

Predicting fluid responsiveness in patients undergoing cardiac surgery: functional haemodynamic parameters including the Respiratory Systolic Variation Test and static preload indicators[†]

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Background. Prediction of the response of the left ventricular stroke volume to fluid administration remains an unsolved clinical problem. We compared the predictive performance of various haemodynamic parameters in the perioperative period in patients undergoing coronary artery bypass surgery. These parameters included static indicators of cardiac preload and functional parameters, derived from the arterial pressure waveform analysis. These included the systolic pressure variation (SPV) and its delta down component (dDown), pulse pressure variation (PPV), stroke volume variation (SVV), and a new parameter, termed the respiratory systolic variation test (RSVT), which is a measure of the slope of the lowest systolic pressure values during a standardized manoeuvre consisting of three successive incremental pressure-controlled breaths.

Methods. Eighteen patients were included into this prospective observational study. Seventy volume loading steps (VLS), each consisting of 250 ml of colloid administration were performed before surgery and after the closure of the chest. The response to each VLS was considered as a positive (increase in stroke volume more than 15%) or non-response. Receiver operating characteristic curves were plotted for each parameter to evaluate its predictive value.

Results. All functional parameters predicted fluid responsiveness better than the intrathoracic blood volume and the left ventricular end-diastolic area. Parameters with the best predictive ability were the RSVT and PPV.

Conclusions. Functional haemodynamic parameters are superior to static indicators of cardiac preload in predicting the response to fluid administration. The RSVT and PPV were the most accurate predictors of fluid responsiveness, although only the RSVT is independent of the settings of mechanical ventilation.

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One of the common manoeuvres to augment cardiac output is fluid administration. Volume expansion with colloid solution was shown to reduce the incidence of gut mucosal hypoperfusion and improve clinical outcome in patients undergoing cardiac surgery.¹ However, unnecessary volume load may cause further deterioration in myocardial function with the development of acute heart failure. Given the notoriously low sensitivity and specificity of cardiac filling pressures for preload monitoring and prediction of response to fluid administration, new methods for haemodynamic

assessment have been developed. These methods use the cyclic changes in stroke volume caused by the increase in

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[‡]*Declaration of interest.* Azriel Perel, MD, is the inventor of the Respiratory Systolic Variation Test (US Patent # 5,769,082). He cooperates as an investigator with Draeger-Siemens in a clinical research project concerning the Respiratory Systolic Variation Test, and is a member of the medical advisory board of Pulsion Medical Systems, Munich, Germany.

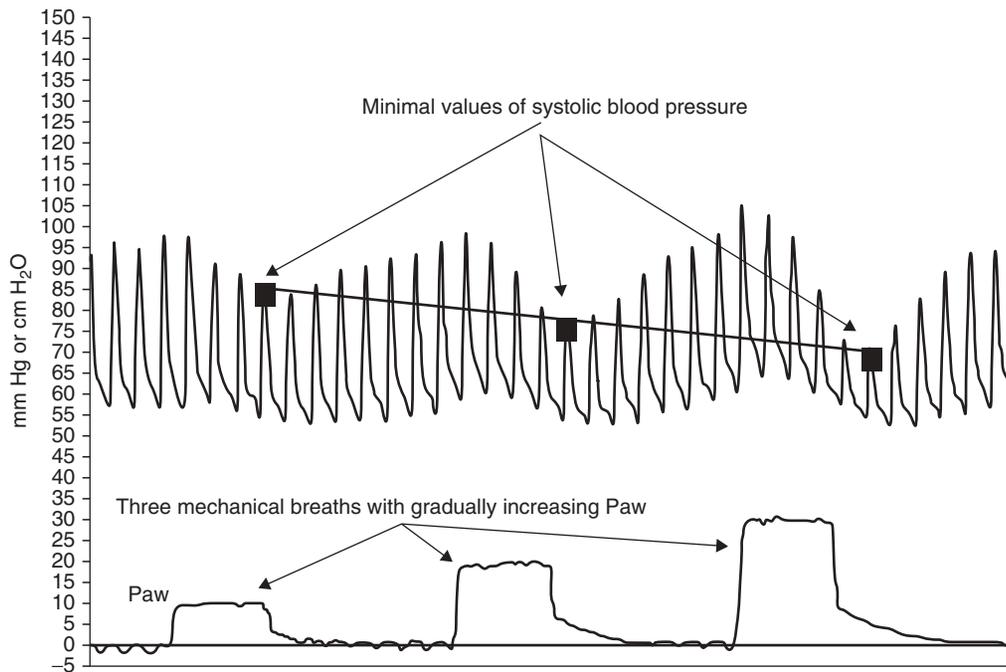


Fig 1 Response of the arterial BP to the RSVT. Three consecutive mechanical pressure-controlled breaths are delivered with inspiratory pressures of 10, 20, and 30 cm H₂O. Minimal values of systolic BP in response to each breath are recorded and then the slope of the relationship between the decrease in BP and inspiratory pressure is calculated.

the intrathoracic pressure during a mechanical breath^{2,3} and are termed functional parameters of fluid responsiveness.

