Stroke volume is determined by cardiac preload, contractility, and afterload. Accordingly, the optimal management of cardiac preload is crucial for maintaining proper cardiac output and tissue oxygen delivery. Too little fluid administration can cause hypovolemia or tissue hypoperfusion, whereas too much fluid can induce pulmonary edema or heart failure. Inadequate volume management can cause adverse clinical outcomes after surgery. The increase in cardiac output after fluid administration is determined by the position of preload on the Frank-Starling curve (Fig. 1). When the preload is located in a steeply inclined position on the graph, the cardiac output is likely to have increased in response to fluid administration. If it can be predicted whether cardiac output would be increased by fluid administration, then fluid management can be improved during the perioperative period.

Traditionally, volume status was assessed on the basis of static monitoring parameters such as heart rate, arterial blood pressure, and central venous pressure (CVP), as well as clinical signs such as urine output. However, many previous studies have demonstrated that static parameters cannot predict fluid responsiveness [1]. On the other hand, the ability of dynamic parameters based on the heart-lung interaction has been validated for the prediction of fluid responsiveness [2].

Many researchers have evaluated parameters based on arterial pressure waveforms, such as pulse pressure variation (PPV),
systolic pressure variation (SPV), stroke volume variation (SVV), ΔDown (apneic systolic blood pressure minus minimal systolic blood pressure during expiration), and ΔUp (maximal systolic blood pressure during inspiration minus apneic systolic blood pressure) (Fig. 2). Variables derived from plethysmography, such as the respiratory variation of pulse oximeter plethysmography waveform amplitude (ΔPOP) and the pleth variability index (PVI), have received attention. Additionally, parameters measured using ultrasound, such as the respiratory variation in peak blood flow velocity of the aorta (ΔVpeak) or the carotid artery (ΔVpeak_CA), the variation in the diameter of the inferior vena cava (ΔIVC), and esophageal Doppler indices, have been assessed in relation to fluid responsiveness.

Many reliable parameters proven in adults are unable to predict fluid responsiveness in the pediatric population [1]. The reasons for the discrepancies in the reliability of dynamic parameters for predicting fluid responsiveness between children and adults are complex and multifactorial [3]. This article reviews the potential predictors of fluid responsiveness and some important considerations for the interpretation of data on fluid responsiveness in the pediatric population.

**Potential Predictors of Fluid Responsiveness**

The potential predictors of fluid responsiveness in the pediatric population are summarized in Table 1.

### Parameters derived from blood pressure

#### Parameters of arterial blood pressure (pulse waveform analysis)

The ability to predict fluid responsiveness based on the respiratory change in the arterial pressure waveform has been
Table 1. Parameters that Can Predict Fluid Responsiveness according to Prospective Pediatric Studies

| Parameter     | Publication                  | Population                  | Age          | Responder/Total (n) | Fluid          | Responder | Reference | Cutoff | AUC  | Sensitivity | Specificity | Comment                  |
|---------------|------------------------------|-----------------------------|--------------|--------------------|----------------|------------|-----------|--------|-----|-------------|-------------|---------------------------|
| PPV_PICCO     | Renner et al. 2012 [14]     | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg, 6% HES | SVI > 15%   | TEE       | 16%    | 0.79| 61%         | 96%         | Arterial pressure wave    |
| PPV_PICCO     | Renner et al. 2012 [14]     | OR, after correction        | 14 ± 12* mo  | 15/26              | 10 ml/kg, 6% HES | SVI > 15%   | TEE       | 15%    | 0.86| 93%         | 72%         |                           |
| PPV_PRAM      | Han et al. 2017 [12]        | OR, before correction       | < 2 yr       | 27/38              | 20 ml/kg/h for 15 min, 5% alb, FFP | CI > 15% | PRAM     | 17.4%  | 0.89| 89%         | 91%         |                           |
| PPV_PRAM      | Han et al. 2017 [12]        | OR, after correction        | < 2 yr       | 26/36              | 20 ml/kg/h for 15 min, 5% alb, FFP | CI > 15% | PRAM     | 13.4%  | 0.79| 81%         | 80%         |                           |
| PVI           | Byon et al. 2013 [15]       | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 10%   | TTE       | 11%    | 0.77| 73%         | 87%         | Plethysmography            |
| PVI           | Renner et al. 2011 [17]     | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| PVI           | Julien et al. 2013 [23]     | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Lee et al. 2017 [6]         | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Renner et al. 2011 [17]     | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Byon et al. 2013 [15]       | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Choi et al. 2010 [16]       | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Pereira et al. 2011 [21]   | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Lee et al. 2014 [32]        | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Kim et al. 2019 [4]         | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Morparia et al. 2018 [5]   | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Lee et al. 2015 [33]        | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| SVV USCOM     | Cheng et al. 2018 [35]      | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak_CA     | Kim et al. 2019 [4]         | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| ΔVpeak        | Choi et al. 2010 [16]       | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
| Peak velocity | Weber et al. 2015 [8]       | OR, before correction       | 14 ± 12* mo  | 15/26              | 10 ml/kg for 10 min, 6% HES | SVI > 15%   | TEE       | 13%    | 0.78| 84%         | 61%         |                           |
Table 1. Continued

