A Novel Mobile Phone Application for Pulse Pressure Variation Monitoring Based on Feature Extraction Technology: A Method Comparison Study in a Simulated Environment

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BACKGROUND: Pulse pressure variation (PPV) can be used to assess fluid status in the operating room. This measurement, however, is time consuming when done manually and unreliable through visual assessment. Moreover, its continuous monitoring requires the use of expensive devices. Capstesia™ is a novel Android™/iOS™ application, which calculates PPV from a digital picture of the arterial pressure waveform obtained from any monitor. The application identifies the peaks and troughs of the arterial curve, determines maximum and minimum pulse pressures, and computes PPV. In this study, we compared the accuracy of PPV generated with the smartphone application Capstesia (PPV_{app}) against the reference method that is the manual determination of PPV (PPV_{man}).
METHODS: The Capstesia application was loaded onto a Samsung Galaxy S4™ phone. A physiologic simulator including PPV was used to display arterial waveforms on a computer screen. Data were obtained with different sweep speeds (6 and 12 mm/s) and randomly generated PPV values (from 2% to 24%), pulse pressure (30, 45, and 60 mm Hg), heart rates (60–80 bpm), and respiratory rates (10–15 breaths/min) on the simulator. Each metric was recorded 5 times at an arterial height scale X1 (PPV_{5appX1}) and 5 times at an arterial height scale X3 (PPV_{5appX3}). Reproducibility of PPV_{app} and PPV_{man} was determined from the 5 pictures of the same hemodynamic profile. The effect of sweep speed, arterial waveform scale (X1 or X3), and number of images captured was assessed by a Bland-Altman analysis. The measurement error (ME) was calculated for each pair of data. A receiver operating characteristic curve analysis determined the ability of PPV_{app} to discriminate a $PPV_{man} > 13\%$.
RESULTS: Four hundred eight pairs of PPV_{app} and PPV_{man} were analyzed. The reproducibility of PPV_{app} and PPV_{man} was 10% (interquartile range, 7%–14%) and 6% (interquartile range, 3%–10%), respectively, allowing a threshold ME of 12%. The overall mean bias for PPV_{appX1} was 1.1% within limits of −1.4% (95% confidence interval [CI], −1.7 to −1.1) to +3.5% (95% CI, +3.2 to +3.8). Averaging 5 values of PPV_{appX1} with a sweep speed of 12 mm/s resulted in the smallest bias (+0.6%) and the best limits of agreement (±1.3%). ME of PPV_{app} was <12% whenever 3, 4, or 5 pictures were taken to average PPV_{app}. The best predictive value for PPV_{app} to detect a $PPV_{man} > 13\%$ was obtained for PPV_{appX1} by averaging 5 pictures showing a PPV_{app} threshold of 13.5% (95% CI, 12.9–15.2) and a receiver operating characteristic curve area of 0.989 (95% CI, 0.963–0.998) with a sensitivity of 97% and a specificity of 94%.
CONCLUSIONS: Our findings show that the Capstesia PPV calculation is a dependable substitute for standard manual PPV determination in a highly controlled environment (simulator study). Further studies are warranted to validate this mobile feature extraction technology to predict fluid responsiveness in real conditions.   (Anesth Analg 2016;XXX:00–00)

Invasive arterial pulse pressure variation (PPV) is based on the cardiopulmonary interactions in mechanically ventilated patients under general anesthesia.[1] In specific settings,[2] PPV can predict fluid responsiveness (FR).[3] Although various techniques can be used to measure PPV at the bedside without specialized monitoring devices, these techniques cannot discriminate between responders and nonresponders to volume expansion.[4] Moreover, visual determination of PPV is not reliable,[5] and thus, PPV measurement requires manual calculation, a dedicated monitoring system, or additional devices. These approaches are often time consuming, not always available, and costly. A new Android™/ iOS™ application called Capstesia™ (GalenicApp, Vitoria, Spain), running on commercially

available mobile phones, calculates PPV using a digital photograph of the arterial waveform displayed by any monitor. The application measures PPV (pulse pressure variation calculated by the Capstesia application [PPV_{app}]) by detecting peaks and troughs of the arterial curve, but it has not been tested against manual calculation of PPV (PPV_{man}).

The goal of our study was to assess reproducibility, accuracy, and precision of PPV_{app} when compared with PPV_{man} in a simulation environment by altering hemodynamic values, components of the arterial waveform (sweep speed and arterial scale), and the number of values to average the final PPV_{app} value.

METHODS

Description of the Smart Phone Application

Capstesia is a new smart phone application (version 1.1.1), functioning on iOS or Android. Launching this application displays the camera mode with a focus. The entire monitor screen is photographed, prompting a green box signal to crop the image including only the arterial pressure wave. The cropped picture of the arterial waveform is adjusted to exclude any other trace, and 10 arterial peaks are selected. The picture is then sent to proprietary software through WiFi, and the determination of PPV is generated by digitalization of the arterial waveform. Of note, the application's PPV calculation does not require hemodynamic data. The result displays a PPV value (PPVapp). The corresponding file on the phone provides access to the screen picture and cropped image, and arterial pressure waveform (Fig. 1). This scan displays circles placed on peak values and arrows placed on minimal arterial values. Figure 2 represents the different steps required to obtain a PPVapp value (Supplemental Digital Content, Video, http://links.lww.com/AA/B412).