The first of these parameters, named the systolic pressure variation (SPV), based on the arterial blood pressure waveform analysis, explores the difference between maximal and minimal values of systolic arterial pressure during one mechanical breath. The SPV, and its delta down (dDown) component, which is the difference between the systolic arterial pressure during the short apnoea and its minimal value during one mechanical breath, have been shown to correlate with the volumetric measures of left ventricular (LV) preload,^{4,5} and to predict the response of the cardiac output to volume loading in septic patients.⁶

More recently, the pulse pressure variation (PPV), which is the difference between the maximal and minimal pulse pressure values during mechanical breath divided by their mean, has been shown to be an even more accurate predictor of fluid responsiveness in septic patients.⁷

The introduction of the pulse contour method for the monitoring of continuous cardiac output⁸ enabled the on-line calculation of the variation of left ventricular stroke volume (LVSV) itself during mechanical ventilation. This parameter, named stroke volume variation (SVV), reflects changes in other indicators of the preload of LV during volume administration⁹ and has been found to be another accurate predictor of the response of LVSV to fluid challenge in patients with normal cardiac function¹⁰ and left ventricular dysfunction.¹¹

The clinical use of these functional haemodynamic parameters has certain limitations. First of all, these methods

may be used only for the assessment of mechanically ventilated patients with no arrhythmias, whose arterial pressure is monitored invasively. Other limitations include a dependency on the delivered tidal volume,¹² as well as the fact that the SPV, PPV, and SVV are calculated as the difference between the maximal and minimal values of systolic arterial pressure or stroke volume during mechanical breath. However, the maximal value is often influenced by an early inspiratory augmentation of LVSV, which is not related to fluid responsiveness. This phenomenon may explain the recently observed lesser sensitivity and specificity of SVV in patients with reduced LV function.¹¹

We have therefore developed a new functional haemodynamic test for the prediction of volume responsiveness, which is termed the respiratory systolic variation test (RSVT). This test is not influenced by tidal volume or early inspiratory increase of LVSV. It consists of the delivery of three consecutive pressure-controlled breaths of incremental peak inspiratory pressures of 10, 20, and 30 cm H₂O (Fig. 1). The minimal values of the systolic arterial pressure following each of these three breaths are measured and plotted against their respective airway pressures, producing the slope (RSVT slope).¹³ A similar method has been preliminary evaluated in clinical practice.¹⁴

Although some of the functional methods for the prediction of fluid responsiveness have been investigated in different patients' populations,^{5,6,8-10} their ability to predict LV response to fluid load has not been compared. The aim of the current study was to compare the ability of different functional haemodynamic parameters (SPV and dDown,

PPV, RSVT, and SVV) to predict the response of LV to volume expansion in patients with normal and abnormal LV function. We also compared these methods with volumetric parameters of cardiac preload-LV end-diastolic area (LVEDA), measured by transoesophageal echocardiography (TOE), and the intrathoracic blood volume (ITBV). As a gold standard we used the change of LVSV, measured by arterial thermodilution, in response to fluid load.

Patients and methods

After institutional ethics committee for human studies approval and personal informed consent, 18 patients undergoing elective coronary artery bypass surgery were included into the study. Patients with peripheral vascular disease involving femoral arteries, significant arrhythmias, clinically evident pulmonary disease, concomitant aortic aneurysms, oesophageal pathology precluding the use of TOE and patients undergoing repeated operations were considered ineligible for the study. Patients were divided into two groups. Patients with normal LV function (LVEF >40%, assessed by preoperative ventriculography) comprised Group 1, whereas Group 2 consisted of patients with preoperative LV dysfunction (LVEF <40%).

Anaesthetic protocol

Patients were NPO and no i.v. fluids were administered in the 8 h preceding the operation. Patients were pre-medicated with their usual cardiovascular medication and with 5–10 mg oral diazepam 1–2 h before arrival to the operating room. Induction of anaesthesia included 0.05–0.1 mg kg⁻¹ midazolam and 5–7 µg kg⁻¹ fentanyl. Tracheal intubation was facilitated by pancuronium 0.1 mg kg⁻¹. Mechanical ventilation was instituted with Servo900C ventilator (Siemens, Sweden) in the pressure control mode with $F_{I_{O_2}}$ 1.0, peak inspiratory pressure 15–20 cm H₂O, ventilatory frequency 8–10 min⁻¹ and I:E ratio 1:2, so that end tidal carbon dioxide was kept in the 30–35 mm Hg range. These parameters of mechanical ventilation were used throughout the surgery. Anaesthesia was maintained by isoflurane 0.5–1% and by fentanyl up to a total dose of 15–20 µg kg⁻¹. All patients received 500 ml of lactated Ringer solution during the induction period.

Haemodynamic monitoring

Transoesophageal multiplane echocardiographic transducer (HP 21364A, Sonos 5500 System, Hewlett-Packard, Andover, USA) was inserted and positioned so that transgastric short axis LV view on middle papillary muscle level was obtained. Images were recorded for off-line evaluation. A 14G triple lumen catheter was inserted into the right internal jugular vein. A thermistor-tipped 4F arterial catheter (PV2024, Pulsion Medical Systems, Munich, Germany) was introduced into the femoral artery and then connected to the PiCCO monitoring system (Pulsion Medical Systems,

Munich, Germany). This system enables the measurement of arterial blood pressure, cardiac output and ITBV by means of transpulmonary (arterial) thermodilution with consequent continuous monitoring of cardiac output and SVV by the pulse contour analysis. Waveforms of arterial blood pressure (BP), central venous pressure (CVP) and airway pressure were recorded using dedicated software (Polyview, Grass Instruments, USA).

