ANESTHESIOLOGY

# Respiratory Variation of Internal Carotid Artery Blood Flow Peak Velocity Measured by Transfontanelle Ultrasound to Predict Fluid Responsiveness in Infants

## A Prospective Observational Study

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## ABSTRACT

**Background:** Cranial sonography is a widely used point-of-care modality in infants. The authors evaluated that the respiratory variation of the internal carotid artery blood flow peak velocity as measured using transfontanelle ultrasound can predict fluid responsiveness in infants.

**Methods:** This prospective observational study included 30 infants undergoing cardiac surgery. Following closure of the sternum, before and after the administration of 10ml · $kg^{-1}$ crystalloid, the respiratory variation of the aorta blood flow peak velocity, pulse pressure variation, and central venous pressure were obtained. The respiratory variation of the internal carotid artery blood flow peak velocity was measured using transfontanelle ultrasound. Response to fluid administration was defined as an increase in stroke volume index, as measured with transesophageal echocardiography, greater than 15% of baseline.

**Results:** Seventeen subjects (57%) were responders to volume expansion. Before fluid loading, the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity (means ± SD) of the responders were 12.6 ± 3.3% and 16.0 ± 3.8%, and those of the nonresponders were 8.2 ± 3.2% and 10.9 ± 3.5%, respectively. Receiver operating characteristic curve analysis showed that the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity could predict fluid responsiveness; the area under the curve was 0.828 ($P < 0.0001$; 95% CI, 0.647 to 0.940) and 0.86 ($P = 0.0001$; 95% CI, 0.684 to 0.959), respectively. The cutoff values of the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity were 7.8% (sensitivity, 94%; specificity, 69%) and 13% (sensitivity, 77%; specificity, 92%), respectively.

**Conclusions:** The respiratory variation of the internal carotid artery blood flow peak velocity as measured using transfontanelle ultrasound predicted an increase in stroke volume in response to fluid. Further research is required to establish any wider generalizability of the results.

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## EDITOR'S PERSPECTIVE

### What We Already Know about This Topic

- Several ultrasound parameters for assessing fluid responsiveness have been described
- Transfontanelle ultrasound can be easily used in small children undergoing surgery, and the anterior fontanelle is an optimal site for Doppler examination of the internal carotid artery
- Previous studies have identified a relationship between fluid responsiveness and respiratory variation in the arterial blood flow peak velocity in the ascending aorta and/or the proximal branches of the aorta

### What This Article Tells Us That Is New

- In infants having cardiac surgery, the respiratory variation of the internal carotid artery blood flow peak velocity as measured using transfontanelle ultrasound predicts an increase in stroke volume in response to an intravenous fluid bolus

In the era of ultrasound, the use of perioperative point-of-care ultrasound has expanded beyond central line placement and regional block, with the advantages of real-time application at the bedside, noninvasiveness, repeatability, and a short learning curve.[1–4] Ultrasound can be used to assess if fluid administration can increase stoke volume. A number of ultrasound parameters for assessing fluid responsiveness have been introduced, including distensibility of the inferior vena cava,[5,6] and respiratory variation of blood flow peak velocity at the brachial artery,[7] the carotid artery,[8] and the aorta.[9–11]

Cranial sonography is a widely used point-of-care modality in infants with advantages of accuracy, cost-effectiveness, and easy applicability at the bedside for the evaluation of cranial morphology and pathology.[12,13] As the anterior fontanelle remains open until 12 to 14 months of age, color Doppler ultrasound can easily visualize the vascular structures including the basilar artery, internal carotid artery, and anterior and middle cerebral arteries, which form the circle of Willis.[14] Transfontanelle ultrasound can be easily used in small children undergoing surgery other than neurosurgery.

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A portable ultrasound device with high-frequency transducers (5 to 8 MHz) can provide high-resolution imaging of the cranium.[12,13] At our institution, we apply transfontanelle ultrasound as a point-of-care cerebral blood flow monitoring method during congenital cardiac operations, and we have reported the clinical utility of this monitoring tool.[15–17]

The internal carotid artery is a terminal branch of the common carotid artery and has seven segments according to the Bouthillier classification.[18,19] Among the segments, the supraclinoid or cerebral portion of the internal carotid artery can be visualized using transfontanelle Doppler ultrasound through a coronal scan.[13] Furthermore, the internal carotid artery blood flow direction is parallel to the Doppler angle of insonation from the anterior fontanelle.[15,20] Accordingly, the accuracy of measurements can be preserved without angle adjustment.[21] Therefore, the anterior fontanelle is an optimal site for Doppler examination of the internal carotid artery blood flow.