Description of the PPV Generated by the Hemodynamic Simulator

The arterial waveforms were displayed by a hemodynamic simulator on a computer screen (Dell™, Round Rock, TX). This simulator has been described elsewhere[6,7] and was previously used as a reference for visual estimation.[8] The display mode allows setting of the following hemodynamic values: systolic and diastolic arterial pressure (SAP and DAP, respectively), heart rate (HR), central venous pressure, systolic and diastolic pulmonary pressure, respiratory rate (RR), tidal volume, and PPV. Briefly, the waveform PPV appearance is generated in 3 steps. First, the length of the respiratory cycle is determined (equal to 60/RR) in seconds. Once the cycle length is known, a sine wave is extrapolated over the length of the cycle going from 0 to 1 and back. The sine value at any point on the wave is subtracted from 1, and this value is multiplied by the percent PPV output by the simulator, and the waveform height at that point is reduced by the resulting proportion, creating systolic pressure variation. Finally, the baseline of the waveform is modulated in the same way, but at only 20% of the height effect. The net modifications result in a smooth graphical waveform that, when measured, yielded the PPV dictated by the simulator.

The arterial waveform in the display mode is specifically dependent on the following variable settings: SAP, DAP,

HR, RR, and PPV. The sweep speed and scale of the arterial pressure waveform can also be adjusted. Because the arterial waveform is generated by the simulator software, there is no time variability of the waveform shape. A sample screen from the hemodynamic simulator is presented in Appendix 1.

Study Protocol

The study protocol was devised to assess the repeatability, accuracy, and precision of PPV_{app} compared with PPV_{man}. The smart phone was fastened to a tripod at a fixed distance from the simulator screen (0.6 m). A Samsung Galaxy S4™ (Daegu, South Korea) with Android version 4.4.2, and a camera resolution of 13 megapixels was used. Luminosity of 105 lux was maintained throughout the experiment without use of the camera zoom function. A Dell monitor (dimensions: 14.5 inches width × 12 inches height) displayed hemodynamic data from the simulator. Twenty-four series of measurements in 17 values of PPV predefined by the simulator were tested (2%, 4%, 5%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 19%, 21%, and 24%). For each series, some combination of the following hemodynamic variables and arterial waveforms was set on the simulator: SAP value (90 or 120 mm Hg), DAP value (45 or 60 mm Hg), HR value (60 or 80 bpm), RR value (10 or 15 per minute), sweep speed of the arterial waveform (6 or 12 mm/s, to obtain at least 10 arterial peaks on the computer screen), and height of arterial waveform (nonoptimized scale [1X] or optimized scale [3X]).

Nonoptimized (PPV_{appX1}) and optimized scale PPV_{app} (PPV_{appX3}) were recorded as either 1 reading (PPV_{1app}) or the average of 2, 3, 4, or 5 values (PPV_{5app}) within the same hemodynamic profile. The number of attempts required to obtain an acceptable PPV_{app} value (defined as a scan showing circles placed on peak values and arrows placed on minimal arterial values) and the time (for the first 200 PPV_{app} determinations) between the snapshot and the displayed value for each specific hemodynamic combination were also recorded. PPV_{man} values were considered the reference method against PPV_{app}. PPV_{man} was calculated by measuring the amplitude of the maximum and the minimum pulse pressures during a respiratory cycle on the screen capture from the monitor immediately after the photograph was taken to generate the PPV_{app}. Therefore, 1 PPV_{man} was calculated for each PPV_{app}. For example, PPV_{man} was calculated 5 times for PPV_{5app}. This calculation was done off-line by an observer blinded to the results of PPV_{app} (AJ).

Statistical Analyses

Distributions of values were evaluated by a Kolmogorov-Smirnov test. Values were expressed in mean (± SD) or median (interquartile range) according to their distribution.

Repeatability of PPV_{app} and PPV_{man}

Repeatability was assessed as precision error, measured by calculating the variation of 5 PPV values within the same hemodynamic profile. Precision error (%) at each time point was calculated using:

$$\text{Precision error} = 1.96 \times \frac{\text{CV}}{\sqrt{n}}, \tag{1}$$
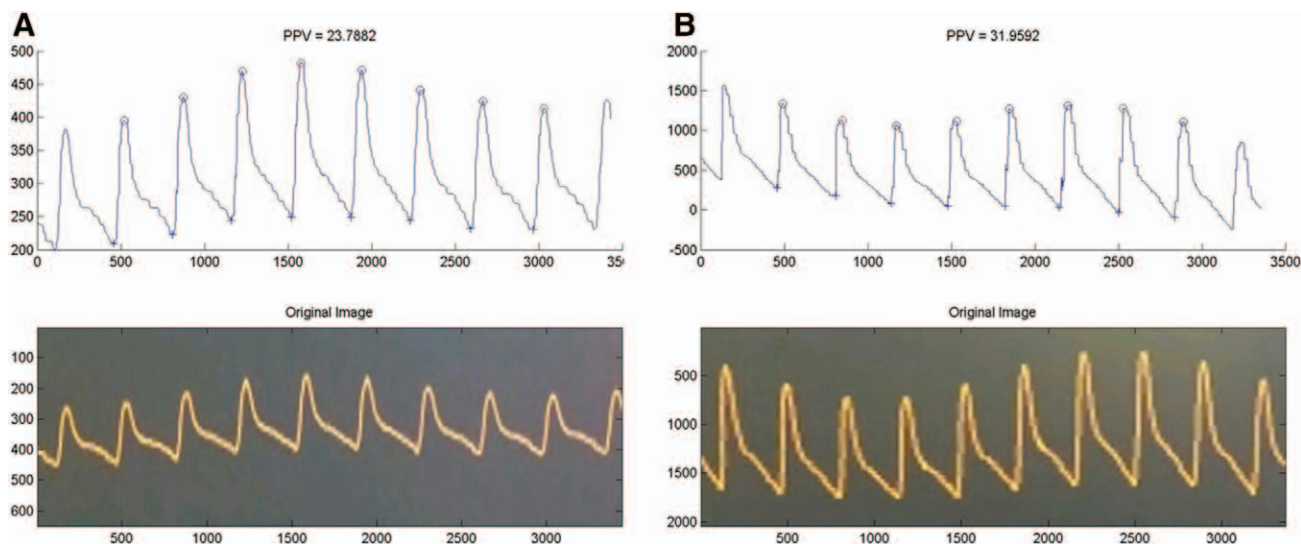
Figure 1. Two examples of pictures digitalized by the Capstesia. A, Sweep speed 12 mm/s; arterial waveform scale X1. B, Sweep speed 6 mm/s; arterial waveform scale X3. PPV = 24%; SAP = 90 mm Hg; DAP = 60 mm Hg; HR = 80 bpm; RR = 10 breaths/min. Notes: The arterial waveform pictured has been obtained after an initial focus of a screen image. The automated scan identifies peaks (circles) and troughs (crosses) to generate a pulse pressure variation (PPV) value. These 2 pictures have been obtained with a predefined PPV displayed by the simulator of 24%. Note that a low definition of the arterial waveform (sweep speed 6, scale X3) of the simulator can drive an erroneous PPV$_{app}$ value. DAP = diastolic arterial pressure; HR = heart rate; RR = respiratory rate; PPV = pulse pressure variation; SAP = systolic arterial pressure.

