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Evaluation of stroke volume variation obtained by arterial pulse contour analysis to predict fluid responsiveness intraoperatively

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Background. Fluid management guided by oesophageal Doppler monitor has been reported to improve perioperative outcome. Stroke volume variation (SVV) is considered a reliable clinical predictor of fluid responsiveness. Consequently, the aim of the present trial was to evaluate the accuracy of SVV determined by arterial pulse contour (APCO) analysis, using the FloTrac™/Vigileo™ system, to predict fluid responsiveness as measured by the oesophageal Doppler.

Methods. Patients undergoing major abdominal surgery received intraoperative fluid management guided by oesophageal Doppler monitoring. Fluid boluses of 250 ml each were administered in case of a decrease in corrected flow time (FTc) to $<$350 ms. Patients were connected to a monitoring device, obtaining SVV by APCO. Haemodynamic variables were recorded before and after fluid bolus application. Fluid responsiveness was defined as an increase in stroke volume index $>$10%. The ability of SVV to predict fluid responsiveness was assessed by calculation of the area under the receiver operating characteristic (ROC) curve.

Results. Twenty patients received 67 fluid boluses. Fifty-two of the 67 fluid boluses administered resulted in fluid responsiveness. SVV achieved an area under the ROC curve of 0.512 [confidence interval (CI) 0.32–0.70]. A cut-off point for fluid responsiveness was found for SVV $\geq$8.5% (sensitivity: 77%; specificity: 43%; positive predictive value: 84%; and negative predictive value: 33%).

Conclusions. This prospective, interventional observer-blinded study demonstrates that SVV obtained by APCO, using the FloTrac™/Vigileo™ system, is not a reliable predictor of fluid responsiveness in the setting of major abdominal surgery.

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Hypovolaemia during major abdominal surgery is a common problem and a constant threat for organ dysfunction.[1] Furthermore, it is associated with poor outcome after surgery.[1–4] However, fluid overload is also reported to increase complications and length of stay after surgery.[5–7] Therefore, adequate intraoperative fluid management has the potential to improve postoperative outcome.[8] Goal-directed fluid optimization was reported to reduce postoperative complications.[9–14]

Different methods to detect fluid responsiveness have been investigated.[13 15–22] Stroke volume variation (SVV) was suggested to be a reliable predictor of hypovolaemia

and fluid responsiveness in cardiac surgery, cardiac failure, and sepsis.[18 20 23] Recently, a new device that determines cardiac output (CO), stroke volume (SV), and SVV by arterial pulse contour analysis was introduced into clinical practice.[24 25] We studied the accuracy of SVV determined by arterial pulse contour analysis in predicting fluid responsiveness compared with an established oesophageal Doppler-based algorithm, which was reported to improve outcome after major abdominal surgery.[12–14]

Methods

After approval from the local ethics committee (Medical University of Vienna, Austria), written informed consent was obtained from patients undergoing elective major abdominal surgery. We included 20 patients with ASA physical status I or II between January 2007 and November 2007. We excluded patients with documented coronary or peripheral artery disease, severe pulmonary disease, arterial hypertension, diabetes mellitus, cardiac arrhythmias, coagulopathies, and symptoms of infections.

Patients were allowed to drink clear liquids until 2 h before surgery, did not receive bowel preparation, and received Ringer's lactate solution (RLS) 500 ml on the ward at the day of surgery. All patients were premedicated with oral midazolam (7.5 mg). On arrival to the operating theatre, a baseline fluid administration of RLS 2 ml kg^{-1} h^{-1} was started. Anaesthesia was induced by fentanyl (1–3 μg kg^{-1}), propofol (2 mg kg^{-1}), and rocuronium (0.6 mg kg^{-1}) and maintained with sevoflurane at a minimum alveolar concentration between 0.9 and 1.5. A fentanyl bolus of 3–5 μg kg^{-1} was administered when required. After tracheal intubation, volume-controlled ventilation with PEEP 5 cm H_2O, tidal volume 8 ml kg^{-1}, and ventilatory frequency between 10 and 12 bpm to achieve an end-tidal carbon dioxide partial pressure between 4.66 and 6 kPa was initiated.