Previous studies have identified the relationship between fluid responsiveness and respiratory variation in the arterial blood flow peak velocity in the ascending aorta and/or the proximal branches of the aorta.[7,8,22] We also observed the respiratory variation of the internal carotid artery blood flow peak velocity when we checked the blood flow to the brain using transfontanelle Doppler ultrasound. The purpose of this study was to evaluate the potential role of point-of-care transfontanelle ultrasonography by determining whether the respiratory variation of the internal carotid artery blood flow peak velocity measured by transfontanelle Doppler ultrasound can predict fluid responsiveness in pediatric cardiac patients.

## Materials and Methods

After obtaining approval from the Seoul National University Hospital Institutional Review Board (H1511-105 to 0724; approval date, December 8, 2015; Republic of Korea), the trial was registered at clinicaltrials.gov. The trial registration number was NCT02632227, and the data collection started January 7, 2016, and ended March 14, 2017. One author explained the study protocol and obtained written informed consent from the guardians of the pediatric patients. This study conformed to the Declaration of Helsinki.

Thirty-four infants undergoing general anesthesia for cardiac surgery (atrial or ventricular septal defect) were prospectively enrolled in this study. The anesthesiologist in charge of the patient decided whether the patient would be included in the study after the sternum closed and before the measurement of study parameters. The inclusion criteria were as follows: central venous pressure less than 7 mmHg, systolic blood pressure less than 85% of the baseline value measured after anesthetic induction and before incision, decreased end-diastolic volume compared with the value measured after anesthetic induction and prior to incision, or presence of other clinical sign of dehydration such as decreased skin turgor or decreased urine output (less than $0.5\,ml \cdot kg^{-1} \cdot h^{-1}$). Patients with preexisting premature closure of the anterior fontanelle, pulmonary hypertension, aortic arch abnormalities, cardiac dysfunction (ejection fraction less than 40%), and lung disease were excluded.

Anesthesia was induced with thiopental sodium 5 mg/kg, fentanyl 2 μg/kg, and rocuronium 0.6 mg/kg. Invasive arterial blood pressure, central venous pressure, regional cerebral oxygen saturation, and transesophageal echocardiography (TEE) parameters were monitored. Anesthesia was maintained with 1.5 to 2.0% sevoflurane, continuous infusion of remifentanil (0.2 to 0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$), and rocuronium. Vasoactive-inotropic score was calculated as follows: dopamine dose (in $\mu g kg^{-1}\ min^{-1}$) + dobutamine dose (in $\mu g kg^{-1}\ min^{-1}$) + [epinephrine dose × 100 (in $\mu g kg^{-1}\ min^{-1}$)] + [milrinone dose × 10 (in $\mu g kg^{-1}\ min^{-1}$)] + [vasopressin dose × 10 000 (in $U\ kg^{-1}\ min^{-1}$)] + [norepinephrine dose × 100 (in $\mu g kg^{-1}\ min^{-1}$)].[23]

### Study Protocol

Responders to fluid administration were defined as patients with an increase in stroke volume (SV) index, as measured with TEE, greater than 15% of the baseline value.

After weaning from the cardiopulmonary bypass, TEE confirmed that there were no residual intracardiac shunts. At the completion of surgery and closure of the sternum, the mechanical ventilation was changed to a tidal volume of 10 ml/kg with no positive end expiratory pressure, inspiratory to expiratory ratio of 1:2, and respiratory rate of 20 to 25 breaths/min to maintain the arterial partial pressure of $CO_2$ at 35 to 40 mmHg. Then, echocardiographic measurements and vital sign recording were commenced. Details of echocardiographic measurements are described in the next section. Fluid administration was commenced with 10 ml/kg crystalloid infusion for 10 min.

### Echocardiographic Measurements: Respiratory Variation of the Internal Carotid Artery and the Aorta Blood Flow Peak Velocity and SV Index

Echocardiographic variables were derived from the iE33 ultrasound imaging system (Philips Medical System), and all measurements were done by a single investigator (J.-T.K.) with experience of greater than 100 transfontanelle ultrasound examinations. J.-T.K. measured the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity and SV index in sequence. First, the investigator gently placed the S8-3 sector array transducer (Philips Medical System) at the anterior fontanelle and obtained a coronal plane image of the brain structure and cerebral basal vessels. Color Doppler was used to identify cerebral arteries. Both internal carotid arteries were identified, and the blood

