Central pulse wave velocity and augmentation index are repeatable and reproducible measures of arterial stiffness

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Research Article

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Abstract

Purpose: Arterial stiffness is an important cardiovascular risk factor. Pulse wave velocity (PWV) and augmentation index (Alx) are established indicators of arterial stiffness. The present study aimed to evaluate the repeatability and reproducibility of PWV and Alx in healthy individuals.

Methods: Forty healthy participants (age 33±11 years, 17 females) underwent resting supine PWV and Alx assessments. Measurements were made in triplicate and repeated one week apart. Alx was measured by brachial occlusion and PWV was measured from the carotid artery to the femoral artery by the tonometer - oscillometric method. Repeatability and reproducibility were assessed using intra-class correlation coefficient (ICC). Inter-operator reproducibility was performed on ten participants.

Results: The average values for week-to-week visits for PWV and Alx were 6.20±0.91 vs 6.13±0.91 ms⁻¹ and 14.0±11.8 vs 16.3±12.2 %. For same-day measurements, both PWV and Alx showed excellent repeatability (PWV: ICC=0.96, 95% CI 0.92-0.98, p<0.01; and Alx: ICC=0.90 95% CI 0.84-0.94, p<0.01) and inter-operator reproducibility (PWV: ICC=0.98, 95% CI 0.93-1.00, p<0.01; and Alx: ICC=0.93 95% CI 0.69-0.98, p<0.01). Measurements were repeated one week apart and showed good reproducibility (PWV: ICC=0.77, 95% CI 0.61-0.87, p=<0.01; and Alx: ICC=0.73 95% CI 0.73-0.86, p<0.01).

Conclusion: PWV and Alx demonstrate excellent repeatability and good reproducibility. Considering these variables are non-invasive and easy-to-measure, arterial stiffness may have a role in routine clinical practice to facilitate risk stratification in cardiovascular diseases.

Introduction

Arterial stiffness is a measure of vascular capability, and can provide useful information on cardiovascular risk, in addition to the standard blood pressure measurement [1]. Arterial stiffening occurs as a natural consequence of ageing and may be a precursor to disease [2]. Stiffening is accelerated by the build-up of fatty streaks within the endothelium of blood vessels, particularly large arteries, and is a major factor responsible for cardiovascular disease in older adults [3]. Historically, arterial stiffness was determined using Poiseuille's equation which assessed a steady flow of liquid through a tube whilst accounting for blood viscosity, and pressure, radius, volume, and length of the vessel [4]. However, Poiseuille's law assumes laminar flow, and flow through the arterial system is mainly turbulent. Current measures of arterial stiffness now consider this turbulent, pulsatile flow (created by the contraction and relaxation of the heart) [5].

Increased arterial stiffness is seen habitual smokers (augmentation index (Alx) being independently associated with exhaled carbon monoxide) [6]. Furthermore, engagement in moderate-to-vigorous physical activity with avoidance of sedentary activity is also associated with slower progression on age-related progression of arterial stiffness [7].
Arterial stiffness is independently associated with COVID-19 infection [8] and can predict cardiovascular events in coronary artery disease [9] and diabetes [10]. Arterial stiffness has been shown to independently predict death and standard cardiovascular end points [1]. Increased arterial stiffness has been seen to be a consistent feature in patients with heart failure and preserved ejection fraction (HFpEF) which may be a key feature in its pathophysiology and appears to increase incrementally with common comorbidities such as hypertension and diabetes [11]. Additionally, high arterial stiffness is associated with disease progression (and mortality) in chronic kidney disease [12]. However, clinical assessment of arterial stiffness is still not standard practice in the UK.

Arterial stiffness is commonly evaluated through pulse wave velocity (PWV) and pulse wave analysis (PWA) (with Al\(\alpha\)) being an output of PWA). PWV is a measure of velocity of blood flow through an artery and is calculated as the ratio between the distance the pulse travels and the time it takes to travel down the artery [1]. In multivariate modelling, Mitchell et al. discovered that adding PWV into the Framingham risk prediction increased the cardiovascular disease risk predictive value by 0.7% [13]. The 2018 European Society of Hypertension guidelines suggest a value of carotid to femoral PWV of 10ms\(^{-1}\) requiring further investigation [14], with reference values for age groups also available [15].