where CV is the coefficient of variation of each measurement (CV = $\frac{SD}{Mean}$) and n is the number of replications kept for each measurement.[9] To evaluate the maximal variation of PPV$_{app}$ and PPV$_{man}$ (i.e., the maximal change because of random error with a probability of 95%), we calculated the least significant changes of PPV proposed by Cecconi et al.,[9] where

$$LSC(\%) = Precision\ error \times \sqrt{2}.$$

Mean and SD or median and interquartile range of precision error and least significant changes were then calculated according to the mean values of each time plot.

Agreement and Responsiveness

The agreement between the measurements obtained with PPV$_{app}$ and those obtained with PPV$_{man}$ was determined using the coefficient of determination (R^2) and the Bland-Altman method.[10] If the mean difference between PPV$_{man}$ and PPV$_{app}$ (bias) was normally distributed, the mean bias and limits of agreement (LOA; 1.96 × SD of the bias) were calculated.[11] In addition, the measurement error (ME) was computed for each set of data as follows[12]:

$$ME = \frac{PPV_{app} - PPV_{man}}{0.5*(PPV_{app} + PPV_{man})} \times 100.$$

This calculation of ME is possible regardless of the distribution of the bias (PPV$_{app}$ – PPV$_{man}$), and ME is also impacted by the range of mean PPV [(PPV$_{app}$ + PPV$_{man}$) × 0.5].[13] Distribution of the ME was expressed in median (95% confidence interval [CI]). Because the ME depends on the precision of each technique,[9] we calculated a posteriori the threshold ME value to accept a good agreement between PPV$_{app}$ and PPV$_{man}$ according to the formula[13]:

Upper limit of the 95% CI of ME

$$< \sqrt{Precision\ PPV_{man}^2 + precision\ PPV_{app}^2}. \tag{2}$$

ME was calculated for each component of PPV$_{app}$: scale optimization (X1 or X3), number of PPV$_{app}$ values averaged (mean of 2, 3, 4, or 5 PPV$_{app}$ values), and sweep speed (6 or 12 mm/s). In addition, the relationship between PPV$_{man}$ and ME was assessed with the coefficient of determination R^2.

Ability of PPV$_{app}$ to Discriminate a PPV$_{man}$ > 13%

To assess the ability of PPV$_{app}$ to identify a PPV$_{man}$ > 13%, receiver operating characteristic (ROC) curves were generated. The areas under the ROC curves were calculated for 3 different components of determining PPV$_{app}$ (scale, sweep speed, and average) and compared as described previously.[14] The Youden Index was determined for each ROC curve (the maximum difference between sensitivity and 1 – specificity).[15] Ninety-five percent CI of the threshold PPV$_{app}$ value was considered the gray zone.[16]

Sample Size Estimation

Because the precision of each PPV calculation (PPV$_{man}$ and PPV$_{app}$) was unknown before performing the experiment, we estimated a precision error of 20% (Equation 1) for both PPV calculations for sample size determination. Therefore, an acceptable ME would have an upper limit of the 95% CI of 28% according to the Equation 2. Considering a potential large distribution of the ME (SD of 25%) and a mean ME of 20%, we needed to compare 41 pairs of data by subgroup analyses (sweep speed, height of scale) according to the following calculation:

