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Prediction of fluid responsiveness in infants and neonates undergoing congenital heart surgery

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Editor's key points

- Dynamic tests of preload are increasingly used to assess fluid responsiveness (FR) in adults.
- This study compared several static and dynamic measures in infants undergoing surgery to correct congenital heart defects.
- Pulse pressure variability predicted FR before and after surgery.
- Stroke volume variability and static variables were less useful.

Background. Dynamic variables reliably predict fluid responsiveness (FR) in adults, but no data are available regarding their performance in infants. The aim of this prospective study was to assess whether pulse pressure variation (PPV) and stroke volume variation (SVV), in contrast to central venous pressure (CVP) and global end-diastolic volume (GEDV), are applicable in infants undergoing congenital heart surgery and to assess threshold values that may help to guide fluid administration in these patients.

Methods. Twenty-six anaesthetized infants, mean (SD) weight 9.7 (4.3) kg, were studied during closed-chest conditions and changing loading conditions before and after repair of congenital heart disease. Stroke volume index was measured by transoesophageal echocardiography (SVI_{TOE}), CVP was measured via a central venous line, GEDV index (GEDVI) was measured by transpulmonary thermodilution, and PPV and SVV were monitored using the PiCCO monitoring system.

Results. Fifteen infants had increased SVI_{TOE} with fluid loading $\geq$15% (responders); 11 infants were defined as non-responders. Analysing the relationship between CVP, GEDVI, SVV, and PPV at baseline with volume-induced percentage change in SVI_{TOE}, only PPV was significantly correlated with ΔSVI_{TOE} both before (r=0.54, P=0.004) and after (r=0.73, P>0.0001). As assessed by receiver-operating characteristic curve analysis, only PPV accurately predicted FR before surgical repair [area under the curve (AUC): 0.79, P=0.01] and after surgical repair (AUC: 0.86, P=0.002).

Conclusions. PPV, in contrast to SVV, CVP, and GEDVI, predicted FR in infants undergoing congenital heart surgery both before and after repair of congenital heart disease.

Keywords: echocardiography; haemodynamics; infants; neonates; physiological monitoring; pulse pressure

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Since hypovolaemia is a common cause of perioperative circulatory failure in both adults and infants, the assessment of the volume status in the critically ill is of paramount importance. Apart from clinical skills, traditional variables such as central venous pressure (CVP) and mean arterial pressure (MAP) are mainly used to guide fluid therapy in infants and neonates.[1] However, numerous studies have shown that the measurement of preload and change in preload alone is not sufficient to show whether a patient will increase stroke volume index (SVI) after a fluid bolus or not.[2–4] More recently, variables such as pulse pressure variation (PPV) and stroke volume variation (SVV), which are based on the heart–lung interaction induced by mechanical ventilation, have been shown to reliably predict the response to a fluid load in adults in different clinical scenarios.[5–7] Whether these dynamic variables are able to predict fluid responsiveness (FR) also in infants and neonates is not yet known. Some experimental data using a paediatric porcine model are available, demonstrating conflicting results in comparison with adults.[4 8 9] This emphasizes the need for a clinical study regarding the application of dynamic variables in infants and neonates. We hypothesized that the predictive power of these variables is not necessarily conferrable to infants and neonates, since there are fundamental differences in physiology between them and adults.

The aim of this study was to investigate whether PPV and SVV in comparison with the static variables CVP and global end-diastolic volume (GEDV) are reliable indicators of FR in paediatric patients undergoing congenital heart surgery.

Methods

The study was conducted in accordance with the principles of the Declaration of Helsinki and the Guidelines for Good

Clinical Practice. The protocol was approved by our institutional Ethics committee (Christian Albrecht University Kiel) and all parents gave informed consent for participation in the study.

