

Stroke volume variation and indexed stroke volume measured using bioreactance predict fluid responsiveness in postoperative children[†]

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Editor's key points

- This study assessed the ability of dynamic haemodynamic variables measured using a bioreactance device to predict fluid responsiveness.
- Stroke volume (SV) and stroke volume variation (SVV) measured by bioreactance were predictive for fluid responsiveness.
- Optimal threshold values for SV and SVV were 29 ml m⁻² and 10%, respectively.

Background. Postoperative fluid management can be challenging in children after haemorrhagic surgery. The goal of this study was to assess the ability of dynamic cardiovascular variables measured using bioreactance (NICOM[®], Cheetah Medical, Tel Aviv, Israel) to predict fluid responsiveness in postoperative children.

Methods. Children sedated and mechanically ventilated, who require volume expansion (VE) during the immediate postoperative period, were included. Indexed stroke volume (SVi), cardiac index, and stroke volume variation (SVV) were measured using the NICOM[®] device. Responders (Rs) to VE were patients showing an increase in SV measured using transthoracic echocardiography of at least 15% after VE. Data are median [95% confidence interval (CI)].

Results. Thirty-one patients were included, but one patient was excluded because of the lack of calibration of the NICOM[®] device. Before VE, SVi [33 (95% CI 31–36) vs 24 (95% CI 21–28) ml m⁻²; $P=0.006$] and SVV [8 (95% CI 4–11) vs 13 (95% CI 11–15)%; $P=0.004$] were significantly different between non-responders and Rs. The areas under the receiver operating characteristic curves of SVi and SVV for predicting fluid responsiveness were 0.88 (95% CI 0.71–0.97) and 0.81 (95% CI 0.66–0.96), for a cut-off value of 29 ml m⁻² (grey zone 27–29 ml m⁻²) and 10% (grey zone 9–15%), respectively.

Conclusions. The results of this study show that SVi and SVV non-invasively measured by bioreactance are predictive of fluid responsiveness in sedated and mechanically ventilated children after surgery.

Keywords: children; equipment, monitors; measurement techniques, transthoracic electrical impedance; monitoring, cardiopulmonary

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Postoperative fluid management after haemorrhagic surgery can be challenging. On the one hand, undiagnosed and uncorrected hypovolaemia may lead to organ dysfunction;¹ on the other hand, fluid overload may be associated with impaired oxygenation.² Therefore, to avoid hypovolaemia and overload, it is mandatory to accurately assess the preload state of the patients.

Static haemodynamic variables, corresponding to static measurement of cardiac filling pressures [mainly central venous pressure (CVP)], are unable to reliably assess fluid responsiveness in adults^{3–4} and in children.^{5–10} A more dynamic approach using variables based on the heart–lung interaction induced by mechanical ventilation has been proposed.¹⁰ When the two cardiac ventricles are working on the

steep portion of the Frank–Starling curve, the respiratory variations are high; the heart is preload-dependent; and the patient is more likely to be a fluid responder (R). In contrast, if at least one of the two ventricles works on the plateau of this relationship, then the respiratory variations are low and the heart is preload independent; the patient is more likely to be a fluid non-responder (NR). The use of respiratory variation of stroke volume or surrogates to predict fluid responsiveness has some limitations that are now identified:¹¹ (i) spontaneous breathing activity; (ii) cardiac arrhythmias; (iii) increased abdominal pressure; (iv) open-chest surgery; (v) high-frequency ventilation, with respiratory rates over 40 bpm; (vi) insufficient variations in intra-thoracic pressure [tidal volume (V_t) < 7 ml kg⁻¹ or decreased compliance of the respiratory system].

