of arterial length is an average derived from only 15 individuals (Butlin *et al.*, 2013), but comparable to published values (Avolio *et al.*, 1983). This constant is thought to be independent of sex, age, blood pressure and ethnicity. However, the use of individualised or population specific constants may improve correlation and minimize differences between US and oscillometric techniques. A caveat is that this approach would likely make the simple XCEL technology more technically and logistically challenging. Finally, despite a significant main effect for device, faPWV changes induced by the postural shift between supine and seated postures were similar between XCEL and US devices (Table 3) and no interaction effect was observed.

The observed ICC of 0.83 (95%CI: 0.65, 0.93) indicates that the XCEL demonstrates good between-day reliability when measuring faPWV. Perhaps surprisingly, the ICC for faPWV was greater than the quality control measure, cfPWV, a measure previously shown to be highly precise (Hwang *et al.*, 2014). This finding further indicates the reproducibility of XCEL-based faPWV measures in the supine position. While clinically relevant data is not available for the lower-limbs, the typical error of XCEL derived faPWV (0.8 m/s, 95% CI: 0.4, 1.0) is also less than the clinically

meaningful mean difference of 1.0 m/s observed for the quality control measure, cfPWV (Vlachopoulos *et al.*, 2010).

Seated Pulse Wave Velocity

Unlike supine measures, seated XCEL faPWV values did not meet the validity criteria, with the absolute SEE (1.2 m/s, 95% CI: 0.9, 1.3) being above the clinically meaningful difference of 1.0 m/s set *a priori*. While these findings indicate that the accuracy of the XCEL may not be adequate in the seated position, there may be a number of reasons for this. The algorithm presented by Butlin and colleagues (Butlin *et al.*, 2013) was only validated in the supine position and may be impacted by postural shift and/or greater vascular tortuosity (hip and knee bend) in the seated position. Additionally, the contrasting technologies used to obtain and analyse arterial pressure waveforms may simply demonstrate greater divergence when arterial geometry is changed. ICC values for faPWV in the seated position also demonstrated poor reliability (ICC: 0.29, 95% CI: 0.23, 0.63). Interestingly, XCEL measures of cfPWV only demonstrated moderate reliability; a measure previously observed to be both highly accurate and reliable in the supine position (Butlin *et al.*, 2013; Hwang *et al.*, 2014).

The present findings indicate that postural change may have a significant impact on the ability of XCEL to accurately and precisely measure central and lower-limb PWV. During orthostasis there is a propensity for blood to pool in the sub-diaphragmatic venous system (Stone *et al.*, 2016). This likely occurred in the current study, as indicated by the reduction in SV, CO, and Pb (Stoner *et al.*, 2018). To compensate for blood pooling, and attempt to ensure adequate venous return, the baroreflex response results in lower extremity vasoconstriction and increased SVR, as evident in the current study (Tahvanainen *et al.*, 2009). Accordingly, both faPWV and cfPWV measures are likely to be influenced by the interaction of the variability of the test (XCEL) device and the response of the

autonomic nervous system to orthostatic induced venous pooling. Accordingly, blood pooling during sitting may lead to greater variability and divergence between the XCEL and US PWV techniques with regards to the timing and characteristics of the recorded pulse waveform.

Implications and future direction

The growth in sedentary behaviours in today's society necessitates the need for the identification of novel, simple tools to help unmask the link between sedentary behaviour and cardiovascular health, as well as enable the early detection and monitoring of CVD development. Whilst it is acknowledged that further research determining the validity and reliability in populations of varying age and health states is needed, the findings of the current study indicate that the oscillometric XCEL device can be used to simply, accurately and precisely measure lower-limb PWV in the healthy young, in a supine position. Although faPWV assessments in a seated position did not meet the validity or reliability criteria, cardiovascular assessments are routinely conducted in a supine position, including FMD (Thijssen *et al.*, 2011), due to the potential for orthostatic induced haemodynamic shifts to confound measures. Whilst postural manoeuvres are unavoidable, this technique does confer several advantages over traditional vascular health assessments. Specifically, measurement of PWV via oscillometry is easier to perform, less operator dependent and more reliable than FMD, particularly in the legs. For example, FMD of the popliteal artery demonstrated extremely poor between-day reliability (ICC = 0.25) in the only study to report lower-limb FMD reliability, to the authors knowledge (McLay *et al.*, 2016). To give a clinical context, the absolute SEM for the current study was 0.53 m/s, meaning that a change of greater than 6.1%, from a mean of 8.6 m/s, is required to infer a true effect, In contrast, using an average baseline FMD of 4.1% and an absolute SEM of 1.74% (calculated from data) (McLay *et al.*, 2016), a change of greater than 42% would have to be observed to be determined true when the FMD technique is used on the leg.

