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Prediction of fluid responsiveness in patients during cardiac surgery

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Background. Left ventricular stroke volume variation (SVV) has been shown to be a predictor of fluid responsiveness in various subsets of patients. However, the accuracy and reliability of SVV are unproven in patients ventilated with low tidal volumes.

Methods. Fourteen patients were studied immediately after coronary artery bypass grafting (CABG). All patients were mechanically ventilated in pressure-controlled mode [tidal volume 7.5 (1.2) ml kg^{-1}]. In addition to standard haemodynamic monitoring, SVV was assessed by arterial pulse contour analysis. Left ventricular end-diastolic area index (LVEDAI) was determined by transoesophageal echocardiography. A transpulmonary thermodilution technique was used for measurement of cardiac index (CI), stroke volume index (SVI) and intrathoracic blood volume index (ITBI). All variables were assessed before and after a volume shift induced by tilting the patients from the anti-Trendelenburg (30° head up) to the Trendelenburg position (30° head down).

Results. After the change in the Trendelenburg position, SVV decreased significantly, while CI, SVI, ITBI, LVEDAI, central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP) increased significantly. Changes in SVI were significantly correlated to changes in SVV ($r = 0.70$; $P < 0.0001$) and to changes in LVEDAI, ITBI, CVP and PAOP. Only prechallenge values of SVV were predictive of changes in SVI after change from the anti-Trendelenburg to the Trendelenburg position.

Conclusions. In patients after CABG surgery who were ventilated with low tidal volumes, SVV enabled prediction of fluid responsiveness and assessment of the haemodynamic effects of volume loading.

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Hypotension is one of the most frequently encountered haemodynamic disturbances in the perioperative setting. In most patients, absolute or relative depletion of intravascular volume is the principal cause of arterial hypotension.[1] However, impaired ventricular contractility, for example after cardiac surgery, may also cause arterial hypotension. In this situation, further volume loading is not accompanied by an increase in cardiac output but may lead to deterioration of cardiopulmonary function.[2 3] Therefore, it is important to identify patients in whom augmentation of cardiac preload leads to an increase in stroke volume. Routinely used static variables of cardiac preload, such as filling pressures [central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP)] and volumetric variables [intrathoracic blood volume index (ITBI) and left ventricular end-diastolic area index (LVEDAI)] have been studied extensively for their ability to predict fluid responsiveness, often with conflicting results.[1 2 4–9]

Recently, dynamic preload variables, such as pulse contour-derived stroke volume variation (SVV), have been introduced into clinical practice.[9–11] SVV is derived from cyclic changes of stroke volume induced by heart–lung interactions during mechanical ventilation. Therefore, both cardiac filling and tidal volume, accompanied by the associated changes in intrathoracic pressure, can influence SVV. Recent studies have demonstrated the usefulness of

SVV as a sensitive indicator of fluid responsiveness in patients during neurosurgical procedures[10] and in the critical care unit.[9 12 13] However, the value of SVV in predicting fluid responsiveness in patients ventilated with lower tidal volumes remains controversial.[14–17] The present study was performed to investigate the value of static preload variables and SVV in predicting fluid responsiveness in cardiac surgical patients ventilated with low tidal volumes.

Patients and methods

After approval by the institutional review board committee of the medical faculty of the university hospital, Aachen, and written informed consent, 16 patients undergoing elective CABG-surgery participated in the study. Patients with emergency operations, occlusive peripheral arterial disease, intracardiac shunts, significant valvular heart disease, and severely decreased left ventricular function (ejection fraction ⩽30%) were excluded from the study. All patients were receiving regular β-blocking agents before surgery, which were continued until the day of surgery.