| Parameter | Publication          | Population       | Age      | Responder/total (n) | Fluid                  | Responder | Reference | Cutoff | AUC       | Sensitivity | Specificity | Comment              |
|-----------|----------------------|------------------|----------|---------------------|------------------------|-----------|-----------|--------|-----------|-------------|-------------|----------------------|
| FTc       | Tibby et al. 2001    | PICU, noncardiac  | 4 day to 16 yr | NA/36 | 10 ml/kg for 30 min, 5% alb, FFP | SV > 10% | TD        | 0.394 s | 0.76      | 90%         | 62%         | Esophageal Doppler    |
|           | Lee et al. 2017      | OR, cardiac surgery | < 5 yr   | 17/30 | 10 ml/kg for 20 min, 6% HES | SVI > 15% | TEE       | 5%     | 0.78      | 82%         | 69%         | Abdominal compression |
| SVI_CAC   | Jacquet-Lagreze et al. 2018 | PICU   | 0.3–75 mo | 20/39 | 10 ml/kg for 10 min, crystalloid | SVI > 15% | TTE       | 11%    | 0.94      | 75%         | 95%         |                      |
| CI_PLR    | Lukito et al. 2012   | PICU             | 1–13 yr  | 20/40 | 10 ml/kg, crystalloid | CI > 10% | TTE       | 10%    | 0.71      | 55%         | 85%         |                      |
| SVV NICOM | Lee et al. 2014      | PICU, cardiac surgery | 6 mo to 6 yr | 13/26 | 10 ml/kg for 10 min, 6% HES | SV > 10%  | TEE       | 10%    | 0.89      | 85%         | 77%         | NICOM                |
| SVV NICOM | Vergnaud et al. 2015 | PICU             | 0–16 yr  | 15/30 | 20 ml/kg for 15–30 min, colloid | SV > 15%  | TTE       | 10%    | 0.81      | 80%         | 74%         |                      |
| SVI NICOM | Vergnaud et al. 2015 | PICU             | 0–16 yr  | 15/30 | 20 ml/kg for 15–30 min, colloid | SV > 15%  | TTE       | 29 ml/m² | 0.88      | 71%         | 100%        |                      |

*Values are presented as mean ± SD. n: number of patients, AUC: area under the curve, PPV: pulse pressure variation, PICCO: pulse index continuous cardiac output, PRAM: pressure recording analytical method, PVI: pleth variability index, ΔVpeak: respiratory variation in aortic blood flow peak velocity, SVV: stroke volume variation, USCOM: ultrasonic cardiac output monitor, ΔVpeak_CA: respiratory variation in internal carotid artery blood flow peak velocity, ΔVIVC: respiratory variation in inferior vena cava diameter, FTc: flow time corrected, DAP_LC: diastolic blood pressure change during liver compression, SV: stroke volume, VTI: velocity time integral, TEE: transesophageal echocardiography, TTE: transthoracic echocardiography, NA: not applicable, US: ultrasound, TCD: transcranial Doppler.
proven in adults [2]. Parameters such as SPV, PPV, ΔDown, and ΔUp have been suggested to predict an increase in the cardiac output in response to volume loading in mechanically ventilated patients. However, these arterial pressure-based variables poorly predict fluid responsiveness in children [1,4–7]. SVV derived from a pulse contour analysis algorithm system (LiDCOrapid system; LiDCO Ltd., UK) is also a poor predictor in the pediatric population [8].

Considering that the predictive ability of PPV is improved by increasing the tidal volume in adults [9,10], there is a possibility that the predictive value of PPV can be improved in children with increased tidal volume. This can be deduced from the finding that the area under the receiver operating characteristic (ROC) curve was increased when the tidal volume was increased from 5 ml/kg to 10 ml/kg and 15 ml/kg in piglets [11]. However, this has not been confirmed in children.

