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CLINICAL PRACTICE

Non-invasive prediction of fluid responsiveness during major hepatic surgery† ‡

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Background. The aim of this study was to evaluate potential predictors of fluid responsiveness obtained during major hepatic surgery. The predictors studied were invasive monitoring of intravascular pressures (radial and pulmonary artery catheter), including direct measurement of respiratory variation in arterial pulse pressure (PPVart), transoesophageal echocardiography (TOE), and non-invasive estimates of PPVart from the infrared photoplethysmography waveform from the Finapres® (PPVfina) and the pulse oximetry waveform (PPVsat).

Methods. We conducted a prospective study of 54 fluid challenges (250 ml colloid) given for haemodynamic instability in eight patients undergoing hepatic resection. Fluid responsiveness was defined as an increase in stroke volume index (SVI) $\geqslant$10%. The following variables were recorded before each fluid challenge: right atrial pressure (RAP), pulmonary artery occlusion pressure (PAOP), PPVart, PPVfina, PPVsat, and the TOE-derived variables left ventricular end-diastolic area index (LVEDAI), early/late (E/A) diastolic filling wave ratio, deceleration time of the E wave (MDT) of mitral flow and the systolic fraction of the pulmonary venous flow (SF).

Results. Only PPVfina, PPVart (both $P<0.001$), PPVsat ($P=0.02$), LVEDAI and MDT (both $P=0.04$) were different in responder *vs* non-responder fluid challenges. The areas under the receiver operating characteristic (ROC) curves were 0.81 (PPVfina), 0.79 (PPVart), 0.70 (LVEDAI), 0.68 (PPVsat and MDT), 0.63 (RAP), 0.62 (E/A), 0.55 (PAOP) and 0.42 (SF). The areas under the ROC curves for RAP, E/A, PAOP and SF were significantly less than that for PPVfina ($P<0.05$ in each case). Only PPVart ($r=0.59$, $P=0.0001$) and PPVfina ($r=0.56$, $P=0.0001$) correlated with the fluid challenge-induced changes in SVI.

Conclusions. PPVart and PPVfina predict fluid responsiveness during major hepatic surgery. This suggests that intraoperative monitoring of fluid responsiveness may be implemented simply and non-invasively.

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Recent studies have shown that intraoperative optimization of cardiac output (CO) by repeated volume loading reduces postoperative morbidity and shortens hospital stay following abdominal surgery.[1] However, unnecessary i.v. fluids may be deleterious, and intraoperative fluid restriction has also been shown to improve clinical outcome.[2] During major hepatic surgery, intravascular volume expansion is constantly required, but the safety margin in fluid management is quite narrow, as high central venous pressure may increase blood loss, transfusion requirements and length of

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hospital stay.[3] Preload assessment is therefore crucial to guide fluid therapy and to prevent excessive fluid loading. Haemodynamic variables obtained through pulmonary artery catheterization have long been a mainstay for preload and volume status assessment, although increasingly questioned in critical care and perioperative monitoring.[4] Over the past few years, new indices, often qualified as 'dynamic' (as opposed to 'static') indicators of cardiac preload, based on respiratory variations of invasively measured arterial pressure or of stroke volume [measured using transoesophageal echocardiography (TOE) or Doppler], have been shown to predict haemodynamic response to volume expansion in mechanically ventilated patients in the intensive care unit.[5–7] More specifically, these indices, when measured before a fluid challenge, distinguish between responders who will increase their stroke volume in response to fluid and non-responders whose stroke volume will not change.[5–7] From these studies, optimal threshold (cut-off) values to guide fluid administration have been determined and are now proposed for clinical practice.[7] Several studies have extended this assessment to the perioperative period, but, apart from one study in neurosurgery,[8] measurements were performed exclusively before[9–11] or after surgery.[11–14] Such experimental conditions do not necessarily reflect intraoperative haemodynamic instability. In addition, tidal volumes, aortic compliance, peripheral resistance and abdominal pressure are likely to vary during abdominal surgery. As a result, threshold values for dynamic predictors during surgery may be different from those reported in other patients. Finally, because the widespread use of arterial catheters and transesophageal echocardiography cannot be advocated in routine surgery, potential non-invasive predictors of fluid responsiveness, such as pulse oximetry plethysmographic waveform,[15] should also be evaluated. The aims of the present study were to measure, before repeated fluid challenges, a number of static and dynamic variables derived from invasive and non-invasive monitoring, to determine their optimal thresholds for predicting fluid responsiveness and to compare their ability to predict fluid responsiveness in patients undergoing hepatic surgery. The hypotheses tested were that (i) dynamic indices predict fluid responsiveness better than static indices under intraoperative conditions and (ii) non-invasive dynamic indices are as sensitive and specific predictors as invasive indices for predicting fluid responsiveness.