Al\(\alpha\) is the percentage of the ratio between augmentation pressure and pulse pressure Fig. 1. Al\(\alpha\) is used as a measure of arterial stiffness, requiring only brachial occlusion making it a considerably easier method. Augmentation pressure is obtained by measuring the reflected brachial pulse wave; whilst pulse pressure is the difference between systolic and diastolic pressure [16]. The common mechanism of increase in Al\(\alpha\) is faster forward pulse propagation and a more rapid reflected wave [16]. In a meta-analysis Al\(\alpha\) has been shown to predict clinical events independently of peripheral blood pressure [17] and as Al\(\alpha\) increases linearly until age 50, this could be a more sensitive marker of arterial ageing in younger adults [18].

Carotid-femoral PWV is the gold standard assessment of arterial stiffness, with the probe-based method remaining the gold standard of obtaining PWV [2]. However, obtaining PWV via the probe method requires skill and specific training [16]. Wilkinson et al. indicated the potential advantage of measuring arterial stiffness in practice to identify at risk patients, but highlighted that this assessment should be used to risk stratify medium-risk hypertensive patients rather than the high-risk hypertensive patients, who are able to be stratified by standard blood pressure measurement alone [2].

Previous studies have shown that the Sphygmocor MM3 technology which utilises applanation tonometry to assess stiffness, is reliable [19], [20]. Limited number of studies have evaluated the functionality of the most recent models of this technology. Thus, the aim of the current study is to evaluate the reliability and repeatability of both PWV and Al\(\alpha\) in younger adults.

**Methods**

**Study Design and Procedure:**
Forty healthy adult volunteers aged 18 to 65 years were recruited for the study. Data were collected between April 2021 and January 2022. Healthy participants were defined as those without history of chronic or acute cardiovascular, respiratory, or neurological conditions. Participants were excluded if they used medication that was known to effect cardiovascular function, they were a current smoker, or their body mass index (BMI) was greater than 35kg.m\(^{-2}\). Ethical approval was obtained through the Coventry University Research Ethics Committee (project reference number: P109193). Participants were required to attend the clinical physiology laboratory on two occasions (one week apart and at the same time of day) and provide written informed consent.

Participants were asked to lay in the supine position for at least 10 minutes in a temperature controlled room prior to taking arterial stiffness measurements. The Sphygmocor Xcel unit (AtCor Medical, Naperville, Illinois, USA) was used to obtain arterial stiffness measurements. Alx was obtained using a brachial cuff and obtaining a blood pressure and pulse pressure from the left brachial artery (approximately midway between the shoulder and the elbow). Measurements were performed in triplicate, and all measures passed the internal quality control criteria [21]. PWV measurement used applanation tonometry over the carotid artery and a partly inflated cuff over the top of the thigh. Assessment required height, sex, date of birth of the participant, and pulse transit distance. Pulse transit distance was obtained by subtracting the distance from the carotid to sternal notch and cuff to the femoral pulse (predetermined at 200mm to avoid need for invasive procedure) from the distance from the sternal notch to the top of the femoral cuff. When appropriate signals from both the cuff and tonometer are obtained, concurrent femoral and carotid pulse waves were captured for a period of 10 seconds. The internal quality control criteria were used to ensure quality of data [21].

Participants returned one week later, at the same time of day, to repeat all measures. A subset of 10 participants underwent inter-operator reproducibility, with a second, trained operator obtaining triplicate values for Alx and PWV, during the same period that the participant is in the supine position.

**Statistical Analysis:**

Data were analysed using the SPSS statistical package version 26 (SPSS Inc., Chicago, IL, USA). Data are expressed as mean ± standard deviation, unless otherwise indicated. Before statistical analysis, data were screened for univariate and multivariate outliers using standard Z distribution cut-offs. Intra-class correlation coefficient (ICC) was performed to determine repeatability, inter-rater reproducibility, and week-to-week reproducibility.

Intra-test repeatability was based on single measure, absolute agreement, 2-way mixed effect model. Inter-rater and week-to-week reproducibility was based on a mean rating (k = 3), single rater, absolute agreement, 2-way mixed effect model. Values < 0.5 were considered poor reliability; 0.5–0.75 moderate reliability; 0.75–0.9 good reliability and > 0.9 considered excellent reliability [15]. Statistical significance was indicated as an alpha level of \( p < 0.05 \).