We studied 26 mechanically ventilated children with congenital heart disease with a mean (SD) age of 14 (12) months and weight of 9.7 (4.3) kg, undergoing elective congenital heart surgery [secundum atrial septal defect (ASD), ventricular septal defect (VSD)] after induction of general anaesthesia. Exclusion criteria were: any contraindication for transoesophageal echocardiography (TOE), atrial fibrillation and/or ventricular arrhythmias distorting variation in SV or its surrogates, and acute need for inotropic drugs after induction of anaesthesia. Induction and maintenance of anaesthesia were standardized. Anaesthesia was induced with etomidate (0.4–0.6 mg kg^{-1}) followed by a bolus of sufentanil (0.5–1 μg kg^{-1}) and rocuronium (0.6–0.9 mg kg^{-1}), and thereafter infants were intubated and their lungs mechanically ventilated with a fixed tidal volume of 10 ml kg^{-1} and a frequency adapted to age and to maintain the Pa_{CO_2} between 4.5 and 5.5 kPa. Positive end-expiratory pressure was set between 3 and 5 cm H_2O and F_{IO_2} maintained between 0.3 and 0.5. Anaesthesia was then maintained with sevoflurane and boluses of sufentanil (0.5–1 μg kg^{-1}) before and after cardiopulmonary bypass, whereas during cardiopulmonary bypass, sufentanil was combined with a continuous infusion of propofol (3–5 mg kg^{-1} h^{-1}).

A 4–5.5 Fr central venous catheter was inserted in the right internal jugular vein or alternatively in the right or left subclavian vein to measure CVP. A 7 cm 3 Fr thermistor-tipped catheter for arterial pressure tracing, for arterial thermodilution, and for pulse contour analysis (PiCCO Plus®, Version 6.0, Pulsion Medical Systems, Munich, Germany) was inserted percutaneously into the right or left femoral artery. The arterial catheter allows discontinuous measurement of transpulmonary thermodilution cardiac index (CI_{TPTD}), SVI (SVI_{TPTD}), and global end-diastolic volume index (GEDVI) as described previously.[10] Additionally, PPV and SVV were monitored continuously. SV was calculated based on a modified algorithm originally described by Wesseling and colleagues.[11] This algorithm enables continuous calculation of SV by measuring the systolic portion of the aortic pressure waveform and dividing the area under the curve (AUC) by the aortic impedance. Initially, the specific aortic impedance is determined by transpulmonary thermodilution.[10] Five millilitres of ice cold saline were injected three times at random points in the respiratory cycle into the proximal port of the central venous catheter to assess CI_{TPTD} and to calibrate pulse contour-derived CI. All thermodilution curves were analysed and accepted or, if necessary, rejected and calibration repeated.

The PiCCO monitor also calculates the mean transit time (mtt) and the down-slope time (dst) of the aortic thermodilution curve which enables GEDV calculation.[12] GEDV is calculated according to:

$$\mathrm{GEDV} = \mathrm{CO} \times (\mathrm{mtt} - \mathrm{dst})$$

SVV is generated from the mean values of four minimum and maximum SVs averaged during the last 30 s as follows:

$$\mathrm{SVV}(\%) = 100 \times \frac{(\mathrm{SV_{max}} - \mathrm{SV_{min}})}{[(\mathrm{SV_{max}} + \mathrm{SV_{min}})]/2}$$

Additionally, PPV can be determined during the same time interval:

$$\mathrm{PPV}(\%) = 100 \times \frac{(\mathrm{PP_{max}} - \mathrm{PP_{min}})}{[(\mathrm{PP_{max}} + \mathrm{PP_{min}})]/2}$$

A paediatric multiplane probe (dimensions of 10.7×7.5 mm, 5 MHz) was used in all children (GE Vivid 7; GE Vingmed Ultrasound AS, N-3190; GE, Horten, Norway). Echocardiographic images were recorded together with the ECG. In all children undergoing elective congenital heart surgery, echocardiography approved the presence of a left-to-right shunt and the absence of any right-to-left shunt. Using a mid-oesophageal long-axis approach, the diameter of the left ventricular outflow tract (LVOT) was obtained for estimation of LVOT area. Conventional pulsed-wave Doppler was performed to measure velocity–time integrals (VTI) in the LVOT, using a longitudinal transgastric position of the echo probe at an angle of 110–130° (Fig. 1). To rule out unforeseeable effects on the accuracy of SVI_{TOE} obtained in the presence of a perimembranous VSD, a deep transgastric approach was aimed alternatively to obtain the diameter and the pulsed-wave Doppler flow of the ascending aorta (Fig. 1). Before each measurement, the probe position was verified to ensure optimal acquisition of the maximal velocity signal. SVI_{TOE} was calculated multiplying the area of the LVOT, respectively, the area of the ascending aorta, with the corresponding VTI of the Doppler measurement. Cardiac index (CI_{TOE}) then was automatically computed by the echo machine as SVI_{TOE} times heart rate. This method was originally described by Darmon and colleagues[13] and has been confirmed by several investigators.[14–16] None of the children had a significant residual shunt as demonstrated by colour Doppler echocardiography at the end of the operation. All TOE measurements were obtained by one experienced investigator and analysed offline by two investigators blinded for the haemodynamic data.