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In adult patients, dynamic variables, such as pulse pressure variation (PPV) and stroke volume variation (SVV), have been shown to reliably predict fluid responsiveness.^{12–14} In contrast, conflicting results have been obtained regarding the predictive values of dynamic variables in children.^{5 6 8 10 15–17}

Continuous efforts have been made to develop non-invasive methods for cardiac output (CO) and other haemodynamic variables measurement. One of the most widely studied non-invasive techniques relies upon bioimpedance, which involves the analysis of intra-beat variations in transthoracic voltage in response to applied high-frequency transthoracic currents.¹⁸ However, the analysis of published studies found discrepancies between CO measured using bioimpedance and thermodilution, and also numerous artifacts that interfered with measurement.^{19 20} Bioreactance is an innovative evolution of the bioimpedance device, processing, and analysing the electrical signal using a new technique. The bioreactance technique sends a high-frequency current, with known low amplitude, through the thorax and measures the frequency and phase modulations resulting from the changes in thoracic blood volume. With bioreactance, a much higher signal quality is obtained, because it is not the changes in the amplitude of the signal that are measured but the changes in frequency, allowing to significantly reduce background noise. In addition, bioreactance does not depend upon the distance between the electrodes for the calculations of CO, which significantly reduces the potential for error in the results. Controversial results have been published regarding the reliability of bioreactance for predicting fluid responsiveness in adult patients.^{21–23} Only one study is available on the use of bioreactance for predicting fluid responsiveness in children.¹⁶ In this study, SVV measured by bioreactance reliably predicted fluid responsiveness after cardiac surgery in children.¹⁶

The aim of this study was to assess the ability of dynamic haemodynamic variables measured using a bioreactance device to predict fluid responsiveness in children after craniostosis repair.

Methods

This prospective single-centre observational study was approved by the Institutional Review Board (IRB) (i.e. Comité de Protection des Personnes Ile-de-France VI) and was conducted in the paediatric neurosurgical intensive care unit of the Necker University Hospital (Paris, France). The patients and their parents (or legal guardians) were informed about the study, but the requirement for signed informed consent was waived by the IRB because of the design of the study, a prospective observational study without any change in the standard management of the children.

Patient population

Postoperative children, aged 0–16 yr, sedated and mechanically ventilated, and who require volume expansion (VE) in the early postoperative period (before postoperative hour 2) after craniostosis repair, could be included in the study.

Exclusion criteria were: patient or legal guardian refusal, cardiac dysrhythmia, severe systolic cardiac dysfunction, significant valvular heart disease, and intra-cardiac shunt.

Patient management and monitoring

Intraoperative anaesthesia management and fluid maintenance were left at the discretion of the anaesthetist in charge of the patient. In our institution, invasive monitoring is standard practice for paediatric patients undergoing craniostosis repair. Briefly, routine monitoring included ECG, invasive arterial and CVP, core temperature, pulse oximetry, end-tidal carbon dioxide (E'_{CO_2}), and urine output (bladder catheter). Isovolaemic compensation of blood loss was observed, with fluid replacement based upon haemodynamic variables, to maintain mean arterial pressure in the range of 45–55 mm Hg and CVP > 2 mm Hg, using artificial colloids and blood transfusion. Transfusion of packed red blood cells (PRBC) was used to maintain intraoperative haemoglobin level in the range of 7–10 g dl⁻¹ and fresh-frozen plasma (FFP) as required (FFP:PRBC transfusion ratio of 1.5–2). During the immediate postoperative period, sedation was maintained using a continuous i.v. infusion of midazolam, to maintain a Richmond Agitation Sedation Scale between –3 and –1, and analgesia was ensured with i.v. morphine and i.v. paracetamol. Mechanical ventilation was provided using: a V_t of 7–8 ml kg⁻¹ body weight, a PEEP of 3–4 cm H₂O, an I/E ratio of 1/1.5 to 1/1.7 (Servo-I Universel, System version 6.1 or 7.0, Maquet Critical Care, Sweden), while the respiratory rate was set to maintain an E'_{CO_2} between 35 and 40 mm Hg. Children were connected to an IntelliVue MP70™ patient monitor (Philips Medical Systems, Suresnes, France), which continuously recorded heart rate (HR, beats min⁻¹), systolic/diastolic/mean invasive arterial pressure (SAP/DAP/MAP, mm Hg), and CVP (mm Hg).