Before induction of anaesthesia, a 5-F thermistor-tipped catheter (PV2015L20A, Pulsiocath; Pulsion Medical Systems, Munich, Germany) was inserted into the femoral artery. After induction of anaesthesia, a 7.5-F central venous catheter (AG-15854-E; Arrow International; Reading, PA, USA) and a 8.5-F introducer sheath (SI-09880; Arrow International) were placed in the right internal jugular vein. A 7-F pulmonary artery catheter (PV2047, VoLEF Catheter PACC 947, Pulsion Medical Systems) was inserted into the pulmonary artery. Pressure transducers (PV8115; Pulsion Medical Systems) were positioned on the mid-axillary line and fixed to the operation table so that they remained at the atrial level during the Trendelenburg manoeuvre.

Haemodynamic monitoring

Routine haemodynamic variables (heart rate, mean arterial pressure and CVP) were recorded continuously (S/5; Datex-Ohmeda, Duisburg, Germany). Transpulmonary thermodilution curves were measured with an arterial thermodilution catheter connected to a haemodynamic computer (PiCCO-plus V 5.2.2; Pulsion Medical Systems), allowing the discontinuous measurement of cardiac index (CI), stroke volume index (SVI), global end-diastolic volume index (GEDI) and ITBI by aortic thermodilution. In addition, arterial pressure, left ventricular CI, SVI and SVV were monitored continuously by pulse-contour analysis. The pulmonary artery catheter was connected to a haemodynamic monitor (VoLEF V 1.0; Pulsion Medical Systems), recording pulmonary artery pressure.

Indicator dilution measurements were performed by triple bolus injections of ice-cooled saline 0.9%, 20 ml, into the right atrium. Injections were spread randomly over the respiratory cycle. Each value represents the average of three measurements. Results were normalized to body surface area. In addition, the transpulmonary thermodilution measurements were required for initial calibration of pulse-contour analysis by the assessment of aortic impedance.[18]

Cardiac index (CI_{TDao}) and SVI were assessed from the aortic thermodilution curves according to the Stewart–Hamilton principle.

ITBI and GEDI were calculated with the mean transit time (mtt_{TDao}) and the down-slope time (dst_{TDao}) of the aortic thermodilution curve:

$$GEDI = CI_{TDao} \times (mtt_{TDao} - dst_{TDao}) \quad (1)$$

$$ITBI = 1.25 \times GEDI \quad (2)$$

SVV represents the variation (as a percentage) of the beat-to-beat pulse contour-derived stroke volume (SV) averaged during the last 30 s (SV_{mean}):

$$SVV = (SV_{max} - SV_{min})/SV_{mean} \quad (3)$$

For determination of the highest SV (SV_{max}) and the lowest SV (SV_{min}), a continuously sliding time period of 30 s was divided into four 7.5-s periods. The highest and lowest SVs of the four periods were then averaged to SV_{max} and SV_{min}.[11]

Transoesophageal echocardiography (TOE)

A multiplane TOE probe (Omniplane II T6210; Philips Medical Systems, Eindhoven, The Netherlands), connected to an ultrasonograph (Sonos 5500; Philips Medical Systems, Eindhoven, The Netherlands) was positioned to visualize the transgastric short-axis view of the left ventricle, at the level of the mid-papillary muscles. This position was maintained throughout the whole study period. Simultaneously acquired TOE images and ECG signals were recorded on a magneto-optical disk and analysed off-line by an experienced investigator blinded to the haemodynamic results. Left ventricular end-diastolic area was measured at the peak of the electrocardiographic R-wave and by manually tracing the endocardial border including the papillary muscles. For each measurement, an average of at least four consecutive cardiac beats throughout the respiratory cycle was evaluated.

Study protocol

Of the 16 participating patients, two were excluded from analysis: one because of acute right ventricular failure after weaning from cardiopulmonary bypass, the other due to poor quality of the echocardiographic images. The remaining 14 patients were studied at the end of surgery, immediately after chest closure and before transfer to the intensive care unit. No adverse effects were observed during the study. Echocardiographic evaluation of left ventricular contractility revealed no significant impairment of systolic function or new regional wall motion abnormalities before the study.

All patients were anaesthetized and underwent mechanical ventilation in pressure-controlled mode with 100% oxygen. The inspiratory pressure level was adjusted to achieve a tidal volume of approximately 8 ml kg^{-1} throughout the

procedure. Inspiratory-to-expiratory time ratio was set to 1:1. Vasoactive medication was not changed during the study period.