For the treatment of anaemia, a strict transfusion protocol was followed. The target haematocrit was 26% in patients aged <65 yr and 28% in patients aged >65 yr. Patients were kept normothermic using upper forced-air warming (Bair Hugger®, Augustine Medical Inc., Eden Prairie, MN, USA). Fluid administration was continued with RLS 3 ml kg^{-1} h^{-1} and increased to 7 ml kg^{-1} h^{-1} after viscera were exposed.

After induction of anaesthesia, a catheter was inserted in the left radial artery as part of the standard monitoring and connected additionally to the FloTrac™/Vigileo™ system (Edwards Lifesciences, USA, version 1.07) to obtain CO, SV, and SVV measurements. The FloTrac™/Vigileo™ system is attached to an existing arterial cannula by a special transducer. The SV is calculated by measuring the area under the pulse pressure curve and multiplying with a correctional factor influenced by sex, age, height, and weight.[24] The version 1.07 can detect and eliminate premature ventricular contractions or other arrhythmias when assessing SVV.[16]

An oesophageal Doppler probe (CardioQ™, Deltex Medical, USA) was inserted to measure CO, SV, and corrected flow time (FTc). A central venous catheter was placed at the discretion of the attending anaesthetist. Peripheral catheters (18 G) were placed on the left arm.

Investigators were instructed to interpret low FTc values with caution and to verify measurements after interrupting surgical manipulation and repositioning of the probe. When the FTc remained below 350 ms, a 250 ml fluid bolus of hydroxyethyl starch 130/0.4 6% (Voluven®, Fresenius Kabi GmbH, Graz, Austria) or RLS was administered over 10 min. In each patient, the choice of fluid bolus was at the discretion of the anaesthetist, but crystalloid and colloid boluses were not mixed in individual patients. An FTc below 350 ms after the complete fluid bolus administration necessitated another fluid bolus. Haemodynamic study variables (CO, SV, SVV, and FTc) were recorded before the start and at the end of each fluid bolus administration.

The FloTrac™/Vigileo™ screen was turned away from the attending anaesthesiologist and covered. The FloTrac™/Vigileo™ variables were collected by independent research staff as part of the blinded study design. Volume responsiveness was defined as an increase in the stroke volume index (SVI) ≥10% (calculated from oesophageal Doppler obtained SV).[26 27]

We report both pooled data and also the effects of colloid (colloid group) and crystalloid (crystalloid group) boluses separately. This analysis was performed to elucidate the separate effect of the crystalloid and colloid boluses on the overall results. However, we did not intend to compare the effects of crystalloid *vs* colloid boluses in this study.

Statistical analysis

Statistical analyses were performed using SPSS® 15.0 (©SPSS Inc., Chicago, IL, USA) and SAS® 9.2 (©SAS Institute Inc., Carry, NC, USA). The haemodynamic variables such as heart rate, mean arterial pressure, CO (FloTrac™), SVV (FloTrac™), and FTc were rank-transformed before statistical analyses due to their skewed distributions and outlying observations. For the comparison of haemodynamic data before and after fluid bolus administration within the groups of patients, analysis of variance (ANOVA) models were performed, accounting for the repeated measurements on the same patient by inclusion of a random block factor. Comparing the changes in the haemodynamic variables due to fluid bolus administration between the groups, analysis of covariance models were performed on the post-administration values, including the pre-administration value as a covariate and the patient-factor as a random block factor. A Bonferroni correction was used for adjusting the significance levels of multiple comparisons. A Mann–Whitney *U*-test was used

for comparing the number of fluid boluses applied between the groups.

Prediction of fluid responsiveness based on SVV was tested by calculation of the area under the receiver operating characteristic (ROC) curve for an increase in SVI $\geq$10% after a fluid bolus administration. The 95% CI for the area under the ROC curve was calculated using the bootstrap percentile method, accounting for the dependence of repeated measurements on the same patient by block resampling as described by Davison and Hinkley.[28] The optimal cut-off point (maximizes sensitivity and specificity) for SVV to predict fluid responsiveness was determined. Accordingly, the positive and negative predictive values for SVV were calculated.