Haemodynamic parameters

All off-line measurements were carried out by an observer blinded to patients' identity, group and stage of the experiment (S.P.).

Left ventricular end-diastolic area index (LVEDAI) and fractional area change (FAC). End-diastole was defined as the frame with the largest LV cross-sectional area immediately after the R-wave, while end-systolic area (LVESA) was measured as the smallest LV area near the peak of the T-wave of the electrocardiogram. LVEDA and LVESA were measured by planimetry using leading edge to leading edge technique. Measurements of all cardiac cycles corresponding to one mechanical breath were analysed and averaged. LVEDA was indexed by dividing it by the body surface area. FAC was calculated as (LVEDA–LVESA)/LVEDA. Intra-observer variability for EDAI was 7 (2)% as determined by repeating measurements in eight randomized patients.

Intrathoracic blood volume index (ITBVI). ITBVI (ITBV indexed to the body surface area) was derived from the PiCCO monitoring system using the transpulmonary thermodilution curve following the triplicate injection of 0.2 ml kg⁻¹ cold saline via the central venous catheter for cardiac output measurement.

Left ventricular stroke volume index (LVSVI). LVSVI was calculated from cardiac output, measured by transpulmonary thermodilution by means of PiCCO monitor, divided by heart rate, and indexed to body surface area.

Systolic pressure variation (SPV) and dDown. The SPV was calculated off-line as a difference between the maximal and minimal values of the systolic BP during one mechanical breath immediately preceding an apnoea interval of 10 s. The dDown was determined as a difference between the minimal value of systolic BP during this breathing cycle and the value of systolic BP at the end of the period of apnoea.¹⁵

Pulse pressure variation (PPV). PPV was calculated as a difference between the maximal and minimal values of the pulse pressure (systolic arterial pressure minus diastolic arterial pressure of the same cardiac cycle) during one mechanical breath related to the average between these values.⁷

Stroke volume variation (SVV). SVV was obtained on-line from the PiCCO monitoring system. The SVV is calculated continuously as a difference between the maximal and minimal values of LVSV related to the mean LVSV within the 7.5-s period, the displayed value being a floating mean over the period of 30 s.

Table 1 Methods of measurement and calculation of haemodynamic parameters used in the study (see also Fig. 1)

Abbreviation	Name of parameter	Measurement	Formula for calculation
LVEDAI	Left ventricular end-diastolic area index	Off-line by planimetry from the video recording made by means of echocardiographic machine, then indexed by body surface area	Measured directly
LVESAI	Left ventricular end-systolic area index	Off-line by planimetry from the video recording made by means of echocardiographic machine, then indexed by body surface area	Measured directly
FAC	Fractional area change	Calculated after analysis of echocardiographic video recording	LVEDA-LVESA LVEDA
ITBVI SPV	Intrathoracic blood volume index Systolic pressure variation	Estimated by PiCCO system Measured off-line by analysis of arterial BP waveform	Difference between minimal and maximal values of systolic BP during mechanical breath
dDown	Delta Down	Measured off-line by analysis of arterial BP waveform	Difference between the minimal value of systolic BP during mechanical breath and its value during apnoea
PPV	Pulse pressure variation	Measured off-line by analysis of arterial BP waveform	Difference between the maximal and minimal values of the pulse pressure during one mechanical breath related to the average between these values
SVV RSVT	Stroke volume variation Respiratory systolic variation test	Estimated by PiCCO system Measured and calculated off-line from the recording of the response of arterial BP to respiratory manoeuvre	See explanation in text

Slope of the respiratory systolic variation test (RSVT). The RSVT manoeuvre was performed by sequence of three consecutive mechanical breaths with inspiratory pressures of 10, 20, and 30 cm H₂O (Fig. 1). The minimal values of the systolic BP during each of the three breaths of the RSVT manoeuvre were measured off-line from the recorded arterial pressure waveform and plotted against the corresponding values of the inspiratory pressure. The slope of the line of best fit for these three points was calculated using Microsoft Excel software.

CVP was determined as mean pressure during the end of expiration.

Methods for measurement and calculation of all haemodynamic parameters are summarized in Table 1.

Experimental protocol

After the induction of anaesthesia and initiation of haemodynamic monitoring the patients were observed for 10–15 min with no other interventions, fluid administration or changes in anaesthetic concentrations. A period of at least 5 min of stable BP, heart rate, CVP, and continuous cardiac output was required before obtaining the baseline set of haemodynamic measurements. Two consecutive volume loading steps (VLS) were then performed, each consisting of 250 ml of colloid solution (Haemaccel, 3.5% urea cross-linked degraded gelatin, Aventis Pharma, Germany), given over 5–7 min. Haemodynamic measurements were performed 3 min after each VLS.