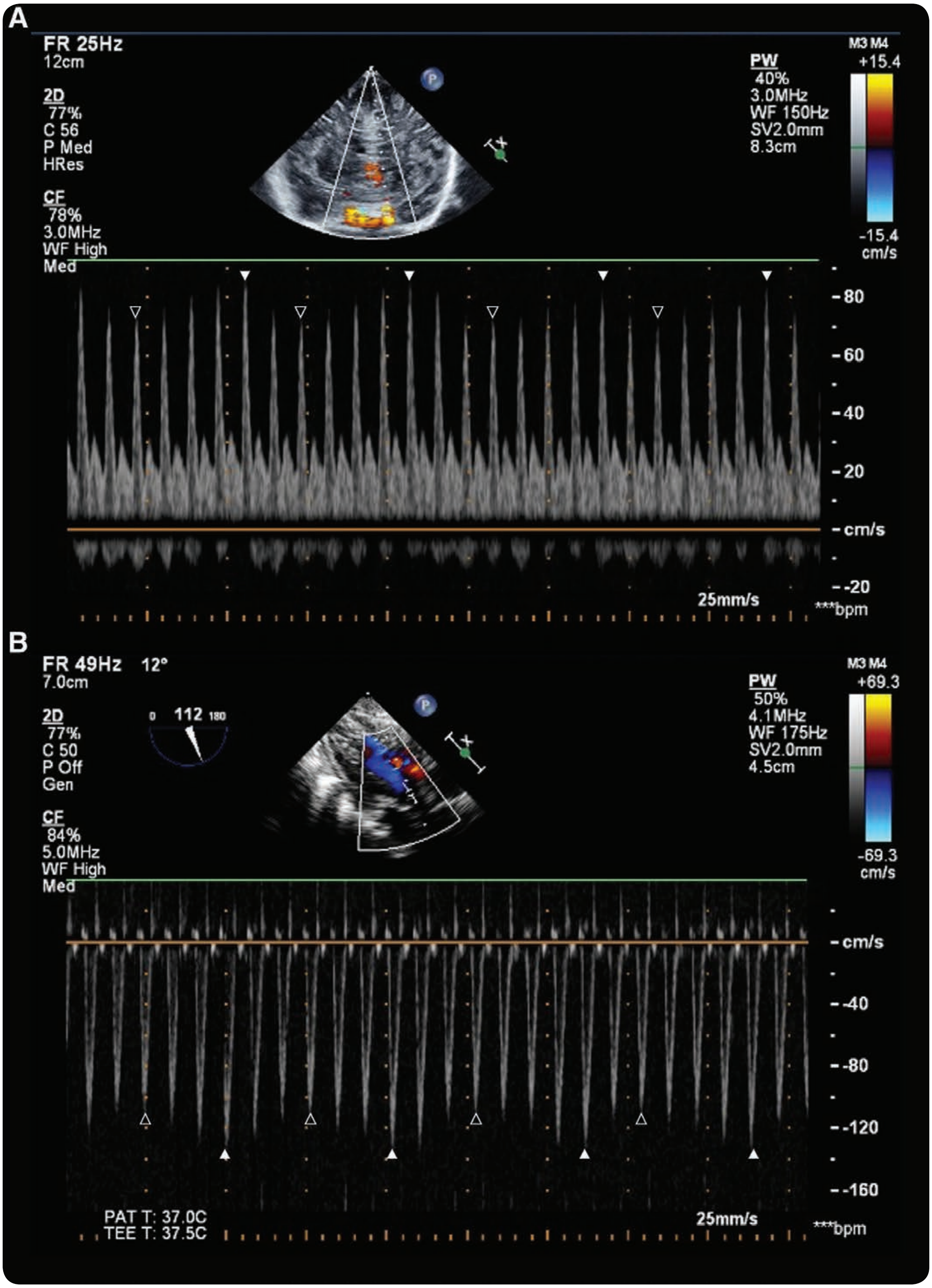


**Fig. 1.** (*A*) Coronal plane image of the brain and the blood flow velocity at the internal carotid artery. (*B*) Deep transgastric long-axis view using pulsed wave Doppler, and the aortic blood flow waveform at the level of the aortic annulus. bpm, beats per minute; C, compression; CF, color flow; FR, frame rate; Gen, general; HRes, high resolution; Med, median; PAT T, patient temperature; P, persistence; PW, pulsed wave; SV, sample volume; TEE T, transesophageal echocardiography probe temperature; WF, wall filter; 2D, two-dimensional echo.