Patients and methods

After institutional approval by the *Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale de Lille* and written informed consent, eight patients scheduled for major hepatic surgery were enrolled. Patients with valvular heart disease or a history of arrhythmias were excluded. Anaesthesia was induced with sufentanil 0.5 $\mu g\ kg^{-1}$, propofol 2 $mg\ kg^{-1}$ and atracurium 0.5 $mg\ kg^{-1}$, and maintained with isoflurane at an expired fraction of 0.5% in a 50% oxygen/50% nitrogen mixture and continuous i.v. sufentanil 0.3 $\mu g\ kg^{-1}\ h^{-1}$. Intraoperative muscle paralysis was maintained by the continuous i.v. administration of atracurium 0.5 $mg\ kg^{-1}\ h^{-1}$. Controlled mechanical ventilation was maintained throughout the procedure with a tidal volume of 8–10 $ml\ kg^{-1}$ and an inspiratory:expiratory ratio of 1:2. The ventilatory frequency was set to maintain an end-tidal P_{CO_2} 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 sternum up to the shoulders with a forced-air warming blanket.

Haemodynamic measurements

All patients were monitored using a 20-G radial arterial catheter (Seldicath 3 French, Plastimed, Saint Lieu la Forêt, France) and a pulmonary artery catheter (PAC, Swan-Ganz catheter, 7.5 French; Baxter Edwards, Lifescience, LLC, Irvine, CA). In addition, finger arterial pressure was monitored non-invasively through a Finapres™ (Ohmeda Monitoring Systems, Englewood, CO). Transducers were positioned at the mid-axillary level with atmospheric pressure used as the zero reference level. Calibration of both monitors was confirmed using calibration tests providing series of 100 or 150 mm Hg square pulses. The correct position of the pulmonary artery catheter in West's zone 3 was verified using a method described previously.[16] Right atrial pressure (RAP) and pulmonary artery occlusion pressure (PAOP) were measured at end-expiration and averaged over three consecutive respiratory cycles. CO was measured by thermodilution, using the average of five measurements obtained by the injection of 10 ml of dextrose at room temperature randomly during the respiratory cycle. Cardiac index (CI) and stroke volume index (SVI) were calculated using standard formulas.

Data acquisition

To record the invasive arterial pressure and the pulse oximetry plethysmographic curve onto a computer (Machintosh LC III, Apple, Cupertino), the analog output (M1084, MP) from the anaesthesia monitor (Monitor Hewlett-Packard, M1165A, Model 56, Les Ulis, France) was converted using an analog-to-digital interface (Biopac MP 100, Systems Inc., Santa Barbara, CA) and acquired using Acknowledge software version 3.1.2 (Biopac. Systems Inc., Santa Barbara, CA). The non-invasive arterial pressure curve signal obtained from the Finapres™ device was simultaneously recorded via the same interface and software. Recordings were analysed off-line with the reviewer unaware of the haemodynamic data. After confirming the absence of artifact, arterial pressure (invasive and non-invasive) curves and pulse oximetry waveform were measured on a beat-to-beat basis. Pulse pressure (PP), the

difference between systolic and diastolic pressure of the preceding beat, was calculated from the invasive arterial (PPart) and Finapres™ non-invasive (PPfina) pressure curves. Likewise, the difference between the maximal and minimal values of the pulse oximetry curve was calculated beat-to-beat and assimilated to a pulse pressure (PPsat), expressed in arbitrary units. Maximal and minimal values for all the aforementioned PPs (PPmax and PPmin, respectively) were determined over a respiratory cycle. All PP measurements were automatically calculated by the software, thus preventing any inter- or intra-observer variations. The PP variation (PPV) was calculated as described previously: PPV (%)=100*(PPmax−PPmin)/[(PPmax+PPmin)/2].[5] PPVs were calculated in triplicate over three consecutive respiratory cycles. The mean value of the three determinations was used for the analysis.

