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# Indices of cardiovascular function derived from peripheral pulse wave analysis using radial applanation tonometry: a measurement repeatability study

Mike Crilly<sup>a</sup>, Christoph Coch<sup>b</sup>, Margaret Bruce<sup>c</sup>, Hazel Clark<sup>c</sup> and David Williams<sup>c</sup>

**Abstract:** Pulse wave analysis (PWA) using applanation tonometry is a non-invasive technique for assessing cardiovascular function. It produces three important indices: ejection duration index (ED%), augmentation index adjusted for heart rate (AIX@75), and subendocardial viability ratio (SEVR%). The aim of this study was to assess within- and between-observer repeatability of these measurements. After resting supine for 15 minutes, 20 ambulant patients (16 male) in sinus rhythm underwent four PWA measurements on a single occasion. Two nurses (A & B) independently and alternately undertook PWA measurements using the same equipment (Omron HEM-757; SphygmoCor with Millar hand-held tonometer) blind to the other nurse's PWA measurements. Within- and between-observer differences were analysed using the Bland-Altman 'limits of agreement' approach (mean difference  $\pm$  2 standard deviations, 2SD). Mean age was 56 (blood pressure, BP 136/79; pulse rate 64). BP/PWA measurements remained stable during assessment. Based on the average of two PWA measurements the mean  $\pm$  2SD between-observer difference in ED% was  $0.3 \pm 2.0$ ; AIX@75  $1.0 \pm 3.9$ ; and SEVR%  $1.7 \pm 14.2$ . Based on a single PWA measurement the between-observer difference was ED%  $0.3 \pm 3.3$ ; AIX@75  $1.7 \pm 6.9$ ; and SEVR%  $0.6 \pm 22.6$ . Within-observer differences for nurse-A were ED%  $0.0 \pm 5.4$ ; AIX@75  $1.5 \pm 7.0$ ; and SEVR%  $1.7 \pm 39.0$  (nurse-B:  $0.1 \pm 3.8$ ;  $0.1 \pm 8.0$ ; and  $0.6 \pm 23.3$ , respectively). PWA demonstrates high levels of repeatability even when used by relatively inexperienced staff and has the potential to be included in the routine cardiovascular assessment of ambulant patients.

**Key words:** applanation tonometry; measurement error; pulse wave analysis; radial artery; reproducibility

## Introduction

Routine clinical assessment of cardiovascular function traditionally relies upon evaluation of the radial pulse and the brachial systolic and diastolic blood pressure. Interest in the non-invasive assessment of cardiovascular function has increased over recent times, particularly around the relationship between the stiffness of large arteries and blood pressure.<sup>1,2</sup> One particularly promising non-invasive method for assessing cardiovascular function that has emerged is the novel technique of pulse wave analysis (PWA) using applanation

tonometry.<sup>1,3–5</sup> Advances in computer technology mean that it is now possible to rapidly assess central aortic pressures and waveforms without the need for cardiac catheterization.<sup>1,2</sup> Until recently, the use of PWA has largely been restricted to research, but commercial PWA devices such as the SphygmoCor system are now available for use in routine clinical practice.<sup>1</sup>

## Pulse wave analysis (PWA)

PWA uses a high-fidelity tonometer to capture electronically the shape of a peripheral arterial pulse.<sup>1</sup> The tonometer probe is 'applanated' (applied so as to flatten, but not occlude an artery) at a convenient site such as the radial artery. The shape of the peripheral pulse wave obtained is then calibrated with the brachial systolic and diastolic pressure (measured in the traditional manner with an inflated cuff at the brachial artery) to derive the shape and dimensions of the central aortic pressure wave.<sup>1</sup> The SphygmoCor system converts the peripheral waveform to a central waveform using a proprietary algorithm ('general transfer function').<sup>5,6</sup> PWA permits the non-invasive

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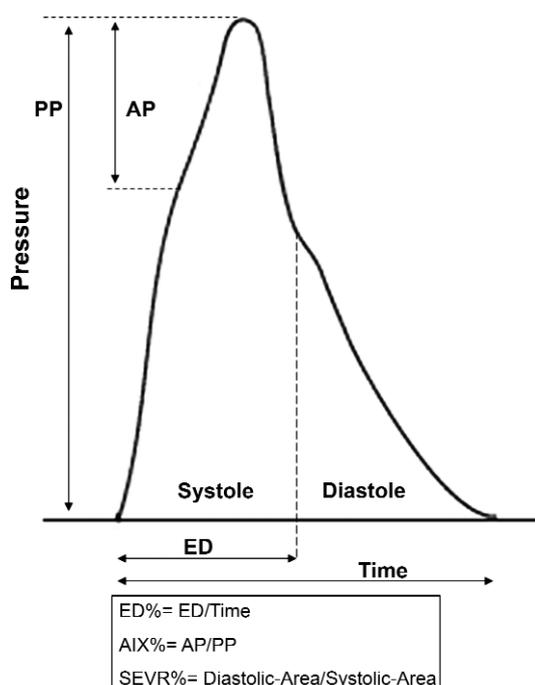
measurement of three main indices of cardiovascular function: augmentation index adjusted to a heart rate of 75 beats per minute (AIX@75), subendocardial viability ratio (SEVR%), and the ejection duration index (ED%).<sup>1</sup> The derivation of these indices are shown schematically in Figure 1 and described below.