After baseline haemodynamic and echocardiographic measurements, the patients were raised to the anti-Trendelenburg position (30° head up), inducing relative depletion of central blood volume. Mean arterial blood pressure decreased significantly but remained above the safety limit of 55 mm Hg. A shift of volume from the extrathoracic into the intrathoracic compartment was then achieved by performing the Trendelenburg manoeuvre (30° head down), thus inducing a shift of intravascular volume from the extra- to the intrathoracic compartment. Haemodynamic and echocardiographic measurements were performed in each position after at least 5 min of stabilization. To investigate the relation between changes in static (EDAI, ITBI, PAOP, CVP) and dynamic variables (SVV) (Δ preload variable) and concomitant changes in SVI (Δ SVI), linear regression analysis was performed after each step. To study the ability to predict fluid responsiveness, changes in SVI (Δ SVI) and cardiac index (Δ CI) in response to the volume shift were correlated to corresponding SVV values in the anti-Trendelenburg position and static preload variables by linear regression analysis.

Statistics

On the basis of a previous study, power analysis revealed a sample size of eight patients for a 25% effect on volumetric indices, when a level of significance of 0.05% and a power of 80% were to be achieved.[19] All data in the tables and figures are presented as mean (SD). Results were analysed using a commercially available software package (Statistica© for Windows version 6.0; Statsoft, Tulsa, OK, USA). The effects of the volume challenge on haemodynamic variables were tested with analysis of variance for repeated measurements (ANOVA). If there were significant differences, *post hoc* testing was performed using Tukey's honest significant difference (HSD) test. Pearson's product moment correlation (r) and Spearman's rank correlation (p) were used for linear regression analysis. A level of $P<0.05$ was considered statistically significant.

Results

Data concerning biometric variables and pharmacological haemodynamic support are given in Table 1. After positioning the patients in the anti-Trendelenburg position, all haemodynamic variables except heart rate, ITBI and systemic vascular resistance index decreased significantly compared with baseline (Table 2). As expected, SVV increased significantly in the anti-Trendelenburg position compared with baseline. When the position was changed from the anti-Trendelenburg to the Trendelenburg position, all patients responded with an increase in SVI of more than 5%. With the exception of heart rate and systemic vascular resistance index, all other haemodynamic variables, including SVV, changed significantly from the anti-Trendelenburg to the Trendelenburg position (Table 2). Airway pressures and tidal volumes showed no significant differences between the neutral, Trendelenburg and anti-Trendelenburg positions.

Changes in SVI showed a significant correlation to Δ ITBI ($r=0.89$; $P<0.0001$), to Δ LVEDAI ($r=0.93$; $P<0.0001$) and to Δ SVV ($r=-0.70$; $P<0.0001$) (Fig. 1). Moreover, Δ SVI had a significant correlation to Δ PAOP ($r=0.60$; $P<0.001$) and to Δ CVP ($r=0.71$; $P<0.0001$) in this setting. A significant interaction between Δ SVV and Δ LVEDAI ($r=-0.77$, $P<0.0001$) was observed.

Prechallenge values of SVV correlated significantly to Δ SVI ($r=0.61$; $P<0.05$) (Fig. 2) and to Δ CI ($r=0.71$; $P<0.01$). In contrast, prechallenge values of PAOP and CVP were not significantly correlated to Δ SVI (Fig. 2) and Δ CI.

The volumetric variables ITBI and LVEDAI were also not correlated to Δ SVI and Δ CI, suggesting that neither can predict the individual response to fluid challenge in this setting.