Bioreactance measurements

The bioreactance-based non-invasive CO and stroke volume measurement system relies upon an analysis of relative phase shifts of an oscillating current that occur when the current passes through the thorax.²⁴ The NICOM® device (NICOM®, Cheetah Medical, Tel Aviv, Israel) monitors CO using four electrodes. Two upper electrodes are placed on the right and left mid-clavicular lines of the thorax, respectively, and two lower electrodes are placed on the midpoints of the right and left 12th ribs, respectively. After placing the electrodes and entering patients' characteristics, the NICOM® device automatically calibrates and then provides continuous values of: stroke volume (SV), indexed stroke volume (SVI), CO, cardiac index, and SVV.

Echocardiographic measurements

Transthoracic echocardiography (TTE) was performed using a Siemens Acuson CV70™ (Siemens Medical Solutions, Issaquah, WA, USA). All measurements were performed by the same investigators (E.V. and C.V.). The aortic diameter (D , mm) was measured at the aortic annulus level in a two-dimensional view from the parasternal long-axis view.

Pulsed Doppler waves aortic flow was recorded at the exact level of the aortic annulus in the apical five-chamber view. Maximal and minimal aortic velocity–time integral (VTI) was measured over a single respiratory cycle on two sets of measurements; then VTI_{mean} was calculated. Stroke volume measured using TTE (SV_{TTE}) was calculated as follows:

$$SV_{TTE} \text{ (ml)} = \frac{VTI_{mean} \times \pi(D)^2}{4}$$

Data recording

In addition to the usual patient's characteristics, respiratory settings and haemodynamic variables were recorded, and also data measured by thoracic bioimpedance (SV_i and cardiac index) immediately before and after VE. The PPV index, based on Aboy and colleagues,^{25 26} was continuously displayed by the Philips® monitor (Intellivue MP70, Philips Medical System). In accordance with our unit policy, children who were clinically judged to require VE (tachycardia, hypotension, oliguria, or delayed capillary refilling) received an i.v. bolus of 20 ml kg^{-1} of artificial colloids (Plasmion®, Fresenius Kabi, France) over 15–30 min.

Statistical analysis

Data were analysed with the Shapiro–Wilk and Kolmogorov–Smirnov tests. Data are expressed as mean (SD) or median (95% confidence interval), as appropriate, and as numbers of patients (%). Rs to VE were defined as patients showing an SV_{TTE} increment of at least 15% after VE and non-responders

(NRs) as those showing an SV increment of <15%. Comparisons between R and NR were assessed using a two-sample Student *t*-test or a Mann–Whitney *U*-test, as appropriate. The predictive ability of a variable for fluid responsiveness was assessed using receiver operating characteristics (ROC) curve analysis. For each variable, a threshold value was determined to maximize both sensitivity and specificity. The grey zone corresponds to a range of values for which the variable of interest does not provide conclusive information. Inconclusive responses are defined for pre-challenge values of the variable of interest with a sensitivity <90% or specificity <90% (diagnosis tolerance of 10%).^{27 28} Grey zone limits are expressed as (low limit–high limit). A power analysis showed that 25 patients were necessary to detect a difference of 0.3 between SVV and CVP areas under the ROC curves (5% type I error rate, 80% power, two-tailed *t*-test). Allowing for possible dropouts, 31 patients were included in the current study. Data were also analysed according to two age strata: 0–3 and >3–16 yr. A *P*-value of 0.05 was considered statistically significant. The statistical analysis was performed with the BiostaTGV software (INSERM and Pierre et Marie Curie University, Paris, France, <http://marne.u707.jussieu.fr/biostatgv/>).

Results

Between August 2012 and July 2013, 31 patients were included after craniostomy surgical repair (Fig. 1). One patient was excluded from the study because of the lack of calibration of the NICOM® device. Therefore, the data from 30 patients were included in the analysis.