Results

Patients' characteristics are outlined in Tables 1 (before surgery) and 2 (during surgery).

None of the patients suffered from intraoperative cardiac arrhythmias. In total, 20 patients received 67 fluid boluses. Ten patients received 26 colloid boluses and 10 patients received 41 crystalloid boluses. The median (range) fluid bolus administration was 3.0 (1–10) boluses per patient. Ten patients received 4 (2–10) crystalloid boluses and 10 patients 2 (1–6) colloid boluses. Fifty-two fluid boluses were followed by an SVI increase $\geq$10%. Twenty boluses in the colloid group and 32 boluses in the crystalloid group were followed by an SVI increase $\geq$10%.

Haemodynamic variables before and after administration of a fluid bolus are outlined in Table 3. During the study period, no patients received catecholamines and no significant changes in the peak inspiratory pressure or PEEP were identified. Only one patient received packed red blood cells (4 units, crystalloid group).

Table 1 Patient characteristics; data are shown as mean (SD), when not indicated otherwise

Sex (female/male)	10/10
Median age (range) (yr)	52.7 (25–77)
Height (cm)	170.3 (8.5)
Weight (kg)	79.8 (13.7)
Type of surgery	
Hepatic resection	15
Whipple's procedure	3
Partial pancreatic resection	1
Hepatic and sigma resections	1

Table 2 Intraoperative characteristics; data are shown as mean (SD)

	Crystalloid group	Colloid group
Crystalloid baseline infusion (ml)	1775 (719)	1655 (662)
Colloid bolus (ml)	0 (0)	650 (428)
Crystalloid bolus (ml)	1025 (606)	0 (0)
Total urine output (ml)	388 (160)	386 (281)
Blood loss (ml)	550 (543)	410 (455)
Fluid balance (ml)	1862 (1120)	1509 (602)

SVV achieved an area under the ROC curve of 0.51 in both groups [Fig. 1, confidence interval (CI) 0.32–0.70%], of 0.58 in the colloid group (Fig. 2, CI 0.23–0.82%) and of 0.44 in the crystalloid group (Fig. 3, CI 0.23–0.70%).

A cut-off point for fluid responsiveness can be reported for an SVV $\geq$8.5% for all fluid boluses administered and for the colloid and crystalloid groups. This cut-off point showed a sensitivity of 77% and specificity of 43% for all boluses. The sensitivity was 65% for colloid boluses and 85% for crystalloid boluses. The specificity was 67% for colloid boluses and 25% for crystalloid boluses. For all boluses, a positive predictive value of 84% and a negative predictive value of 33% were calculated. The positive predictive value was 87% for colloid boluses and 82% for crystalloid boluses. The negative predictive value was 36% for colloid boluses and 29% for crystalloid boluses.

Discussion

This prospective, interventional observer-blinded study demonstrates that SVV determined by the FloTrac™/Vigileo™ system cannot serve as a reliable predictor of fluid responsiveness in the setting of major abdominal surgery.

Calculation of CO and SV from the area under the pulse pressure curve—and subsequently, calculation of SVV—by semi-invasive devices has been available for more than 10 yr.[29] Because of their bedside availability, dynamic preload variables such as SVV were studied as predictors of fluid responsiveness in several clinical trials using the PICCO catheter.[15–20] SVV can be calculated from the change of SV during a mechanical breath. As a transient decrease in left ventricular preload is the main effect of a mechanical breath, a more preload-dependent patient will demonstrate a larger SVV.[30] Unlike SVV, oesophageal Doppler-guided fluid optimization was reported to reduce morbidity in the setting of major abdominal surgery.[12–14] Therefore, the definition of a reliable SVV threshold value to predict fluid responsiveness is pivotal for the development of an SVV-based fluid optimization algorithm and subsequently for the design of clinical trials investigating its impact on perioperative morbidity.