Upper limit of the 95% CI of the ME

$$= 0.28 = ME + 1.96 \times \frac{SD}{\sqrt{n}},$$
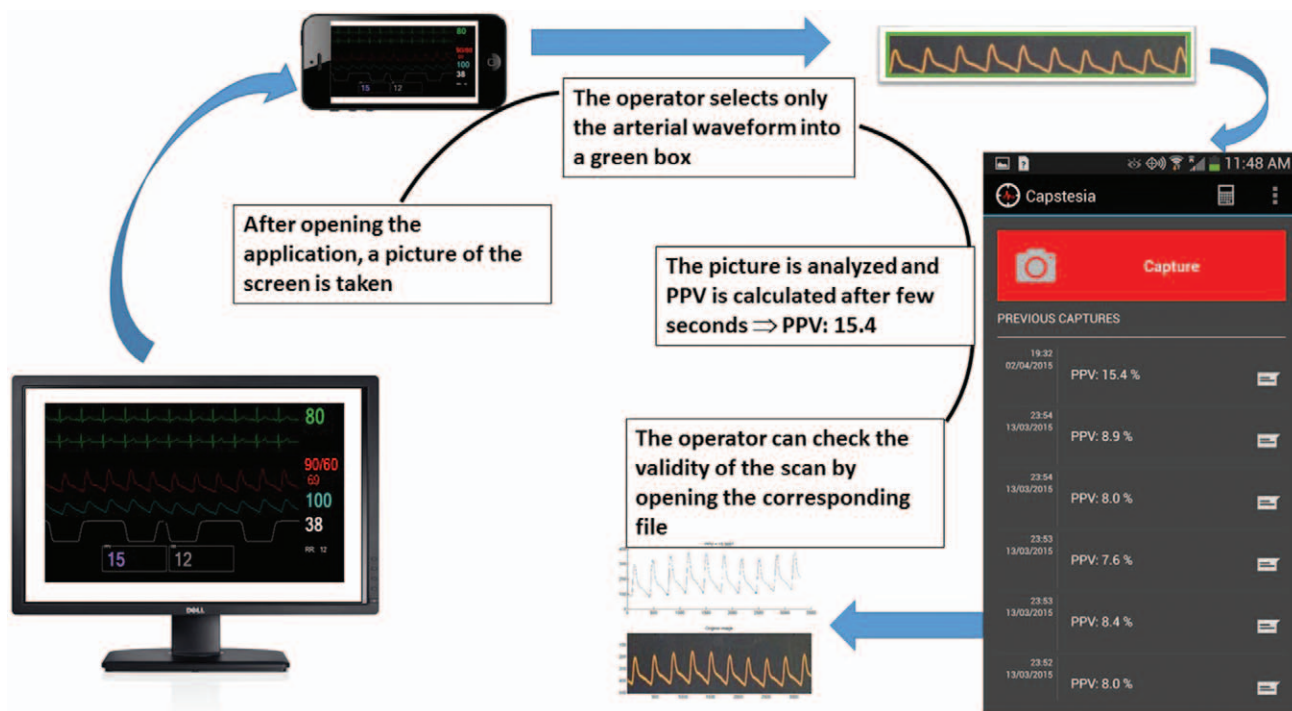
Figure 2. Steps to obtain a PPV$_{app}$ value. PPV$_{app}$ = pulse pressure variation calculated by the Capstesia™ application.

where n is the number of data pairs, ME is the expected mean value of the ME, and SD is the standard deviation of the ME. Because PPV$_{app}$ was also averaged from 5 values, we needed at least 205 pictures by subgroup analyses.

All analyses were performed using MedCalc Statistical Software version 14.8.1 (MedCalc® Software bvba, Ostend, Belgium). $P < 0.05$ was considered as significant.

RESULTS

Two thousand one hundred pictures were recorded, of which 60 (3%) were excluded because of scan process error in the application. Eight hundred sixteen pairs of data (PPV$_{app}$ versus PPV$_{man}$) were ultimately evaluated.

The median time to obtain a PPV$_{app}$ value in the app was 24 seconds (21–28 seconds). Figure 3 describes the number of PPV$_{app}$ values according to the setting of the simulator. Precision error of PPV$_{app}$ and PPV$_{man}$ was 10% (7%–14%) and 6% (3%–10%), respectively (Table 1). An acceptable threshold value for ME between PPV$_{app}$ and PPV$_{man}$ was then calculated at 12%. Mean values of PPV$_{app}$ and coefficient of determination between PPV$_{app}$ and PPV$_{man}$ are presented in Table 2. Distribution of PPV$_{appX3}$ bias was not normally distributed. Figure 4 displays Bland-Altman analysis for 1 value (Fig. 4A) and for 5 averaged values (Fig. 4B) of PPV$_{app}$ at scale X1. The least ME was obtained with a sweep speed of 12 mm/s and the average of 5 values (ME = 6%; 95% CI, 5–10; Table 2). Upper limit of 95% CI of ME was <12% when 3, 4, or 5 pictures were obtained to average PPV$_{app}$ (Appendix 2) at scale X1. There was a significant relationship between ME and PPV$_{man}$ ($R^2 = 0.38$, $P < 0.001$; Fig. 5). Areas under ROC curves for each type of PPV$_{app}$ are presented in Appendix 3. The greatest area was obtained with PPV$_{5appX1}$.

DISCUSSION

The main finding of this pilot study is that, in a highly controlled environment, PPV$_{app}$ shows an acceptable accuracy with PPV$_{man}$ when at least 3 pictures are taken to average PPV$_{app}$ at scale X1 (upper limit of the 95% CI of the ME <12%). The best accuracy is obtained with a sweep speed of 12 mm/s with 5 averaged PPV$_{app}$. Second, with a low rate of unsuccessful scan process (3%) and a short period of time to obtain a PPV value (24 seconds), PPV$_{app}$ determination is feasible. Finally, a PPV$_{app}$ threshold of 13.5% (gray zone, 12.9%–15.2%) is potentially able to discriminate FR (PPV$_{man} > 13\%$).

Cardiac output (CO) optimization has the potential to decrease postoperative complications[17]; however, CO measurement lacks reliability and is expensive.[18] By predicting FR, PPV is an acceptable surrogate for CO optimization.[19] Therefore, the promise of an easy-to-use pocket application capable of guiding fluid therapy is valuable. Also, by providing other advanced hemodynamic variables (CO and inotropy), this application questions the need to buy supplemental equipment for advanced monitoring. However, the accuracy of these advanced hemodynamic variables was not evaluated in this study. More generally, feature extraction technologies are becoming readily available in health care delivery and could soon be an essential tool for the anesthesiologist.[20–22]