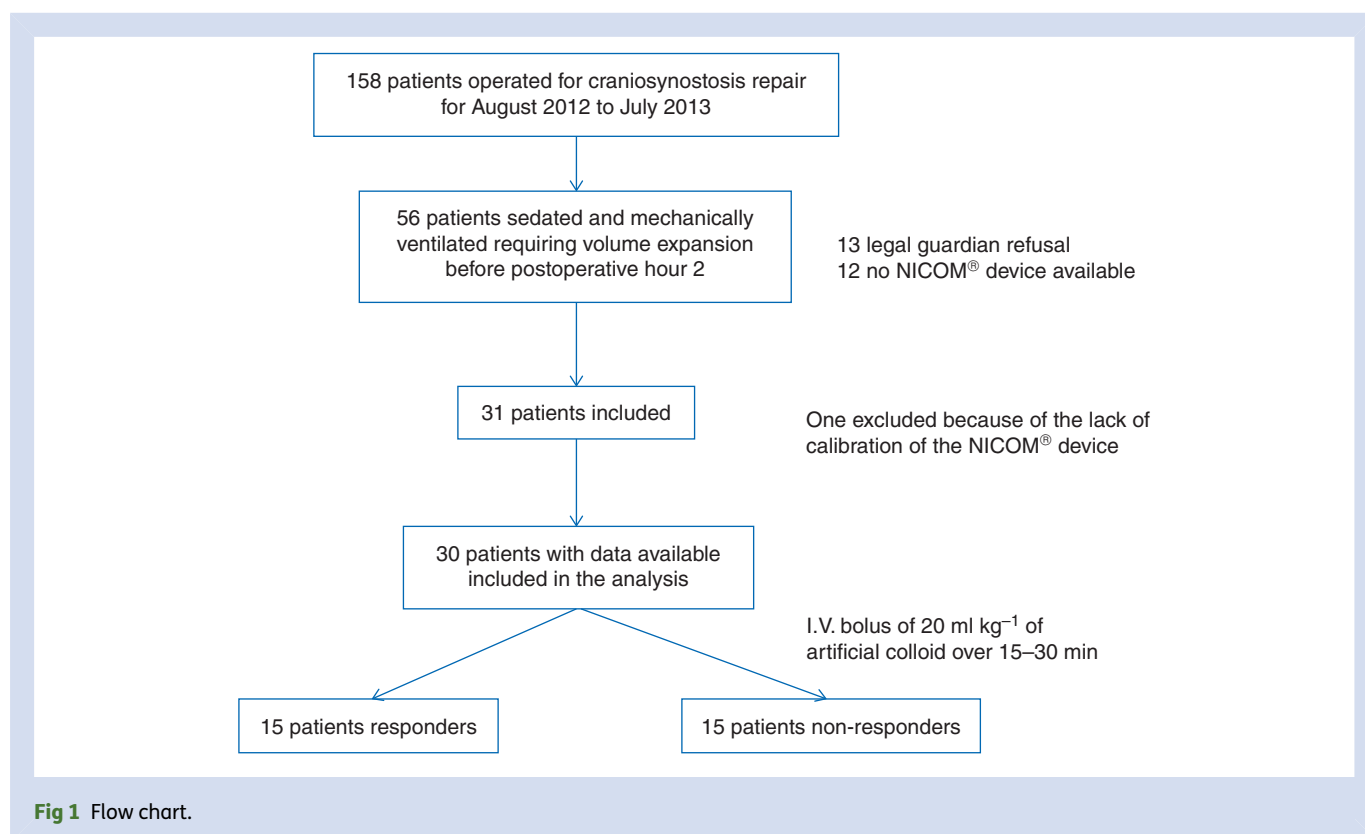


Fig 1 Flow chart.

Table 1 Baseline characteristics of the Rs and the NRs to VE. Data are median (95% CI). BSA, body surface area. *VE was performed using artificial colloid (Plasmion®)