However, data on such SVV threshold values are limited. Hofer and colleagues[15] reported that an SVV threshold value of $\geq$12% is able to predict an SVI increase $\geq$25% with a sensitivity of 74% and a specificity of 71% achieving an area under the ROC curve of 0.808 in patients undergoing off-pump cardiac surgery. Berkenstadt and colleagues[17] calculated a threshold value for SVV above 9.5% to induce a $\geq$5% increase in SVI after administering a stepwise fluid bolus of hydroxyethyl starch 130/0.4 6% (100 ml) in patients undergoing brain surgery. Recently, Hofer and colleagues[16] reported an SVV threshold value of 9.6% (sensitivity 91%, specificity 83%, area under the ROC curve 0.824) for prediction of fluid responsiveness

Table 3 Haemodynamic variables before and after fluid bolus administration and change due to fluid bolus administration; data are shown as median (quartiles); SV, stroke volume; SVV, stroke volume variation; FTc, corrected flow time; *$P<0.00625$ comparing variables before and after fluid bolus administration within the groups; all comparisons between the groups with respect to changes in the variables were not statistically significant (i.e. $P\geq0.00625$). †Rank-transformations were applied before statistical analyses

Variables	Before	After	Change
All boluses			
Heart rate (beats min^{-1})†	73 (64; 82)	74 (66; 87)	1 (−2; 7)
Mean arterial pressure (mm Hg)†	66 (61; 83)	72 (63; 88)	3 (−2; 13)*
Cardiac output (litre min^{-1})	4.6 (3.8; 5.5)	5.7 (4.8; 7.1)	1.2 (0.3; 2.1)*
Cardiac output FloTrac™ (litre min^{-1})†	4.8 (4.2; 5.3)	5.2 (4.6; 6.0)	0.4 (−0.1; 1.1)*
SV (ml)	63 (52; 80)	82 (65; 99)	15 (9; 25)*
SV FloTrac™ (ml)	68 (58; 79)	74 (65; 86)	5 (−1; 12)*
SVV FloTrac™ (%)†	11 (8; 16)	8 (6; 10)	−3 (−5; 0)*
FTc (ms)†	332 (313; 340)	373 (356; 395)	47 (28; 69)*
Crystalloid group			
Heart rate (beats min^{-1})†	72 (62; 81)	73 (65; 88)	1 (−2; 7)
Mean arterial pressure (mm Hg)†	65 (59; 80)	74 (63; 88)	3 (−1; 14)
Cardiac output (litre min^{-1})	4.3 (3.7; 6.1)	5.7 (4.8; 8.1)	1.3 (0.4; 2.1)*
Cardiac output FloTrac™ (litre min^{-1})†	4.5 (4.1; 4.8)	4.9 (4.5; 5.8)	0.6 (−0.1; 1.2)*
SV (ml)	69 (52; 83)	86 (65; 104)	17 (11; 27)*
SV FloTrac™ (ml)	63 (54; 75)	73 (61; 81)	7 (2; 16)*
SVV FloTrac™ (%)†	13 (9; 17)	9 (6; 13)	−3 (−5; 0)*
FTc (ms)†	324 (301; 337)	369 (343; 393)	52 (24; 69)*
Colloid group			
Heart rate (beats min^{-1})†	76 (67; 82)	77 (70; 86)	4 (−3; 9)
Mean arterial pressure (mm Hg)†	68 (64; 83)	70 (64; 85)	3 (−4; 7)
Cardiac output (litre min^{-1})	4.6 (3.8; 5.1)	5.7 (4.9; 6.7)	1.2 (0.2; 2.2)*
Cardiac output FloTrac™ (litre min^{-1})†	5.3 (4.9; 6.3)	5.6 (4.8; 6.5)	0.4 (−0.2; 0.6)
SV (ml)	62 (56; 73)	76 (66; 87)	14 (7; 24)*
SV FloTrac™ (ml)	73 (67; 83)	74 (69; 86)	3 (−2; 10)
SVV FloTrac™ (%)†	9 (7; 12)	7 (5; 9)	−3 (−5; 0)
FTc (ms)†	335 (331; 345)	378 (364; 400)	43 (31; 70)*