**Results**
Demographic and anthropometric characteristics of the participants are presented in Table 1. Participants were classified as healthy with an average BMI of 25 kg/m² and blood pressure of 124/77 mmHg. Mean and standard deviations are presented in Table 2.

### Table 1
Demographic and physical characteristics of study participants

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>33.4 ± 11.0</td>
<td>22–58</td>
</tr>
<tr>
<td>Sex, male/ female</td>
<td>23 / 17</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>174 ± 8.4</td>
<td>158–190</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76.4 ± 13.3</td>
<td>49–114</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25 ± 3.70</td>
<td>18.3–37.4</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>124 ± 11.7</td>
<td>100–142</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>76.8 ± 8.39</td>
<td>63–98</td>
</tr>
</tbody>
</table>

### Table 2
Mean and Standard Deviation of Augmentation Index (Alx) and Pulse Wave Velocity (PWV)

<table>
<thead>
<tr>
<th></th>
<th>PWV (mean ± SD, ms⁻¹)</th>
<th>Alx (mean ± SD, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-test repeatability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repeat 1</td>
<td>6.17 ± 0.89 (n = 40)</td>
<td>5.05 ± 3.81 (n = 40)</td>
</tr>
<tr>
<td>Repeat 2</td>
<td>6.12 ± 0.97 (n = 40)</td>
<td>5.21 ± 4.16 (n = 39)</td>
</tr>
<tr>
<td>Repeat 3</td>
<td>6.05 ± 0.94 (n = 37)</td>
<td>4.82 ± 4.00 (n = 39)</td>
</tr>
<tr>
<td>Test-retest reproducibility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 1</td>
<td>6.20 ± 0.91 (n = 40)</td>
<td>14.0 ± 11.8 (n = 40)</td>
</tr>
<tr>
<td>Week 2</td>
<td>6.13 ± 0.91 (n = 40)</td>
<td>16.3 ± 12.2 (n = 40)</td>
</tr>
<tr>
<td>Inter-rater reproducibility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Researcher 1</td>
<td>6.14 ± 1.04 (n = 10)</td>
<td>20.4 ± 12.7 (n = 10)</td>
</tr>
<tr>
<td>Researcher 2</td>
<td>5.99 ± 1.10 (n = 10)</td>
<td>21.3 ± 13.4 (n = 10)</td>
</tr>
</tbody>
</table>

### Pulse Wave Velocity:

An excellent ICC was obtained for intra-test repeatability (0.92, 95% CI: 0.87–0.95, *p* < 0.05) and inter-rater reproducibility (0.98, 95% CI: 0.92–1.0, *p* < 0.05). Spread of triplicate results are displayed in Fig. 2. There was a very good correlation between measurements taken one week apart (ICC = 0.87, 95% CI: 0.76–0.93, *p* < 0.05) was obtained.

### Augmentation Index:
An excellent ICC was obtained for intra-test repeatability (0.90, 95% CI: 0.84–0.94, p < 0.05) and inter-rater reproducibility was obtained (0.93, 95% CI: 0.69–0.982, p < 0.05). Triplicate measures are displayed in Fig. 3. Measurements taken one week apart also showed very good correlation (ICC = 0.86, 95% CI: 0.73–0.93, p < 0.05) was obtained.

**Discussion**

To the best of our knowledge, this is the first study to assess intra-test, inter-rater repeatability, and test-retest reproducibility of PWV and Alx simultaneously. The primary findings suggest in a sample of healthy adults, excellent repeatability and good reproducibility of the PWV and Alx.

Intra-test repeatability has been demonstrated as excellent by Hwang et al. (PWV and Alx (ICC: 0.996 and 0.983, respectively)) in the SphygmoCor Xcel device [22]. This study included both young and older adults (mean: 33.3, range 22–58 years), however due to a small sample size of older adults, it was not possible to determine if repeatability changed between age groups as suggested by Bortel et al. [23].

Making devices less operator dependent is important for use in clinical practice [24]. The semi-automated device used in this study showed excellent reproducibility for PWV and Alx (ICC: 0.98 and 0.93). Novice vs. experienced operator analysis has previously been assessed using the SphygmoCor device. Results showed that it takes an estimated 30 participants to ensure acceptable Alx measurements, and around 2.5 hours initial training and a further 14 or more practice measures to ensure acceptable PWV measures [23].

