Prediction of fluid responsiveness using a non-invasive cardiac output monitor in children undergoing cardiac surgery


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Abstract

Background: This study evaluated the ability of a non-invasive cardiac output monitoring device (NICOM) to predict fluid responsiveness in paediatric patients undergoing cardiac surgery.

Methods: Children aged <5 yr undergoing congenital heart surgery were included. Once the sternum had been closed after repair of the congenital heart defect, 10 ml kg\(^{-1}\) colloid solution was administered for volume expansion. Transoesophageal echocardiography (TOE) was performed to measure stroke volume (SV) and respiratory variation in aortic blood flow peak velocity (\(\Delta V_{\text{peak}}\)) before and after volume expansion. Haemodynamic and NICOM variables, including SV\(_{\text{NICOM}}\), stroke volume variance (SVV\(_{\text{NICOM}}\)), cardiac index (CI\(_{\text{NICOM}}\)), and percentage change in thoracic fluid content compared with baseline (TFC\(_d0\%), were also recorded. Patients in whom the stroke volume index (SVI), measured using TOE, increased by >15% were defined as fluid responders.

Results: Twenty-nine patients were included (13 responders and 16 non-responders). Before volume expansion, only \(\Delta V_{\text{peak}}\) differed between groups (\(P=0.036\)). The SV\(_{\text{NICOM}}\), HR, and central venous pressure did not predict fluid responsiveness, but \(\Delta V_{\text{peak}}\) did. The CI\(_{\text{NICOM}}\) was not correlated with CI\(_{\text{TOE}}\) (\(r=0.107, P=0.43\)). Using Bland–Altman analysis, the mean bias between CI\(_{\text{TOE}}\) and CI\(_{\text{NICOM}}\) was 0.89 litre min\(^{-1}\) m\(^{-2}\), with a precision of 1.14 litre min\(^{-1}\) m\(^{-2}\). Trending ability of NICOM for SVI and CI was poor when TOE was a reference method.

Conclusions: The SVV\(_{\text{NICOM}}\) did not predict fluid responsiveness in paediatric patients during cardiac surgery. In addition, there was no correlation between CI\(_{\text{TOE}}\) and CI\(_{\text{NICOM}}\). Fluid management guided by NICOM should be performed carefully.

Clinical trial registration: ClinicalTrials.gov NCT01996956.

Key words: cardiac output; cardiac surgical procedure; fluid therapy; paediatrics; stroke volume

In paediatric patients undergoing cardiac surgery, adequate fluid management is important. Hypovolaemia can impair organ perfusion and cause metabolic acidosis; however, excessive fluid overload can cause acute ventricular dysfunction and pulmonary oedema.

It is more difficult to predict the fluid responsiveness in children compared with adults. In adults, pulse pressure variation and stroke volume variation (SVV) reliably predict the fluid loading response and are superior to traditional central venous pressure (CVP).\(^1\)\(^-\)\(^4\) However, evidence that these dynamic variables predict fluid responsiveness in children is limited, with conflicting results.\(^5\)\(^-\)\(^8\) Except for respiratory variation in aortic blood flow peak velocity (\(\Delta V_{\text{peak}}\)), no variables reliably predicted fluid responsiveness in paediatric patients.\(^9\) Furthermore, the need for non-invasive fluid management methods in children continues to increase.
Editor’s key points

- Fluid responsiveness in paediatric patients is difficult to predict, and there are few data on the validity of non-invasive cardiac output monitoring in children.
- This study found that stroke volume variation estimated using the NICOM device did not predict fluid responsiveness.
- There was also poor correlation between cardiac index assessed using NICOM or transoesophageal echocardiography.
- Clinicians should interpret variables derived using NICOM with caution in children undergoing cardiac surgery.