Data collection was performed during closed-chest conditions at the following time points: after induction of anaesthesia and instrumentation of the patients including all required catheters and the transoesophageal echo probe, the first data collection was performed and this time point was defined as baseline before surgical repair of the congenital heart defect (BL-BSR). The second time point during closed-chest conditions was defined after a fluid load with 10 ml kg^{-1} of hydroxylethyl starch 6% (FL-BSR). The third and fourth time points of data collection took place after surgical repair of the congenital heart defect at the end of the operative procedure also during closed-chest conditions: BL after surgical repair of the congenital heart defect (BL-ASR) and after FL with 10 ml kg^{-1} of hydroxylethyl starch 6% (FL-ASR). Haemodynamic measurements were obtained

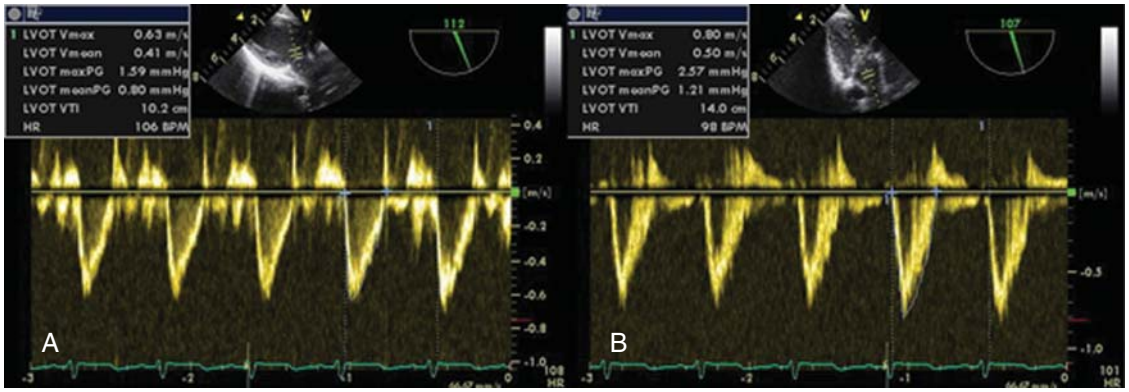

Fig 1 Measurement of Doppler velocity time integral in the LVOT (A) and in the ascending aorta (B).

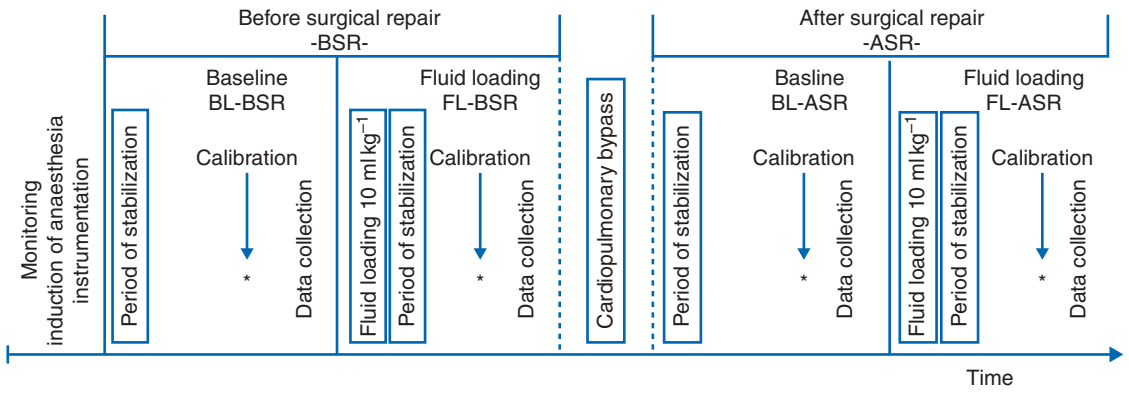

Fig 2 Study design. BSR, before surgical repair; ASR, after surgical repair.

after a short period of stabilization (~3 min) within 10 min after the end of the fluid load and after recalibration of the PiCCO system (Fig. 2). CVP was measured at end-expiration. Children with increased SVI_{TOE} ≥15% in response to fluid administration were considered to be responders; the remaining ones were defined as non-responders.