Although it is still unclear what role functional and structural changes in lower-limb vasculature may have on the heart or the development of central CVD, it is recognised that arterial stiffness in the lower extremities is an important determinant of cardiac afterload. Recently, lower-leg vasodilatory function was observed to decrease and central arterial stiffness (cfPWV) to concomitantly increase in response to 3-hrs of prolonged sitting (Credeur *et al.*, in press). Whilst a direct link could not be made, increased PWV in the legs has been reported to be linked to greater aortic stiffness (Wohlfahrt *et al.*, 2013) and left ventricular mass (Ix *et al.*, 2010). Accordingly, assessments of faPWV, as an adjunct to cfPWV (aortic), may be useful in further understanding the effects of sedentary behaviour on CVD risk and, more specifically, understanding how the lower-limb vasculature interacts with central vasculature and cardiac properties. Given that central and peripheral arterial health can be assessed simply, accurately and precisely in the supine position using the oscillometric XCEL device, this tool may be useful in helping to further understand the pathological mechanisms linking cardiovascular disease to sedentarism.

CONCLUSION

The aim of this study was to determine the accuracy (validity) and precision (reliability) of faPWV measurements obtained using the oscillometric-based XCEL device in supine and seated positions. Findings suggest that faPWV can be determined with acceptable accuracy and precision, but only in the supine position. The use of the XCEL device may provide research scientists with a practical, accurate and precise way of investigating the impact of sedentary behaviour, including prolonged sitting, on lower-limb vascular health. Importantly, this technology may also be useful in helping to understand how the lower-limb vasculature acutely and chronically interacts with central vascular and cardiac properties.

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COMPETING INTERESTS

None.

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AUTHOR CONTRIBUTIONS

K.S., S.F., J.F. and L.S. contributed to the conception and design of the experiment, data collection, analysis, interpretation of the data and the drafting of the manuscript. E.K., K.B., G.Z., D.C., D.L. and E.H. contributed to data collection and critical revision of the manuscript for its intellectual content. All authors have approved the final version of the manuscript.

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TABLES

Table 1. Participant demographic data for validity and reliability analyses.

	Validity		Reliability	
	X	(SD)	X	(SD)
n	31		15	
Age (years)	25.8	(5.8)	22.1	(6.4)
Female (%)	48		60	
Height (m)	1.72	(0.08)	1.69	(0.06)
Weight (kg)	73.9	(13.8)	65.2	(7.7)
BMI (kg/m^2)	24.7	(3.3)	22.8	(1.9)
PA Sessions (No./wk)	4.5	(2.0)	4.2	
PA (mins/session)	69	(41)	54	(16)

Abbreviations: BMI, body mass index; PA, physical activity.

	Supine		Seated			
	X	(SD)	X	(SD)	*P*	*d*
SBP (mmHg)	115	(9.9)	118	(8.4)	**0.028**	-0.28
DBP (mmHg)	67	(7.1)	74	(7.1)	**0.000**	-0.93
MAP (mmHg)	99	(7.9)	103	(7.2)	**0.000**	-0.52
cSBP (mmHg)	101	(8.4)	103	(7.0)	**0.042**	-0.27
AIx (%)	4.9	(10.3)	0.0	(11.4)	**0.022**	0.45
AIx75 (%)	-3.5	(10.7)	-4.9	(13.4)	0.479	0.11
Pb (mmHg)	11.5	(2.2)	10.7	(1.8)	**0.022**	0.40
Pf (mmHg)	25.4	(2.7)	23.8	(3.0)	**0.005**	0.55
RM (%)	45.9	(7.8)	45.0	(5.5)	0.375	0.15
CO (L/min)	4.6	(1.0)	3.7	(0.9)	**0.000**	0.89
HR (bpm)	55	(10.0)	61	(12.1)	**0.000**	-0.53
SV (ml)	84.4	(18.4)	63.1	(17.9)	**0.000**	1.17
SVR (d.s.cm^{-5})	1510	(284.7)	2029	(605.5)	**0.000**	-1.10

Table 2. Mean values for peripheral and central haemodynamic responses to change in posture. Bold indicates significant at $P < 0.05$.