Echocardiographic measurements

Echo-Doppler studies were performed with a System Five Performance (GE Vingmed, Horton, Norway) equipped with a multiplane 5 MHz transesophageal transducer. The probe was first positioned to obtain a left ventricular (LV) short-axis image at the mid-papillary muscle level. The LV short axis, end diastolic, cross-sectional area was measured by manual planimetry of the area circumscribed by the leading edge of the endocardial border. The anterolateral and posteromedial papillary muscles were included within the ventricular area. LV areas were divided by the surface body area of the patient to obtain indexed LV areas at end-diastole (LVEDAI). Then, using a mid-oesophageal approach, a four-chamber view of the cardiac cavities was obtained. Mitral inflow velocities were obtained through pulsed Doppler at the tip of the mitral leaflets and the images were recorded. The peak velocities of the early diastolic filling wave (E) and the late diastolic filling wave (A) were measured and the ratio of these velocities (E/A) was calculated. The deceleration time of the E wave (MDT) was measured as the time between the peak E velocity and the return to zero baseline of the early diastolic flow velocity. Then, in order to measure the pulmonary venous flow (PVF), the pulsed Doppler sample area was positioned in the left upper pulmonary vein approximately 1 cm proximal to the entrance into the left atrium. When necessary, colour Doppler was used to sample maximal flow. From PVF velocity tracing, the velocity-time integrals (VTI) of the peak systolic (S) wave (VTIs) and the peak diastolic (D) wave (VTId) were measured. The systolic fraction (SF) was calculated as described previously:[17] SF=(VTIs)/(VTIs+VTId). All echocardiographic and Doppler measurements were performed over three to four beats throughout the respiratory cycle and averaged for the analysis.

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 250 ml of colloid solution (4% modified fluid gelatin, Gelofusine®, B. Braun Medical SAS, Boulogne Billancourt, France) over 10–15 min. A complete set of haemodynamic and echocardiographic measurements including all the studied variables (RAP, PAOP, PPVart, PPVsat, PPVfina, LVEDAI, E/A, MDT, and SF) was performed and recorded just before VLS (baseline values) and was repeated 2–5 min after VLS.

The SVI increase induced by volume expansion was used to classify each VLS as responder ($\geqslant$10% increase in SVI) or non-responder (<10% increase in SVI). In responders, successive VLSs were performed until non-responder status was reached. When several suspected episodes of hypovolemia occurred during the surgical procedure, the whole protocol was repeated for each episode.

Because the validity of this analysis relies on the absence of haemodynamic changes other than the standardized increase in preload secondary to the 250 ml VLS, the protocol was interrupted before post-VLS measurements in case of evident interference (especially uncontrolled haemorrhage).

Statistical analysis

All haemodynamic and echographic variables are presented as mean (SD). Comparisons between baseline and post-VLSs values used the Wilcoxon signed rank sum test for repeated measures. To assess the ability of the variables to discriminate between responder and non-responder VLSs, the values of each variable (PAOP, RAP, PPVart, PPVsat, PPVfina, LVEDAI, SF, E/A and MDT) measured before VLSs leading to a positive response were compared with those measured before a negative response using the Mann–Whitney *U*-test. Receiver operating characteristic (ROC) curves were generated for all the variables. The most discriminating threshold value (the cut-off value that maximized the sum of the sensitivity and specificity) was determined for each variable. The area under the curve (AUC) of each variable was calculated and AUCs were compared as described previously.[18] Correlations between the pre VLS values of each variable and the SVI response to subsequent fluid infusion were determined using Spearman's rank correlation coefficient calculation. Finally, agreement between the two non-invasive indices of PP variation (PPVfina and PPVsat) and PPVart was assessed using Bland–Altman analysis. Statistical analysis was performed using SPSS software, version 10.1 (SPSS Inc., Chicago, IL). For all comparisons, $P<0.05$ was considered significant.

Results

Patients were classified ASA I or II, with ages ranging between 45 and 71 yr. All underwent right hepatectomy,

Table 1 Changes in haemodynamic variables during volume loading steps (VLSs). Values are mean (SD). HR, heart rate; MAP, mean arterial pressure; CI, cardiac index; SVI, stroke volume index; SVRI, systemic vascular resistance index. *P<0.05 in comparison with responders at the same stage of volume loading. †P<0.05 in comparison with baseline

	Baseline		After 250 ml	
	Responders	Non-responders	Responders	Non-responders
HR (beats min^{-1})	66 (11)	65 (11)	67 (10)	67 (12)
MAP (mm Hg)	68 (10)	73 (12)	75 (10)†	76 (11)
CI (litre min^{-1} m^{-2})	2.2 (0.5)	2.8 (0.5)*	2.8 (0.6)†	2.8 (0.6)
SVI (ml m^{-2})	34 (7)	44 (8)*	43 (6)†	42 (8)
SVRI (dyn s cm^{-5} m^2)	2202 (447)	1843 (475)*	1948 (505)†	1946 (467)

