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Assessing fluid responsiveness during open chest conditions

D. A. Reuter[1]*, M. S. G. Goepfert[1], T. Goresch[1], M. Schmoeckel[2], E. Kilger[1] and A. E. Goetz[1]

[1]Department of Anaesthesiology, University of Munich, Germany. [2]Department of Cardiac Surgery, University of Munich, Germany

**Corresponding author: Department of Anesthesiology, University of Munich, Marchioninistr. 15, 81377 Munich, Germany. E-mail: Daniel.Reuter@med.uni-muenchen.de*

Background. Measurement of ventilation-induced left ventricular stroke volume variations (SVV) or pulse pressure variations (PPV) is useful to optimize preload in patients after cardiac surgery. The aim of this study was to investigate the ability of SVV and PPV measured by arterial pulse contour analysis to assess fluid responsiveness in patients undergoing coronary artery bypass surgery during open-chest conditions.

Methods. We studied 22 patients immediately after midline sternotomy. We determined SVV, PPV, left ventricular end-diastolic area index by transoesophageal echocardiography, global end-diastolic volume index and cardiac index by thermodilution before and after removal of blood 500 ml and after volume substitution with hydroxyethyl starch 6%, 500 ml.

Results. Blood removal resulted in a significant increase in SVV from 6.7 (2.2) to 12.7 (3.8)%. PPV increased from 5.2 (2.5) to 11.9 (4.6)% (both $P<0.001$). Cardiac index decreased from 2.9 (0.6) to 2.3 (0.5) litres min^{-1} m^{-2} and global end-diastolic volume index decreased from 650 (98) to 565 (98) ml m^{-2} (both $P<0.025$). Left ventricular end-diastolic area index did not change significantly. After fluid loading SVV decreased significantly to 6.8 (2.2)% and PPV decreased to 5.4 (2.1)% (both $P<0.001$). Concomitantly, cardiac index increased significantly to 3.3 (0.5) litres min^{-1} m^{-2} ($P<0.001$) and global end-diastolic volume index increased significantly to 663 (104) ml m^{-2} ($P<0.005$). Left ventricular end-diastolic area index did not change significantly. We found a significant correlation between the increase in cardiac index caused by fluid loading and SVV as well as PPV before fluid loading (SVV, $R=0.74$, $P<0.001$; PPV, $R=0.61$, $P<0.005$). No correlations were found between values of global end-diastolic volume index or left ventricular end-diastolic area index before fluid loading and the increase in cardiac index.

Conclusion. Measurement of SVV or PPV allows assessment of fluid responsiveness in hypovolaemic patients under open-chest and open-pericardium conditions. Thus, measuring heart–lung interactions may improve haemodynamic management during surgical procedures requiring mid-line sternotomy.

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According to the Frank–Starling mechanism, preload is one of the main determinants of cardiac performance.[1] Specifically, during cardiac surgery the assessment of cardiac preload and fluid responsiveness, i.e. the prediction of whether fluid loading will result in an increase in cardiac output is of crucial importance. Thus, optimizing preload helps to avoid low cardiac output, hypotension and, in the case of low preload, the inappropriate use of vasopressors or catecholamines. Mechanically ventilated patients suffering from low preload often show visible undulations in the arterial pressure waveform. Those undulations, which can be quantified as systolic pressure variation (SPV) or pulse pressure variation (PPV), are caused by the haemodynamic effects of the cyclic interaction between the heart and the lungs in the closed thorax induced by mechanical ventilation.[2 3] Retrospective analysis of SPV and its Δ-down component as well as PPV have proven to be sensitive markers of fluid responsiveness.[3–5] More recently, different methods of measuring the underlying variation in left ventricular stroke volume (SVV) in real time at the bedside have been reported.