flow velocity sampling site was located in the right internal carotid artery at the carotid canal of the skull base, and the internal carotid artery blood flow waveforms were stored using pulsed wave Doppler (fig. 1A). Second, the S7-3t TEE probe (Philips Medical System) was used to record the aortic blood flow waveform at the level of the aortic annulus from a deep transgastric long-axis view with pulsed wave Doppler (fig. 1B). The maximum and minimum blood flow velocities during one respiratory cycle were measured. The respiratory variation of the internal carotid artery and the aorta blood flow peak velocity were calculated as follows: 100 × (maximum peak velocity − minimum peak velocity) × ([maximum peak velocity + minimum peak velocity] × $2^{-1}$)$^{-1}$. Finally, the aortic annulus diameter was measured from the midesophageal aortic valve long-axis view. SV index was calculated as follows: cross-sectional area = 3.14 × (annulus × $2^{-1}$)$^2$; SV = cross-sectional area × velocity time integral; SV index = SV × body surface area$^{-1}$. Each variable was measured three times, and the average was used for analysis. All measurements were performed at the same sampling sites with the same probe position to obtain identical images. During data collection, we only recorded the internal carotid artery and the aorta blood flow peak velocities, and the arterial and central venous waveforms. After the completion of data collection, a blinded investigator calculated the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity, pulse pressure variation, and SV index without knowledge of the results of the reference standard or index test.

### Vital Sign Recording

The data were transferred from a bedside monitor (Solar 8000M; GE Medical Systems Information Technologies, USA) to a computer by using an analog-to-digital converter (DA 149; DATAQ Instruments, USA) at 1,000 Hz. Pulse pressure variation was calculated as follows: pulse pressure variation (%) = 100 × (maximum pulse pressure − minimum pulse pressure) × ([maximum pulse pressure + minimum pulse pressure] × $2^{-1}$)$^{-1}$. A single blinded investigator performed three consecutive measurements and averaged the values for statistical analysis.

### Statistical Analysis

Previous studies that evaluated fluid responsiveness in pediatric patients concluded that the respiratory variation of the aorta blood flow peak velocity could predict fluid responsiveness with the area under the curve in a receiver operating characteristic curve analysis of 0.79 to 0.86.[9] We hypothesized that the area under the curve of the respiratory variation of the internal carotid artery blood flow peak velocity from the transfontanelle examination would be 0.8. We calculated the required sample size for the comparison of the area under a receiver operating characteristic curve with a null hypothesis value. Considering the α error of 0.05, 80% power, and sample size ratio in the negative/positive group of 1, among responder and nonresponders, 26 patients were needed. Considering the attrition rate of 10%, a total of 30 pediatric patients were included in the study.

The Kolmogorov–Smirnov test was used to test the normality of data distribution. Differences between responders and nonresponders were evaluated using Student's *t* test or the Mann–Whitney U test. The predictors were analyzed using the receiver operating characteristic curve analysis. To test the abilities of dynamic variables to predict fluid responsiveness, the area under the curves in the receiver operating characteristic curve analysis were calculated, and the cutoff value of 0.8 was used to determine the clinically significant predictability. The Youden method was used to define the optimal criterion value. Comparison of receiver operating characteristic curves to test the statistical significance of the difference between the area under the curves followed the method of DeLong *et al.*[24] Statistical significance was considered at $P < 0.05$. Statistical analyses were performed using MedCalc software (version 15.2.2; MedCalc, Belgium) and SPSS software (version 23.0; IBM Corp., USA).

## Results

After four patients were excluded who did not meet the inclusion criteria, 30 pediatric patients were included in the final analysis (fig. 2). Seventeen subjects (57%) were responders to volume expansion. The patients' characteristics of responders and nonresponders are shown in table 1. Table 2 shows the hemodynamic data before and after fluid loading in responders and nonresponders to volume expansion.

At baseline, there was no difference in mean arterial blood pressure, heart rate, central venous pressure, and pulse pressure variation between responders and nonresponders. However, the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity were significantly higher in the responder group than in the nonresponder group (the respiratory variation of the internal carotid artery blood flow peak velocity: $P = 0.001$; mean difference, 4.4%; 95% CI, 1.9 to 6.9%; the respiratory variation of the aorta blood flow peak velocity: $P = 0.001$; mean difference, 5.1%; 95% CI, 2.3 to 7.8%).