Statistical analysis

Data are expressed as mean (SD). Statistical comparisons were performed using commercially available statistics software (GraphPad Prism 5, GraphPad Software Inc., San Diego, CA, USA). One-way analysis of variance was used to analyse data both before and after surgical repair and volume loading, followed by the Bonferroni correction for multiple comparisons. To assess the ability of a variable to identify responders and non-responders, receiver-operating characteristic (ROC) curves were generated, and an optimal threshold value (the value that maximizes the sum of both sensitivity and specificity) was determined. Areas under the ROC curves were calculated and compared as described previously.[17] Pearson correlation coefficients were calculated for static and dynamic variables and subsequent changes in SVI after fluid loading. Values of $P<0.05$ were considered statistically significant.

Results

Twenty-six patients were included in the study: 18 were undergoing VSD closure and eight underwent surgical correction of an ASD. Mean (SD) age, weight, height, and body surface area (BSA) were: age: VSD: 7.8 (3.8) months, ASD: 30.6 (9.4) months; weight: VSD: 7.2 (1.6) kg, ASD: 15.5 (2.7) kg; height: VSD: 71.7 (10.7) cm, ASD: 98.2 (11.7) cm; BSA: VSD: 0.37 (0.06) cm^2, ASD: 0.64 (0.08) cm^2. Details of all patient characteristics regarding congenital heart disease, age, body weight, height, and BSA are described in Supplementary Table S1. None of the children needed continuous vasoactive drugs before the beginning of cardiopulmonary bypass. Infants undergoing surgical repair of the VSD received a single dose of enoximone (0.5 mg kg^{-1}) before weaning from cardiopulmonary bypass in addition to a low dose of epinephrine (0.02–0.05 μg kg^{-1} min^{-1}). Haemodynamic variables are presented in Table 1. Fifteen children

Table 1 Haemodynamic variables [mean (SD)] in all children before and after surgical repair of congenital heart disease. BL-BSR, baseline before surgical repair; FL-BSR, fluid loading before surgical repair; BL-ASR, baseline after surgical repair; FL-ASR, fluid loading after surgical repair; HR, heart rate; MAP, mean arterial pressure; SVRI, systemic vascular resistance index; CI_{TPTD}, cardiac index derived from transpulmonary thermodilution; SVI_{TPTD}, stroke volume index derived from transpulmonary thermodilution; CI_{TOE}, cardiac index obtained by transoesophageal echocardiography; SVI_{TOE}, stroke volume index obtained by transoesophageal echocardiography; CVP, central venous pressure; GEDVI, global end-diastolic volume index; SVV, stroke volume variation; PPV, pulse pressure variation. *Significantly different from BL-BSR; †significantly different from BL-ASR. *P*-value indicated for one-way analysis of variance followed by the Bonferroni correction for multiple comparisons

Variables	BL-BSR	FL-BSR	BL-ASR	FL-ASR
HR (min^{-1})	102 (18)	100 (18)	126 (17)	124 (19)
MAP (mm Hg)	62 (9)	68 (12)	55 (7)	62 (10)†
SVRI (dyne s cm^{-5} m^{-2})	2050 (1053)	1989 (980)	1448 (725)	1398 (692)
CI_{TPTD} (litre min^{-1} m^{-2})	3.1 (1.5)	3.6 (1.0)	3.7 (0.9)	4.5 (1.1)
SVI_{TPTD} (ml min^{-1} m^{-2})	31.0 (12)	37.1 (9)	30.9 (9)	35.8 (8)
CI_{TOE} (litre min^{-1} m^{-2})	3.5 (1.1)	4.2 (1.0)*	3.9 (1.0)	4.6 (0.9)
SVI_{TOE} (ml min^{-1} m^{-2})	33.8 (7.5)	41.8 (9.5)*	32.1 (9.0)	40.7 (9.2)†
CVP (mm Hg)	7.5 (1.9)	11.1 (3.3)*	9.7 (2.2)	11.6 (3.3)†
GEDVI (ml m^{-2})	299 (129)	391 (128)*	415 (167)	595 (223)†
SVV (%)	14.5 (3.2)	10.4 (3.0)*	14.7 (3.5)	11.2 (3.1)†
PPV (%)	16.3 (4.9)	12.2 (3.7)*	16.4 (4.8)	11.4 (2.7)†

