Automated pulse pressure and stroke volume variations from radial artery: evaluation during major abdominal surgery

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Background. Off-line calculation of the pulse pressure variation (PPVref) has repeatedly been shown to be a reliable predictor of fluid responsiveness in mechanically ventilated patients. This study was designed to assess the ability of two algorithms for automated calculation of PPV (PPVauto) (Intellivue MP 70) and stroke volume variation (SVVauto) (FloTrac/Vigileo) to predict fluid responsiveness during abdominal surgery.

Methods. We conducted a prospective study of 56 fluid challenges given for haemodynamic instability in 11 patients undergoing major abdominal surgery. Fluid responsiveness was defined as an increase in stroke volume index (SVI) >10%. PPVref, PPVauto, SVVauto, and SVI (oesophageal Doppler) were recorded simultaneously before and after each fluid challenge.

Results. PPVauto and SVVauto both correlated with PPVref \( r_{corr} = 0.87 \) (\( P<0.001 \)) and 0.84 (\( P<0.001 \)), respectively; \( n=77 \). All three indices measured before fluid challenges were higher in responder (\( n=32 \)) than in non-responder (\( n=24 \)) fluid challenges (\( P<0.02 \)). The mean areas under the receiver operating characteristic curves were 0.96 (PPVref), 0.96 (PPVauto), and 0.95 (SVVauto), and the optimal threshold value for each variable was 13%, 13%, and 12%, respectively. All indices correlated with the fluid challenge-induced changes in SVI (PPVref: \( r_{corr} = 0.65 \); PPVauto: \( r_{corr} = 0.58 \); SVVauto: \( r_{corr} = 0.58 \), \( P<0.001 \) for all).

Conclusions. PPVauto and SVVauto predict fluid responsiveness as accurately as off-line PPVref in patients with haemodynamic instability during major abdominal surgery.

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Recent studies have shown that intraoperative optimization of cardiac output (CO) by repeated volume loading reduces postoperative morbidity after major surgery.1 However, unnecessary i.v. fluids may be deleterious, and intraoperative fluid restriction has also been shown to improve clinical outcome.2 In this context, indices reflecting the haemodynamic changes during mechanical ventilation, the so-called ‘dynamic’ indices of fluid responsiveness, have been proposed for clinical practice. A growing number of studies have demonstrated the ability of these indices to differentiate between patients who will increase their stroke volume (SV) in response to intravascular fluid bolus (responders) and those who will not (non-responders).3 Accordingly, preliminary results suggest that goal-directed fluid management based on pulse pressure variation (PPV) monitoring during high-risk surgery improves postoperative outcome and decreases the length of hospital stay.4 The widespread use of PPV has, however, been limited by the fact that its calculation requires off-line measurements of the pressure changes or the use of particular monitors such as the PiCCOplus (Pulsion Medical Systems, Munich, Germany) which necessitates central venous access and specific (typically femoral) artery catheter.

Recently, new algorithms or devices have been developed for automated and continuous calculation of either
PPV or SV variation (SVV) by pulse contour analysis from standard peripheral (typically radial) arterial line. Although all these devices analyse the same physiological signal (i.e. the respiratory-induced variations in arterial pressure curve), they actually do not provide ‘true’ automated calculation of PPV or SVV but rather create new variables that may not be equivalent to the extensively studied off-line PPV. As a result, measurements obtained by one specific device may not be applied to indices from other manufacturers. This may be particularly true when the index is SVV, as it requires additional beat-to-beat SV measure using a pulse contour analysis algorithm. The best discriminating (between responders and non-responders) threshold value may also be different between devices, emphasizing the need for specific validation of any automated indices before clinical use. Early evaluation studies, performed before and after cardiac surgery, show conflicting results. Reliable prediction of fluid responsiveness was found with automated PPV using two different software systems (IntelliVue MP monitor, Philips Medical Systems, Best, The Netherlands; DX 2020 monitor, Dixtal, Sao Paulo, SP, Brazil), whereas conflicting results were reported with SVV (FloTrac/Vigileo, Edwards Lifesciences, Irvine, CA, USA). However, considering the impact of both clinical (e.g. tidal volume) and experimental (study design) conditions on the predictive value of any index, comparison of different automated indices can be reliably achieved only if measurements are performed simultaneously in the same patients. To date, no such comparison of new automated indices is available in the literature. This study was thus designed to assess, in comparison with offline PPV, the ability of automated PPV (IntelliVue MP 70) and SVV (FloTrac/Vigileo) to predict fluid responsiveness in patients undergoing major abdominal surgery.