Table 2 Haemodynamic and echocardiographic indicators of fluid responsiveness measured before responder and non-responder volume loading steps (VLSs). Values are mean (SD). PPVfina, respiratory changes in non-invasive arterial pulse pressure; PPVart, respiratory changes in invasive arterial pulse pressure; PPVsat, respiratory changes in the pulse oximetry plethysmographic waveform; MDT, mitral deceleration time; LVEDAI, left ventricular end-diastolic area index; RAP, right atrial pressure; E/A, ratio of the early (E) and the late (A) peak velocities of the mitral flow; SF, systolic fraction; PAOP, pulmonary artery occlusion pressure

	Responder VLSs	Non-responder VLSs	P
PPVfina (%)	16 (8)	8 (3)	0.0001
PPVart (%)	15 (7)	9 (4)	0.0005
PPVsat (%)	14 (11)	9 (7)	0.02
MDT (ms)	221 (42)	196 (37)	0.036
LVEDAI (cm^2 m^{-2})	9.8 (3.2)	12.1 (3.9)	0.038
RAP (mm Hg)	6 (4)	8 (4)	0.09
E/A	1.48 (0.37)	1.72 (0.57)	0.17
SF (%)	53 (14)	55 (11)	0.38
PAOP (mm Hg)	8 (4)	9 (4)	0.55

Table 3 Receiver operating characteristic curve analysis of haemodynamic and echographic parameters in prediction of fluid responsiveness. AUC (95% CI), area under ROC curve (95% CI); PPVfina, respiratory changes in non-invasive arterial pulse pressure; PPVart, respiratory changes in invasive arterial pulse pressure; LVEDAI, left ventricular end-diastolic area index; PPVsat, respiratory changes in the pulse oximetry plethysmographic waveform; MDT, mitral deceleration time; RAP, right atrial pressure; E/A, ratio of the early (E) and the late (A) peak velocities of the mitral flow; PAOP, pulmonary artery occlusion pressure; SF, systolic fraction; NA, non applicable (AUC<0.5). *P<0.05 *vs* PPVart and PPVfina

	AUC (95% CI)	Optimal threshold value
PPVfina	0.81 (0.70–0.93)	14.0%
PPVart	0.79 (0.67–0.92)	12.5%
LVEDAI	0.70 (0.53–0.88)	10.5 cm^2 m^{-2}
PPVsat	0.68 (0.54–0.82)	9.5%
MDT	0.68 (0.52–0.84)	234 ms
RAP	0.63 (0.49–0.77)*	10 mm Hg
E/A	0.62 (0.45–0.78)*	1.84
PAOP	0.55 (0.39–0.70)*	8 mm Hg
SF	0.42 (0.26–0.60)*	NA

except one with left hepatic lobectomy. All remained in the supine position during surgery, and hepatic inflow cross clamping was not used. Initial echocardiographic measurements showed normal LV ejection fraction (>50%) in all patients. The mean estimated total blood loss was 820 ml (range: 200–1400 ml). A total of 54 VLSs (range 5–8 per patient) were performed. Twenty-three responder VLSs (increase in SVI ranging between 10 and 75%; 1–4 per patient) and 31 non-responder VLSs (change in SVI ranging between −30 and +9%; 2–5 per patient) were identified. No more than two successive responder VLSs was observed in any patient. Because of intraoperative conditions (gastric mobilization, compression by retractors, or both), echocardiographic data were obtained in only 48 (20 responder and 28 non-responder) VLSs for MDT, SF and E/A, and 39 (16 responder and 23 non-responder) VLSs for LVEDAI. Peak and plateau airway pressures before the first VLS ranged from 12 to 19 cm H_2O and from 9 to 17 cm H_2O, respectively. Moderate intraoperative variations in airway pressures without associated changes in tidal volume were observed in all patients, with the difference between the highest and the lowest plateau pressure ranging between 2 and 9 cm H_2O.