Nevertheless, PPV$_{app}$ determination requires a WiIFi connection, and the picture needs careful attention: avoiding light glares, holding the smart phone parallel to the screen (otherwise at risk of disturbing the ratio between maximal and minimal pulse pressure), and preventing image obstruction by other artifacts in the selected box. A confirmatory visualization of the processed scan
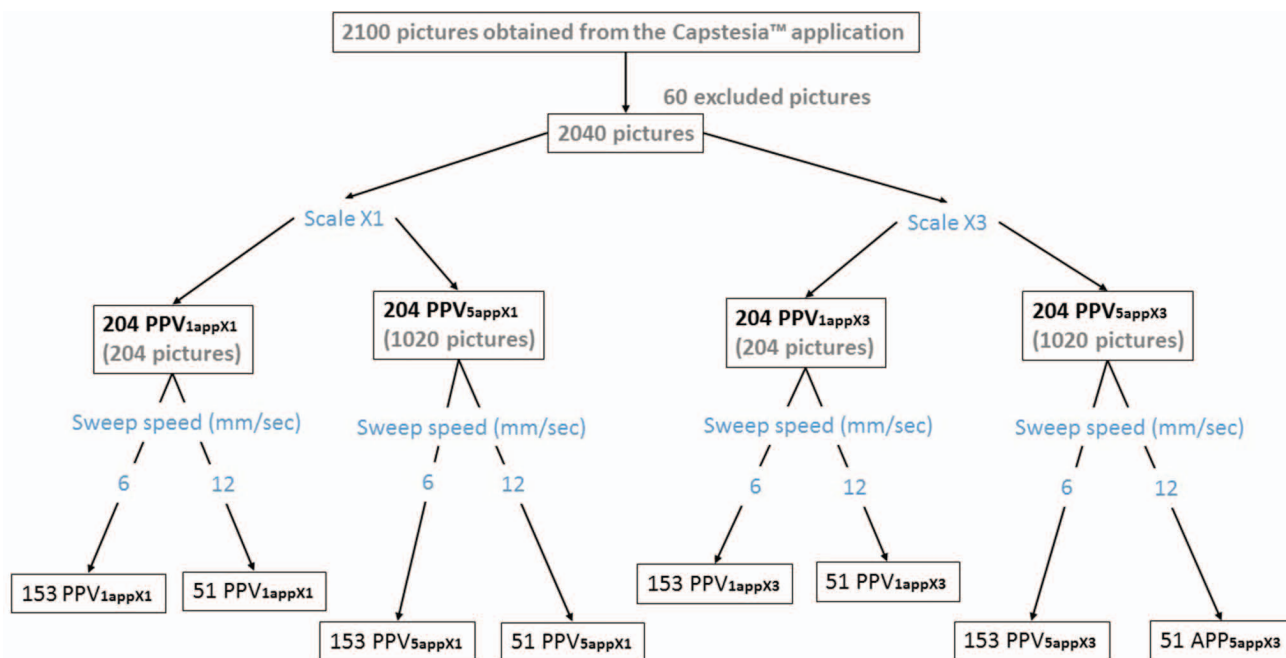
Figure 3. Flowchart of the study protocol. Notes: The first picture obtained by the Capstesia™ application was kept to calculate PPV_{1app}. Five successive pictures of the screen displaying the same hemodynamic variables were averaged to calculate PPV_{5app} (1020 pictures). Note that the PPV_{app} value obtained by the first picture to calculate PPV_{1app} was also averaged with the 4 following values to calculate PPV_{5app}. Not shown is that PPVman was calculated 2040 times, at the time of each PPVapp determination, by manually measuring the amplitude of the maximum and the minimum pulse pressures during a respiratory cycle on a corresponding screen capture. PPV_{app} = pulse pressure variation calculated by the Capstesia application; PPV_{1appX1} = pulse pressure variation displayed by the smart phone application from 1 value at scale X1; PPV_{5appX1} = average of 5 pulse pressure variation values displayed by the smart phone application at scale X1; PPV_{1appX3} = pulse pressure variation displayed by the smart phone application from 1 value at scale X3; PPV_{5appX3} = average of 5 pulse pressure variation values displayed by the smart phone application at scale X3.

Table 1. Random Error (Reproducibility) of PPV_app Measurement

	PPV_{5appX1}	PPV_{5appX3}	PPV_{man}
Coefficient of variation (%)	11 (8–16)	11 (7–22)	7 (4–11)
Precision error (%)	10 (7–14)	10 (6–19)	6 (3–10)
Least significant change (%)	14 (9–20)	13 (8–27)	9 (4–14)

Data are presented as median (interquartile range). Precision error = 1.96 × (coefficient of variation/$\sqrt{n}$); least significant change = precision error × $\sqrt{2}$ (95% confidence interval of the precision). The coefficient of variation (CV = SD/mean) was determined for each hemodynamic combination and n was the number of replications, 5 in our experiment; the precision error was <20%.
PPV_{app} = pulse pressure variation calculated by the Capstesia™ application; PPV_{5appX1} = average of 5 pulse pressure variation values displayed by the smart phone application at scale X1; PPV_{5appX3} = average of 5 pulse pressure variation values displayed by the smart phone application at scale X3; PPV_{man} = manual determination of pulse pressure variation.

also ensures that there is no misinterpreted or erroneous data (Fig. 2). Contrary to our assumptions, increasing the scale and decreasing the sweep speed worsened the LOA. These 2 modifications may have decreased the contrast between red pixels (representing the arterial waveform) and the black screen and also decreased the definition of the waveform. It may, consequently, have altered the scan process. Averaging the number of PPV_{app} values increased the accuracy of the application, consistent with a study demonstrating that determinations of PPV averaged on 3 respiratory cycles were better than 1.[23] Particularly, it has recently been shown that the ability to predict FR depends

on the period of averaging the PPV, a greater interval worsening the results.[4]