The same sequence of haemodynamic measurements and volume loading was repeated after the end of the operation and before the transfer to the ICU. No measurements were

carried out in the presence of haemodynamic instability or immediately following changes of inotropic or anaesthetic medications.

Statistical analysis

All statistical analyses were performed using SPSS software. All variables were expressed as mean (SD). The significance of changes in the parameters during the experiment was analysed by means of ANOVA for repeated measures (General Linear Model) with volume load as a within-subject factor. The effect of LV function on the changes of haemodynamic parameters was analysed as a between-subject factor.¹⁶ Within-subjects contrasts were calculated for the levels of the within-subjects factor (volume of infused fluid).

Correlation between the change of LVSVI after and haemodynamic variables before each VLS was assessed by the Spearman's rank correlation coefficient.

The response to the VLS was considered positive if LVSVI increased by at least 15%. Difference between values of haemodynamic parameters preceding VLS of 'responders' and 'non-responders', that is steps with positive response and no response to fluid challenge (increase of LVSVI of <15%) was evaluated by a two-tailed *t*-test. The distribution of 'responders', between patients with normal and impaired LV function was evaluated by the exact Fisher's test. Comparison of haemodynamic parameters during the experiment between groups with normal and abnormal LV function was done by *t*-test with Dunn-Sidak correction.¹⁶

Evaluation of the ability of the tested parameters to predict positive fluid responsiveness was performed by

constructing receiver operating characteristic (ROC) curves.¹⁷ The area under each curve was calculated, and the respective values were compared.¹⁸ A value of ROC curve of 1.0 indicates perfect performance with 100% sensitivity and 100% specificity for the corresponding indicator, whereas the value of 0.5 means that the predictive performance of the indicator is no better than chance.

A probability value of less than 0.05 was considered significant for all differences.

Results

Eighteen patients (16 males and two females) were included in the study. There were 10 patients in Group 1 (normal LV function), and eight in Group 2 (impaired LV function). Patients in Group 1 were significantly younger than patients in Group 2, but there were no differences between the groups in body weight, body surface area, cardiopulmonary bypass time, or aortic clamp time (Table 2). FAC, determined by TOE at baseline, was significantly higher in patients in Group 1 than in Group 2 [0.52 (0.06) vs 0.35 (0.10), respectively, $P=0.005$], while EDAI was significantly lower [8.0 (1.4) cm² m⁻² vs 12.9 (3.5) cm² m⁻², $P=0.002$]. These differences between groups did not change throughout the study. There were no differences in any of the other

haemodynamic variables between groups at any stage of the experiment.

Fluid loading was not performed in one patient after the operation because of an unexpectedly extensive procedure and a need for massive postoperative inotropic therapy. A total of 70 VLS were performed and analysed whereby 32 (46%) were associated with positive response of the LVSVI to the fluid administration ('responders'), while 38 (54%) were 'non-responders'.

Changes of haemodynamic variables during the study are presented in Table 3.

No influence of preoperative LV function taken as a between-subject factor was found on the haemodynamic response to VLS. The distribution of 'responders' and 'non-responders' was equal between patients with normal and abnormal LV function. Moreover, there were no differences in SVI, MAP (mean arterial pressure), ITBVI, SPV, dDown, SVV, PPV, RSVT, and MAP between the two groups at any stage of the study. We have therefore pooled all data for the entire study population.

Fluid loading both before and after the operation produced a significant increase of EDAI, LVSVI, CVP, and MAP, and a significant decrease of SPV, dDown, PPV, SVV, and RSVT (Table 3). The ITBVI changed significantly in response to volume load before the surgery in Group 2 only.

The MAP, EDAI, SVV, slope of RSVT, PPV, SPV, and dDown, but not the CVP, ITBVI, and HR values before the VLS differed significantly between 'responders' and 'non-responders' (Table 4).

The analysis of ROC curves was performed without separation of patients into two groups because of the lack of the influence of LV function on the observed response to VLS.

The areas under the ROC curves for MAP, ITBVI, EDAI, SPV, dDown, PPV, SVV, and RSVT (Figs 2 and 3; Table 5) are significantly larger than 0.5. The area under the ROC curve for RSVT and PPV was significantly larger than that

Table 2 Patient characteristics of the study population. BSA, body surface area; LVEF, left ventricular ejection fraction, estimated by preoperative ventriculography; CPB, cardiopulmonary bypass; AoCx, aortic cross-clamp. Data are mean (range) or mean (SD). * $P<0.05$

	Good LV	Poor LV	Total
Age, yr	61.9 (49–75)	71.5 (62–84)*	66.2 (49–84)
BSA, m ²	2.0 (0.2)	1.8 (0.16)	1.9 (0.22)
Preoperative LVEF%	59.3 (5.3)	33.1 (5.3)*	45.3 (14.4)
CPB time, min	66.6 (28.8)	66.4 (20.1)	66.5 (23.4)
AoCx time, min	32.4 (13.1)	38.2 (13.9)	35.3 (13.1)