showed increased SVI_{TOE} ≥15% in response to a fluid load (responders: VSD: n=11; ASD: n=4), whereas in the remaining 11 children, SVI_{TOE} increased by ≤15% (non-responders: VSD: n=7; ASD: n=4). Fluid loading induced significant changes in CI_{TOE}, SVI_{TOE}, CVP, GEDVI, SVV, and PPV before surgical repair and in MAP, SVI_{TOE}, CVP, GEDVI, SVV, and PPV after surgical repair of congenital heart defect (Table 2).

Analysing the relationship between CVP, GEDVI, SVV, and PPV and volume-induced percentage change in SVI (ΔSVI_{TOE}) before repair of the congenital heart defect, only PPV significantly correlated with ΔSVI_{TOE} (r=0.54, P=0.004). After surgical repair, GEDVI (r=−0.64, P=0.0005), SVV (r=0.57, P=0.02), and PPV (r=0.73, P<0.0001) significantly correlated with ΔSVI_{TOE} in contrast to CVP (r=−0.03, P=0.81) (Table 2).

At BSR, the best AUC to identify a ≥15% increase in SVI_{TOE} was seen for PPV (AUC=0.79). The optimal threshold value given by ROC analysis was ≥16% for PPV: a value of ≥16% predicted an increase in SVI_{TOE} ≥15% with a sensitivity of 61% and a specificity of 96%. After surgical repair of the congenital heart defect, the best AUC to discriminate between responders and non-responders was seen for PPV (AUC: 0.86), SVV (AUC: 0.78), and GEDVI (AUC: 0.77) (Figs 3 and 4). The optimal threshold value given by ROC analysis was ≥15% for PPV (sensitivity: 93% and specificity: 72%), ≥15% for SVV (sensitivity: 60% and specificity: 81%), and for GEDVI, ROC analysis yielded a threshold value of ≤400 ml m^{-2} (sensitivity: 66% and specificity: 78%).

Table 2 Correlation between preload variables and volume-induced percentage change in SVI_{TOE} ≥15% before and after surgical repair of congenital heart disease in SVI at different PEEP levels. BSR, before surgical repair; ASR, after surgical repair; SVI_{TOE}, stroke volume index obtained by transoesophageal echocardiography; CVP, central venous pressure; GEDVI, global end-diastolic volume index; PPV, pulse pressure variation; SVV, stroke volume variation

Preload variables	BSR		ASR	
	r	*P*-value	*r*	*P*-value
CVP (mm Hg)	−0.17	0.42	−0.03	0.81
GEDVI (ml m^{-2})	−0.13	0.52	−0.64	0.0005
PPV (%)	0.54	0.004	0.73	<0.0001
SVV (%)	0.30	0.14	0.57	0.02

Discussion

The main findings of this study are:

(i) the static variable CVP does not predict FR in infants before and after ASD/VSD closure.

(ii) GEDVI and SVV failed to predict FR in the presence of an intracardiac left-to-right shunt. After surgical repair of the intracardiac shunt, however, both variables enhanced their predictive power.

(iii) PPV in contrast to SVV was the only dynamic variable of FR in this setting and accurately predicted the response to fluid loading both before and after repair of an intracardiac shunt.