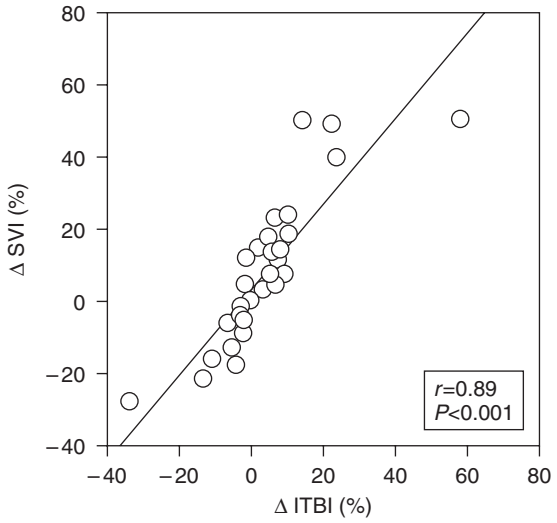
Table 1 Biometric variables and data on pharmacological haemodynamic support (mean (range) or (SD))

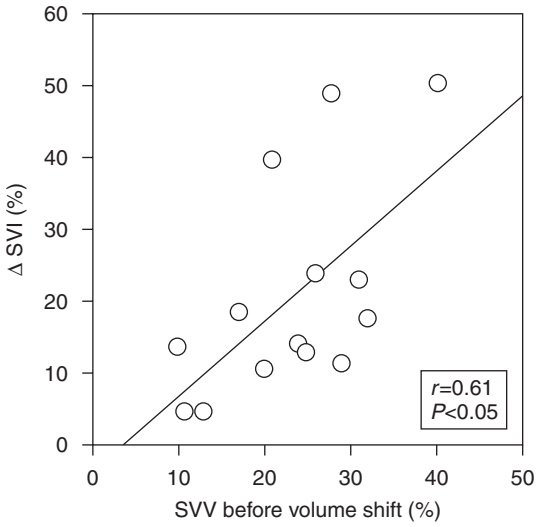
Age (yr) (range)	63 (45–84)
Height (cm)	175.1 (5.5)
Weight (kg)	88.4 (9.9)
Body surface area (m^2)	2.04 (0.12)
Epinephrine ($\mu g\ kg^{-1}\ min^{-1}$)	0.01 (0.01)
Norepinephrine ($\mu g\ kg^{-1}\ min^{-1}$)	0.06 (0.03)

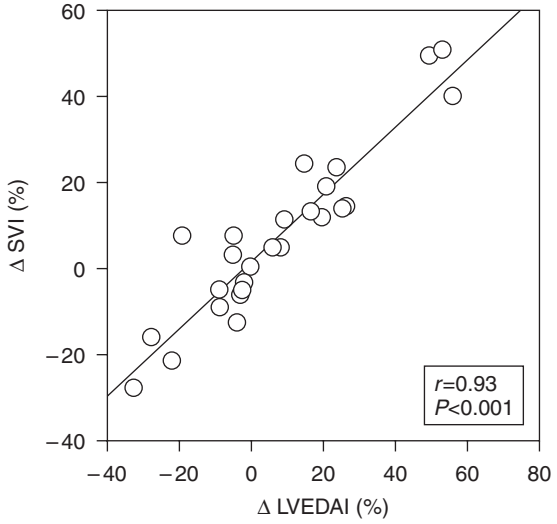
Table 2 Haemodynamic and ventilatory variables (mean (SD)) at baseline, in the anti-Trendelenburg position (30° head up) and in the Trendelenburg position (30° head down).*$P<0.05$, **$P<0.01$ *vs* baseline, °$P<0.05$, °°$P<0.01$, Trendelenburg *vs* anti-Trendelenburg position