Methods

Patients and anaesthesia

After institutional approval by the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale de Lille and obtaining written informed consent, 11 patients undergoing gastrointestinal or vascular surgery were enrolled. Patients with a history of arrhythmia, valvular heart disease, intracardiac shunt or pulmonary artery hypertension, or history of oesophageal or gastrointestinal disease precluding the use of transoesophageal Doppler were excluded. Anaesthesia was induced with sufentanil 0.3–0.5 μg kg⁻¹, propofol 2–3 mg kg⁻¹, and cisatracurium 0.15 mg kg⁻¹, and maintained with continuous i.v. propofol 3–8 mg kg⁻¹ h⁻¹ and sufentanil 0.3–0.5 μg kg⁻¹ h⁻¹. Intraoperative muscle paralysis was maintained by the continuous i.v. administration of cisatracurium 0.15 mg kg⁻¹ h⁻¹. After tracheal intubation, controlled mechanical ventilation was maintained throughout the procedure with a tidal volume of 8–10 ml kg⁻¹ of estimated lean body weight and an inspiratory:expiratory ratio of 1:2, without PEEP. The ventilatory frequency was set to maintain an end-tidal Pco₂ range of 3.8–4.7 kPa (Cato, Dräger, Lübeck, Germany). No changes to the ventilator settings were made during the study period. To minimize intraoperative hypothermia, patients were covered from the sternum up to the shoulders with a forced-air warming blanket.

Haemodynamic measurements and data acquisition

After induction of anaesthesia, a 20 G artery catheter (Sellicath 3 French, Plastimed, Saint Lieu la Forêt, France) was inserted in the left radial artery. Artery pressure was measured using the FloTrac transducer coupled to both Philips and Vigileo monitors. Pressure transducers were zeroed at the mid-axillary level to atmospheric pressure.

Off-line pulse pressure variation

The arterial pressure waveform from the Philips monitor was recorded to a personal computer using data acquisition software (TrendfaceSolo 1.1, Ilexcellence GmbH, Wildau, Germany) and was analysed to calculate PPV using the following equation: PPV (%) = 100 × (PP_max – PP_min) / [(PP_max + PP_min) / 2], where PP_max and PP_min are, respectively, the maximal and minimal values of pulse pressure over a respiratory cycle. All PP measurements were automatically calculated by the software, thus preventing any inter- or intra-observer variations. PPV was measured on three consecutive respiratory cycles and averaged for analysis, as previously described. Recordings were analysed off-line with the reviewer unaware of the haemodynamic data. This ‘off-line PPV’ was used as a reference measurement for prediction of fluid responsiveness, and thus designated as PPV_ref thereafter.

Automated on-line PPV

Automated PPV (PPV_auto) was displayed in real-time by the Philips® IntelliVue MP70 monitor. The algorithm used has been previously published. Briefly, the method is based on automatic detection algorithms, rank-order filters, and kernel smoothing. PP_max, PP_min, and PP_mean are determined over a window of 8 s, and the values from four consecutive windows (32 s) are used to calculate an averaged PPV_auto as (PP_max – PP_min) / PP_mean. In this study, the value of PPV_auto provided by the monitor was continuously recorded from the monitor into the personal computer using the TrendfaceSolo software.