The receiver operating characteristic curve analysis (fig. 3) showed that the respiratory variation of the internal carotid artery blood flow peak velocity and the aorta could predict fluid responsiveness; the area under the curve was 0.83 ($P = 0.0001$; 95% CI, 0.65 to 0.94) and 0.86 ($P < 0.0001$; 95% CI, 0.68 to 0.96), respectively. The cutoff value of the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity was 7.8% (sensitivity, 94%; specificity, 69%) and 13% (sensitivity, 77%; specificity, 92%), respectively. There was no significant difference between the area under the curve of the respiratory variation of the aorta blood flow peak velocity and that of the respiratory variation of the internal carotid artery blood flow peak velocity in predicting fluid responsiveness ($P = 0.792$; difference between area under the curves: 0.03; 95% CI, −0.21 to 0.27). Pulse pressure variation and central venous pressure could not predict fluid responsiveness; the area under the curve was 0.52 ($P = 0.854$; 95% CI, 0.33 to 0.71) and 0.66 ($P = 0.140$; 95% CI, 0.47 to 0.82), respectively.

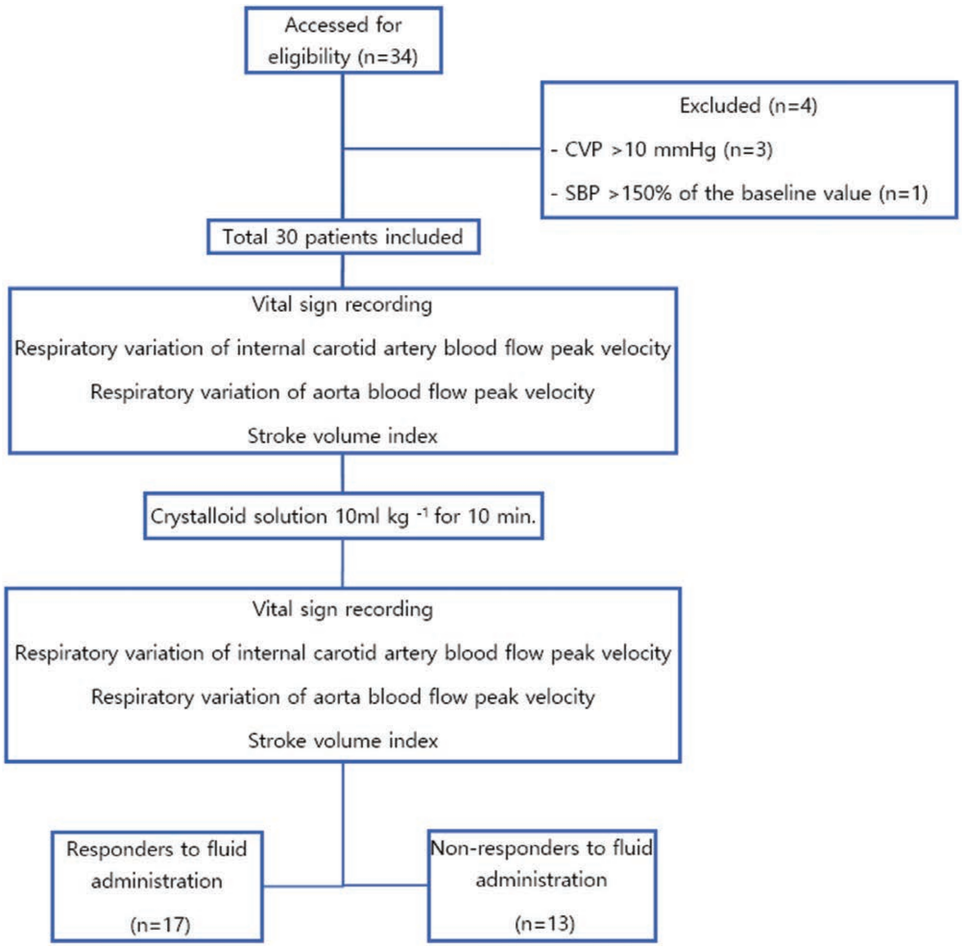


**Fig. 2.** Flow diagram showing the number of patients screened for eligibility, number of patients included in the study, and number of patients with complete ultrasound data for analysis. CVP, central venous pressure; SBP, systolic blood pressure.

## Discussion

In this study, we found that the respiratory variation of the internal carotid artery blood flow peak velocity measured using transfontanelle ultrasound can predict fluid responsiveness in infants undergoing cardiac surgery.