Based on the principle of arterial pulse contour analysis, our group reported on the assessment of SVV in patients immediately after cardiac surgery.[6–8] The usefulness of this variable in predicting volume responsiveness was confirmed under various clinical conditions in patients after cardiac surgery and in other groups of patients.[9–11] However, the extent of SVV, and consequently that of SPV and PPV, is dependent on multiple factors besides volume status. Besides the magnitude of tidal volume and therefore the extent of lung inflation and intrapulmonary pressure, changes in chest wall compliance seem to influence heart–lung interactions.[12–14] Sternotomy and retraction of both hemithoraces, as performed during most cardiac surgical procedures, distinctly reduce the constraint of the chest wall imposed on the heart and the lungs. In consequence, sternotomy leads to distinct changes in those factors determining left ventricular SVV, such as the pattern of venous return to the right ventricle and cardiac preload volume, or changes in left ventricular afterload.[15 16] Thus, SVV and PPV measured after sternotomy, although still present, cannot be simply compared with those measured under closed-chest conditions.

The aim of the present study was to measure SVV and PPV during open-chest conditions under defined changes in cardiac preload. We hypothesized that even under open chest conditions heart–lung interactions induced by mechanical ventilation can be used to assess the individual status of fluid responsiveness.

Methods

The study was performed with approval of the Institutional Review Board. Twenty-five patients scheduled for elective coronary artery bypass surgery were included in the study group. Another five patients were included to serve as controls. Written informed consent was obtained from all patients. Patients with a severely reduced preoperative left ventricular ejection fraction <0.35 and patients with a haemoglobin concentration <120 g litre^{-1} before surgery were excluded.

Prior to surgery a 20 cm 5 Fr thermistor-tipped catheter (PV2025L20; Pulsion Medical Systems, Munich, Germany) was inserted into the femoral artery in each patient. This catheter was connected to a haemodynamics monitor (PiCCO, v. 5.12; Pulsion Medical Systems). Induction of anaesthesia was then performed with midazolam 0.1–0.15 mg kg^{-1} and sufentanil 0.6–1.0 μg kg^{-1}. Orotracheal intubation was facilitated with pancuronium 0.1–0.15 mg kg^{-1}. Anaesthesia was maintained with isoflurane 0.8–1.5% and continuous application of sufentanil 0.7–1.0 μg kg^{-1} h^{-1}. Mechanical ventilation was adjusted in a volume-controlled mode to apply tidal volumes of 10 ml kg^{-1} of ideal body weight, calculated according to the Devine formula. A positive end-expiratory airway pressure of 5 cm H_2O was applied. A triple-lumen central venous catheter was inserted into the internal jugular vein. All transducers were positioned at the level of mid-axillary line and zeroed to atmospheric pressure. Further, an omniplane probe (HP 21364A; Hewlett Packard, Andover, MA, USA) for transoesophageal echocardiography (TOE) was positioned and connected to a Hewlett Packard SONOS Phased Array Imaging System.

Study group

The study protocol started after completion of sternotomy and pericardiotomy and a period of 5 min for haemodynamic stabilization. Haemodynamic parameters were then determined at three time points during harvesting of the left internal mammary artery, with the sternal retractor in place. Those measurements were made before, during and after isovolaemic haemodilution, which is performed in our service routinely before cardiopulmonary bypass in order to minimize the need of allogeneic blood transfusions.[17] All measurements were performed in the supine position. After each intervention, a period of 3 min for stabilization was allowed. The time points were: T_1, baseline, after sternotomy, pericardiotomy and opening of the left pleural cavity; T_2, after removal of 500 ml of whole blood over a period of 10 min; T_3, after volume replacement using hetastarch 6%, 130 kDa, 500 ml, given over 10 min.

Control group

Haemodynamic measurements in the control group were performed at T_1 (after sternotomy and pericardiotomy, with the sternal retractor in place) and 15 min later ($T_{2control}$). During this time interval no haemodynamic intervention (fluid or drug administration) was performed.