Automated on-line SVV

Automated calculation of SVV (SVV_auto) was displayed in real-time by the Vigileo monitor (software version 1.10). SV is assessed using a proprietary algorithm described in
Detail elsewhere. Briefly, the algorithm first assesses pulse pressure by calculating the standard deviation of the instantaneous arterial pressure (100 values per second over 20 s) around its mean value. The pulse pressure, and thus the standard deviation, is proportional to the SV, through a conversion factor which incorporates the effects of both resistance and compliance, via manually entered patient data and arterial waveform analysis. SVV is then assessed using the following equation: 

$$SVV(\%) = \frac{SV_{\text{max}} - SV_{\text{min}}}{SV_{\text{mean}}}$$

where $SV_{\text{max}}$, $SV_{\text{min}}$, and $SV_{\text{mean}}$ are, respectively, the maximum, minimum, and mean SV determined by the system during a time window of 20 s. The system can theoretically detect and eliminate premature ventricular contractions or other arrhythmias for assessment of SVV. In this study, SVV$_{\text{auto}}$ was continuously recorded from the Vigileo© into the computer using an analogue-to-digital interface (Multi-Data-Logger, Edwards Lifesciences).

Other haemodynamic measurements

Central venous pressure was measured at end-expiration using a standard central venous catheter inserted via the right internal jugular vein. Cardiac index (CI) and SV index (SVI) were obtained via an oesophageal Doppler (Hemosonic© 100; Arrow, USA) introduced into oesophagus for measurement of aortic diameter and aortic blood flow. After oral insertion, the position of the probe was adjusted until obtaining the highest value of diameter with complete detection of the descending aortic anterior and posterior walls. Then, the position of the oesophageal Doppler was adjusted to obtain the best aortic blood velocity signal. Once positioned, the oesophageal probe was not moved until the end of the fluid challenge.

Study protocol

During the surgical procedure, haemodynamic instability was suspected by the occurrence of a 20% decrease in invasive systolic arterial pressure, a 20% increase in heart rate, or both compared with preoperative baseline values. For each suspected episode of haemodynamic instability, a volume loading step (VLS) was performed using 4% modified fluid gelatine (Gelofusine®, B. Braun Medical SAS, Boulogne Billancourt, France) over 8–15 min. The volume load was at least 200 ml, but was continued (up to 500 ml) as long as an increase in CVP of at least 2 mm Hg was not obtained. This minimal increase in CVP was included as an endpoint in the volume loading protocol in order to maximize the probability that fluid administration actually increased intravascular volume and thus cardiac preload, even during concomitant blood loss. A complete set of haemodynamic and oesophageal Doppler measurements including the studied variables (PPV$_{\text{ref}}$, PPV$_{\text{auto}}$, and SVV$_{\text{auto}}$) was performed and recorded just before each VLS and repeated 2–5 min after each VLS. The SVI increase induced by volume expansion was used to classify each VLS as responders ($\geq 10\%$ increase in SVI) or non-responders ($<10\%$ increase in SVI). In responders, successive VLSs were performed until non-responder status was reached. When several suspected episodes of hypovolaemia occurred during the surgical procedure, the whole protocol was repeated for each episode. Because the validity of this analysis relies on the absence of significant haemodynamic changes other than the standardized increase in preload secondary to the fluid challenge, the protocol was interrupted before post-VLS measurements if other events that could produce haemodynamic changes occurred (especially uncontrolled haemorrhage or necessity of a vasopressor).

Statistical analysis

All variables are presented as mean (sd) unless otherwise specified. To assess the ability of the variables to discriminate between responder and non-responder VLSs, the values of each variable measured before VLSs leading to a positive response were compared with those measured before a negative response using Student’s t-test, with adjustment of the t-statistic to take into account the presence of several observations for each patient studied. Then, receiver operating characteristic (ROC) curves were generated for all the variables using the first measurement made in each patient. The most discriminating threshold value was determined for each variable using the following equation: 