	NRs (n = 15)	Rs (n = 15)	P-value
Age (months)	60.0 (32.8–96.8), range (4–137)	27.0 (11.5–32.7), range (7–139)	0.077
Body weight (kg)	18.0 (11.5–24.5)	13.0 (9.1–15.0)	0.191
BSA (m ²)	0.72 (0.52–0.94)	0.57 (0.42–0.64)	0.158
Aortic diameter (cm)	13.7 (10.7–15.1)	11.6 (9.7–13.5)	0.329
VE (ml kg ⁻¹ *)	20.0 (20.0–20.0)	20.0 (19.6–20.0)	0.838
PEEP (cm H ₂ O)	3 (3–3)	3 (3–5)	0.287
Mean airway pressure (cm H ₂ O)	8.0 (8.0–9.0)	8.0 (7.2–8.0)	0.135
V _t (ml kg ⁻¹)	8.3 (7.1–9.2)	8.0 (6.9–11.1)	0.85
Haematocrit (%)	32.2 (29.7–37.9)	32.3 (28.7–35.6)	0.62

Table 2 Differences in haemodynamic variables between R and NR before and after VE. Data are expressed as median (95% CI). HR, heart rate; MAP, mean arterial pressure; CVP, central venous pressure; PPV, pulse pressure variation; SVi, indexed stroke volume; SVV, stroke volume variation. *P<0.05 vs before VE (baseline) within a group. †P<0.05 vs NRs

	Before VE		After VE	
	NRs	Rs	NRs	Rs
HR (beats min ⁻¹)	106 (86–116)	130 (106–144)†	108 (89–118)	135 (104–145)†
MAP (mm Hg)	73 (61–91)	67 (63–85)	83 (67–91)	80 (74–93)
CVP (mm Hg)	5.5 (4.0–9.6)	8.0 (3.9–9.0)	10.0 (6.3–16.4)	13.5 (7.0–16.5)*
PPV (%)	7.0 (5.9–10.0)	10.0 (9.0–12.9)†	5.0 (4.2–8.0)	6.0 (5.2–8.2)
SVi (ml m ⁻²)	33 (31–36)	24 (21–28)†	34 (30–38)	35 (26–36)*
SVV (%)	8 (4–11)	13 (11–15)†	7 (4–11)	10 (7–12)
Cardiac index (litre min ⁻¹ m ⁻²)	3.3 (2.8–3.8)	3.1 (2.4–3.6)	3.3 (3.0–4.1)	3.8 (3.3–5.0)*

Table 3 Prediction of the fluid responsiveness by the ROC curves of CVP, PPV, SVi, and SVV measured using the NICOM® device. AUC, area under the ROC curve; Grey zone, range of values with a sensitivity <90% or specificity <90%

	Cut-off value	AUC (95% CI)	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)	Grey zone
CVP	8 mm Hg	0.59 (0.35–0.80)	40	80	57	66	3–9 mm Hg
PPV	8%	0.77 (0.57–0.91)	78	69	72	76	6–10%
SVi	29 ml m ⁻²	0.88 (0.71–0.97)	93	80	71	100	27–29 ml m ⁻²
SVV	10%	0.81 (0.66–0.96)	93	80	74	90	9–15%

Baseline patient characteristics were similar for the Rs and the NRs (Table 1).

Table 2 shows the haemodynamic variables in the Rs and NRs, before and after VE. Before VE, HR [106 (95% CI 86–116) vs 130 (95% CI 106–144); $P=0.016$], PPV [7.0% (95% CI 5.9–10.0) vs 10.0% (95% CI 9.0–12.9), $P=0.0149$], SVi [33 (95% CI 31–36) vs 24 (95% CI 21–28) ml m⁻²; $P=0.006$], and SVV [8 (95% CI 4–11) vs 13 (95% CI 11–15)%; $P=0.004$] were significantly different between NR and R (Table 2). The areas under the ROC curves of SVi (cut-off value: 29 ml m⁻²) and SVV (cut-off value: 10%) for predicting fluid responsiveness were, respectively, 0.88 (95% CI 0.71–0.97) and 0.81 (95% CI 0.66–0.96) (Table 3, Fig. 2). Corresponding grey zone limits were (26–29 ml m⁻²) and (9–15%), respectively. Data from the two age strata (0–3 and 3–16 yr) are presented in Table 4.

Discussion

In this study, SVi and SVV measured by bioreactance were found to be predictive of fluid responsiveness, with optimal threshold values of 29 ml m⁻² and 10%, respectively, in sedated and mechanically ventilated children after craniostomy surgical repair.