Day-to-day reliability assessed by Hwang et al. showed PWV and Alx reliability to be excellent (ICC = 0.979 and 0.939, respectively) in the Sphygmocor Xcel device [22]. These results indicate higher levels of reproducibility compared to the present study. A difference in study population could be attributed to this finding as the present study only assessed mainly younger participants.

Hwang et al. assessed the day-to-day and intra-test reliability of the Xcel and MM3 devices. These devices, both manufactured by SphygmoCor use the semi-automated (applanation tonometry and oscillometric) and tonometry-only methods of data acquisition. Measures of PWV and Alx between devices were strongly related (r = 0.85 and 0.75), suggesting methods of acquisition are in agreement [25]. Studies in clinical populations found no difference between the Vicorder (using oscillometric technique only) and SphygmoCor SCOR-Pvx (using gated pulse wave forms obtained through applanation tonometry only) when assessing PWV [26]. Not only did this study evaluate different models of device (each with different algorithms), but there were also different methods of data acquisition (oscillometric vs. applanation tonometry), which gives rise to multiple points of error, as discussed by Bortel et al. [25]. Conversely, Hickison et al. assessed validity and repeatability of the Vicorder apparatus (using oscillometric techniques only) and the SphygmoCor Xcel (semi-automated, carotid application tonometry and femoral cuff) devices. The Vicorder showed a higher degree of accuracy, especially at high PWV, than the semi-automated SphygmoCor Xcel [27]. This is an important consideration in the trade-off between being able to assess PWV in the clinic, the assessment being a true representation of a patient's
characteristics, and the time taken to obtain the measure (including both clinic time, and the time taken to
train the operator).

Intra-test repeatability assesses only mechanical and minute-to-minute biological variation due to the
tape measure distances staying the same between tests; intra-rater repeatability assesses human error as
well as mechanical and minute-to-minute biological variation and week-to-week reproducibility assesses
human error, mechanical variation, day-to-day biological variation and minute-to-minute biological
variation. With adding additional opportunity for error, we can see that correlation decreases, but it is
promising that there was still an excellent level of reproducibility when operators are different.

One of the major limitations of the present study is that it recruited only healthy individuals, and
employed only the SphygmoCor Xcel. Considering importance of arterial stiffness evaluation in clinical
settings, the present findings should be further confirmed in different clinical populations with gated age
groups to allow generalisability of data and further analysis into the variation between devices and
methods of acquisition used. Additionally, the SphygmoCor assumes uniform stiffness throughout the
artery and also only assesses central artery stiffness. Using ultrasound data acquisition methods may
allow researchers/clinicians to pinpoint specific areas of stiffness.

In conclusion, our results show that assessment of PWV and Alx using the SphygmoCor Xcel
demonstrate good to excellent repeatability and reproducibility in a sample of healthy adults. Considering
high accuracy, non-invasive and easy-to-measure features, arterial stiffness measurements may play a
vital role and should be integrated in routine clinical practice to facilitate risk stratification in
cardiovascular diseases.

Declarations

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the manuscript do not reflect the views and opinions of the funders.

Authors’ Contributions

Study concept and design: DGJ; Study Supervision: NO, DGJ; Acquisition of data: MR, SLR, CJS, NCO,
DGJ; Data analysis and interpretation of data: SLR; Drafting of the manuscript: SLR; Critical review of the
manuscript: DGJ, PB, GM, AEH, MR, NCO.

All authors approved the final version of the manuscript. DGJ acts as the guarantor and take
responsibility for the content of the manuscript, including the data and analysis.

Conflicts of interest/Competing interests
The authors declare that they have no conflicts of interest.

**Availability of data and material**

The corresponding author shall provide data upon reasonable request.

**References**


**Figures**

![Diagram of arterial blood pressure over time](image-url)
Figure 1

Determining augmentation index from the central pressure wave

Profile of Pulse Wave Velocity

Figure 2

Profile of the measures obtained by PWV. Participants’ individually values were plotted for each repeat in ascending order from the mean.
Figure 3

Profile of augmentation index obtained measures. Participants’ individual values were plotted for each repeat in ascending order from the mean.