### Augmentation index (AIX) adjusted to a heart rate of 75 (AIX@75)

In the peripheral arteries the outgoing systolic pulse wave is reflected back towards the heart and adds to ('augments') the central aortic pressure in late systole.<sup>1,3-5</sup> The amount by which the aortic pressure is increased by this phenomenon is the 'augmentation pressure' (AP). AIX is this aortic AP expressed as a percentage of the aortic 'pulse pressure' (PP).<sup>1,3,4</sup> AIX ( $=AP/PP$ ) indicates the combined influence of large artery pulse wave velocity, peripheral pulse wave reflection and vascular function.<sup>3,5,7,8</sup> AIX is the most widely researched index of PWA, with several studies indicating that AIX is independently predictive of adverse cardiac events.<sup>9,10</sup> Since AIX varies with heart rate it is commonly adjusted to a 'standard heart rate' of 75 beats per minute (AIX@75).<sup>11</sup>

### Subendocardial viability ratio (SEVR%, Buckberg ratio)

The 'area under the curve' (AUC) of the systolic and diastolic portions of the central aortic pulse wave can be measured using PWA.<sup>1</sup> Blood flow within the coronary arteries occurs mainly during diastole and the



**Figure 1** Cardiovascular indices derived from arterial pulse wave.

diastolic-AUC indicates myocardial perfusion ('supply of oxygen').<sup>1</sup> The systolic-AUC indicates myocardial contraction ('demand for oxygen'). The subendocardial viability ratio (SEVR%), also known as the Buckberg ratio, is a 'supply to demand' ratio of the diastolic-AUC divided by the systolic-AUC.<sup>1,12</sup> In normal coronary arteries, subendocardial ischaemia occurs when SEVR% falls below 50%.<sup>13</sup>

### Ejection duration index (ED%)

The duration of left ventricular systolic ejection (systolic time interval in milliseconds) can be measured using PWA.<sup>1</sup> The ratio of the duration of systolic ejection to the total duration of a cardiac cycle is the ejection duration index (ED%). Patients with systolic dysfunction have been found to have a higher ED% than those with diastolic dysfunction.<sup>1</sup>

### Repeatability of PWA indices

It is important that clinical innovations, such as PWA, are carefully evaluated before their widespread introduction into routine clinical practice. The diffusion of previous medical innovations into medical practice has not always produced the benefits anticipated for patients.<sup>14</sup> For PWA to be clinically useful it must be a clinically reproducible technique, but a recent review concluded that considerable uncertainty still remains concerning the repeatability of peripheral PWA.<sup>15</sup> Only one previous study has reported on the repeatability of AIX@75 and SEVR%<sup>16</sup> and two further studies have estimated the repeatability of SEVR%,<sup>17,18</sup> although one of these studies only addressed between-observer repeatability.<sup>18</sup> No previous studies have reported on the repeatability of ED%.

The recent introduction of PWA into routine clinical cardiovascular assessment of patients at Aberdeen Royal Infirmary (a 1000-bed university teaching hospital) provided the opportunity to assess the repeatability of the method when undertaken by nursing staff with limited previous experience of using the technique. The aim of this study was to estimate the within- and between-observer repeatability for the three main indices of cardiovascular function (AIX@75, SEVR%, and ED%) obtained from PWA using applanation tonometry.

### Methods

A consecutive series of 20 ambulant patients in sinus rhythm underwent pulse wave analysis (PWA). They were purposively selected to include 10 patients prescribed medication for essential hypertension and 10 patients without hypertension or known cardiovascular morbidity. Blood pressure (BP) and peripheral PWA were each measured a total of four times at a single hospital visit. Two nurses independently undertook all BP/PWA measurements in alternate order

using the same equipment. BP was measured at the left brachial artery and PWA at the right radial artery according to an agreed protocol.

Patients rested supine for 15 minutes before each nurse (A/B) measured BP/PWA twice in alternate order (ABAB or BABA). Each nurse measured BP/PWA alone in a clinical side-room, ensuring that any tonometer pressure mark left at the wrist had disappeared before alternating. Whilst each nurse was aware of their own BP/PWA measurements, each was blind to the measurements obtained by the other. Neither nurse had access to patient medical records nor did they record any other additional clinical information (other than asking patients about their current use of medication for high BP). Patients did not speak or sleep during assessment. They had not been asked to refrain from eating, drinking or smoking prior to assessment. All assessments were undertaken in a quiet temperature-controlled side-room at Aberdeen Royal Infirmary (22 July to 30 September 2004, between 08:30 am to 3:30 pm).