In a 1999 meta-analysis, on CO measurement, Critchley and Critchley[13] introduced the notion of percentage error (PE) to propose an acceptable threshold derived from the LOA of the Bland-Altman analysis. The PE is based on the 95% confidence interval of the bias and on the mean CO (of both methods) of each data set. This value is, therefore, calculated after all the comparisons have been made. It provides a rough estimate against which other clinical study results can be compared at a level that most clinicians can use. However, PE presents some intrinsic limits. First, PE does not consider the range of CO.[24] Second, PE is based on LOA, thus considering that the bias between the 2 assessed methods is normally distributed. Notably, numerous recent method comparison studies did not test the distribution of the bias, with a risk of using inappropriate statistical tools (LOA, 95% CI, PE).[25–27] Finally, PE is a value with no dispersion dimension. To overcome these 3 limits (consider the range of CO, nonnormal distribution of the bias, dispersion of the error measurement between 2 techniques), we calculated the ME that is based on each individual set of data, used in 1992[12] and also described in meta-analysis by Critchley and Critchley.[13] Noteworthy is the citation stating that one should calculate the *"percentage error for each set of data rather than calculating a single percentage error from the averaged data."*[13] Interestingly,

Table 2. Method Comparison Evaluation Between PPV$_{man}$ and PPV$_{app}$

	Median or mean (%)	SD or IR	Coefficient of determination (R^2)	Bias (%), mean or median	SD or IR of the bias	Limits of agreement, % (95% CI) of the bias	Measurement of error, % (95% CI)
PPV$_{man}$ (n = 204)	12.9	7.4; 17.0					
PPV$_{1appX1}$ (n = 204)	13.8	8.8; 18.5	0.92	1.2	1.9	−2.6 (−2.1 to −3.0) +5.0 (+4.5 to +5.4)	13 (11 to 15)
PPV$_{1appX3}$ (n = 204)	14.3	9.1; 19.5	0.72	1.3	−0.1; 2.5		12 (11 to 14)
PPV$_{5appX1}$ (n = 204)	13.8	8.7; 18.3	0.96	1.1	1.3	−1.4 (−1.7 to −1.1) +3.5 (+3.2 to +3.8)	9 (7 to 10)
PPV$_{5appX3}$ (n = 204)	14.2	9.4; 19.4	0.90	1.2	0.4; 2.5		11 (9 to 14)
PPV$_{5appX1}$ (sweep speed = 6 mm/s; n = 51)	14.1	6.7	0.96	1.1	1.5	−1.9 (−2.6 to −1.2) +3.9 (+3.2 to +4.7)	10 (5 to 14)
PPV$_{5appX1}$ (sweep speed = 12 mm/s; n = 51)	13.7	6.7	0.97	0.6	1.1	−1.6 (−2.1 to −1.0) +2.8 (+2.3 to +3.4)	7 (5 to 10)*

All the coefficients of determination were statistically significant (P < 0.001). The bias is the mean difference between PPV$_{man}$ and PPV$_{app}$. PPV$_{app}$ values with scale X3 were not normally distributed. The ME was calculated for each pair of data (ME = difference of PPV$_{app}$ and PPV$_{man}$/ mean of PPV$_{app}$ and PPV$_{man}$); SD of the ME ranged from 19% for PPV$_{5appX1}$, 23% for PPV$_{5appX3}$ and PPV$_{1appX1}$, and 25% for PPV$_{1appX3}$.
CI = confidence interval; IR = interquartile range; ME = measurement error; PPV$_{app}$ = pulse pressure variation calculated by the Capstesia™ application; PPV$_{1appX1}$ = pulse pressure variation displayed by the smart phone application from 1 value at scale X1; PPV$_{5appX1}$ = average of 5 pulse pressure variation values displayed by the smart phone application at scale X1; PPV$_{1appX3}$ = pulse pressure variation displayed by the smart phone application from 1 value at scale X3; PPV$_{5appX3}$ = average of 5 pulse pressure variation values displayed by the smart phone application at scale X3; PPV$_{man}$ = manual determination of PPV.
*P = 0.036 compared with PPV$_{5appX1}$ at sweep speed 6 mm/s.
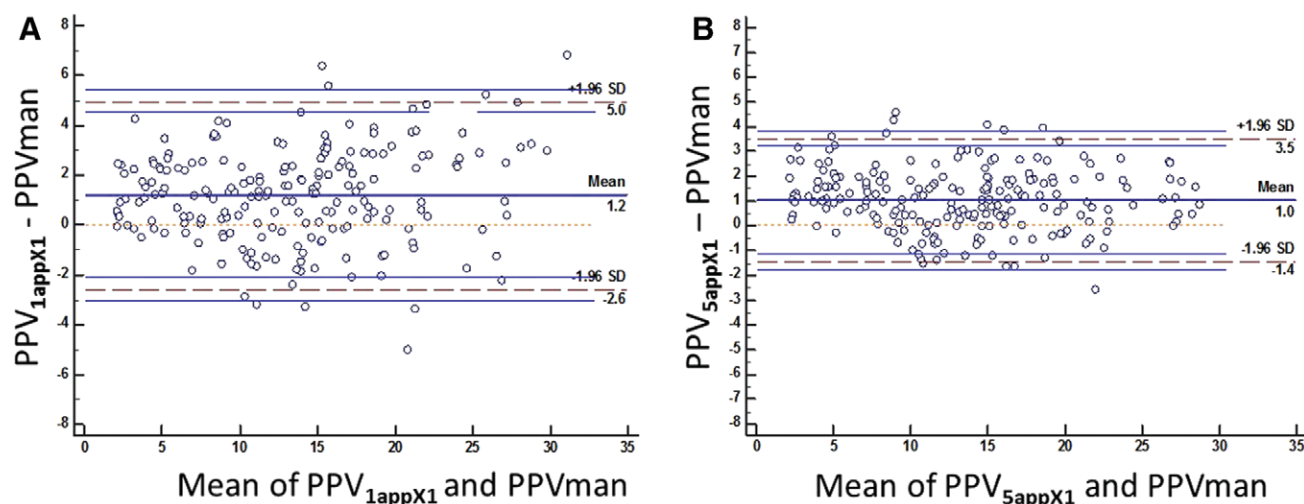
Figure 4. Bland-Altman plots showing the accuracy and the agreement between PPV$_{1appX1}$ and PPV$_{man}$ (A) and between PPV$_{5appX1}$ and PPV$_{man}$ (B). PPV$_{1appX1}$ = pulse pressure variation displayed by the smart phone application from 1 value at scale X1; PPV$_{5appX1}$ = average of 5 pulse pressure variation values displayed by the smart phone application at scale X1; PPV$_{man}$ = manual determination of pulse pressure variation.