Fluid therapy is important for pediatric patients undergoing major surgical procedures. The goal of fluid therapy is to maintain the normal physiologic volume state in children.[25] Only half of pediatric patients respond to intravascular volume expansion.[11,26] Errors such as fluid overload and dehydration cause complications and negative outcomes.[27,28] However, prediction of fluid responsiveness in pediatric patients is difficult and has limited evidence. The respiratory variation of the aorta blood flow peak velocity, SV variation, pulse pressure variation, noninvasive cardiac output monitoring, pleth variability index, and near-infrared spectroscopy could predict fluid responsiveness in some pediatric patients; however, previous studies showed inconsistent results.[29,30] Only the respiratory variation of the aorta blood flow peak velocity has been proven to be predictive in systematic analysis; however, it has limited utility in some clinical situations.[9,10,31,32]

The predictive ability for fluid responsiveness of the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity did not show significant differences in the receiver operating characteristic curve comparison. However, the cutoff values for predicting fluid responsiveness were different between the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity. It is possible that the existence of a solid cranium reduced the respiratory variation of intracranial arterial blood flow velocities. Furthermore, the mechanism of cerebral blood flow autoregulation may explain the difference between the cutoff values of the respiratory variation of the internal carotid artery and the aorta blood flow peak velocity. The optimal cutoff value of the respiratory variation of the aorta blood flow peak velocity for prediction remains

**Table 1.** Patient Characteristics and Intraoperative Variables at the Time of Data Collection

| | Responders (n = 17) | Nonresponders (n = 13) | 95% CI Differences between Groups |
|---|---|---|---|
| Age (months) | 5.2 (1.0–10.0) | 4.9 (1.0–12.0) | 0.3 (–2.1 to 2.9) |
| Height (cm) | 63.5 (53.3–77.5) | 64.1 (54.0–78.6) | 0.6 (–4.6 to 5.9) |
| Weight (kg) | 6.0 (3.4–9.6) | 6.1 (4.1–8.2) | 0.1 (–1.0 to 1.2) |
| Gender, male | 8 (47) | 7 (53) | |
| Operation | | | |
| Atrial septal defect | 4 (23) | 4 (30) | |
| Ventricular septal defect | 13 (77) | 9 (70) | |
| CPB time (min) | 118.8 ± 50.8 | 102.1 ± 25.4 | 16.6 (–14.9 to 48.3) |
| Aorta cross clamping time (min) | 77.8 ± 35.2 | 61.6 ± 16.5 | 16.2 (–5.5 to 38.1) |
| Left $rSO_2$ (%) | 63.3 ± 8.7 | 64.0 ± 7.0 | 0.6 (–5.4 to 6.7) |
| Right $rSO_2$ (%) | 63.5 ± 11.1 | 65.8 ± 7.9 | 2.2 (–5.1 to 9.7) |
| Peak inspiratory pressure (cm $H_2O$) | 18.2 ± 2.8 | 18.5 ± 5.0 | 0.2 (–3.6 to 3.2) |
| Temperature (°C) | 35.9 ± 0.7 | 36.0 ± 0.8 | 0.1 (–0.5 to 0.7) |
| Vasoactive–inotropic score | 9.8 ± 4.6 | 8.8 ± 5.5 | 1.9 (–1.8 to 5.7) |

Values are expressed median (range) and mean ± SD. Categorical variables are expressed as number (%). CPB, cardiopulmonary bypass; $rSO_2$, regional cerebral oxygen saturation.