$$AUC = \frac{(1-\text{specificity})^2 + (1-\text{sensibility})^2}{2}$$

The area under the ROC curve (AUC) was calculated for each variable and AUCs were compared as previously reported. Correlations between automated indices and PPV$_{\text{ref}}$ and then between pre-VLS values of each variable and the SVI response to subsequent fluid infusion, were calculated for the first set of measures obtained in each patient ($n=11$ independent sets of observations) using Pearson’s linear correlation coefficient $r$ or Spearman’s rank (non-linear) correlation coefficient $\rho$ when needed. Bivariate mixed models with a Kronker product covariance were then used to calculate these correlations ($r_{\text{corr}}$) for all (repeated) measurements obtained throughout surgery, as previously described. Statistical analysis was performed using SAS/Stat© software (SAS Institute Inc., Cary, NC, USA). For all comparisons, $P<0.05$ was considered significant.

Results

Patients were all classified ASA II or III, with ages ranging between 48 and 75 yr. The duration of the surgical procedure ranged between 180 and 540 min (median: 300 min). The median estimated blood loss was 750 ml (range: 300–2000 ml). During the study period, no significant changes in peak or plateau inspiratory pressure were identified.

A total of 56 VLSs (range 3–7 per patient) were performed. Thirty-two responder VLSs (mean volume infused: 298 ml; increase in SVI ranging between 10%
and 54%; one to five VLSs per patient) and 24 non-responder VLSs (mean volume infused: 302 ml; change in SVI ranging between –18% and 9%; one to four VLSs per patient) were identified. The response of SVI did not correlate with the volume administered \((r=0.076; P=0.57)\). Off-line analysis of arterial pressure waveform recordings allowed calculation of PPV\(_{\text{ref}}\) in all pre- and post-VLS sets of haemodynamic measurements \([n=82]\) (range 4–12 per patient), as, according to our protocol, 30 measurements performed after responder VLS also served as pre-VLS measurements of subsequent VLS, despite occurrence of ectopic cardiac beats during data recording in five cases (concerning four VLSs, from two patients). In the presence of these ectopic beats, no value of PPV\(_{\text{auto}}\) was provided by the Philips monitor (thus, a total of 77 values only were available for analysis), whereas calculation of SVV\(_{\text{auto}}\) was apparently unaffected (82 values available for analysis). As shown in Figure 1, correlation between PPV\(_{\text{ref}}\) and PPV\(_{\text{auto}}\) was strong \((r=0.88 (P=0.0004)); r_{\text{corr}}=0.87 (P<0.0001)\), for \(n=11\) (one per patient), and 77 sets of measurements, respectively and also between PPV\(_{\text{ref}}\) and SVV\(_{\text{auto}}\) \([r=0.88 (P=0.0003); r_{\text{corr}}=0.82 (P<0.0001)\], for \(n=11\) (one per patient), and 82 sets of measurements, respectively; without ectopic beats (77 measurements): \(r_{\text{corr}}=0.84; P<0.0001\).

Comparisons of variables measured immediately before responder and non-responder VLSs showed that all three indices were higher in the responder group than in the non-responder group \([\text{mean (SD)}\text{ PPV}_{\text{ref}}: 16\text{ (5)% vs 8 (4)%}, \ P=0.003, n=56; \text{PPV}_{\text{auto}}: 18\text{ (8)% vs 10 (3)%}, \ P=0.02, n=52; \text{SVV}_{\text{auto}}: 16\text{ (7)% vs 10 (4)%}, P=0.01, n=56]\) (Fig. 2). The performance of PPV\(_{\text{ref}}\), PPV\(_{\text{auto}}\) and SVV\(_{\text{auto}}\) in discriminating responder and non-responder VLSs was evaluated and compared by constructing ROC curves from the first VLS in each patient (Fig. 3). The areas under the ROC curves \([\text{mean (95% CI)}\text{ of PPV}_{\text{ref}}, \text{PPV}_{\text{auto}}\text{ and SVV}_{\text{auto}}\text{ were, respectively, 0.96 (0.70–1.00), 0.96 (0.72–1.00), and 0.95 (0.65–1.00) (P=NS between areas) and the optimal threshold value for each variable was 13% (sensitivity: 0.88; specificity: 0.92), 13% (sensitivity: 0.89; specificity: 0.91), and 12% (sensitivity: 0.86; specificity: 0.91), respectively. Finally, a significant correlation with the VLS-induced change in SVI was found for the three variables measured before VLS: PPV\(_{\text{ref}}\) \([\rho=0.68 (P=0.03; \ n=11)]; r_{\text{corr}}=0.65 (P=0.0001; n=56)\], PPV\(_{\text{auto}}\) \([\rho=0.73 (P=0.02; n=11)]; r_{\text{corr}}=0.58 (P=0.0002; n=52)\], and SVV\(_{\text{auto}}\) \([\rho=0.77 (P=0.01; n=11); r_{\text{corr}}=0.58 (P=0.0003; n=56)\] (Fig. 4).