In critically ill infants and neonates, adequate fluid therapy is a particular challenge for the anaesthetist and critical care physician, since fluid homeostasis is maintained in a narrow range and physiological compensation of both hypervolaemia and hypovolaemia is limited. Therefore, assessment of each subject's individual position on the Starling curve in order to optimize cardiac preload and avoid deleterious fluid overload is of utmost importance. The basic principle of a dynamic approach to challenge the individual

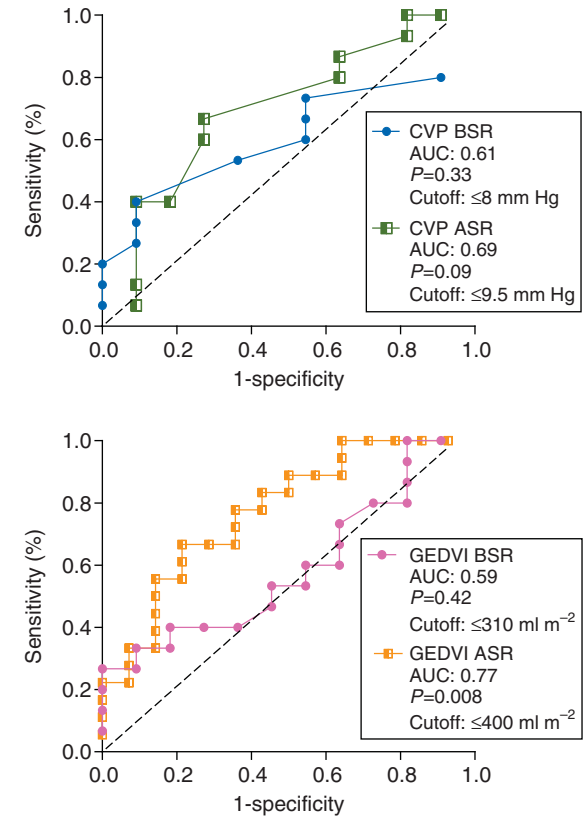

Fig 3 Prediction of FR: area under the ROC curve (AUC) for predicting a ≥15% increase in SVI. BSR, before surgical repair; ASR, after surgical repair; CVP, central venous pressure; GEDVI, global end-diastolic volume index. The straight line indicates line of identity. AUC=0.5: prediction of FR not better than chance; AUC=1.0: best prediction. Cut-off value maximizes the sum of both sensitivity and specificity, helping to discriminate between responders and non-responders.

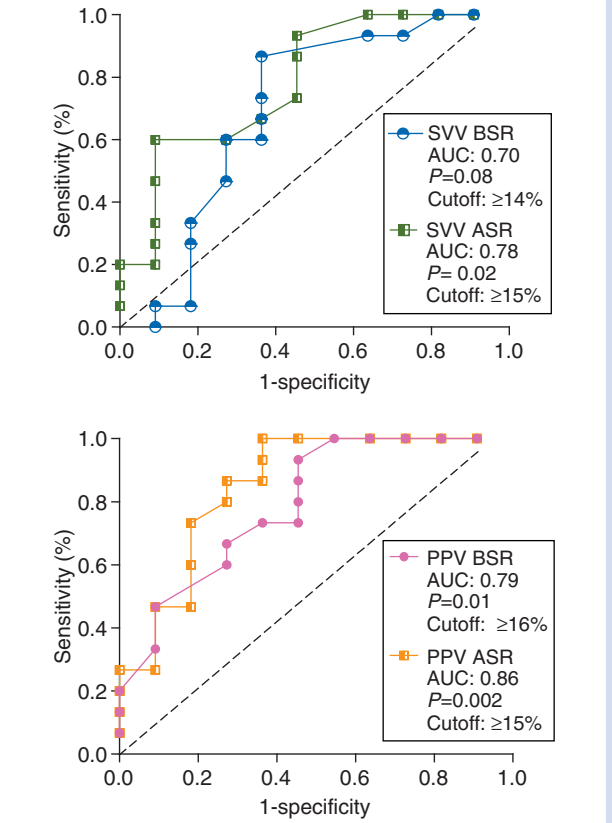

Fig 4 Prediction of FR: area under the ROC curve (AUC) for predicting a ≥15% increase in SVI. BSR, before surgical repair; ASR, after surgical repair; PPV, pulse pressure variation; SVV, stroke volume variation. The straight line indicates line of identity. AUC=0.5: prediction of FR not better than chance; AUC=1.0: best prediction. Cut-off value maximizes the sum of both sensitivity and specificity, helping to discriminate between responders and non-responders.