The non-invasive cardiac output monitoring device (NICOM; Cheetah Medical, Wilmington, DE, USA) uses a non-invasive technique, based on transthoracic bioelectance, which applies a high-frequency electrical current of known amplitude and frequency across the thorax and detects the relative phase shift between the injected current and recorded voltage. Phase shifts occur as a result of pulsatile changes in blood volume in the aorta. Several studies have demonstrated the clinical usefulness and feasibility of the NICOM in adults, but its effectiveness in children remains controversial. However, in one study, NICOM values predicted fluid responsiveness non-invasively in children in the intensive care unit. During operations, the NICOM may facilitate volume administration in paediatric patients.

In the present study, we assessed whether SVV values measured using NICOM (SVVNICOM) can predict fluid responsiveness in children after repair of congenital heart defects and compared NICOM-derived values with other possible predictors of fluid responsiveness. We also evaluated the accuracy of cardiac index (CI) measured using NICOM (CINICOM) vs transoesophageal echocardiography (TOE; CITOE).

Methods

The study was approved by the Institutional Review Board of Seoul National University Hospital and was registered at ClinicalTrials.gov (NCT01996956). Written informed consent was provided by all parents. Children <5 yr of age undergoing congenital heart surgery were enrolled. Patients with a single ventricle, right heart failure, renal failure, respiratory disease, any cardiac arrhythmia, or moderate or severe valvular stenosis and regurgitation were excluded.

No premedications were administered. Anaesthesia was induced with midazolam (0.1 mg kg⁻¹), thiopental (5 mg kg⁻¹) and atropine (0.02 mg kg⁻¹). Rocuronium (0.6 mg kg⁻¹) and fentanyl (5–10 μg kg⁻¹) were used for endotracheal intubation. Anaesthesia was maintained using midazolam (0.1–0.2 mg kg⁻¹ h⁻¹), sufentanil (2.5–5 μg kg⁻¹ h⁻¹), and vecuronium (0.05–0.1 mg kg⁻¹ h⁻¹). Mechanical ventilation was controlled to obtain an arterial partial pressure of CO₂ of 35–40 mm Hg, with a constant tidal volume of 10 ml kg⁻¹ maintained during surgery.

After induction of anaesthesia, a peripheral arterial catheter was placed at the left or right radial artery; a central venous catheter was inserted into the right internal jugular vein. Monitoring using the NICOM device commenced with four NICOM dual electrodes attached to the patient’s back in accordance with the manufacturer’s instructions. A TOE probe (either S8-3t or S7-3t; iE33 Echocardiography System; Philips, Andover, MA, USA) was then inserted.

Following weaning from cardiopulmonary bypass, lung recruitment was performed to prevent atelectasis. Ventilation was commenced using a tidal volume of 10 ml kg⁻¹; the respiratory rate was controlled to maintain normocarbia.

Experimental protocol

The NICOM was recalibrated when the patients were fully weaned from cardiopulmonary bypass. After closure of the sternum, baseline NICOM-derived variables (stroke volume [SVNCOM], SVVNICOM, CINICOM) and percentage change in thoracic fluid content compared with baseline (TFCd0%) were recorded. Volulyte® (6% hydroxyethyl starch 130/0.4) at 10 ml kg⁻¹ was administered for 10 min; after fluid loading, NICOM variables were recorded again. The mean of three serial NICOM values was used in the analysis. Peak inspiratory pressure, CVP, arterial blood pressure, body temperature, and vasoactive and inotropic agent doses were also recorded during the experimental period. Infotrop agent use (vasoactive–inotropic score) was then calculated as follows: dopamine dose (in μg kg⁻¹ min⁻¹) + dobutamine dose (in μg kg⁻¹ min⁻¹) + [epinephrine dose × 100 (in μg kg⁻¹ min⁻¹)] + [milrinone dose × 100 (in μg kg⁻¹ min⁻¹)] + [vasopressin dose × 100 (in U kg⁻¹ min⁻¹)] + [norepinephrine dose × 100 (in μg kg⁻¹ min⁻¹)].