Haemodynamic monitoring

Mean arterial (MAP) and central venous pressure (CVP) were measured continuously. Cardiac output and global end-diastolic volume, the latter reflecting the volume of the four heart chambers, were assessed by transcardiopulmonary thermodilution as described earlier.[18] All thermodilution measurements were performed in triplicate using iced saline 0.9%, 15 ml, which was injected randomly throughout the respiratory cycle into the central venous catheter. SVV was assessed by arterial pulse contour analysis. Therefore, stroke volume (SV) was measured continuously using an algorithm (PiCCO, v. 5.12; Pulsion Medical Systems), which is based on the work of Wesseling and colleagues.[6] With this original algorithm, SV is calculated continuously by measuring the systolic portion of the aortic pressure waveform and dividing this area by the aortic impedance, which is initially determined by transcardiopulmonary thermodilution. The algorithm used here further analyses the actual shape of the pressure waveform and takes into account the patient's specific aortic compliance and systemic vascular resistance, as described earlier.[19] SVV as the variation of beat-to-beat stroke volume from the mean value during the respiratory cycle was

calculated as:

$$SVV = [(SV_{max} - SV_{min})/SV_{mean}] \times 100(\%).^{7-12}$$

SV_{mean} was determined by using a continuously sliding time window of 30 s. This time window is further divided in to four 7.5 s periods; within each period the highest (SV_{max}) and the lowest value (SV_{min}) of SV were determined and the average of the four 7.5 s intervals was used to calculate SVV. Similarly, PPV, expressing the variation of pulse pressure (systolic–diastolic arterial pressure) around the mean, was calculated.[5] For each measurement, both SVV and PPV were recorded continuously over a period of 3 min, after which the mean was calculated.

Echocardiographic monitoring

Left ventricular end-diastolic area was assessed by TOE. All TOE images were acquired at end-expiration in the transgastric midpapillary short-axis view of the left ventricle by one investigator. The position of the probe was not changed throughout the study. TOE images and ECG signal were recorded on videotape. Off-line analysis was performed by an independent and experienced investigator blinded to the condition of the trial subjects. End-diastole was defined as the largest left ventricular cross-sectional area immediately after the R-wave peak in the ECG. Left ventricular end-diastolic area was traced edge to edge, including the papillary muscles. For each measurement, three consecutive cardiac cycles were analysed and an average was obtained.

Statistics

Raw data were indexed to body surface area to calculate thermodilution stroke volume index, global end-diastolic volume index (GEDVI) and left ventricular end-diastolic area index (LVEDAI). Data were tested for normal distribution with the Liliefors modification of the Kolmogorov–Smirnov test. All data are expressed as mean (SD) if not stated otherwise. Haemodynamic variables at time points T_1, T_2 and T_3 were compared by performing one-way analysis of variance for repeated measurements with Bonferroni adjustment (a value of $P<0.025$ was considered significant). In the control group, haemodynamic variables at time points T_1 and $T_{2control}$ were compared by using the non-parametric Wilcoxon rank sum test. Further, to analyse the relation between haemodynamic parameters before volume loading and the increase in cardiac index (CI) induced by volume loading, Pearson product moment correlations were calculated.

Results

In three of the 25 patients investigated in the study group, isovolaemic haemodilution was not performed because of a haemoglobin concentration of less than 120 g litre^{-1} immediately before the start of the study protocol. Those patients were excluded from the study. Twenty-two patients completed the study protocol. Demographic data for the study group and the control group are given in Table 1. In four of the 22 patients of the study group, no sufficient TOE images could be obtained during surgery. All patients tolerated the study regimen well. All patients were haemodynamically stable and did not require any pharmacological support with vasopressors or catecholamines.

Study group

Haemodynamic data at time points T_1, T_2 and T_3 are given in Table 2.

Blood withdrawal

Compared with baseline measurements (T_1), CI was significantly lower after blood withdrawal (T_2), as was GEDVI (both $P<0.025$). LVEDAI and CVP did not change significantly. Concomitantly, SVV and PPV increased significantly (both $P<0.001$).