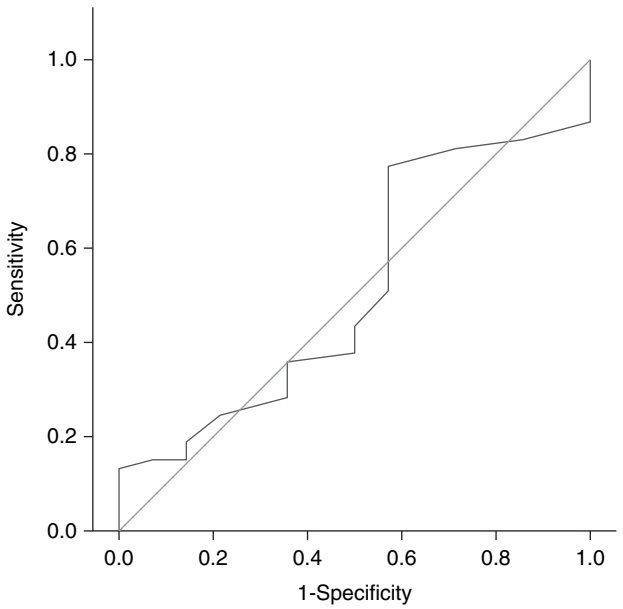

Fig 1 ROC curve for prediction of fluid responsiveness of SVV to an increase of changes in the SVI ≥10% using SVV obtained by the FloTrac™/Vigileo™ system. All boluses (n=67); area under the curve: 0.51

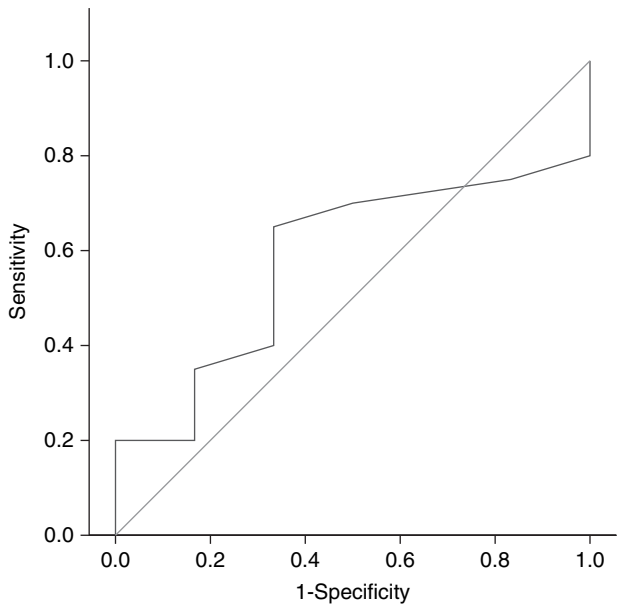

Fig 2 ROC curve in patients receiving colloid boluses (n=26 boluses) for SVV as a predictor of increases SVI ≥10% using the SVV obtained by the FloTrac™/Vigileo™ system. Area under the curve: 0.58

(SVI increase >25%) in patients before elective cardiac surgery using the FloTrac™/Vigileo™ system.

Other studies reported a good inverse correlation between SVV and cardiac index in septic patients and patients undergoing cardiac surgery,[18–20] but failed to define an SVV threshold value for predicting fluid responsiveness.

Our calculated SVV threshold value of ≥8.5% accords with the other published SVV threshold values, although