the ME depends on the value of PPV$_{man}$ (Fig. 5), indicating that unacceptable high ME values involved low PPV$_{man}$ values, wherein its exact value has limited clinical relevance. It has also been proposed that the LOA be defined a priori.[28] However, the LOA and the ME depend on the precision error of both methods. Therefore, if precision error of each technique can be quantified, the interchangeability of 2 methods should be accepted if the 95% CI of the ME are equal to or less than the square root of both square precision techniques [√(precision PPV$_{man}$2+precision PPV$_{app}$2)].[13]

LIMITATIONS OF THE STUDY
We tested PPV$_{app}$ in an ideal simulation environment. The arterial waveform displayed by the simulator is consistent over time, without the effect of other physiologic variables (sympathetic tone, HR variability).[29] We did
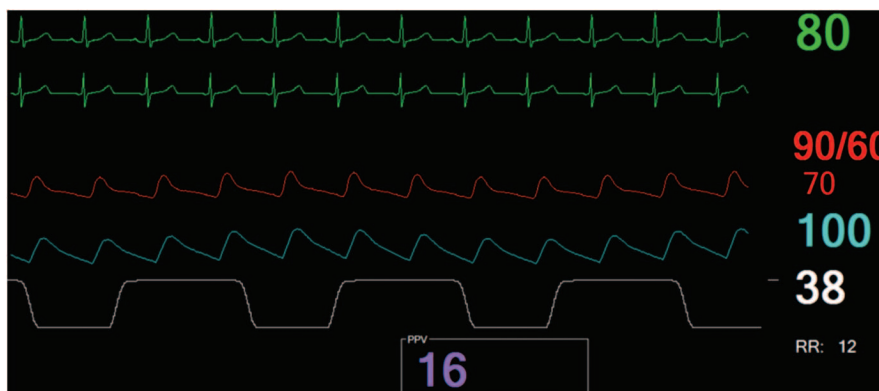
not choose the PPV displayed by the simulator (PPV$_{sim}$) as the reference method for 2 main reasons. First, PPV$_{sim}$ has never been validated. Second, the PPV$_{sim}$ is determined according to a 20% variation between the height and the bottom of the arterial waveform; therefore, it can differ according to the dimensions of the screen on which it is displayed or according to the height of the arterial scale. To avoid any confounding bias between the generated PPV$_{sim}$ and the one actually displayed, recalculating PPV$_{man}$ for each displayed screenshot allowed us to achieve a robust comparison. However, as PPV$_{man}$ was calculated within 1 respiratory cycle, we did not specifically select 10 heart beats contrary to the determination of PPV$_{app}$. These differences in the generation of PPV$_{man}$ and PPV$_{app}$ may have altered the agreement between both PPV determinations. Accordingly, PPV$_{app}$ manufacturers recommend selection of only 7 to 8 peaks to avoid the
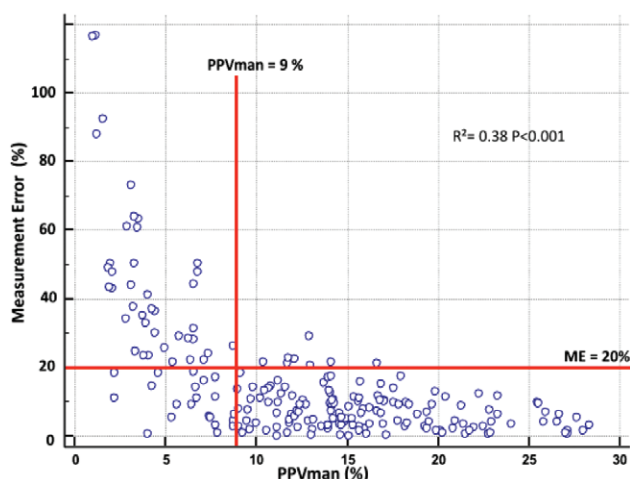
Figure 5. Relationship between the measurement of error of PPV$_{5appX1}$ and the PPV$_{man}$. Note: For clinical decision making (PPV$_{man}$ > 9%), only 5% (8/166) of data pairs presented a measurement error >20%. ME = measurement error; PPV$_{5appX1}$ = average of 5 pulse pressure variation values displayed by the smart phone application at scale X1; PPV$_{man}$ = manual determination of pulse pressure variation.

pollution by low arterial frequencies, which could alter the peak and the trough arterial values. Furthermore, PPV applicability may vary in an operating room environment where light reflection is greater, and the conditions of use are not respected (smart phone parallel to the screen for instance). Finally, other computer monitors may produce different results because of variability in definition and resolution.

CONCLUSIONS

With a low precision error and accurate LOA compared with manual PPV, PPV$_{app}$ could predict FR. We demonstrated that an arterial scale of 1X combined with an average of at least 3 pictures of the same screen were the best conditions for obtaining a valuable PPV$_{app}$, especially for a sweep speed of 12 mm/s. Nonetheless, real conditions are warranted to test this application with these settings.