Table 1 Patient data. All data are mean (SD) and median (range). CAD, coronary artery disease; 2-VD, two-vessel disease; 3-VD, three-vessel disease

	Study group (*n*=22)	**Control group (*n*=5)**
Sex (female/male)	5/17	2/3
Age (yr)	60 (14)	63 (10)
	61 (38–77)	63 (54–78)
Body weight (kg)	83 (16)	78 (17)
	89 (51–117)	87 (56–94)
Body mass index	27.4 (5.0)	26.6 (3.9)
(kg m^{-2})	27.5 (18.7–38.4)	27.2 (22.1–31)
Ejection fraction	0.66 (0.11)	0.63 (0.05)
	0.67 (50–83)	0.64 (56–68)
CAD: 2-VD/3-VD	3/19	0/5

Table 2 Haemodynamic data of the study group. All data are mean (SD). *Significantly different from T_1; §significantly different from T_2; (all $P<0.025$). *n*, number of patients; T_1, before blood withdrawal; T_2, immediately after blood withdrawal; T_3, after volume replacement; MAP, mean arterial pressure; HR, heart rate; CI, cardiac index; CVP, central venous pressure; SVV, stroke volume variation; PPV, pulse pressure variation; LVEDAI, left ventricular end-diastolic area index; GEDVI, global end-diastolic volume index; $P_{AW\ peak}$, peak airway pressure; $P_{AW\ mean}$, mean airway pressure; Hb, haemoglobin concentration; n.a., not assessed

	n	**T_1**	**T_2**	**T_3**
MAP (mm Hg)	22	86 (11)	69 (10)*	78 (12)§
HR (beats min^{-1})	22	69 (10)	64 (11)	65 (11)
CI (litre min^{-1} m^{-2})	22	2.9 (0.6)	2.3 (0.5)*	3.2 (0.5)*,§
CVP (mm Hg)	22	0 (3)	−3 (4)	3 (4)*,§
SVV (%)	22	6.7 (2.2)	12.7 (3.8)*	6.8 (2.2)§
PPV (%)	22	5.2 (2.5)	11.9 (4.6)*	5.4 (2.1)§
LVEDAI (cm^2 m^{-2})	18	11.1 (4.1)	8.2 (3.9)	11.3 (4.8)
GEDVI (ml m^{-2})	22	650 (98)	565 (98)*	663 (104)§
$P_{AW\ peak}$ (cm H_2O)	22	23 (2.8)	23 (2.9)	24 (3.2)
$P_{AW\ mean}$ (cm H_2O)	22	9.4 (1.5)	9.4 (1.5)	9.6 (1.6)
Hb (g litre^{-1})		133 (10)	n.a.	114 (14)§

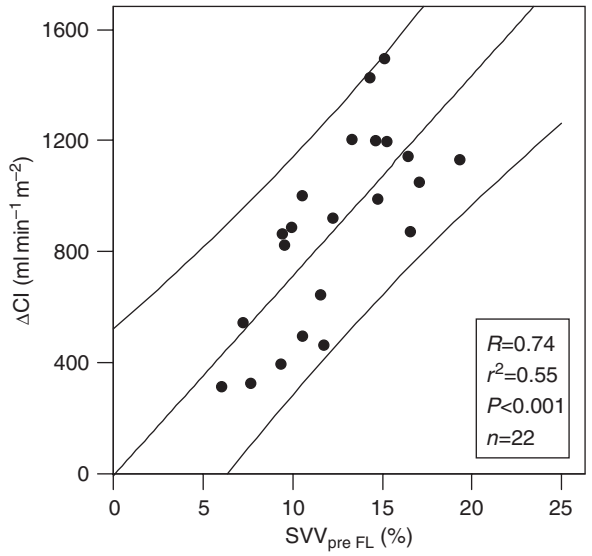

Fig 1 Relation of stroke volume variation ($SVV_{pre\ FL}$) before fluid loading (*x*-axis) and changes in cardiac index (ΔCI) caused by fluid loading (*y*-axis). Spearman correlation coefficient *R*, r^2 and 95% confidence interval of *R* are shown.