The main haemodynamic variables recorded before and after VLSs are summarized in Table 1. Comparison of variables measured immediately before responder and non-responder VLSs showed that PPVart, PPVfina, PPVsat and MDT were higher, and the LVEDAI lower, in the responder VLS group than in the non-responder group (Table 2). There was no significant difference in RAP, PAOP, E/A and SF between the two groups (Table 2). The performance of variables in discriminating responder and non-responder VLSs was evaluated by constructing ROC curves. The areas under the ROC curves and the optimal threshold value for each variable are reported in Table 3. Greater areas were obtained with indices derived from respiratory changes in arterial pressure (PPVart and PPVfina) while areas obtained with RAP, PAOP, E/A and SF were not significantly different from 0.5 (i.e. the test variable was no better than chance) (Fig. 1). A significant correlation with the VLS-induced change in SVI was found for only four variables measured before VLS: PPVart (r=0.59, P=0.0001), PPVfina (r=0.56, P=0.0001) (Fig. 2), PPVsat (r=0.29, P=0.04) and MDT (r=0.29, P=0.05). Bland–Altman analysis demonstrated a small bias between non-invasive estimates of PPV (PPVfina and PPVsat) and PPVart (mean difference: −0.1 and 1.0%, respectively), but precision, as assessed by the 95% limits of agreement, was better with PPVfina than with PPVsat (Fig. 3).

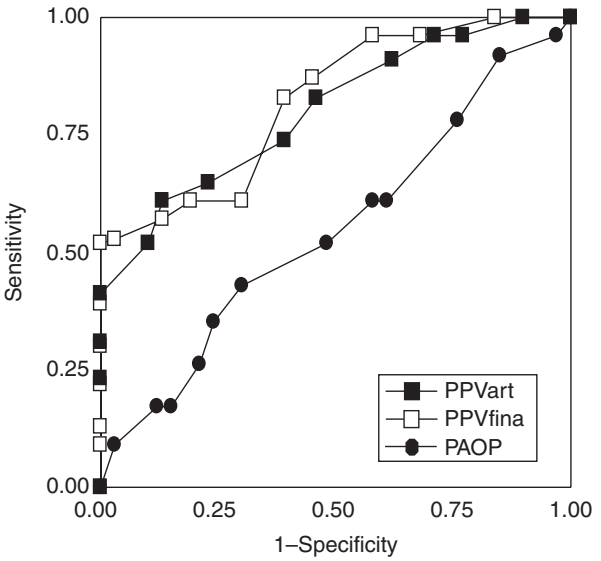

Fig 1 Receiver operating characteristic (ROC) curves for PPVart, PPVfina and PAOP.

Discussion

Recent studies have consistently shown that intraoperative optimization of SVI by repeated volume loading (probably by preventing 'occult' peripheral hypoperfusion), and also i.v. fluid restriction (to avoid deleterious fluid overload), improves clinical outcome and shortens hospital stay following abdominal surgery.[1 2] Accurate predictors of fluid responsiveness are thus needed in the operating theatre. The data from the present study demonstrate that PPVart is a better predictor of fluid responsiveness than static variables, including the TOE-derived ones, during hepatic surgery with haemodynamic instability. Moreover, non-invasive PPVfina provides a prediction as accurate as that obtained from invasive PPVart measurements. Estimated optimal thresholds for both dynamic indices were in the same range as those previously established for PPV in the ICU. This suggests that monitoring of fluid responsiveness may be implemented simply and non-invasively to optimize fluid therapy during surgery.