### Blood pressure (BP)

BP was measured with a standard adult cuff at the left brachial artery (a large adult cuff was used if the upper arm circumference was greater than 32 cm). Patients had their supine BP measured four times (nurses alternating twice) using the Omron HEM-757 IntelliSense BP monitor (marketed commercially as the M5-I in the UK by Omron Healthcare Inc., Bannockburn, IL, USA). The Omron M5-I/HEM-757 is an automated oscillometric BP monitor that had been successfully validated independently against international criteria.<sup>19</sup>

### Radial pulse wave analysis (PWA)

A hand-held tonometer probe (Millar tonometer, Houston, Texas, USA) was used to capture the peripheral pulse wave. The tonometer was 'applanated' (applied so as to flatten but not occlude) at the right radial artery with the wrist supported by a pillow. The shape of the peripheral pulse wave was captured electronically using a laptop computer (Toshiba Satellite Pro) linked to a desktop SphygmoCor pulse wave analysis system (SCOR-Px, software version 7.01, AtCor Medical Pty Ltd., Sydney, Australia).<sup>1</sup> The SphygmoCor system generated an average peripheral pulse wave contour from a 10 second recording period. The quality of the pulse waves captured was assessed by the nurse both visually (on the PC screen) and numerically using the SCOR-Px built-in quality index score, QI% (derived from pulse height, pulse height variation and diastolic variation).

The two nurses were registered general nurses, with more than 20 years clinical experience each. Both had previous expertise in intensive care nursing. Prior to the start of this study they had practised PWA around 35 times on a small number of work colleagues after

having attended a 2-day PWA theoretical-practical course some 6 months previously. Only high-quality pulse wave traces, both visually (uninterrupted steep upstroke with second systolic shoulder before a sharp incurva inflection and smooth exponential decline in diastole) and numerically (QI%  $\geq 85\%$ ; pulse height  $\geq 100$  units; pulse height variation  $\leq 5\%$ ; and diastolic variation  $\leq 5\%$ ) were considered acceptable.<sup>1</sup>

### Statistical approach

Analysis is based on individual patient data as the unit of analysis. Only anonymized individual patient data were available for this analysis. The 'Bland-Altman 95% limits of agreement' approach (mean difference  $\pm 2$  standard deviations, 2SD) was used to assess within- and between-observer differences in paired measurements,<sup>20,21</sup> with the mean of all four measurements (ED%, AIX@75, SEVR%) assumed to be the best estimate of the true underlying value.<sup>21</sup> This approach assumes that observer differences are normally distributed over a range of measurements and uses SD as an index of measurement error.<sup>21</sup> Intraclass correlation coefficients (ICC) were calculated for between- and within-observer repeatability using one-way analysis of variance (ANOVA). Standard methods were used to calculate 95% confidence intervals.<sup>22</sup> All data were double-entered for analysis into SPSS (version 14). No participants or 'outlying values' were excluded from any part of the analysis.

### Results

Pulse wave analysis was successfully undertaken in a consecutive series of 20 ambulant patients (four female) in sinus rhythm referred for PWA from among patients attending Aberdeen Royal Infirmary (ARI). Ten patients were on medication for essential hypertension (four mono-therapy, four dual-therapy and two triple-therapy). Mean age was 56 (range 27–82; SD 14.6). Mean brachial BP was 136/79. Excluding the initial 15 minutes rest, PWA took a mean of 30 (range 12–54; SD 11.8) minutes per patient. The quality of PWA recording was high with a mean quality index (QI%) of 97.1% (range 90–100; SD 2.9). Mean QI% was similarly high for both nurses (96.9% and 97.3%). For 12 patients the nurse assessment followed a sequence of 'ABAB' (and 'BABA' for eight patients).

### PWA and BP measurements

Both nurses recorded very similar PWA and BP measurements for this group of patients. The values and ranges of the clinical measurements obtained are shown in Table 1. The pulse rate shown is that recorded by the SphygmoCor machine. SEVR% had the widest range of values (extending over 79 points), whilst the ED% had the narrowest range (12 points).

**Table 1** Measurements of blood pressure (BP) and pulse wave analysis (PWA) undertaken by two observers,  $n = 20$ .

	Mean	(SD)	Range (low to high)	Mean Nurse-A	(SD)	Mean Nurse-B	(SD)
Ejection duration ratio, ED%	34	(3.0)	12 (30 to 42)	35	(3.0)	34	(3.1)
Augmentation index at 75 bpm, AIX@75	19	(11.0)	43 (-3 to 41)	19	(11.4)	18	(10.8)
Subendocardial viability ratio, SEVR%	158	(20.8)	79 (122 to 201)	157	(21.0)	159	(21.3)
Pulse rate (bpm)	64	(8.9)	37 (51 to 88)	64	(8.9)	63	(9.1)
Brachial diastolic blood pressure (mmHg)	79	(8.5)	28 (60 to 88)	79	(8.2)	78	(9.1)
Brachial systolic blood pressure (mmHg)	136	(19.6)	80 (93 to 173)	136	(18.9)	135	(20.6)

Because of rounding of decimal places the range may not equal the highest minus the lowest value.