Testing PPV$_{app}$ during general anesthesia and test FR is the next step to validate this tool before its wider use can be recommended. ∎

APPENDIX 1

Example of a Screen Displaying a PPV Value of 16%

Notes: The sweep speed is 12 mm/s, allowing to crop 10 peaks to determine the PPV$_{app}$. PPV$_{app}$ = pulse pressure variation calculated by the Capstesia application.

Appendix 2. Relationship Between PPV$_{man}$ and PPV$_{app}$ According to the Number of Averaged Values (1, 2, 3, 4, or 5 Pictures), with a 1X Arterial Scale

	Median (%)	IR (%)	Coefficient of determination (R^2)	Bias (%)	SD (%)	Limits of agreement, % (95% CI)	Measurement error, % (95% CI)
PPV$_{man}$	12.9	7.4 to 17.0					
PPV$_{1app}$ (n = 204)	13.8	8.8 to 18.5	0.92	1.2	1.9	−2.6 (−2.1 to −3.0) 5.0 (4.5 to 5.4)	13 (11 to 15)
PPV$_{2app}$ (n = 204)	13.9	8.7 to 18.6	0.96	1.2	1.4	−1.7 (−2.0 to −1.3) 4.0 (3.6 to 4.3)	11 (9 to 13)
PPV$_{3app}$ (n = 204)	13.9	8.7 to 18.4	0.96	1.1	1.4	−1.6 (−1.9 to −1.3) 3.7 (3.4 to 4.0)	10 (8 to 12)
PPV$_{4app}$ (n = 204)	13.8	8.8 to 18.3	0.96	1.1	1.3	−1.5 (−1.8 to −1.2) 3.6 (3.3 to 3.9)	9 (8 to 11)
PPV$_{5app}$ (n = 204)	13.8	8.7 to 18.3	0.96	1.1	1.3	−1.4 (−1.7 to −1.1) 3.5 (3.2 to 3.8)	9 (7 to 10)

All the coefficients of determination were statistically significant ($P < 0.001$). The bias is the mean difference between PPV$_{man}$ and PPV$_{app}$ values, and it was normally distributed. The limits of agreement are calculated as 1.96 × SD of the bias; upper and lower limits of agreement are presented with the 95% CI. The upper limit of 95% CI of the ME was ≤12% for 3, 4, or 5 averaged value of PPV$_{appX1}$, showing an acceptable accuracy against PPV$_{man}$.

CI = confidence interval; IR = interquartile range; PPV$_{app}$ = PPV displayed by the smartphone application; mean of 2 (PPV$_{2app}$), 3 (PPV$_{3app}$), 4 (PPV$_{4app}$), and 5 (PPV$_{5app}$) pulse pressure variations values (arterial scale X1) calculated by the smartphone application per hemodynamic combination; n = numbers of PPV values obtained; PPV$_{man}$ = manual determination of PPV.

APPENDIX 3

ROC Curves Comparing the Ability of PPV$_{app}$ to Discriminate Between PPV$_{man}$ Under or Upper 13%
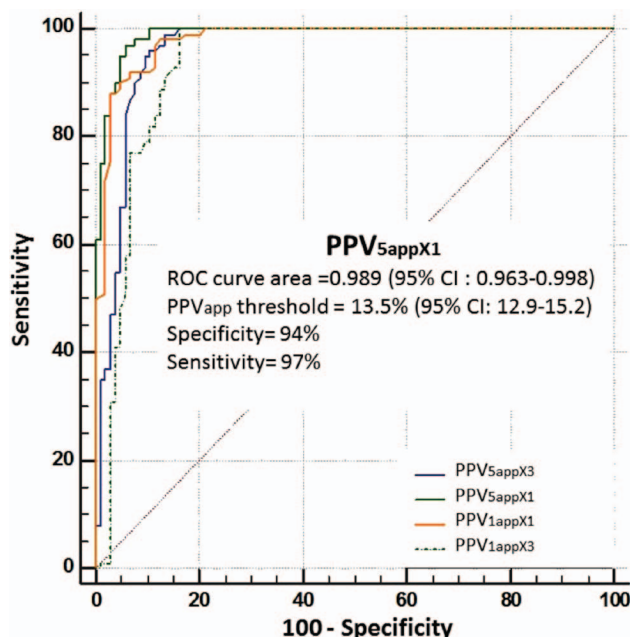
CI = confidence interval; PPV$_{app}$ = pulse pressure variation calculated by the Capstesia™ application; PPV$_{1appX1}$ = pulse pressure variation displayed by the smart phone application from 1 value at scale X1; PPV$_{5appX1}$ = average of 5 pulse pressure variation values displayed by the smartphone application at scale X1; PPV$_{1appX3}$ = pulse pressure variation displayed by the smart phone application from 1 value at scale X3; PPV$_{5appX3}$ = average of 5 pulse pressure variation values displayed by the smartphone application at scale X3; ROC = receiver operating characteristic curve.

DISCLOSURES

Name: Olivier Desebbe, MD.
Contribution: This author was the first author and helped design the study, conduct the study, data collection, data analysis, and manuscript preparation.
Attestation: Olivier Desebbe approved the final manuscript, attests to the integrity of the original data and the analysis reported in this manuscript, and is the archival author.
Conflicts of Interest: Olivier Desebbe declares no conflicts of interest.
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Contribution: This author helped design the study, conduct the study, data collection, data analysis, and manuscript preparation.
Attestation: Alexandre Joosten approved the final manuscript and attests to the integrity of the original data and the analysis reported in this manuscript.
Conflicts of Interest: Alexandre Joosten is a consultant for Edwards Lifesciences™.
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Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.

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RECUSE NOTE

Dr. Maxime Cannesson is the Section Editor for Technology, Computing, and Simulation for *Anesthesia & Analgesia*. This manuscript was handled by Dr. Steven L. Shafer, Editor-in-Chief, and Dr. Cannesson was not involved in any way with the editorial process or decision.

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