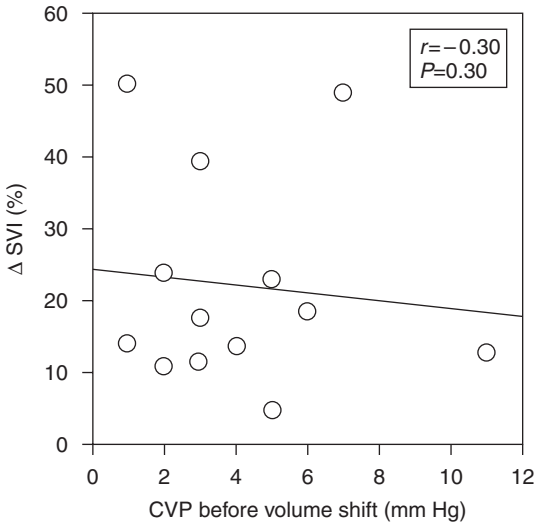
	Baseline	Anti-Trendelenburg	Trendelenburg
HR (min^{-1})	86 (11)	86 (10)	85 (15)
MAP (mm Hg)	72 (6)	65 (7)*	90 (10)°°,**
CVP (mm Hg)	11 (3)	4 (4)**	19 (3)°°,**
MPAP (mm Hg)	24 (4)	16 (4)	33 (4)°°,**
PAOP (mm Hg)	12 (3)	6 (3)**	20 (4)°°,**
CI (litre $min^{-1}\ m^{-2}$)	2.93 (0.63)	2.72 (0.61)*	3.17 (0.50)°°,*
SVI (ml $min^{-1}\ m^{-2}$)	34.71 (8.96)	32.43 (8.82)*	38.49 (8.83)°°,**
SVRI (dyn s $cm^{-5}\ m^{-2}$)	1719 (359)	1868 (393)	1811 (391)
SVV (%)	17.5 (4.2)	23.4 (8.3)**	14.00 (5.11)°°
ITBI (ml m^{-2})	786 (152)	741 (96)	830 (157)°°
LVEDAI ($cm^2\ m^{-2}$)	5.78 (1.68)	5.24 (1.87)**	6.36 (1.80)°°,**
P_{insp} (mm Hg)	21.31 (3.55)	21.75 (2.68)	22.00 (3.38)
PEEP (mm Hg)	2.81 (1.84)	2.88 (1.54)	3.43 (1.18)
V_T (ml kg^{-1})	7.51 (1.25)	7.29 (0.79)	6.65 (1.28)
RR (min^{-1})	12 (1)	12 (1)	12 (1)

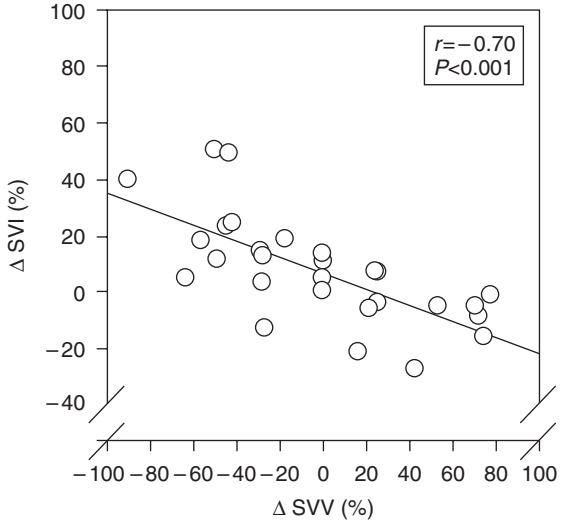
HR=heart rate; MAP=mean arterial pressure; CVP=central venous pressure; MPAP=mean pulmonary artery pressure; PAOP=pulmonary artery occlusion pressure; CI=cardiac index measured by aortic thermodilution; SVI=stroke volume index; SVRI=systemic vascular resistance index; SVV=stroke volume variation; ITBI=intrathoracic blood volume index; LVEDAI=left ventricular end-diastolic area index; P_{insp}=peak inspiratory pressure; PEEP=positive end-expiratory pressure; V_T=tidal volume; RR=respiratory rate.