Values are based on four measurements (except values for individual nurses based on two measurements).

SD, standard deviation; ED%, ejection duration index; bpm, beats per minute; AIX@75, augmentation index adjusted to a pulse rate of 75 bpm using the SphygmoCor machine's inbuilt algorithm; SEVR%, subendocardial viability ratio; mmHg, millimetres of mercury.

SEVR% had a similar range and SD to systolic BP, whilst AIX@75 had a similar range (43 points) and SD to pulse rate.

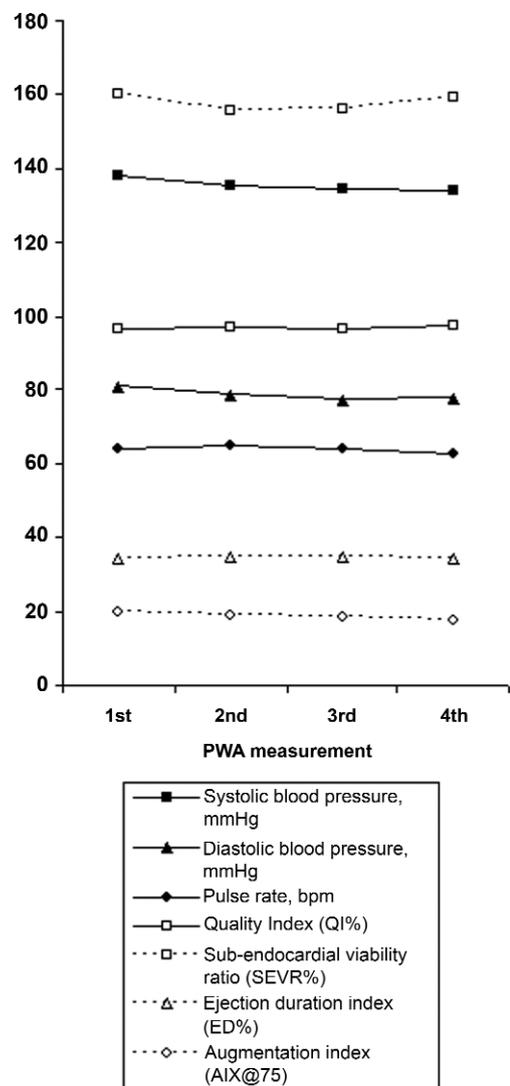
### Trends in PWA assessment

Each patient had four sequential measurements of BP and PWA. Figure 2 shows the stability of mean BP and PWA measurements over time. Systolic and diastolic BP decreased (by 3.6 and 3.1 mmHg respectively) with the majority of the reduction occurring between the first and second measurements. Pulse rate declined by 1.3 beats per minute, whilst AIX@75 declined by 2.0 points. SEVR% initially declined (by 4.5 points between the first and second measurements) before gradually returning to its initial value. Both ED% and QI% showed no real change over time.