In children, there is an urgent need for a tool enabling to predict fluid responsiveness to avoid undue fluid loading, carrying a risk of impaired oxygenation.² In our study, we have noted that VE based on standard clinical monitoring was inappropriate in 50% of children. This result is in accordance with the adult literature^{12–29} and has been also recently confirmed in paediatric patients.^{5–8, 10} Before VE, MAP and CVP were not different between R and NR in our study. In contrast, HR was

significantly different between R and NR. However, while increased HR may indicate some degree of hypovolaemia, the interpretation of tachycardia in the perioperative period is not univocal and may be related to different causes, including, for example, pain or other cause of discomfort. Lastly, anaesthetists may be confronted with difficulty distinguishing whether a patient had responded positively or negatively to VE.⁷ Therefore, a tool enabling them to know when to start and when to stop fluid loading in children could be useful.

Thoracic bioimpedance was among the first and most widely used non-invasive method of measuring CO.³⁰ However, the

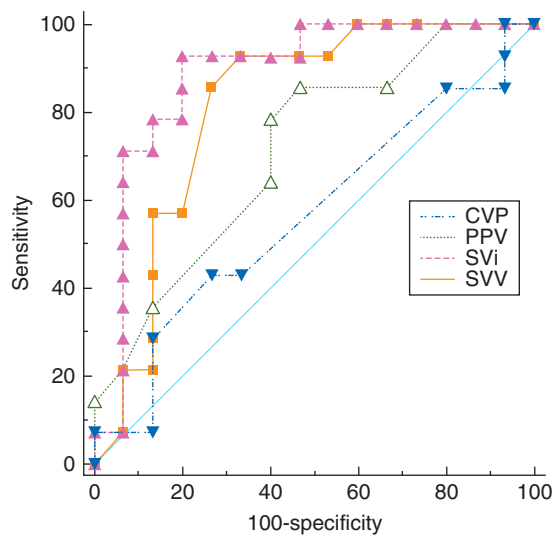


Fig 2 Prediction of the fluid responsiveness by the ROC curves of indexed stroke volume (SVi, cut-off value: 29 ml m⁻²) and stroke volume variation (SVV, cut-off value: 10%) measured using the NICOM[®] device. The straight line is a reference line. The areas under the ROC curves of SVi and SVV are 0.88 (95% CI 0.71–0.97) and 0.81 (95% CI 0.66–0.96), respectively.

analysis of published studies found discrepancies between CO measured using bioimpedance and thermodilution and also numerous artifacts that interfered with measurement.^{19 20} Bioreactance has the advantage over bioimpedance of getting a much higher signal quality, by reducing the background noise. Unlike bioimpedance, bioreactance does not use static impedance and does not depend upon the distance between the electrodes for the calculations of CO, which significantly reduces the potential for error in the results. Paediatric studies assessing the performance of bioimpedance and bioreactance devices for the measurement of CO are limited and have provided contrasting results.^{31–34} Up to now, only one study has assessed the ability of haemodynamic variables provided by the NICOM[®] device to predict fluid responsiveness in mechanically ventilated children.¹⁶ This study has shown that SVV measured by NICOM[®] reliably predicted fluid responsiveness in children during mechanical ventilation after cardiac surgery.¹⁶ Thus, the results from this study are in agreement with our own results, with an optimal cut-off value of SVV of 10% which is similar to the cut-off value found in our study.¹⁶

Dynamic variables such as SVV, pulse pressure, and systolic pressure variation are clinically reliable variables for predicting fluid responsiveness in adults.^{3 4 12 29} However, they are underexplored in children and the few results available are controversial. In paediatric patients, the respiratory variation in aortic blood flow velocity (ΔV_{peak} , derived by echocardiography) is now considered as reliable for predicting fluid responsiveness.¹⁰ More recently, measurements of SVV¹⁶ and SVi^{7 35} were also found to be predictive of fluid responsiveness in children. In our study, PPV was significantly different between Rs and NRs before VE (Table 2). However, the area under the ROC curve for PPV was <0.80 (Table 3), confirming that peripheral dynamic index does not predict fluid responsiveness in children,¹⁰ in contrast to central index, such as SVi and SVV in children more than 3 yr of age (Table 4).