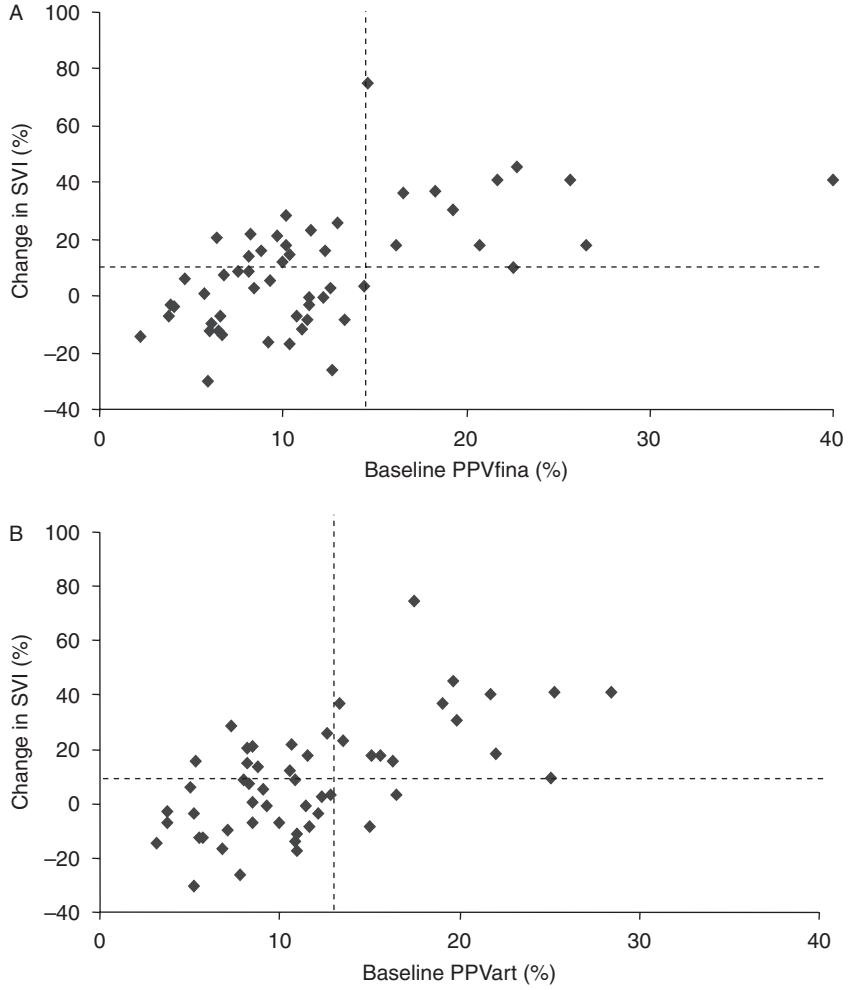

Fig 2 The relation between PPVfina (A) or PPVart (B) measured before volume loading steps (baseline values) and the changes in stroke volume index (SVI) induced by volume infusion. Horizontal dotted lines=10% increase in SVI (separating responder from non-responder volume loading steps). Vertical dotted lines=optimal threshold value.