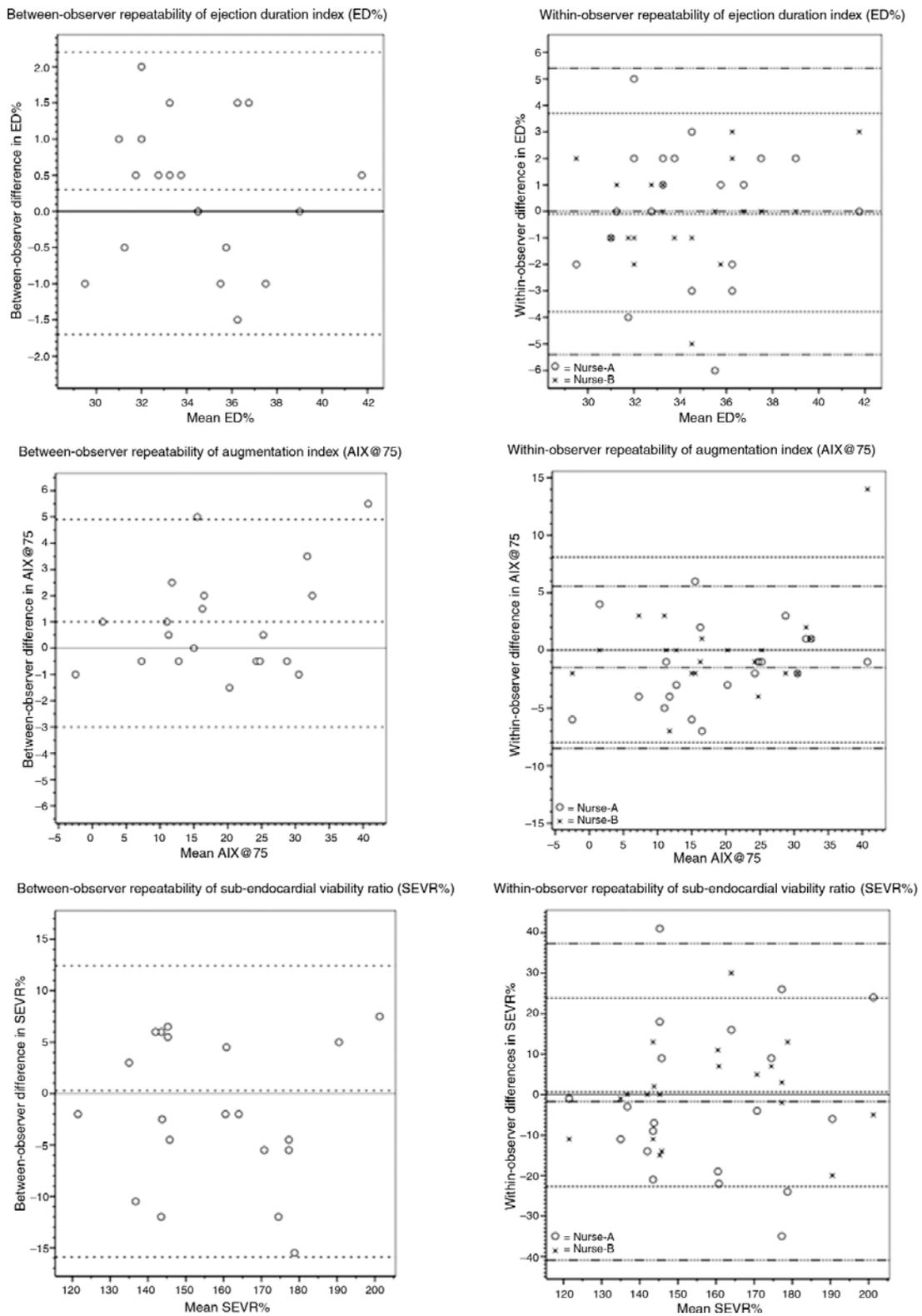
Between- and within-observer repeatability (ED%, AIX@75 and SEVR%) are shown in Tables 2 and 3. Pulse rate is included as a comparison measure. The related Bland-Altman plots are shown in Figure 3. For the between-observer differences the solid horizontal line represents the line of no difference, whilst the three dashed horizontal lines represent the mean (and  $\pm 2SD$ ) of the difference between measurements. For the within-observer differences the dashed-dotted lines represent nurse-A and the dashed lines nurse-B.

### Between-observer repeatability

The ICCs based on the average of two PWA measurements were very high ( $\geq 0.94$ ) (Table 2). They were lower when based on a single PWA measurement, but remained above 0.92 for AIX@75. The upper section of Table 2 shows the between-observer differences (mean difference, SD, limits of agreement) in PWA measurements based on the average of two PWA measurements made on each patient by each nurse. All the differences are small (less than 2 points), but the spread of these differences (indicated by SD) are wider for those indices with a wider range of values. SEVR% has the widest range (79 points) and also the



**Figure 2** Trends in serial blood pressure and pulse wave analysis (PWA) measurements: four measurements on 20 patients made alternately by two nurses.



**Figure 3** Between-observer and within-observer repeatability of three cardiovascular indices.

**Table 2** Between-observer repeatability of pulse wave analysis (PWA): based upon two independent measurements made alternately by two observers on 20 patients (differences are 'nurse-A' measurement minus 'nurse-B' measurement).