Abbreviations: AIx, augmentation index; AIx@75; augmentation index normalized to a heart rate of 75 bpm; CO, cardiac output; cSBP, central systolic blood pressure; *d*, Cohen's d; DBP, diastolic blood pressure; HR, heart rate; MAP, mean arterial pressure; Pb, aortic backward wave pressure; Pf, aortic forward wave pressure; RM, reflection magnitude; SBP, systolic blood pressure; SV, stroke volume; SVR, systemic vascular resistance.

Table 3. Comparison of femoral-ankle pulse wave velocity determined by SphygmoCor XCEL and Doppler ultrasound devices.

	Ultrasound		XCEL		aSEE (95% CI)		sSEE (95% CI)		RSE (95% CI)	
	X	(SD)	X	(SD)	m/s		SD		%	
Supine										
PTT (ms)	68.4	(8.6)	78.8	(9.0)	7.4	(4.3, 8.7)	0.9	(0.5, 1.0)	10.8	(6.3, 12.7)
PWV (m/s)	9.8	(1.2)	8.6	(1.1)	0.8	(0.4, 1.0)	0.7	(0.3, 0.9)	8.4	(3.8, 10.3)
Seated										
PTT (ms)	52.5	(7.1)	58.6	(6.0)	5.83	(4.8, 5.9)	0.8	(0.7, 0.8)	11.1	(9.1, 11.4)
PWV (m/s)	12.8	(1.8)	11.6	(1.3)	1.21	(0.9, 1.3)	0.7	(0.5, 0.7)	9.4	(7.1, 10.1)
Δ										
PTT (ms)	15.9	(6.7)	20.2	(8.6)	8.2	(6.4, 8.5)	1.2	(0.9, 1.3	51.4	(40.4, 53.7)
PWV (m/s)	3.0	(1.5)	2.9	(1.2)	1.2	(1.0, 1.2)	0.8	(0.7, 0.8)	39.8	(33.4, 40.0)

Abbreviations: aSEE, absolute standard error of estimate; CI, confidence interval; PTT, pulse transit time; PWV, pulse wave velocity; RSE, relative standard error; sSEE, standardised standard error of estimate.

Table 4. Reliability of the SphygmoCor XCEL to determine central and peripheral PWV in supine and seated positions.

	ICC (95% CI)		SEM (95% CI)		RC (95% CI)	
Supine						
faPWV (m/s)	0.83	(0.65-0.93)	0.53	(0.33-0.75)	1.46	(0.92-2.09)
cfPWV (m/s)	0.67	(0.40-0.86)	0.48	(0.31-0.65)	1.34	(0.87-1.80)
Seated						
faPWV (m/s)	0.29	(0.23-0.63)	1.19	(0.86-1.39)	3.29	(2.37-3.86)
cfPWV (m/s)	0.57	(0.25-0.81)	0.54	(0.36-0.71)	1.51	(1.00-1.97)

Abbreviations: cfPWV, carotid-femoral pulse-wave velocity; CI, confidence interval; faPWV, femoral-ankle pulse-wave velocity; ICC, intra-class correlation coefficient; RC, repeatability coefficient; SEM, standard error of measurement.

FIGURES LEGENDS

Figure 1. Examples of waveforms recorded at the superficial femoral artery (SFA) and ankle or posterior tibial artery (PTA) using SphygmoCor XCEL (a) and Doppler ultrasound (b) devices.

Figure 2. Bland-Altman plots (top panels) and correlation analysis (bottom panels) for femoral-ankle PWV (faPWV) obtained by SphygmoCor XCEL (XCEL) and Doppler ultrasound (US) devices in supine (closed circles) and seated (open circles) positions.