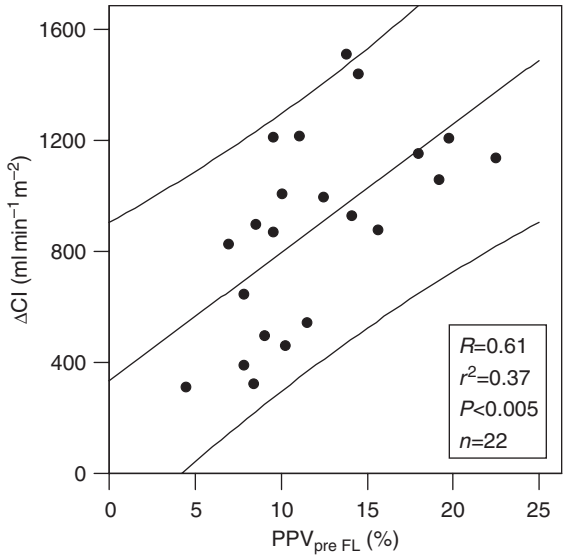

Fig 2 Relation of stroke volume variation ($PPV_{pre\ FL}$) before fluid loading (*x*-axis) and changes in cardiac index (ΔCI) caused by fluid loading (*y*-axis). Spearman correlation coefficient *R*, r^2 and 95% confidence interval of *R* are shown.

Fluid loading

After fluid loading (T_3), CI was significantly higher than at (T_2) ($P<0.001$); mean ΔCI caused by fluid loading was 880 (347) ml m^{-2}. CVP ($P<0.001$) and GEDVI ($P<0.005$) were also significantly higher after fluid loading. The increase in LVEDAI was not significant. SVV and PPV were significantly lower after volume loading (both $P<0.001$) (Table 2).

Prediction of fluid responsiveness

There were no significant correlations between values of CVP, GEDVI or LVEDAI at T_2 (before fluid loading) and ΔCI caused by fluid loading (CVP, $R=0.20$; GEDVI, $R=-0.32$; LVEDAI, $R=-0.45$; all $P>0.05$). In contrast, SVV and PPV at T_2 (before fluid loading) showed highly significant correlations to ΔCI (SVV, $R=0.74$; $P<0.001$; PPV, $R=0.61$; $P<0.005$) (Figs 1 and 2).

Control group

In the control group, there were no significant differences between values of MAP [81 (3) *vs* 78 (20) mm Hg], CVP [3 (1) *vs* 3 (1) mm Hg], CI [2.6 (0.6) *vs* 2.7 (0.4) litres min^{-1} m^{-2}], GEDVI [784 (229) *vs* 802 (254) ml m^{-2}], SVV [7 (2) *vs* 7 (3)%] and PPV [5 (1) *vs* 5 (1)%] at T_1 (baseline) and $T_{2control}$ (15 min after T_1, without intervention). LVEDAI was not measured.

Discussion

Our study indicates that heart–lung interactions caused by positive-pressure ventilation can be quantified by SVV and PPV also under open-chest conditions, and that SVV and PPV are predictive of fluid responsiveness.

Measuring SVV and PPV has been shown to be useful in detecting fluid responsiveness in mechanically ventilated patients after cardiac surgery in closed-chest conditions.[9 10] In the closed thorax, changes in intrathoracic pressure during each respiratory cycle cause predominantly cyclic changes in venous return, preload and SV. However, during most cardiac surgery procedures the thorax and the pericardium are opened widely. This has an important effect on haemodynamics and the interactions between the heart and the lungs.[16]