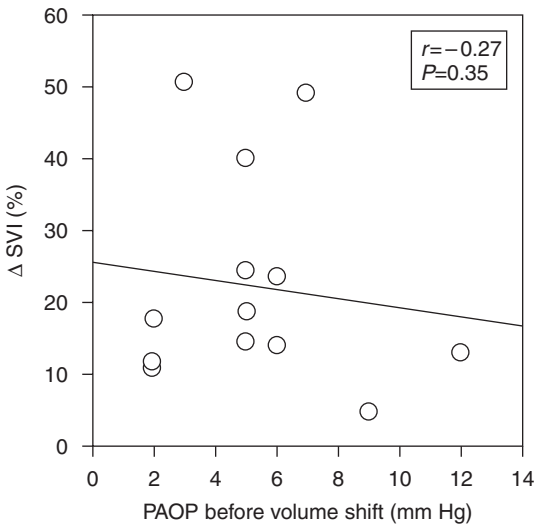


Fig 1 Linear correlation analysis of the relationship between changes in stroke volume index (Δ SVI) and changes in intrathoracic blood volume index (Δ ITBI), left ventricular end diastolic index (Δ LVEDAI) and stroke volume variation (Δ SVV) associated with changes in body position.

Fig 2 Linear correlation analysis of the relationship between changes in stroke volume index (Δ SVI) after volume challenge and stroke volume variation (SVV), central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP) before volume challenge. Volume challenge was performed by changing the patient's position from 30° head-up to 30° head-down.

Discussion

The results suggest that pulse contour-derived variation in SVV is predictive of the fluid response in cardiac surgical patients ventilated with low tidal volumes. In contrast, routinely used static variables of cardiac preload, such as PAOP, CVP, EDAI and ITBI, failed to predict volume responsiveness.

The use of SVV as a functional haemodynamic variable is based on the heart–lung interactions during mechanical ventilation.[20–23] Respiratory-induced changes in left ventricular preload result in cyclic changes in left ventricular stroke volume and in arterial pressure.[20–23] In the presence of hypovolaemia, the left ventricle usually operates on the ascending part of the Frank–Starling curve. Thus, changes in stroke volume should be more pronounced when compared with normovolaemia. SVV and the surrogate variables systolic pressure variation (SPV) and pulse pressure variation (PPV) have been studied previously in patients during brain surgery, in critically ill patients after cardiac surgery and in patients suffering from septic shock.[7 9 10 12 24] SVV, SPV and PPV are highly sensitive in predicting fluid responsiveness in these settings. Thus, dynamic preload variables were considered to be important in guiding fluid and catecholamine therapy in critically ill patients.[3 25]

However, SVV depends not only on cardiac filling status but also on changes in intrathoracic pressure associated with the application of tidal volume.[14 17] It has been demonstrated that accurate prediction of volume responsiveness by SVV is feasible when tidal volumes of 10[10 12] or 13–15 ml kg^{-1} are used.[11] In contrast, Wiesenack and colleagues were not able to demonstrate a predictive value of SVV in cardiac surgical patients ventilated with tidal volumes of 10 ml kg^{-1} when studying a volume challenge with colloid solutions.[15] However, the interpretation of these results is difficult as variables of baseline cardiac preload, such as ITBI and LVEDAI, and thus the degree of hypovolaemia, were not given.[15] In addition, there was relatively wide variation in baseline SVV [13.6 (8.1%)], suggesting a heterogeneous patient population. Therefore, it remained unclear whether SVV was a reliable predictor of fluid responsiveness during mechanical ventilation with low tidal volume. In the present study, we administered tidal volumes of 6.7–7.5 ml kg^{-1} in a pressure-controlled mode, which is more common in clinical practice than tidal volumes of 15 ml kg^{-1}.[11]

In contrast to previously published studies, in the present study the volume challenge was induced by a defined change in the patient's position. We have recently demonstrated that this technique is effective in the study of cardiac preload in anaesthetized and mechanically ventilated patients.[26] By raising the patients to the anti-Trendelenburg position, we induced arterial hypotension by relative depletion of cardiac preload. The decrease in left ventricular preload, as indicated by the decrease in LVEDAI, was followed by a decrease in SVI. For ethical reasons, it was not appropriate to induce hypotension and hypovolaemia in our patients by decreasing intravascular volume. In a second step, a shift of volume from the extrathoracic to the intrathoracic compartment was achieved by performing the Trendelenburg manoeuvre (30° head down). In clinical practice, this manoeuvre is used in the initial treatment of suspected hypovolaemia and thus for testing preload responsiveness. The Trendelenburg manoeuvre has been shown in cardiac surgical patients to be more effective than passive leg raising.[27] In contrast to data of Reuter and colleagues,[28] all our patients responded immediately to this manoeuvre with a significant increase in left ventricular preload and consecutively SVI, demonstrating that this manoeuvre was effective in inducing a relevant volume challenge.