Echocardiographic measurement

All echocardiography data were measured by a single expert, who was blinded to all values measured by NICOM.

Stroke volume and cardiac index

To measure SVT, the aortic annulus diameter (D) was measured during the systolic phase mid-oesophageal aortic valve long-axis view. A TOE probe was then advanced to obtain a deep transgastric long-axis view. Using pulsed wave Doppler, the aortic blood flow waveform at the level of the aortic annulus was recorded. The mean velocity time integral (VTI) was calculated from three consecutive waves at the end of the expiratory period.

Variables were calculated as follows:

\[ SV = 3.14 \times (D/2)^2, \]
\[ CO = SV \times HR, \]
\[ CI = CO \times BSA^{-1}, \]

where CO is the cardiac output, HR the heart rate, and BSA the body surface area.

Respiratory variation in aortic blood flow peak velocity

Using pulsed wave Doppler, the maximal and minimal blood flow velocity (Vpeak) during one respiratory cycle was measured, at the aortic valve level in the deep transgastric long-axis view. The respiratory variation in Vpeak (ΔVpeak) was calculated as follows:

\[ \Delta V_{peak} = \frac{(V_{peak_{max}} - V_{peak_{min}}) \times (V_{peak_{max}} + V_{peak_{min}})^2}{100}. \]

The mean ΔVpeak was calculated using three consecutive respiratory cycles.

Statistics

The required number of patients was determined according to data from previous studies, in which the area under the receiver operating characteristic (ROC) curve for variable predictors...
ranged from 0.77 to 0.86, with a responder to non-responder ratio of approximately 1:1.57. We assumed that the SVV\textsubscript{NICOM} would predict fluid responsiveness with an area under the ROC curve of >0.8. We calculated a required sample size of 29 using the PASS software 2008 (version 8.0.16; NCSS Statistical Software, Kaysville, UT, USA), with an \( \alpha \) error of 0.05, a power of 0.8, and an estimated 10% attrition rate.

Following fluid challenge, we defined two study groups: the fluid responder group, comprising patients in whom fluid administration increased SV\textsubscript{TOE} by >15%; and the non-responder group, comprising the remaining patients.

Statistical analyses were performed using SPSS (version 20; SPSS Inc., Chicago, IL, USA) and MedCalc software (version 12.7.7; MedCalc, Ostend, Belgium). Student’s unpaired \( t \)-test or the Mann–Whitney \( U \)-test was used to evaluate group differences. To determine the ability of all variables to predict fluid responsiveness, ROC curves were generated, and the area under the ROC curve was calculated. To assess correlation between TOE and NICOM in SV, SVI, and CI, linear regression analysis was performed. The concordance between C\textsubscript{NICOM} and C\textsubscript{TOE} was evaluated using the Bland–Altman method. The mean difference (bias) and precision (SD) between C\textsubscript{NICOM} and C\textsubscript{TOE} was also calculated. The 95% limits of agreement were calculated using the interval defined by the observed bias (1.96 SD). Polar plot was used to evaluate the trending ability of NICOM compared with TOE. A value of \( P<0.05 \) was taken to indicate statistical significance.

**Results**

The study included a total of 29 paediatric patients (15 males and 14 females) who had undergone either ventricular septal defect (n=5), ventricular septal defect with atrial septal defect (n=7), ventricular septal defect with infundibular muscle resection (n=3), atrial septal defect (n=6), atrioventricular septal defect (n=1), or tetralogy of Fallot operations (n=1). After surgery, no significant valvular regurgitation or ventricular dysfunction occurred in any patient. Table 1 lists the patient characteristics and intraoperative variables.

In total, 13 patients were volume responders and 16 non-responders (Fig. 1). No significant group difference was observed in clinical characteristics or intraoperative variables. Before volume expansion, only the \( \Delta V \text{peak} \) differed between the two groups.