Frank–Starling curve at the bedside is to induce a cyclical change in cardiac preload induced by mechanical ventilation. Positive pressure ventilation intermittently decreases right ventricular end-diastolic volume and consequently decreases left ventricular preload due to a reduction in venous return.[18] SVV and PPV have been introduced as dynamic variables of FR, which reflect ventilation-induced cyclic changes in left ventricular SV. Several recent studies have shown that SVV and PPV are superior to the measurement of static filling pressures.[4–7 19 20] However, only a few animal studies[4 8 9] and one clinical observation[21] are available in infants and neonates addressing the impact of volumetric and dynamic variables on preload assessment and prediction of FR.

In the present study, we challenged the ability of the static variables CVP and GEDVI and the dynamic variables PPV and SVV to predict FR in this particular patient population. These variables were monitored during two completely different circulatory conditions: the presence of an intracardiac shunt, that is, left-to-right shunt, and after surgical treatment, in the absence of an intracardiac shunt.

In terms of the static variable CVP, our results are in good agreement with previous investigations in adults[2 22] and in a paediatric porcine model.[4] On the basis of these and several other studies, a systematic review concluded that dynamic variables are superior to static filling pressures in predicting FR.[3] In our study, CVP was not able to predict FR either with or without an intracardiac shunt. The static volumetric variable GEDVI was not superior to CVP in the presence of left-to-right shunt. After closure of the shunt, however, the predictive power of GEDVI in terms of FR was substantially improved. The area under the ROC curve was significant only after surgical repair of the congenital heart defect, yielding a sensitivity of 66% and a specificity of 78%. As with any thermodilution technique, intracardiac shunts, substantial valvular insufficiencies, or both may affect absolute values of CI and additionally absolute values of GEDVI. Although both variables are derived from the same thermodilution curve, it has been shown that the mean transit time of an indicator may change independently of changes in CI, disarming the assumption of mathematical coupling between CI

and GEDVI.[23–25] In the presence of a left-to-right shunt, recirculation of the indicator prolonged the thermodilution curve resulting in an underestimation of CI, which is in accordance with our investigation. Conversely, Cecchetti and colleagues demonstrated a significant linear correlation between CI and GEDVI in infants with haemorrhagic and cardiogenic shock.[26] Our data support the findings of Cecchetti and colleagues in at least two ways, first, since the accuracy of SVI_{TPTD} compared with SVI_{TOE} has been enhanced after closure of the intracardiac shunt, one could assume that the accuracy of GEDVI obtained by the same thermodilution curve has been improved likewise. This might explain the ability of GEDVI to predict FR after the intracardiac shunt was eliminated. Currently, normal values for intracardiac and intrathoracic blood volumes in infants and neonates have not yet been defined. In a study of infants after cardiac surgery, values of GEDVI [427 (38) ml m^{-2}] were comparable with values obtained in our study.[27]

Regarding the ability of PPV and SVV to discriminate between responders and non-responders, only PPV met the criteria of a reliable dynamic variable of FR both before and after repair of the intracardiac shunt. At BSR, a threshold value of PPV $\geq$16% reliably predicted an increase in SVI_{TOE} $\geq$15% with a sensitivity of 73% and a specificity of 63%. The predictive power of PPV was increased at ASR, yielding a threshold value of $\geq$15% with a sensitivity of 93% and a specificity of 72%. An SVV value of $\geq$15% was able to predict FR only in the absence of an intracardiac shunt with a sensitivity of 60% and a specificity of 90%, indicating a less predictive power compared with PPV. These findings differ, at least in part, to previously reported results. Our group recently showed in a paediatric porcine model applying different loading conditions that SVV but not PPV was able to accurately predict FR, when animals' lungs were ventilated with a tidal volume of 10 ml kg^{-1}.[4] Since these findings were counterintuitive compared with previously reported results in adults, we hypothesized that they may be explained by differences between the physiology in young *vs* adult subjects, specifically heart rate, chest wall compliance, mean arterial pressure and pulse pressure, arterial vasomotor tone, and aortic compliance and elastance, all of which may influence pulse pressure and PPV in a differing way compared with adults. Moreover, frequent calibration of the PiCCO monitoring system used to obtain SVV repeatedly adjusted pulse contour-derived SVV to potential changes in arterial elastance and compliance, giving SVV an edge over PPV in this setting. Accordingly, it was suggested that though PPV is still a surrogate of SVV, the influence of vasomotor tone on PPV and systolic pressure variation (SPV) is more pronounced compared with SVV.[28]