Table 3 Changes of haemodynamic variables during the experiment. Data presented as mean (SD). HR, heart rate; MAP, mean arterial pressure; LVSVI, left ventricular stroke volume index; CVP, central venous pressure; ITBVI, intrathoracic blood volume index; EDAI, left ventricular end-diastolic area index; FAC, fractional area change; SVV, stroke volume variation; SPV, systolic pressure variation; dDOWN, delta DOWN; PPV, pulse pressure variation; RSVT, slope of respiratory systolic variation test. * $P<0.05$ in comparison with the value at the previous stage of the volume load sequence

	Before surgery			After surgery		
	Baseline	After 250 ml	After 500 ml	Baseline	After 250 ml	After 500 ml
HR, beats min ⁻¹	62.3 (10.9)	60.3 (10.9)	60.9 (14.0)	84.1 (14.0)	83.0 (15.2)	81.9 (14.6)
MAP, mm Hg	77.9 (13.5)	82.0 (13.1)	88.3 (16.5)*	74.9 (11.5)	79.7 (11.2)	83.6 (11.4)*
LVSVI, cc m ⁻²	33.4 (9.8)	38.1 (12.2)*	40.5 (11.7)*	27.5 (5.9)	32.8 (5.5)*	36.1 (5.2)*
CVP, mm Hg	7.8 (3.1)	9.1 (2.9)*	11.2 (3.9)*	9.3 (2.6)	10.8 (3.3)*	12.1 (3.1)*
ITBVI, cc m ⁻²	999 (394)	1009 (337)	1003 (272)	931 (268)	938 (233)	985 (256)*
EDAI (good LV), cm ² m ⁻²	8.0 (1.4)	9.3 (1.9)*	10.5 (1.8)*	6.3 (0.7)	7.2 (0.8)*	8.0 (0.8)*
EDAI (poor LV), cm ² m ⁻²	12.9 (3.5)	13.9 (3.8)*	15.1 (3.7)*	11.4 (2.6)	12.6 (2.5)*	13.5 (2.7)*
FAC (good LV)	0.52 (0.06)	0.58 (0.08)	0.59 (0.08)	0.58 (0.05)	0.59 (0.06)	0.58 (0.07)
FAC (poor LV)	0.35 (0.10)	0.37 (0.10)	0.37 (0.12)	0.39 (0.09)	0.42 (0.10)	0.41 (0.09)
SVV, %	12.2 (7.8)	6.8 (4.8)*	5.8 (5.1)*	18.6 (5.5)	11.5 (4.5)*	8.0 (3.4)*
SPV, mm Hg	8.1 (3.4)	5.5 (3.2)*	3.1 (1.8)*	12.8 (5.8)	9.6 (4.6)*	7.0 (4.7)*
DDOWN, mm Hg	6.3 (4.2)	4.3 (3.8)*	2.4 (2.4)*	7.7 (4.4)	4.7 (3.8)*	2.9 (4.2)*
PPV, %	10.3 (10.9)	5.3 (5.8)*	1.2 (3.5)*	18.0 (10.2)	10.9 (5.8)*	5.8 (6.7)*
RSVT slope, mm Hg/cm H ₂ O	0.56 (0.25)	0.28 (0.24)*	0.15 (0.17)*	0.73 (0.31)	0.57 (0.25)*	0.37 (0.24)*

Table 4 Differences in indicators of LVSV response to volume load between VLS with positive response and VLS with no response [mean (SD)]. MAP, mean arterial BP; EDAI, left end-diastolic area index; SVV, stroke volume variation; PPV, pulse pressure variation; RSVT, the slope of respiratory systolic variation test; SPV, systolic pressure variation; dDOWN, delta DOWN; CVP, central venous pressure; ITBVI, intrathoracic blood volume index. * $P < 0.005$; ** $P < 0.001$

	MAP (mm Hg)	EDAI ($\text{cm}^2 \text{m}^{-2}$)	SVV (%)	PPV (%)	RSVT [mm Hg/ cm H_2O]	SPV (mm Hg)	dDOWN (mm Hg)	CVP (mm Hg)	ITBVI (cc m^{-2})
Responders	73.9 (12.2)*	8.9 (2.6)*	17.0 (6.3)**	17.5 (8.5)**	0.75 (0.23)**	12.4 (4.4)**	8.8 (3.4)**	8.7 (2.3)	901 (316)
Non-responders	83.5 (10.7)	11.7 (3.8)	8.2 (4.9)	4.5 (4.8)	0.31 (0.18)	5.6 (2.9)	2.8 (2.3)	10.0 (3.6)	1031 (299)