**Discussion**

The results of the present study show that real-time monitoring of two different automated indices obtained from standard radial arterial line (PPV from Philips Intellivue and SVV from FloTrac/Vigileo) allows prediction of fluid responsiveness as accurately as off-line PPV\(_{\text{ref}}\) in patients with haemodynamic instability during major abdominal surgery. Areas under the ROC curves, the most commonly used measure of diagnostic accuracy, and estimated optimal thresholds for both automated indices were within the range of values previously obtained with PPV\(_{\text{ref}}\).\(^{10}\) These indices have thus potential for intraoperative goal-directed fluid administration based on monitoring of fluid responsiveness of SVI.

Only limited data are available regarding automated indices of fluid responsiveness and, to the best of our knowledge, this study was the first to assess the value of such indices for fluid responsiveness during surgery. Our results are in accordance with the single published study.
having evaluated PPV_{auto} from Philips Intellivue in the clinical setting and which found, in anaesthetized patients under stable haemodynamic conditions before start of surgery for coronary artery bypass grafting, that PPV_{auto} was an accurate predictor of fluid responsiveness, with a best threshold value of 10%. We also confirm the value of SVV_{auto} from the FloTrac/Vigileo, as recently evidenced for the response of SVI to changes in body positioning in patients after cardiac surgery, with an optimal threshold value of 9.6%. Consistent with this study, our data contradict the negative results initially reported with SVV from FloTrac. It has been proposed that these differences may be attributed to modifications in the device’s software (especially reduction in the time window for adjustment in vascular tone) that have followed early evaluation and which resulted in improved measurement of CO. Our study evaluated simultaneously PPV_{auto} and SVV_{auto} and thus allowed comparison of both devices. Our results suggest that using a sophisticated algorithm to

Fig 2 Off-line arterial pulse pressure variation (PPV_{ref}), automated pulse pressure variation (PPV_{auto}), and automated stroke volume variation (SVV_{auto}) before responder (R) and non-responder (NR) VLSs. Boxplots = inter-quartile range and median; whiskers = smallest and largest observations that are less than 1.5 inter-quartile range from the end of the box; *P* ≤ 0.02, R vs NR for all indices.

Fig 3 ROC curves comparing the ability of PPV_{ref}, PPV_{auto} and SVV_{auto} to discriminate between responder and non-responder VLSs. The curves for PPV_{ref} and PPV_{auto} are superimposed.

Fig 4 The relation between PPV_{ref}, PPV_{auto}, or SVV_{auto} measured before VLSs and the changes in SVI induced by volume infusion. Vertical dotted lines represent the optimal threshold value.
derive SV from arterial pulse pressure does not add anything when evaluating fluid responsiveness in the operating theatre. Such observation has already been reported when comparing SVV and PPV calculated by the PiCCOplus system (Pulsion Medical Systems).\(^{20,21}\)