We observed a positive correlation between prechallenge values of SVV in the anti-Trendelenburg position (i.e. during hypovolaemia) and the corresponding changes in SVI and CI after volume challenge. SVV was the only variable that could predict fluid responsiveness. However, when compared with other studies, the correlation between prechallenge values of SVV and Δ SVI was lower.[11 12] This was most probably a result of the relatively small tidal volumes used in the present study.

In contrast to SVV, all other preload variables failed to predict fluid responsiveness. Although the static measurements of intracardiac pressures and volumetric variables accurately reflected changes in left ventricular preload and were thus able to detect hypovolaemia (Table 2, Fig. 1), they were not able to predict the patients' response to a fluid challenge. Our findings are in accordance with most studies, in which static preload variables failed to predict fluid responsiveness.[1 2] As the slope of the Frank–Starling curve (i.e. the relationship between ventricular preload and stroke volume) depends on ventricular contractility, the prechallenge filling status is not the only variable determining the response to a volume challenge.[2 29] In the situation of impaired ventricular contractility, the resulting increase in stroke volume as a response to an increase in preload is decreased compared with patients with unimpaired ventricular contractility. Patients after CABG surgery often present with a modest deterioration of global or regional ventricular contractility caused by myocardial stunning.

Our study has some limitations. First, the validity of pulse-contour analysis for the assessment of SVV has not yet been proven by direct comparison with other techniques. However, our findings are strongly supported by a study in which SVV was determined echocardiographically and was found to be a predictor of fluid responsiveness.[9] Secondly, the patients studied did not show a physiological heart rate response to either position change. This is presumably due to residual β-blockade, which might alter the interpretation of our results. However, in the cardiac surgical setting, most patients are treated perioperatively with β-blocking agents, so that our results reflect a common clinical situation. Thirdly, our patients were already hypovolaemic at baseline, as demonstrated by low values of LVEDAI. Hypovolaemia was aggravated when the patients were brought to the anti-Trendelenburg position. As a result, prechallenge

values of SVV were rather high. Because of the study design, we were not able to evaluate the predictive value of SVV in normo- or even hypervolaemic patients with SVV values within or below the normal range. However, it seems likely that the present setting is close to the most common clinical situation, with hypovolaemia as the principal cause of arterial hypotension. Fourthly, the changes in body position induced in our patients possibly resulted in alterations in respiratory mechanics, which may have influenced SVV. To our knowledge, it has never been studied whether changes in airway pressure or in tidal volume affect SVV to a different degree. In the present study, airway pressure was adjusted in an attempt to achieve comparable tidal volumes throughout the study procedure. In practice, airway pressures were slightly lower in the anti-Trendelenburg position and elevated after the head-down tilt when compared with baseline. However, the changes in ventilatory settings that had to be made were small. Neither the differences in inspiratory airway pressures nor the resulting changes in tidal volumes were of statistical significance (Table 2). Therefore, it seems unlikely that the predictive value of prechallenge SVV was significantly influenced by changes in respiratory mechanics associated with the head-down tilt.

In summary, our results strengthen the importance of functional haemodynamic monitoring. Assessment of hypovolaemia in the anti-Trendelenburg position by static preload variables alone could not predict the response to the change in body position. Only values of SVV in the anti-Trendelenburg position correlated with the increases in SVI and CI associated with volume challenge. The dynamic index SVV proved to be a reliable variable in cardiac surgical patients ventilated with low tidal volumes. Moreover, assessment of SVV allowed real-time monitoring of left ventricular preload.

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