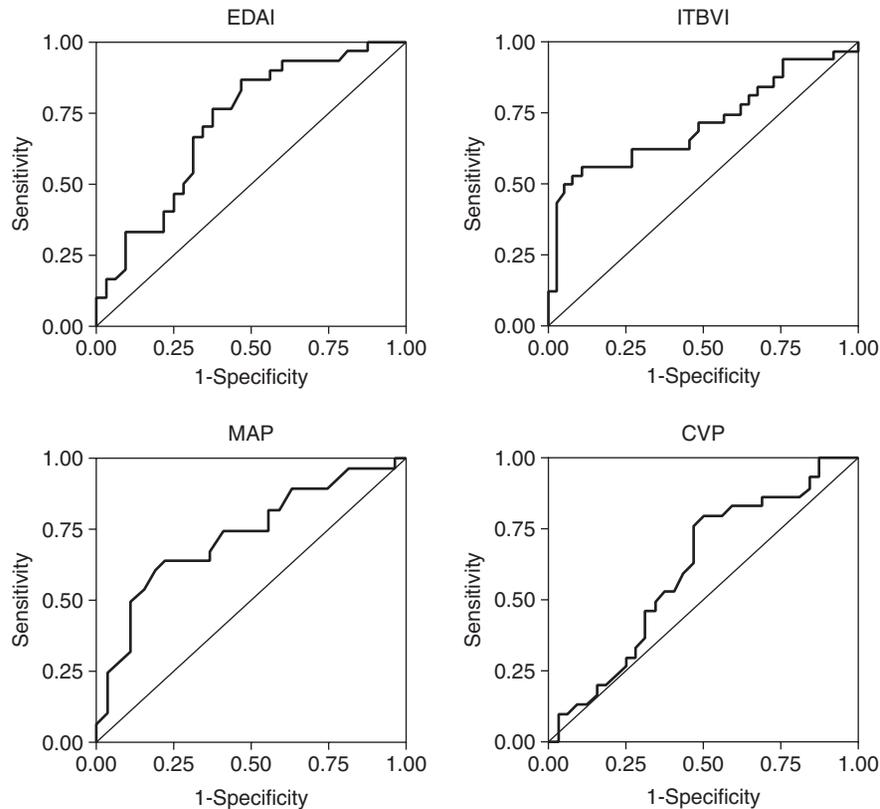


Fig 2 ROC curves for EDAI, ITBVI, MAP, and CVP.

for SVV, EDAI, ITBVI, and MAP. The area for CVP was not significantly different from 0.5.

Significant correlation was found between the change of LVSVI following VLS and the slope of RSVT, PPV, dDown, SPV, SVV, EDAI, and ITBVI before volume loading with rho-values of 0.70, 0.68, 0.67, 0.62, 0.58, -0.52 ($P < 0.01$), and -0.32 ($P < 0.05$), respectively. No significant correlation between the volume loading induced change of LVSVI and the CVP was found.

Discussion

Optimization of cardiac output by repeated volume loading has been shown to improve clinical outcome in patients undergoing anaesthesia and surgery.^{1 19 20}

However, this method might carry the risk of potentially deleterious fluid overload. Indeed, other reports have shown that more restrictive fluid regimen may lead to better

outcome after abdominal²¹ and vascular surgery.²² It is possible that any therapeutic approach to fluid management will depend on the chosen method of haemodynamic assessment in general, and on the accurate prediction of fluid responsiveness in particular.²³

In mechanically ventilated patients, functional haemodynamic parameters, derived from the analysis of the response of the arterial pressure to the mechanical breath, have been shown to be superior to static indicators of cardiac preload in their ability to predict fluid responsiveness,^{2 4 6 7 10 11} and distinguish between ‘responders’, who will significantly increase their stroke volume after fluid administration, and ‘non-responders’, who have already reached or are approaching the flat part of their Frank–Starling curve. Our present study confirms once more that these parameters reflect fluid responsiveness better than the CVP, EDA, or ITBV. We have found, that EDAI, which is frequently regarded as a ‘gold standard’ for the evaluation of LV