	Intraclass correlation coefficient	(95% CI)	Mean difference	(95% CI)	SD (2SD)	Limits of agreement <sup>a</sup>
Average of both PWA measurements						
Ejection duration ratio, ED%	0.94	(0.86 to 0.98)	0.3	(-0.2 to 0.7)	1.0 (2.0)	-1.7 to 2.2
AIX adjusted for heart rate, AIX@75	0.98	(0.95 to 0.99)	1.0	(0.0 to 1.9)	2.0 (3.9)	-3.0 to 4.9
Subendocardial viability ratio, SEVR%	0.94	(0.85 to 0.98)	-1.7	(-5.0 to 1.6)	7.1 (14.2)	-15.9 to 12.4
Pulse rate (bpm)	0.98	(0.94 to 0.99)	0.5	(-0.4 to 1.4)	1.9 (3.8)	-3.3 to 4.3
First PWA measurement						
Ejection duration ratio, ED%	0.85	(0.66 to 0.94)	0.3	(-0.5 to 1.0)	1.7 (3.3)	-3.1 to 3.6
AIX adjusted for heart rate, AIX@75	0.93	(0.84 to 0.97)	1.7	(0.1 to 3.3)	3.5 (6.9)	-5.2 to 8.6
Subendocardial viability ratio, SEVR%	0.86	(0.68 to 0.95)	-0.6	(-5.9 to 4.7)	11.3 (22.6)	-23.2 to 22.0
Pulse rate (bpm)	0.92	(0.82 to 0.97)	0.4	(-1.3 to 2.0)	3.6 (7.1)	-6.8 to 7.5
Second PWA measurement						
Ejection duration ratio, ED%	0.78	(0.51 to 0.91)	0.3	(-0.8 to 1.4)	2.3 (4.5)	-4.2 to 4.8
AIX adjusted for heart rate, AIX@75	0.96	(0.91 to 0.99)	0.2	(-1.3 to 1.7)	3.2 (6.4)	-6.2 to 6.6
Subendocardial viability ratio, SEVR%	0.77	(0.50 to 0.91)	-2.9	(-10.1 to 4.4)	15.6 (31.2)	-34.1 to 28.4
Pulse rate (bpm)	0.89	(0.75 to 0.96)	0.7	(-1.4 to 2.7)	4.3 (8.6)	-7.9 to 9.2

95% CI, 95% confidence interval around differences; SD, standard deviation (2SD = twice the standard deviation); PWA, pulse wave analysis; ED%, ejection duration index; AIX@75, augmentation index adjusted for heart rate; SEVR%, subendocardial viability ratio; bpm, beats per minute.

<sup>a</sup>Limits of agreement = mean difference  $\pm$  2SD.

widest 'limits of agreement' (-16% to +12%). Both ED% and AIX@75 have narrower limits of agreement (-2 to +2; -3 to +5, respectively); limits that are comparable with pulse rate (-3 to +4). The between-observer differences, when expressed as a proportion of the range (mean difference/range of values) were small: 2.2% for ED%, AIX@75 and SEVR%; compared with 1.4% for pulse rate.

The lower two sections of Table 2 show the between-observer differences for the first and second PWA measurements. As would be anticipated, the between-observer variability is greater when based on a single measurement as opposed to the average of two readings. For example, the between-observer limits of agreement for ED% was -3% to +4% when based on the first PWA measurement; -4% to +5 when based on the second measurement; but -2% to +2% when based on the average of these two measurements.

### Within-observer repeatability

The within-observer differences in PWA measurements for the two nurses (A & B) are shown in Table 3. The ICCs for AIX@75 were high for both nurses ( $\geq 0.93$ ), but somewhat lower for ED% and SEVR ( $\leq 0.86$ ). The actual numerical differences for all three indices were small (less than 2 points). ED% and

AIX@75 both had limits of agreement that were broadly comparable with those for pulse rate. For example, the values for nurse-B were -4 to +4, -8 to +8, and -8 to +5 (for ED%, AIX@75 and pulse rate respectively). Nurse-A showed greater variability in the measurement of ED% and SEVR%, whilst nurse-B showed greater variability in the measurement of AIX@75. The widest 'limits of agreement' was for SEVR% measured by nurse-A (-41 to +37). Focusing on the other PWA measurements, from the nurse with the higher level of variability, within-observer limits of agreement were -5 to +5 for ED%, -8% to +8 for AIX@75, and -12 to +10 for pulse rate. The within-observer absolute differences, when expressed as a proportion of the range (mean difference/range of values) were small: 0.4% for ED%; 0.1% for AIX@75; 0.8% for SEVR% and 3.1% for pulse rate.

### Discussion

PWA using radial artery tonometry has very high levels of within- and between-observer repeatability, even when used by nurses with limited previous experience of the technique. Both between-observer and within-observer

**Table 3** Within-observer repeatability of pulse wave analysis (PWA): based upon two independent measurements made alternately by two observers on 20 patients (differences are second measurement minus first measurement).

	Intra-class correlation coefficient	(95% CI)	Mean difference	(95% CI)	SD (2SD)	Limits of agreement <sup>a</sup>
Nurse-A measurement of PWA						
Ejection duration ratio, ED%	0.66	(0.31 to 0.86)	0.0	(-1.3 to 1.3)	2.7 (5.4)	-5.4 to 5.4
AIX adjusted for heart rate, AIX@75 (%)	0.95	(0.87 to 0.98)	-1.5	(-3.1 to 0.2)	3.5 (7.0)	-8.5 to 5.6
Subendocardial viability ratio, SEVR%	0.64	(0.28 to 0.85)	-1.7	(-10.8 to 7.5)	19.5 (39.0)	-40.6 to 37.3
Pulse rate (bpm)	0.82	(0.59 to 0.93)	-0.9	(-3.4 to 1.7)	5.5 (11.1)	-11.9 to 10.2
Nurse-B measurement of PWA						
Ejection duration ratio, ED%	0.83	(0.61 to 0.93)	-0.1	(-0.9 to 0.8)	1.9 (3.8)	-3.8 to 3.7
AIX adjusted for heart rate, AIX@75 (%)	0.93	(0.83 to 0.97)	0.1	(-1.8 to 1.9)	4.0 (8.0)	-8.0 to 8.1
Subendocardial viability ratio, SEVR%	0.86	(0.68 to 0.94)	0.6	(-4.8 to 6.0)	11.7 (23.3)	-22.7 to 23.9
Pulse rate (bpm)	0.93	(0.82 to 0.97)	-1.2	(-2.7 to 0.4)	3.3 (6.6)	-7.7 to 5.4