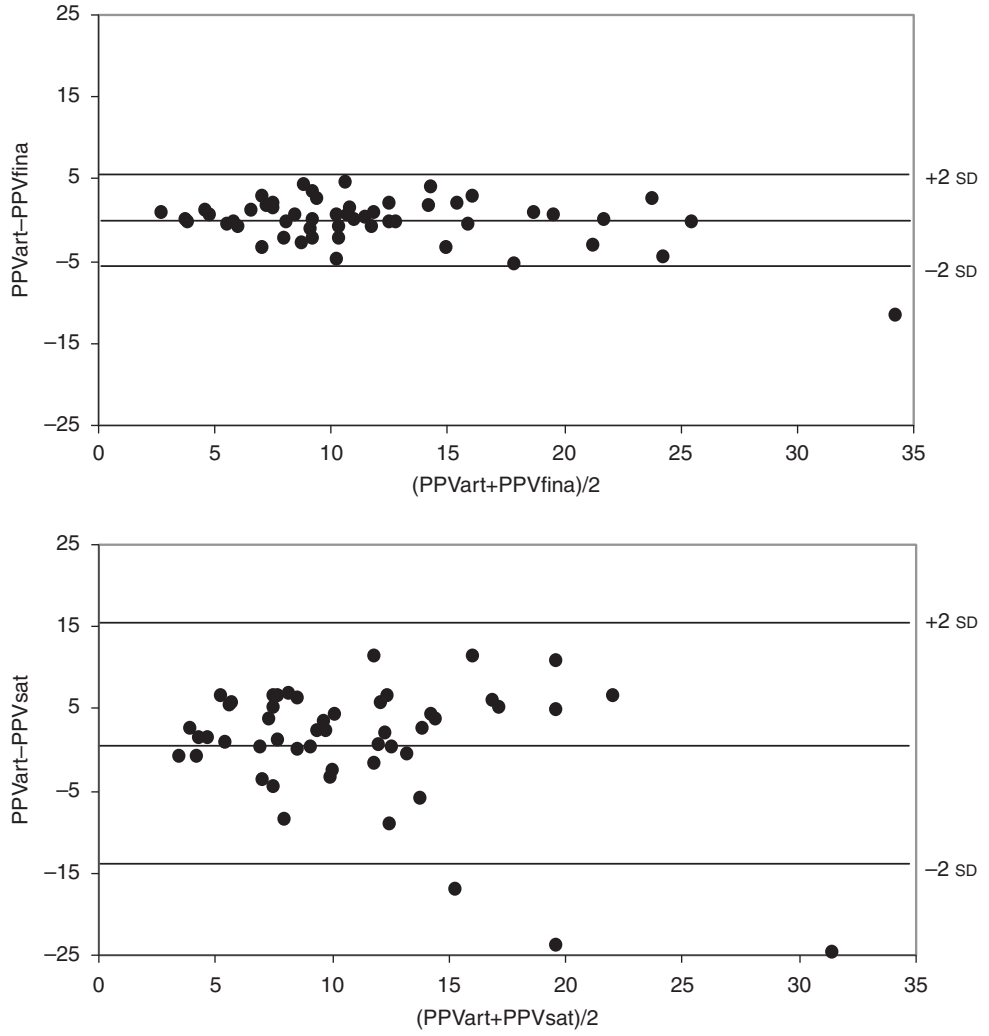

Fig 3 Representation of Bland–Altman analysis of the relation between PPVfina (upper panel) or PPVsat (lower panel) and PPVart. Horizontal lines represent the mean (2 SD) range of the differences between PPVfina or PPVsat and PPVart, defining the 95% limits of agreement between the two methods tested.

Haemodynamic monitoring to assess preload responsiveness using arterial pressure or LV stroke volume variation has been validated primarily in ICU patients.[5–7] Several studies have extended this assessment to the perioperative period, but measurements in these studies were performed under conditions of haemodynamic stability before[9–11] or after surgery.[11–14] Our study is the first to determine the relevance of ventilation-induced arterial PP variation in cases of haemodynamic instability (recent hypotension, tachycardia, or both) while abdominal surgery is still underway. In contrast with intensive care patients, during major hepatic surgery, chest and abdominal compliance, airway pressures, aortic compliance and peripheral resistance are expected to vary over several minutes rather than several hours or days. In fact, we observed only moderate variations in airway pressure throughout surgery in all patients. Our findings strongly suggest that intraoperative conditions do not alter the clinical usefulness of respiratory variations in PP. Indeed, the optimal PPVart threshold value (12.5%) found in the present study is in the range of those previously obtained in ICU patients (from 11 to 13%).[7]

In agreement with previous reports, dynamic variables performed better than ventricular filling pressure-derived indices (RAP and PAOP) in predicting fluid responsiveness.[5–7] The area under the ROC curve for PPVart in the present study (0.79) was lower than those found for ventilation-induced arterial pressure variation variables in ICU patients (between 0.94 and 0.98), but is in the same range as that established in most (0.81[9]; 0.82[12]) but not all (0.87–0.96[11]) studies before or after surgery. In the present study, this result appeared essentially to be because of 'false negative cases', that is patients responding to VLSs who were predicted to be non-responders (PPVart <12.5%) (the left upper quadrant in Fig. 2). Recent studies have shown that the degree of tidal volume and chest wall compliance influence the magnitude of PPVart, with small variations in pleural and transpulmonary pressures (resulting from small tidal volume or increased chest compliance)

leading to such false negative cases.[7 19 20] However, in our study, patients responding to VLS with PPVart <12.5% and those with PPVart >12.5% (true positives) had similar tidal volumes and airway pressures (data not shown). In fact, most of the responders to VLS with PPVart value less than 12.5% had to moderate increases in SVI (between 10 and 20%), with pre-VLS values of PPVart greater than 8% (Fig. 2). This implies that PPVart values ranging from 8 to 13% may constitute an inconclusive or 'grey zone'[21] where its predictive value is uncertain.

Non-invasiveness is of importance in anaesthesia. Improved outcome following intraoperative optimization of SVI by fluid therapy has been shown even in routine surgery,[1 2] where invasive monitoring is usually not recommended. A major finding of the study is that PPVfina provides a reliable non-invasive index of fluid responsiveness. One preliminary report demonstrated good agreement between PPVfina and PPVart in ICU patients but did not assess the value of PPVfina itself in predicting SVI response to fluid loading.[22] The Finapres™ is a non-invasive continuous beat to beat monitor of the finger arterial pressure waveform. The finger arteries are compressed at a fixed diameter, by applying an external pulsating pressure determined through infrared photoplethysmography in the finger cuff. Finapres™ data have not been found to be a reliable substitute for radial or brachial intra-arterial pressures in anesthetized patients.[23] We also found a poor agreement between arterial pressure from the Finapres and invasive monitoring in our patients (data not shown). However, a recent article showed that, in experimental conditions, SV variations can be modelled through pulse waveform analysis and PPV can be derived from the signal and is correlated for blood loss.[24] Our results show not only a good agreement between PPVfina and PPVart but also that PPVfina has the same predictive value as PPVart in anaesthetized patients undergoing hepatic surgery. The correlations between the VLS-induced change in SVI and PPVart and PPVfina, although not very close, confirm that these variables are associated, that is the VLS-induced changes in SVI tend to be higher for higher values of PPV.