**Table 2.** Hemodynamic Data in Responders and Nonresponders at Baseline and after Fluid Loading

| | Before Fluid Administration | | | After Fluid Administration | | |
|---|---|---|---|---|---|---|
| | Responders (n = 17) | Nonresponders (n = 13) | *P* value, 95% CI Differences between Groups | Responders (n = 17) | Nonresponders (n = 13) | *P* value, 95% CI Differences between Groups |
| Heart rate (beats/min) | 142 ± 16 | 138 ± 17 | 0.500, 4.3 (–8.8 to 17.4) | 139 ± 15 | 137 ± 19 | 0.723, 2.3 (–11.1 to 15.8) |
| Mean arterial pressure (mmHg) | 55 ± 10 | 61 ± 7 | 0.097, 5.7 (–1.1 to 12.6) | 70 ± 11 | 71 ± 12 | 0.759, 1.4 (–8.0 to 10.8) |
| Central venous pressure (mmHg) | 8 ± 2 | 6 ± 3 | 0.195, 1.3 (–0.7 to 3.4) | 10 ± 2 | 9 ± 2 | 0.268, 1.1 (–0.9 to 3.2) |
| Stroke volume index (ml · $m^{-2}$) | 18.2 ± 4.9 | 20.7 ± 8.1 | 0.168, 1.7 (–0.8 to 4.4) | 23.3 ± 6.6 | 21.2 ± 7.8 | 0.331, 1.2 (–1.3 to 3.7) |
| Cardiac index (l · $min^{-1}$ · $m^{-2}$) | 2.5 ± 0.7 | 2.8 ± 0.1 | 0.441, 0.2 (–0.4 to 0.9) | 3.2 ± 0.9 | 2.8 ± 0.2 | 0.256, 0.4 (–0.3 to 1.1) |
| Pulse pressure variation (%) | 18.2 ± 2.8 | 18.5 ± 5.0 | 0.759, 0.7 (–4.3 to 5.8) | 15.8 ± 4.8 | 13.2 ± 2.5 | 0.119, 2.6 (–0.7 to 5.9) |
| Respiratory variation of aorta blood flow peak velocity (%) | 16.0 ± 3.8 | 10.9 ± 3.5 | 0.001, 5.1 (2.3 to 7.8) | 9.0 ± 3.0 | 11.4 ± 6.0 | 0.215, 2.3 (–1.5 to 6.2) |
| Respiratory variation of internal carotid artery blood flow peak velocity (%) | 12.6 ± 3.3 | 8.2 ± 3.2 | 0.001, 4.4 (1.9 to 6.9) | 8.2 ± 3.0 | 7.8 ± 2.8 | 0.437, 0.8 (–1.3 to 3.0) |

Values are expressed as mean ± SD.

uncertain, ranging from 7 to 20%.[10] We found that the cutoff value of the respiratory variation of the aorta blood flow peak velocity was 13% for predicting fluid responsiveness in infants, which was similar to the previously published data at our institution.[32,33] The cutoff value of 7.8% of the respiratory variation of the internal carotid artery blood flow peak velocity should be validated in a further study.

We used the aortic velocity time integral at the level of the aortic annuls as our reference method for cardiac output measurement. As the respiratory variations of the aorta blood flow peak velocity and SV index were determined in the same aortic pulsed Doppler measurement, these two variables tightly correlated physiologically and mathematically.[10] This relationship could lead to an overestimation of the predictive accuracy of the respiratory variation of the aorta blood flow peak velocity and could be a potential source of bias.

The respiratory variation of the internal carotid artery blood flow peak velocity has several benefits over the respiratory variation of the aorta blood flow peak velocity. For obtaining the respiratory variation of the aorta blood flow peak velocity, transthoracic echocardiography or TEE is needed. If the surgical field is close to the chest, transthoracic echocardiography cannot be applied. TEE also has some problems associated with the TEE probe, especially in infants. On the other hand, the respiratory variation of the internal carotid artery blood flow peak velocity can be applied without limitation if the fontanelle remains open. Furthermore, the respiratory variation of the internal carotid artery blood flow peak velocity as measured using