Ectopic beats appeared transitorily during study in two patients, during four VLSs (two responders and two non-responders). As reported in the Results section, no PPV\(_{\text{auto}}\) value was given by the Philips monitor whereas SVV\(_{\text{auto}}\) values remained continuously displayed. Although these cases were too rare to alter significantly the global results with SVV\(_{\text{auto}}\), individual analysis of the two non-responding VLSs (Case 1: PPV\(_{\text{ref}}\)=9%; SVV\(_{\text{auto}}\)=19%; Case 2: PPV\(_{\text{ref}}\)=1%; SVV\(_{\text{auto}}\)=12%) suggest that ectopic beats, probably because of post-extrasystolic potentiation, may result in overestimation of SVV\(_{\text{auto}}\) and, in turn, in ‘false positive’ prediction of fluid responsiveness. These observations also suggest that some devices are probably more robust than others to misdirection of ectopic beats. In practice, we would recommend viewing with caution large values of any automated indices in the presence of ectopic beats before deciding fluid administration.

In contrast with most previous studies assessing fluid responsiveness in the operating room, all our VLSs were performed during surgery, that is, in ‘real life’ situations. It was thus a priori possible that, despite our aiming to discard VLSs with uncontrolled haemodynamic variations, changes other than the standardized increase in preload by VLS occurred between pre- and post-VLS measurements and affected the results. It is in order to minimize this eventuality that a minimal increase in CVP, which, in the absence of change in ventricular compliance and afterload, is likely to attest to an increase in intravascular volume preload, was included in the volume loading protocol in the present study. The choice of a CVP increase of 2 mm Hg is debatable, especially as it was essentially based on the literature on shock.\(^{15}\) but the results obtained with PPV\(_{\text{ref}}\) suggest a posteriori that this precaution was pertinent and contributed to reliable assessment of automated indices in the present study. The fact that the protocol included non-standardized VLSs (range: 200–500 ml) represented a potential further source of bias which can be a posteriori discarded, since the response of SVI did not correlate with the volume administered.

Other methodological aspects and potential limitations of this study must be considered. First, we measured descending aortic blood flow using oesophageal Doppler to estimate SVI, and thus to classify responder and non-responder VLSs. Studies comparing oesophageal Doppler estimates of CO with those derived from simultaneous measurements using thermodilution found that oesophageal Doppler has limited clinical agreement with any single thermodilution measurement of CO.\(^{22}\) However, these studies also showed that oesophageal Doppler has high validity (no bias and high clinical agreement with pulmonary artery thermodilution) for monitoring changes in CO during patient management.\(^{22}\) Accordingly, most studies having shown that intraoperative optimization of SVI by repeated volume loading improved clinical outcome using oesophageal Doppler.\(^{23}\) Secondly, repeated measurements were performed throughout surgery in each patient. An advantage of analysing the response of SVI to repeated VLSs was that it reproduced daily practice when fluid responsiveness has to be evaluated both in different patients and in the same patient on different occasions. However, this may have led to overestimation of the tightness of the correlations. Statistical analysis was thus adjusted to multiple observations per patient whenever indicated. Thirdly, in contrast with most previous studies assessing various indices of fluid responsiveness, we did not quantify agreement (using Bland and Altman analysis) between indices. This, however, was deliberate, since (i) indices using slightly different formulae (see Methods) or derived from different physiological variables (volumes vs pressures) can theoretically all be accurate predictors of fluid responsiveness, despite relatively weak agreement between them, and (ii) assessing agreement over a wide range of values of two indices can be misleading, as, for example, the conclusions for clinical practice of a given limit of agreement obtained from large values would be irrelevant for small values of any indices.

In conclusion, PPV assessed using the Philips Intellivue monitor and SVV via the FloTrac/Vigileo system exhibited performances comparable with that of off-line PPV\(_{\text{ref}}\) in terms of predicting fluid responsiveness during major abdominal surgery. Whether using one of these automated measures may alter outcome remains, however, to be demonstrated. Further investigation is thus clearly needed to establish whether goal-directed fluid administration based on monitoring of such indices will result in improvement of postoperative outcome.

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### References