Another surrogate variable for PPVart could be PPVsat. The pulse plethysmographic waveform represents pulse-dependent changes in volume of arterial blood and is related to stroke volume. Indeed, several reports have found a consistent correlation between dynamic indices derived from plethysmographic waveform and corresponding invasive variables.[15 25] Changes in the plethysmographic waveform after blood withdrawal also correlate well with corresponding changes in the arterial waveform,[15] but no study has tested the relation of these indices with fluid responsiveness. However, in our study, both the agreement between PPVsat and PPVart and the prediction of VLS-induced change in SVI with PPVsat were weak. This may be explained by the sensitivity of the plethysmographic signal to humoral and neurogenic factors.[26] In addition, proprietary software included in pulse oximeters are designed to provide a graphic display for pulse oximetry monitoring and not for PP variation assessment. The software generates a signal that is substantially filtered, amplified and smoothed before display.[27] As a result, whether using different pulse oximeters would provide similar results remains to be investigated.

While filling pressure-derived indices (RAP and PAOP) did not predict fluid responsiveness, the TOE-derived static variables exhibited contrasting results. TOE has been reported to be of value for fluid management during hepatic surgery.[28] We found that LVEDAI was a potentially useful variable for TOE monitoring of fluid responsiveness with an AUC of 0.70, although there was no significant correlation between LVEDAI and VLS-induced changes in SVI. Previous reports on correlation between LVEDAI and SVI variation in response to volume expansion have led to conflicting results.[5 6] Operator dependency and difficulty of measuring ventricular surfaces through manual planimetry in real-time may account for these discrepancies. In addition, the estimation of the LV end diastolic area by TOE does not always accurately reflect LVED volume and hence LV preload.[5] Nevertheless, LVEDAI is usually considered an acceptable measure of LV preload in clinical practice,[6] and its value as an index of preload responsiveness is thought to mainly depend on whether biventricular function is normal or not.[5]

Doppler measurement of mitral flow allows indirect evaluation of the individual LV diastolic pressure/volume relationship and has been proposed as a predictor of the increase in CO after intravascular fluid challenge. E-wave deceleration time (expressed as MDT in the present study) has long been known as a preload-dependent transmitral flow Doppler variable.[29] Our study is the first to show that MDT predicts fluid responsiveness in patients, but it did not perform as well as dynamic variables. Although pulmonary vein flow has been found to be correlated to E-wave MDT,[30] we did not find it to be of value for fluid responsiveness prediction.

Finally, only one study, performed by Lattik and colleagues,[31] has shown that E/A may predict fluid responsiveness. Our data did not confirm the results of Lattik's study, although the area under ROC curve obtained in our patients (0.62) was only slightly smaller than that reported in their study (0.71). The larger volume used for fluid challenges (twice that given in our study) and the definition of fluid responsiveness (20% increase in SVI) used in that study may account for these differences. In fact, several recent studies have shown that reliable prediction of fluid responsiveness by echocardiography is likely to require the use of dynamic indices.[5 6]

The present study was designed to evaluate the predictive value of various indices during surgery conditions. It is possible that, despite our aiming to discard VLS with uncontrolled haemodynamic variations, changes other than the standardized increases in preload by 250 ml VLSs may have occurred between pre- and post-VLSs measurements and affected the validity of our results. Because we tested a

number of different measures as possible predictors of fluid responsiveness, the risk of type 1 error may have been underestimated. However, PPVart and PPVfina were the only predictors of fluid responsiveness, and very significant differences between responder and non-responder VLSs were found only for these two variables (Table 2). In addition, repeated measurements were performed throughout surgery in each patient and then treated as independent observations for the analysis. However, this was done for all studied variables, and the large intra-individual haemodynamic variations that occur in any patient undergoing major hepatic surgery make it unlikely that these repeated measurements biased the analysis. We also verified that results were not biased by measurements derived from a particular patient (data not shown). Another limitation of our study was that some TOE measurements could not be performed, but this limitation must be acknowledged as representing real clinical practice. Non-invasive indices of PP variation could be measured in all patients throughout surgery. In practice, however, the signals of both the Finapres™ device and the pulse oximeter may be unstable or non-satisfactory, thus altering or preventing respiratory variation measurements, especially in patients with severe peripheral hypoperfusion. There are no monitors currently available that display these non-invasive indices of fluid responsiveness in real-time, and such measurements still necessitate off-line analysis of computer or graphic recordings. Finally, because no patient received epidural analgesia, whether the same results would be observed in patients with neuraxial blockade remains to be demonstrated.

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