95% CI, 95% confidence interval around differences; SD, standard deviation (2SD = twice the standard deviation); PWA, pulse wave analysis; ED%, ejection duration index; AIX@75, augmentation index adjusted for heart rate; SEVR%, subendocardial viability ratio; bpm, beats per minute.

<sup>a</sup>Limits of agreement = mean difference  $\pm$  2SD.

differences in the measurement of ED%, AIX@75 and SEVR% were small, whether based on a single initial measurement or the average of two readings. Mean absolute differences between measurements were less than 2 points for all three indices. SEVR% had the widest range of values and demonstrated the widest limits of agreement. On the basis of this study we would predict that for 95% of patients assessed in a similar manner, the absolute differences between-observers undertaking a single measurement would fall within a range of -2 to +2 (ED%), -3 to +5 (AIX@75), and -16 to +12 (SEVR%). Based on a conservative estimate, the equivalent limits for absolute differences within-observers are -5 to +5 (ED%), -8 to +8 (AIX@75), and -41 to +37 (SEVR%).

### Study strengths and limitations

We adopted a rigorous approach to this evaluation of PWA repeatability, taking account of consensus guidelines on the performance of PWA. We assessed all of our patients supine after 15 minutes of rest.<sup>23</sup> Our patients had a broad range of PWA values and the number of patients recruited is comparable with other published studies.<sup>16-18</sup> All BP/PWA measurements were made using the same equipment by two nurses who were blind to each other's measurements, although it was not possible to avoid each nurse being aware of their own BP/PWA measurements and any resulting bias will have tended to reduce within-observer variability.

The nurses independently and alternately measured PWA on the same patients at a single session. PWA was undertaken to a very high-quality standard and BP

was recorded using a validated and automated machine.<sup>19</sup> Both BP and PWA indices remained stable during the assessment period. Our primary interest was the repeatability of PWA, not the ability of PWA to distinguish between patients with or without specific medical conditions. In order to avoid unduly influencing BP/PWA measurement, the nurses collected only limited patient demographic data (age and gender). Other than drug therapy for essential hypertension they were kept blind to the patient's medical history.

A limitation of the study is that the sequence of nurse BP/PWA measurement was not random, but depended pragmatically upon which nurse was most readily available to undertake the first measurement. Consequently, the first PWA/BP measurement was undertaken by nurse-A (sequence ABAB) for 12 (nine male) patients. This is unlikely to have biased our results as those patients assessed initially by nurse-A were similar to those initially assessed by nurse-B (mean age of 57 vs 56; BP 133/78 vs 140/79; and pulse rate 66 vs 61).

We did not confirm that BP was the same in both arms. Radial PWA and brachial BP were measured on opposite arms, as it was more convenient to place the Omron BP machine and SphygmoCor device on opposite sides of the patient. Since both nurses followed the same procedure this will not have influenced our assessment of repeatability. But if any of our patients had significant left subclavian artery stenosis, then the subsequent miscalibration of the SphygmoCor device will have distorted the central aortic values obtained from the true value.

We intentionally attempted to select patients to provide a broad range of PWA values across which we could assess repeatability (as opposed to assessing the ability of PWA to distinguish between different patient groups). Since a wider range of values will have tended to inflate the ICCs, undue emphasis should not be placed on the potential generalizability of the ICCs that we observed.<sup>20,21</sup> Since we assessed our patients at a single session, we have not accounted for within-patient variability that would operate when assessing the same patient on more than one occasion; for example, in prospectively monitoring clinical changes in PWA.

### Comparison with other studies

The 'limits of agreement' approach is the most useful approach to the assessment of measurement error and repeatability.<sup>20,21</sup> A comparison of our findings with the published literature is shown in Table 4. One additional study has evaluated the repeatability of SEVR%, but provides insufficient information to derive 'limits of agreement' to permit its inclusion.<sup>23</sup> Whilst several studies have reported on the repeatability of AIX unadjusted for heart rate,<sup>17,24</sup> only one previous study has reported on the repeatability of AIX (mean  $\pm$  2SD) adjusted for heart rate (AIX@75).<sup>16</sup> Two studies have estimated the repeatability of SEVR%,<sup>17,18</sup> but no previous studies have reported on the repeatability of ED%.