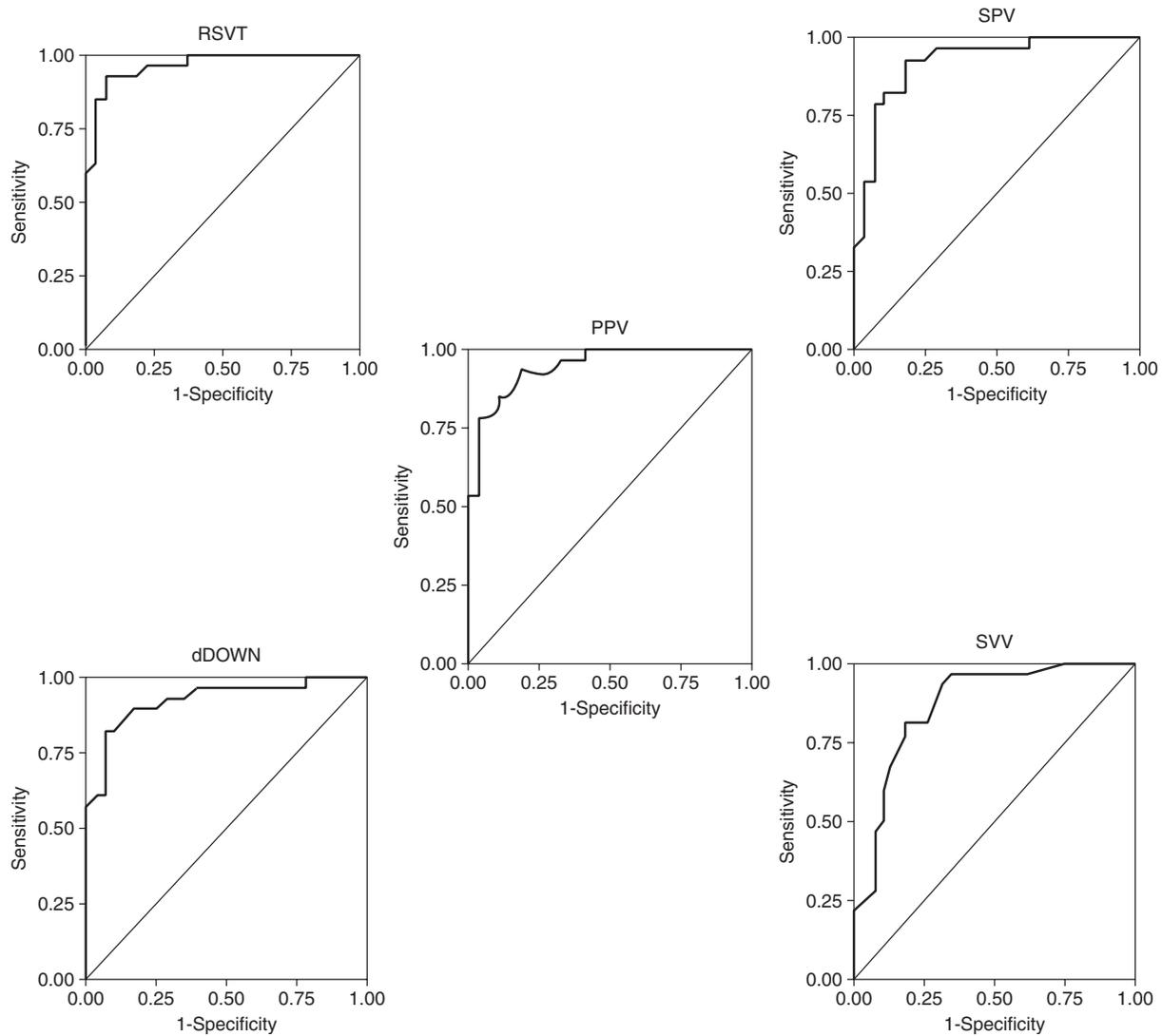


Fig 3 ROC curves for RSVT, dDOWN, SPV, SVV, and PPV.

Table 5 Comparison of areas under the ROC curves for the indicators used for the prediction of the response of LVSV to fluid administration. MAP, mean arterial blood pressure; CVP, central venous pressure; ITBVI, intrathoracic blood volume index; EDAI, left ventricular end-diastolic area; SPV, systolic pressure variation; dDOWN, delta DOWN; SVV, stroke volume variation; PPV, pulse pressure variation; RSVT, respiratory systolic variation test. * $P < 0.05$ in comparison with RSVT; ** $P < 0.001$ in comparison with RSVT

	ROC area	95% CI	Proposed threshold value	Sensitivity	Specificity
MAP	0.73**	0.60–0.87	<76.5 mm Hg	64%	77%
CVP	0.61**	0.47–0.75	NS		
ITBVI	0.71**	0.59–0.84	<845 cc m ⁻²	63%	73%
EDAI	0.71**	0.59–0.84	<9.05 cm ² m ⁻²	63%	69%
SPV	0.92	0.85–0.99	>8.5 mm Hg	82%	86%
dDOWN	0.92	0.85–1.0	>5.0 mm Hg	86%	86%
SVV	0.87*	0.79–0.96	>11.5%	81%	82%
PPV	0.95	0.89–1.0	>9.4%	86%	89%
RSVT	0.96	0.92–1.0	>0.51 mm Hg/cm H ₂ O	93%	89%

preload in patients with both good and abnormal LV function,²⁴ was indeed higher in patients with impaired LV function, and increased significantly further following fluid loading. However, its predictive value, as reflected by the

area under the ROC curve, was relatively low. In our study population volume loading failed to increase LVSVI in some patients with EDAI less than 7 cm² m⁻², while it caused a positive response in some patients with EDAI larger than

15 cm² m⁻². Moreover, patients with impaired preoperative systolic LV function and relatively large baseline EDA had the same LVSVI as well as the number of responses as did those patients with normal LV function and dimensions.

These findings indicate that despite their relatively large LV dimensions and lower FAC, patients with impaired LV function may often be on the steep part of the Frank–Starling curve and be equally responsive to volume load as patients with preserved LV function. Although we did not find differences in response to volume load between groups of patients with preserved and abnormal LV systolic function, this may not be true in patients with very poor LV function (LVEF <30%).

Another volumetric parameter that we examined was the ITBVI, which was shown previously to correlate significantly with the SPV and dDown during experimental haemorrhage.⁵ Although the area under the ROC curve for ITBVI was significantly larger than 0.5, this parameter also had lower predictive ability of fluid responsiveness compared with functional haemodynamic parameters.

The CVP, which is still probably the most common parameter, which is being used for the evaluation of intravascular volume status, have been found to lack any predictive value at all.

These findings confirm the hypothesis that the preload and fluid responsiveness are two different physiological entities, and that even the most precise estimation of cardiac preload does not consistently provide the correct information regarding the patient's response to fluid administration.