![Fig 1 Consolidated Standards of Reporting Trials (CONSORT) diagram.](image-url)
Value of predicted a 15% increase in SVI (SVVNICOM and activity of 78.6%. There was positive relationship between responsiveness was not predicted by SVVNICOM, H R, and CVP, but with thoracic fluid content compared with baseline; TOE, transoesophageal echocardiography. *P < 0.05 before FL is after FL. †P < 0.05 between responders and non-responders in both before FL. P-value was adjusted for multiple comparisons. Variables are expressed as mean (sd) or number.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Responders (n=13)</th>
<th>Non-responders (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before FL</td>
<td>After FL</td>
</tr>
<tr>
<td>Heart rate (beats min⁻¹)</td>
<td>135 (22)</td>
<td>127 (22)*</td>
</tr>
<tr>
<td>Systolic arterial pressure (mm Hg)</td>
<td>97 (12)</td>
<td>116 (12)*</td>
</tr>
<tr>
<td>Diastolic arterial pressure (mm Hg)</td>
<td>47 (4)</td>
<td>63 (14)*</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>61 (6)</td>
<td>74 (12)*</td>
</tr>
<tr>
<td>Central venous pressure (mm Hg)</td>
<td>5 (3)</td>
<td>8 (3)*</td>
</tr>
<tr>
<td>SVI_TOE (ml m⁻²)</td>
<td>20.5 (6.2)</td>
<td>21.4 (8.2)*</td>
</tr>
<tr>
<td>CI_TOE (litre min⁻¹ m⁻²)</td>
<td>2.7 (0.6)</td>
<td>3.2 (0.8)*</td>
</tr>
<tr>
<td>SVV_NICOM (ml m⁻²)</td>
<td>16.0 (4.8)</td>
<td>19.1 (7.4)*</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>2.1 (0.4)</td>
<td>2.1 (0.9)</td>
</tr>
<tr>
<td>SVV_NICOM (%)</td>
<td>13.6 (4.4)</td>
<td>11.4 (4.6)*</td>
</tr>
<tr>
<td>TFCd0%</td>
<td>3.4 (7.6)</td>
<td>6.1 (8.1)*</td>
</tr>
<tr>
<td>ΔV_peak (%)</td>
<td>15.5 (6.3)</td>
<td>8.7 (2.6)*</td>
</tr>
</tbody>
</table>

Comparison of areas under receiver operating characteristic curves before volume expansion. The areas under the curve for SVV_NICOM, HR, CVP, and ΔV_peak were 0.51 (95% confidence interval 0.32-0.70), 0.507 (95% confidence interval 0.32-0.70), 0.68 (95% confidence interval 0.48-0.84), and 0.77 (95% confidence interval 0.57-0.91), respectively. A ΔV_peak of >13.5% alone predicted fluid responsiveness, with a sensitivity of 69.2% and specificity of 78.6%. CVP, central venous pressure; HR, heart rate; SVV_NICOM, stroke volume variation measured by non-invasive cardiac output monitoring device (NICOM); ΔV_peak, respiratory variation in aortic blood flow peak velocity.

Discussion

This study demonstrated that the NICOM device cannot be used to predict fluid responsiveness in paediatric patients <5 yr of age undergoing cardiac surgery. The correlation between NICOM- and TOE-derived CI following volume expansion was weak. In addition, the trending ability of NICOM was poor.

The NICOM device uses bioreactance to measure cardiac output, with four dual electrodes attached to the thorax; this has been considered as an innovative method that is potentially applicable in children. Some studies report a strong correlation between NICOM and echocardiographic measurements of CI in both neonates and children. However, in another report using a paediatric haemorrhagic shock model, CI values measured by bioreactance were not correlated with values recorded using the pulmonary artery thermodilution technique and did not reflect the changes in SVI_TOE induced by volume expansion (r=0.08, P=0.7).