Durand and colleagues investigated 26 infants with a median age of 26 months requiring ventilation and volume expansion. They showed that respiratory variations of aortic blood flow obtained by echocardiography accurately predicted FR, whereas PPV and SPV did not.[21] They hypothesized that at least one physiological factor may have contributed to the low predictive power of PPV and SPV in their observation: based on the physiology of the Windkessel model, pulse pressure is directly proportional to left ventricular SV and inversely related to arterial compliance.[29 30] Therefore, they speculated that PPV or SPV in their responder group was limited in their predictive power due to the higher arterial elastic properties observed in children. In addition, the children in Durand's study were ventilated with a mean tidal volume of 7.4 ml kg^{-1}, a tidal volume that has been shown to be too low to induce meaningful intrathoracic pressure swings, since cyclic variations in left ventricular pressure highly depend on absolute value of tidal volume applied.[4 20]

In a recent systematic review of the literature, it was pointed out that PPV, SVV, and SPV are highly reliable variables of FR and that the diagnostic accuracy of PPV appears to be significantly superior compared with SVV and SPV.[31] The findings of our investigation emphasize the robustness of PPV compared with SVV to reliably predict FR in different clinical scenarios and in different patient populations. Although still a surrogate variable of SVV, PPV is a simple measure of pulse pressure (defined as the difference between the systolic and diastolic pressure). In contrast, SVV is a variable based on a complex algorithm obtained by pulse contour analysis, consequently highly dependent on changes in aortic compliance.[32] With respect to the impact of dynamic variables of FR in optimizing fluid management, it must be kept in mind that there are clearly defined limitations. In a recent review on PPV, Cannesson and colleagues[33] stressed the importance of a sound knowledge about physiological and technological background essential to accurately interpret dynamic variables, that is, PPV. A newly introduced and recently improved non-proprietary and publicly available algorithm for automatic determination of PPV from arterial pressure signals has been compared with the PiCCO system in an experimental setting of rapid haemodynamic changes due to severe haemorrhagic shock.[34] The PiCCO system, that is, PPV performed well during haemodynamic stable conditions; however, the systems failed to accurately estimate the PPV during severe haemorrhage and during aggressive fluid administration. These findings, however, do not affect our results, since the two time points of data collection were not during severe haemorrhage. Especially data collection before surgical repair was performed under stable haemodynamic conditions. Also the second time point of data collection after surgical repair at the end of the operation was characterized by stable haemodynamics, even though some children received inotropic pharmacological support. Moreover, in a recent investigation, Pinsky and colleagues were able to show in patients after cardiac surgery requiring fluid administration, vasoactive support, or both that both SVV and PPV appear to be unaffected by varying doses of vasopressor and inotropic agents.[35]

Our results are limited by the lack of an experimental gold standard for SVI determination, such as an ultrasound flow probe measuring instantaneous aortic blood flow. Instead, we used a clinical acceptable method to determine CI and

SVI, TOE. In paediatrics, echocardiography has been proven to be interchangeable with the Fick and pulmonary artery thermodilution method with a bias of around 10%.[36] An advantage of using TOE as the reference method for CO determination, however, is the possibility to determine instantaneous blood flow in the LVOT or in the ascending aorta, independent from the amount of the shunt fraction and beyond this to rule out any residual shunt at the end of the surgical procedure. Furthermore, the type of congenital heart defect (i.e. ASD/VSD) and consequently the associated specific pathologies regarding right and/or left atrial and ventricular compliance may influence the performance of dynamic variables of FR in different ways. Since we did not obtain data on atrial, ventricular, or both compliance, we cannot substantially comment on this particular point of interest. Further investigations highlighting these specific questions would be very helpful to more precisely define indications and limitations of dynamic variables of FR in infants. By implication, our results cannot be extrapolated to critically ill infants without congenital heart disease. However, we have chosen children with intracardiac shunts that benefit from curative surgery and consequently make them more comparable with infants and neonates being critically ill due to different diagnosis. Nevertheless, more data are needed in different paediatric clinical scenarios to more clearly define the relevance of dynamic variables of FR helping to guide fluid administration more precisely.

In conclusion, in infants and neonates undergoing congenital heart surgery, PPV but not SVV, CVP, and GEDVI accurately predicted FR both before and after repair of an intracardiac shunt.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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Declaration of interest

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