SVV and PPV have so far not been studied in detail under open-chest conditions with changes in preload volume. Scott and colleagues investigated the effect of a passive Valsalva manoeuvre using 25–30 mm Hg of PEEP, which is also known to influence preload in patients with right lateral thoracotomy and the pleura widely opened.[20] They found that the application of PEEP, even with the direct transmural effect of the raised intrathoracic pressure released from the lungs, still resulted in a fall in arterial pressure of the same extent as that in closed-chest conditions. They therefore concluded that the decrease in systemic arterial pressure, i.e. the Δ-down component of SPV, is mainly caused by occlusion of small pulmonary vessels and capillaries, leading to a reduction in left ventricular preload. Further, the transmurally transmitted compression of the great veins reducing the venous return to the right ventricle seemed responsible for the decrease in arterial pressure only to a minor extent. This hypothesis was supported by the change in CVP when PEEP was applied in their patients. This change was similar whether the chest was open or closed. However, in contrast to their investigation, our patients underwent sternotomy with a retractor placed to keep both hemithoraces widely open. This certainly minimized

the transmittance of transmural pressure. Nevertheless, SVV increased significantly when preload was reduced by blood withdrawal. In contrast, in the control patients, in whom no blood was withdrawn during the same stage of surgery, SVV, PPV and CI did not change; so other potential reasons—for example, recovery from sternotomy and its associated endogenous sympathetic activation—seemed unlikely for the changes in SVV and PPV in the study group.[21] This strengthens the hypothesis that under open-chest conditions the effect of ventilation-induced occlusion of the intrapulmonary vessels is mainly responsible for the temporary reduction of left ventricular filling. Further, this basic mechanism responsible for SVV, which is aggravated during low-preload conditions, appears to be independent of transthoracic pressure in its origin, although it is enhanced by it.[15 16]

Moreover, under open-chest conditions in the present study, high SVV values were associated with a high degree of fluid responsiveness, as indicated by the significant relation between SVV before fluid loading and the increase in CI provoked by this manoeuvre. But, importantly, the absolute level of SVV was lower compared with data for patients with closed chest.[9–12]

A recent study by Wiesenack and colleagues examined SVV in patients undergoing cardiac surgery.[22] In this study, which was performed in the early phase of surgery, no correlation was found between SVV and the increase in cardiac index induced by fluid loading, which is in contrast to the data presented here and by others.[10–12] This divergence of results may have arisen if these data[22] were not all acquired uniformly before sternotomy. A mean SVV of 4.8 ± 1.8% during closed-thorax conditions, as reported in that study, even after fluid loading and at tidal volumes of 10 ml kg^{-1}, represents an extremely low value compared with other studies that have used the same ventilator settings.[11 12] On the other hand, the data on SVV of the present study, measured after fluid replacement and using tidal volumes of 10 ml kg^{-1} under open-thorax conditions (6.8 ± 2.2%), are comparable to those of Wiesenack and colleagues.

Importantly, in all our patients the pericardium was opened widely before onset of measurements. Thus, potential pericardial constraint on both ventricles under fluid loading was minimized. However, this reduction of pericardial constraint under fluid loading may have influenced right ventricular performance and, further, the coupling between the right and left ventricle, making the mechanism of generation of left ventricular SVV under these conditions not comparable to the closed-chest condition. Experimental and clinical data, however, support the contention that, at least under hypo- and normovolaemic conditions, left ventricular performance is not substantially altered by pericardiotomy.[23 24] In parallel, right ventricular function under normal or moderately elevated cardiac loading has been shown not to be significantly influenced by the pericardium.[25 26] Thus, the basic mechanisms leading to left ventricular SVV and its changes under fluid loading seem also transferable to the post-pericardiotomy phase of cardiac surgery procedures. However, further experimental studies assessing right and left ventricular function synchronously under open-thorax and open-pericardium conditions are needed to further elucidate heart–lung interactions. This accounts specifically for the situation of fluid overload and ventricular overdistension. This may also enable to identify the Δ-up and Δ-down components of SVV within this clinical situation. Further, threshold values for SVV and PPV that clearly discriminate fluid-responsive from fluid-unresponsive patients have to be defined.

In conclusion, our data indicate that assessing the haemodynamic consequences of ventilation-induced heart–lung interactions allows the prediction of fluid responsiveness in patients undergoing cardiac surgery during open-chest and open-pericardium conditions. On-line assessment of functional preload parameters such as SVV and PPV are therefore useful clinical tools to optimize the haemodynamic management of patients during cardiac surgery procedures.

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