Values of SVV_NICOM and SVV_NICOM were correlated with SVI_TOE and SVI_TOE (r=0.751 and 0.409, P<0.001 and P=0.001, respectively). However, CVP was not correlated with CVP (r=0.107, P=0.43; Fig. 3). The CVP values were 2.12 (0.56) litre min⁻¹ m⁻², which was significantly lower than the CVP value of 3.01 (1.07) litre min⁻¹ m⁻² (P<0.01). Using Bland-Altman analysis, the mean bias and precision of CVP and CVP were 0.89 and 1.14 litre min⁻¹ m⁻², respectively (Fig. 4). The limits of agreement were −1.3 and 3.1 litre min⁻¹ m⁻².

Polar plots were created to assess the trending ability of NICOM for CI when TOE was a reference method; however, it showed poor trending ability (Fig. 5).
In addition, CI values measured by bioreactance differed from normal-range values, particularly in smaller children. Similar results were obtained in another neonate study, in which NICOM underestimated CI values when compared with echocardiographic data; in the present study, NICOM also underestimated CI values by ~30% compared with TOE. We observed no correlation between CI

change significantly during hypovolaemia and volume expansion. In addition, CI values measured by bioreactance differed according to the weight of the patient and were lower than normal-range values, particularly in smaller children. Similar results were obtained in another neonate study, in which NICOM underestimated CI values when compared with echocardiographic data; in the present study, NICOM also underestimated CI values by ~30% compared with TOE. We observed no correlation between CI

Predicting fluid responsiveness in children is important in instances of low cardiac output. The predictive ability of several haemodynamic variables of fluid responsiveness has been evaluated. Static variables, such as HR and CVP, were assessed during major paediatric operations, with area under the ROC curve values of 0.53–0.55 in HR and 0.47–0.61 in CVP. In our study, the areas under the ROC curves of HR and CVP were 0.51 (95% confidence interval 0.32–0.70) and 0.68 (95% confidence interval 0.48–0.84), respectively. Although typically used to estimate intravascular volume status, HR and CVP are poor predictors of fluid responsiveness.

The ΔVpeak has been known to be the only variable shown to predict fluid responsiveness in children. The ΔVpeak is considered an accurate method of evaluating preload in ventilated patients with septic shock. Suggested cut-off values are 7–20%. Variations in study population, such as surgical patients without concomitant disease or critically ill patients, explain the wide range of cut-off values. In the present study, ΔVpeak was also a good predictor of fluid responsiveness, with cut-off values of ~13.5%, consistent with previous studies.

Although evidence that SVV can be a predictor of fluid responsiveness is still insufficient, there was still a possibility that SVV would be a target parameter for volume management in children. Recently, two studies showed that the dynamic parameters of NICOM can guide fluid management in paediatric patients after major surgery. According to these reports, SVV

In a recent study, SVV

Fig 3 Correlation between the transoesophageal echocardiography (TOE) and non-invasive cardiac output monitoring device (NICOM) variables. (a) Stroke volume (SV). (b) Stroke volume index (SVI). (c) Cardiac index (CI).

"Fig 4 Bland–Altman plot of cardiac indices measured by NICOM and TOE. The bias and precision of the two methods were 0.89 and 1.14 litre min⁻¹ m⁻², respectively."
the ROC curve was 0.57 in younger children. This result coincides with our findings, because the range of age of our patients was between 1 and 36 months.

The present study had several limitations. First, echocardiographic measurement errors may have occurred, even though the same expert obtained all of the echocardiographic data. Second, electrodes were sometimes folded or applied to different sites because of limited space in smaller patients, which may have influenced the NICOM variables. Finally, the reason for inaccuracy of NICOM has not been clearly determined yet, as commented in a previous report.26

In conclusion, SVV measured using the NICOM system did not predict fluid responsiveness in pediatric patients during cardiac surgery. In addition, there was no correlation between the CI obtained using NICOM and echocardiography. Careful fluid management is needed when using NICOM during pediatric cardiac surgery.

Authors’ contributions

Declaration of interest
None declared.

References

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