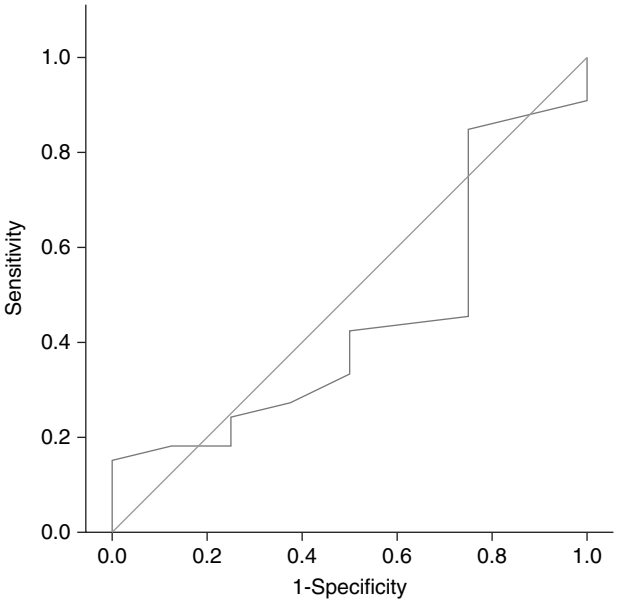

Fig 3 ROC curve in patients receiving crystalloid boluses (n=41 boluses) for SVV as a predictor of increases SVI ≥10% using the SVV obtained by the FloTrac™/Vigileo™ system. Area under the curve: 0.44

volume responsiveness was defined differently.[15–17] However, in contrast to Hofer and colleagues,[16] the sensitivity and specificity and the area under the ROC curve of only 0.44 in the crystalloid group and of 0.58 in the colloid group in our study underline the very limited clinical usefulness of our FloTrac™/Vigileo™ system obtained SVV threshold value as a predictor of fluid responsiveness. Therefore, more work is required before recommending its clinical use.

Recently, de Waal and colleagues[31] demonstrated that SVV assessed by the FloTrac™/Vigileo™ system using the first generation software (version 1.01) failed to predict fluid responsiveness in patients undergoing coronary artery bypass grafting. The authors speculate that the 10 min recalibration interval might be too long to accurately detect changes in SVV.[31] The SVV is defined as a per cent change of SV, regardless of the absolute SV values. Therefore, changes in the recalibration interval should not influence the accuracy of SVV. This might explain why SVV failed to predict fluid responsiveness, although the recalibration interval of the FloTrac™/Vigileo™ system was reduced to 1 min in the software generation (version 1.07) used in our trial.

Our results and those of de Waal and colleagues[31] might have been not only influenced by the long re-calibration interval but also by other flaws in the FloTrac™/Vigileo™ algorithm or other systematic errors. This is supported by Kubitz and colleagues,[32] who demonstrated in an animal model that pulse contour analysis tends to underestimate SVV during decreased cardiac afterload and vice versa. None of our study patients received vasoactive drugs as used in the animal model, but the anaesthesia-induced reduction of cardiac afterload could have generated a similar effect.

Although an enhanced volume effect of hydroxyethyl starch, especially in hypovolaemic patients, has been reported,[33] we were not able to observe this trend. However, it was not the primary goal of this study to compare the effects of crystalloid and colloid fluid boluses. Therefore, our non-randomized study design might not be suitable for drawing further conclusions regarding this question.

Our study has several limitations. First, one might criticize the intra-observer variability of oesophageal Doppler obtained parameters.[34] Although this may influence the accuracy of absolute CO values, directional changes in SV can be measured reliably.[34] However, all oesophageal Doppler probes were placed and handled by device experienced anaesthetists in order to minimize this source of inaccuracy.[35] Secondly, we did not use an alternative device to obtain additional SVV values. This could have led to further conclusions on the source of the inaccuracy of FloTrac™/Vigileo™ system obtained SVV. Thirdly, during hepatic resections, surgically induced haemodynamic instability may occur, especially due to compression of the caval vein. This may mimic intravascular hypovolaemia and result in misinterpretations of the FTc. Therefore, investigators were carefully instructed to clarify this issue as described in the Methods section. Hence, we consider this bias in our results as unlikely. Finally, as part of the study design, we only applied fluid boluses in patients with an FTc below 350 ms. Therefore, we cannot report whether a positive fluid response could have occurred in patients having an FTc above 350 ms and a high SVV at the same time. We are aware that this preselection might bias our results.

In conclusion, our findings emphasize the need for further evaluation of FloTrac™/Vigileo™ determined SVV as a predictor of fluid responsiveness.

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