Among many advantages of SVV and SVi measured using bioreactance, one may underline: a totally non-invasive aspect (as opposed to oesophageal Doppler which may be considered

Table 4 Prediction of the fluid responsiveness by the ROC curves of CVP, PPV, SVi, and SVV measured using the NICOM[®] device in children under and more than 3 yr of age. AUC, area under the ROC curve; Grey zone, range of values with a sensitivity <90% or specificity <90%; R, responder to VE; NR, non-responder to VE

	Cut-off value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Grey zone
Children < 3 yr (n = 17, R = 12, NR = 5)							
CVP	6 mm Hg	0.74 (0.38–0.95)	100	43	34	100	3–5 mm Hg
PPV	12%	0.60 (0.33–0.83)	28	100	37	100	9–11%
SVi	26 ml m ⁻²	0.92 (0.68–0.99)	75	100	100	63	27–28 ml m ⁻²
SVV	9%	0.57 (0.31–0.81)	91	40	80	100	7–17%
Children > 3 yr (n = 13, R = 3, NR = 10)							
CVP	5 mm Hg	0.76 (0.41–0.96)	100	43	44	100	8–9 mm Hg
PPV	8%	0.81 (0.48–0.97)	67	100	100	87	6–6%
SVi	33 ml m ⁻²	0.81 (0.49–0.96)	100	60	52	100	28–32 ml m ⁻²
SVV	10%	0.97 (0.70–1.00)	100	90	81	100	10–11%

as semi-invasive), the possibility of continuous monitoring (as opposed to echocardiography), and the fact that it is easy to use ('plug and play').

In our study, Rs to VE were defined as patients showing an increase in SV_{TTE} of at least 15% after VE. We have decided to choose this cut-off value of 15% based on the results of previous studies in children, which suggested that this difference is clinically significant.¹⁰

One possible limitation of our study is related to the relatively wide age range of patients included in our study. This could potentially result in a heterogeneous population, in particular from a cardiovascular physiology point of view. However, no patient was aged more than 12 yr and <6 months, while the major differences in cardiovascular physiology are usually observed between children under and more than 6 months of age.³⁶ In the NR and R groups, the age ranged from 6 to 137 and 7 to 139 months, respectively, without patients younger than 6 months. Moreover, other authors studying fluid responsiveness in children have included patients with wider age range. For example, in a very recent study assessing the utility of SVV as a predictor of fluid responsiveness in children, the authors have included 13 children aged 2 months to 14 yr.³⁷ On the other hand, we also performed an analysis after stratification for age under and above 3 yr. Such a subgroup analysis was able to provide further insights into the effect of age on fluid responsiveness assessment (Table 4). However, we recognize that these results should be interpreted with caution because stratifying by age may generate a problem of statistical power. Indeed, power and sample size calculations were based on the total number of patients and not on the number of patients included in each subgroup.

Bioreactance has its own shortcomings. The mathematical model of the bioreactance is based on several anatomical and physiological assumptions, including the fact that blood resistivity is supposed to remain constant. However, blood resistivity is proportional to haematocrit; therefore, significant haemodilution might skew bioreactance CO measurement. Nevertheless, previous studies have shown that this limitation was not significant for haematocrit values ranging from 25% to 45%.³⁸ All the patients included in our study had haematocrit values included in this range. In addition, the bias and precision of the NICOM[®] device measurements are comparable with what is published in the literature for other methods of CO measurements used in the paediatric population.^{39 40}

In conclusion, the results of this study show that SVi and SVV non-invasively measured by bioreactance are predictive of fluid responsiveness in sedated and mechanically ventilated postoperative children.

Authors' contributions

E.V.: study design, patient recruitment, data collection, and data analysis; C.V.: patient recruitment, data collection, and data analysis; J.V., J.M., and P.M.: patient recruitment and data collection; P.C.: data analysis and writing up of the paper. G.O.: study design, data analysis, writing up of the paper, and archiving of the study files.

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Declaration of interest

None declared.

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