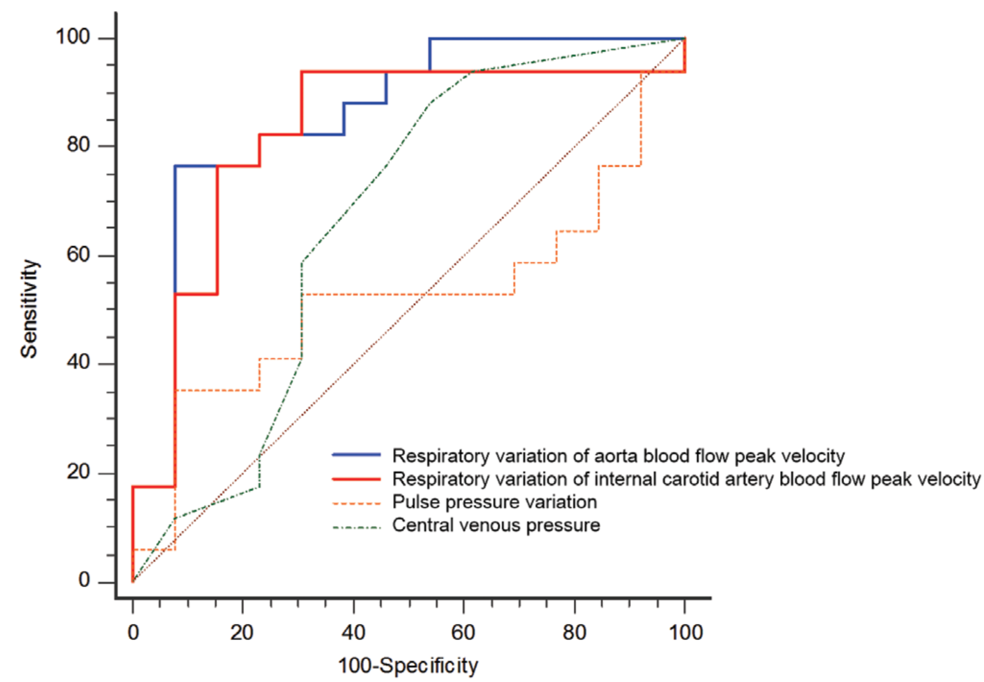


**Fig. 3.** Receiver-operating characteristic curves of the respiratory variation of the aorta blood flow peak velocity (*solid blue line*), the respiratory variation of the internal carotid artery blood flow peak velocity (*solid red line*), pulse pressure variation (*dashed orange line*), and central venous pressure (*dashed green line*) at baseline to discriminate between responders and nonresponders to intravascular volume expansion.

transfontanelle ultrasound has less potential bias associated with Doppler beam angle adjustment than the respiratory variation of the aorta blood flow peak velocity.

In the study protocol, several measurement points could be a potential source of bias. We sequentially recorded the respiratory variation of the internal carotid artery blood flow peak velocity (index test), the respiratory variation of the aorta blood flow peak velocity (index test), and SV index (reference standard). We considered that the change in SV index during the measurements could be a potential source of bias, and tried to minimize the time gap between measurements to less than 3 min. However, the measurement time point of the respiratory variation of the aorta blood flow peak velocity was closer to the reference standard than that of the respiratory variation of the internal carotid artery blood flow peak velocity. Accordingly, the accuracy of the respiratory variation of the internal carotid artery blood flow peak velocity may be theoretically underestimated compared with that of the respiratory variation of the aorta blood flow peak velocity. The knowledge of index test or reference standard results during data collection could be a potential source of bias. Therefore, we interpreted the index test and reference standard after the completion of data collection by a blinded investigator.

Consistent with our results, Song *et al.*[8] reported that the respiratory variation of the internal carotid artery blood flow peak velocity obtained using Doppler ultrasound is superior to pulse pressure variation in predicting fluid responsiveness in adults. Because of the preferential diversion of blood flow toward the carotid arteries and away from the peripheries in hemodynamically unstable patients, pulse pressure variation at the radial artery could result in erroneous information about systemic vascular resistance and respiratory variations.[34–36] Therefore, the respiratory variation of the internal carotid artery blood flow peak velocity can be a useful indicator of fluid responsiveness in hemodynamically unstable infants or in patients with continuous infusion of vasopressors.

This was an observational study performed at a single center. Only 30 infants undergoing cardiac surgery were included. The application of these results in patients undergoing general surgery or in infants without general anesthesia or muscle paralysis needs to be done with caution. An external validation in other circumstances, such as other surgeries and time spent in the intensive care unit, is required to validate and determine the generalizability of these findings. Another consideration is the clinical outcome of fluid management based on the prediction of fluid responsiveness with transfontanelle ultrasound examination. As far as we know, the clinical consequence of fluid administration guided by this or a similar method has not been proved in pediatric patients. Further study is needed to determine the clinical significance of fluid management based on the respiratory variation of the internal carotid artery blood flow peak velocity.

This study has several limitations. First, the ultrasound examinations were performed by one experienced anesthesiologist and had no inconclusive measurements in this study. However, the transfontanelle ultrasound examination needed a trained operator. Characteristics of transfontanelle ultrasound, such as the learning curve and intra- and interoperator variability, have yet to be defined. Second, transfontanelle ultrasound cannot be used in patients with a closed fontanelle and in those with arch vessel anomalies, such as carotid artery stenosis and patent ductus arteriosus. Furthermore, we included only patients with biventricular anatomy, without left ventricular outflow tract obstruction, without moderate to severe aortic valve stenosis or regurgitation, and without severe myocardial dysfunction. Therefore, more data are needed to apply our results to this population. Third, transfontanelle ultrasound is a noncontinuous monitoring system.

In conclusion, transfontanelle ultrasound is a noninvasive point-of-care imaging modality that can predict fluid responsiveness in infants undergoing cardiac surgery. Further studies are required to confirm these results in infants undergoing other general surgical procedures and those in the intensive care unit.

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Support was provided solely from institutional and/or departmental sources.

## Competing Interests

The authors declare no competing interests.

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