All three previous studies (Table 4) were hospital-based.<sup>16-18</sup> Two studies measured PWA supine on a single occasion,<sup>16,17</sup> whilst the third study measured PWA seated on three separate days.<sup>18</sup> Only one study rested patients for as long as 15 minutes supine.<sup>16</sup> Participants in our study were older (with a higher average brachial blood pressure) than the two studies recruiting healthy hospital volunteers,<sup>16,18</sup> but had a similar age to the study involving patients with renal failure.<sup>17</sup> Differences in patient characteristics, duration of rest before assessment, observer expertise and the influence of diurnal variation at the time of assessment may explain differences in repeatability between studies.<sup>25</sup> Whilst our analysis is based on individual patients as the 'unit of analysis', the previous studies have used 'all PWA measurements performed' as their unit of analysis (e.g. three PWA measurements on 25 patients contributes 75 units of analysis). Such a 'pooling of PWA measurements' has the effect of artificially inflating the sample size and reducing the influence of individual patient variability.

Our within-observer 'limits of agreement' for AIX@75, SEVR% and heart rate were very similar to those from the study that also rested patients 15 minutes supine before PWA (Table 4). But is narrower for SEVR% than the study involving patients with renal failure.<sup>17</sup> Our between-observer LoA were consistently narrower than the other three studies. Two studies reported much wider LoA for SEVR% than ours.<sup>16,18</sup>

**Table 4** Repeatability of PWA from this study compared with previously published data: 'limits of agreement' (LoA, mean difference  $\pm$  2SD) for the SphygmoCor device.

	This study	Frimodt-Moller <sup>16</sup> (2006)	Siebenhofer <sup>18</sup> (1999)	Savage <sup>17</sup> (2002)
Type observer	Trained nurses	Trained observers	Trained observers	Investigators
Setting	Ambulatory hospital patients – Scotland	Hospital recruited healthy volunteers – Denmark	Hospital recruited healthy volunteers – England	Patients with renal failure and hospital staff – England
Assessment	Single day Rested supine 15 minutes	Single day Rested supine 15 minutes	3 separate days Rested seated 10 minutes	Single day Rested supine 5 minutes
Number of patients	20	22	25	188
Mean age (male)	56 years (80%)	40 years (52%)	33 years (60%)	56 years (57%)
Mean BP	136/79	113/68	118/75	–
Within-observer LoA <sup>a</sup>				
AIX@75	0.1 $\pm$ 8.0	0.0 $\pm$ 11.3	–	–
SEVR%	0.6 $\pm$ 23.3	0.4 $\pm$ 25.2	–	0.3 $\pm$ 36
Heart rate	1.2 $\pm$ 6.6	0.1 $\pm$ 6.5	–	–
Between-observer LoA				
AIX@75	1.7 $\pm$ 6.9 <sup>b</sup> 1.0 $\pm$ 3.9 <sup>c</sup>	0.6 $\pm$ 14.5 <sup>b</sup> 0.6 $\pm$ 11.8 <sup>c</sup>	– –	– –
SEVR%	0.6 $\pm$ 22.6 <sup>b</sup> 1.7 $\pm$ 14.2 <sup>c</sup>	2.6 $\pm$ 35.6 <sup>b</sup> 2.4 $\pm$ 30.6 <sup>c</sup>	– 2.7 $\pm$ 30.8 <sup>c</sup>	– 0.6 $\pm$ 18 <sup>c</sup>
Heart rate	0.4 $\pm$ 7.1 <sup>b</sup> 0.5 $\pm$ 3.8 <sup>c</sup>	0.4 $\pm$ 9.3 <sup>b</sup> 0.4 $\pm$ 7.8 <sup>c</sup>	– –	–

AIX@75, augmentation index AIX adjusted for heart rate; SEVR%, subendocardial viability ratio.

<sup>a</sup>Within-observer LoA included from our study are for nurse B;

<sup>b</sup>based on a single (first) PWA measurement;

<sup>c</sup>based on the average of two or more PWA measurements.

The high levels of repeatability seen in our study may relate to our nurses' previous experience in intensive care nursing and use of complex clinical devices, as well as the fact that our patients rested supine for a full 15 minutes before assessment. Whilst our nurses were aware that their performance was being scrutinized, and consequently may have been particularly diligent in their measurements, a similar influence will operate in any formal repeatability studies.<sup>16–18,25</sup>

In conclusion, we found high levels of both within- and between-observer repeatability for the cardiovascular indices of ED%, AIX@75 and SEVR%, even when PWA is undertaken by relatively inexperienced staff. There was no discernable time trend in either the quality or in the variability of PWA measurement, suggesting that PWA is a technique that can be easily and rapidly acquired for use in clinical practice. Our study supports suggestions that peripheral PWA using applanation tonometry has the potential to be included in the routine cardiovascular assessment of ambulant patients.

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