Our study offers the first systematic comparison of the various functional haemodynamic parameters that are derived from the respiratory-induced variations in the arterial pressure in the mechanically ventilated patients, in regard to their ability to predict the LV response to volume load. In patients, undergoing cardiac surgery and ventilated in the pressure-controlled mode with inspiratory pressures of 15–20 cm H₂O, we have found that the PPV has a significantly better predictive ability than the SVV, while the performance of SPV and dDOWN is intermediate (Table 4). Indeed concerns have been raised concerning the lack of sufficient validation of pulse contour analysis to accurately follow instantaneous changes in the SV.²⁵ Although several studies established good ability of SVV to predict volume responsiveness,^{10,11} another study, performed in a population of patients similar to ours, could not confirm this finding.²⁶

Our current study clearly demonstrates that the SVV, though somewhat less accurate than the PPV, is still an excellent predictor of fluid responsiveness, and as such is far better than static parameters of LV preload.

However, the major limitations of the clinical use of the SVV, PPV, SPV, and dDown is that they can be used reliably only during fully controlled mechanical ventilation, and may become unreliable in patients who breathe spontaneously or who are on partial ventilatory support.²⁷ In fact, all these parameters were validated only during

volume-controlled mechanical ventilation with tidal volume of 8–12 ml kg⁻¹.²⁵ Obviously, larger or smaller tidal volumes will create respectively larger or smaller fluctuations of the LVSV and hence in these parameters.¹²

The main advantage of the new functional haemodynamic parameter that is presented in our study, the RSVT, is in the standardized stimulus that is being used to test fluid responsiveness independently of the set tidal volume. The uniqueness of the RSVT relative to the other functional haemodynamic parameters stems also from the fact that it actually estimates the slope of the Frank–Starling curve by producing sequential incremental challenge to LV filling, caused by standardized respiratory manoeuvre. In addition, since the RSVT is calculated only from the lowest values of the systolic arterial pressure, it is not influenced by the early inspiratory augmentation of the LVSV.¹³ This phenomenon becomes the predominant component of BP fluctuations during hypervolaemia and/or congestive heart failure and is associated with the lack of fluid responsiveness.^{4,6,13,28} The fact that the SPV and SVV are based on the difference between the maximal and minimal values of systolic arterial pressure during the mechanical breath, may potentially reduce their accuracy in the prediction of volume responsiveness, especially in the presence of impaired LV function.¹¹

Our results show that the RSVT may indeed be a more accurate predictor of fluid responsiveness in comparison with established functional haemodynamic parameters. Together with PPV, the RSVT has the best sensitivity and specificity, which, when combined with the standardization it offers, make it very promising for future evaluation. In its current form, however, the performance of RSVT demands complex respiratory manoeuvre and is dependent on off-line measurements and calculations, which precludes its clinical use. However, with the introduction of the RSVT manoeuvre into existing ventilators, and interfacing the ventilator with monitors that are capable of calculating the RSVT on-line in real time, the performance of this test in future may become feasible for clinical use in mechanically ventilated patients.

The major limitation of our study is that we have arbitrarily defined both the volume load that was used (250 ml of plasma expander) as well as what was considered to be 'a positive response to volume load'. We defined our primary outcome variable as a 'response' (increase of SVI of 15% or more of its previous value). This choice was done in order to obtain data comparable to findings from similar research.² In the study, performed in a similar patient's population, an excellent agreement has been found between arterial thermodilution and pulmonary thermodilution, which remains the current clinical standard for cardiac output measurement.²⁹ Since triple measurement of cardiac output using pulmonary artery thermodilution can reliably detect differences of 12–15% in cardiac output value,³⁰ we assume that the technique we used was accurate enough to detect changes of this magnitude.

One may claim, that the response of SVI to fluid load should be considered as a continuous variable, and that multivariate analysis, which combines other physiological parameters characterizing preload, would be more appropriate in its prediction. However, the ROC curve is a valid statistical method for the assessment and comparison of the ability of different physiological parameters to diagnose or predict absence or presence of a certain physiological condition³¹ (in our case, fluid responsiveness), which was, actually, the goal of our study. Supplying the clinician with the complex information which includes several physiological variables and results derived from multivariate analyses, appeared to us to be of less practical value, than a simple 'yes' or 'no' answer as to the predicted effect of fluid administration.

Another limitation of our study is that it was conducted in elective haemodynamically stable patients undergoing cardiac surgery. It might not reflect the haemodynamic situation in septic or trauma patients.

The other limitation of our study is the fact that multiple measurements were carried out, both before and after surgery, in the same patients, and that these measurements were then treated as independent observations for the construction of ROC curves. However, this is true for the statistical analysis performed for all investigated variables, and hence the difference found between parameters may be real.

We conclude that functional haemodynamic parameters based on the analysis of the arterial pressure waveform predict volume responsiveness of ventilated patients with either preserved or abnormal LV function better than static indicators of cardiac preload. Of these functional parameters, the newly introduced RSVT seems to have a promising potential as it presents the first standardized respiratory manoeuvre for haemodynamic assessment and has better ability to predict fluid responsiveness.

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