Some studies using the pressure recording analytical method (Vygon; Vytech, Italy) or the PiCCO monitoring system (PiCCO Plusw, version 6.0; Pulsion Medical Systems, Germany) have shown that PPV can predict fluid responsiveness in pediatric cardiac surgery [12–14] (Table 1). However, in a study in children after the surgical repair of a ventricular septal defect or tetralogy of Fallot [12], PPV was measured in an open chest and the amount of fluid administered was 20 ml/kg/h for 15 min, making it difficult to compare the results with those from patients in whom measurements were taken with the chest closed or those who received 10 ml/kg/h fluid for volume expansion. In addition, the reference value for assessing an increase in cardiac index was measured using the same device that measured PPV [12]. Another study had the limitations of having a retrospective design and a small number of patients [13]. Accordingly, there is still little evidence suggesting that PPV is a reliable parameter for predicting fluid responsiveness in children.

Central venous pressure

Most previous studies consistently demonstrated that CVP has no ability to predict fluid responsiveness both in adults and in children [14–19]. Most static parameters such as CVP are poor predictors of fluid responsiveness.

Parameters derived from plethysmography

The plethysmographic waveform is generated by the blood volume change in the vessels of tissues, not by the pressure change. ΔPOP has been suggested as a potential dynamic parameter for predicting fluid responsiveness. ΔPOP can be calculated as follows:

\[
\Delta \text{POP}(\%) = 100 \times \frac{(\text{amplitude max} - \text{amplitude min})}{(\text{amplitude max} + \text{amplitude min}) / 2}.
\]

However, a pulse oximeter plethysmograph is usually displayed after automatic resizing of amplitude in a patient monitor, and calculation of ΔPOP requires specific tools and software. For convenience, PVI (Masimo Corp., USA) has been introduced to obtain the respiratory variations in the plethysmographic waveform. PVI is automatically calculated as \([\text{perfusion index (PI) max} - \text{PI min}] / \text{PI max}\), where PI is the ratio between a pulsatile ‘alternating current’ (AC) component and a non-pulsatile ‘direct current’ (DC) component of the infrared signal of pulse oximeter plethysmograph. Both ΔPOP and PVI are attractive parameters for use in pediatric patients because they are measured noninvasively.

ΔPOP and PVI have been shown to be equally effective for predicting fluid responsiveness in ventilated adults in normal sinus rhythm [20]. Although a study has shown that PVI cannot predict fluid responsiveness [21], a meta-analysis [22] concluded that PVI is a reliable predictor in the pediatric population [15,17,23] (Table 1). The mean threshold for the identification of responders to volume expansion was 14% ± 3%, and the area under the summary ROC curve of PVI was 0.86 [22].

Although a strong relationship between ΔPOP and PPV was found in mechanically ventilated children [24], plethysmography-derived parameters have different characteristics from pressure-associated parameters. This may be one of the reasons why parameters derived from plethysmography have a higher predictive ability than those derived from arterial pressure waveforms in children.

Plethysmographic waveforms are known to be influenced by stroke volume, arterial and venous distensibility, and the venous pressure of the sampling site [25–27]. Accordingly, the reliability of ΔPOP and PVI can be influenced by peripheral perfusion, microcirculation, sampling site, and contact pressure of the probe. Although PVI measured at various sites, including the forehead, ear, and fingers, can predict fluid responsiveness in mechanically ventilated adults, the cutoff values for predicting fluid responsiveness differ with the sampling site (15% for the forehead, 16% for the ear, and 12% for the finger) [28]. These findings can be extrapolated to the pediatric population. The contacting force between the pulse oximeter sensor and the measurement site can affect the plethysmography amplitude and reliability of ΔPOP as a predictor of fluid responsiveness in pediatric patients [29,30]. In addition, use of vasopressors such as norepinephrine may decrease the reliability of ΔPOP and PVI, as demonstrated in a previous study in adult patients [31].

Parameters derived from ultrasound

Respiratory variation of aortic blood flow peak velocity

ΔVpeak is measured at the aortic annulus or the left ventricular outflow tract by using pulsed wave Doppler with transtho-
Fluid responsiveness in children

VOL. 72, NO. 5, October 2019

Radic or transesophageal echocardiography (Fig. 3). It is a promising marker for optimization of perioperative fluid therapy in the pediatric population [5] and is calculated as follows:

\[ \Delta V_{\text{peak}} (\%) = 100 \times \frac{V_{\text{peak \ max}} - V_{\text{peak \ min}}}{\left(\frac{V_{\text{peak \ max}} + V_{\text{peak \ min}}}{2}\right)} . \]

\( \Delta V_{\text{peak}} \) is a consistent predictor of fluid responsiveness in pediatric patients under mechanical ventilation [4–6,15–17,21,32,33] (Table 1). One thing that needs to be considered is that the cardiac index and the stroke volume index are obtained from the velocity time integral at the aortic annulus by using the same ultrasound device that measures \( \Delta V_{\text{peak}} \). This measurement coupling might make \( \Delta V_{\text{peak}} \) better correlated with the cardiac index or the stroke volume index than other dynamic parameters.

Respiratory variation of aortic blood flow peak velocity measured at the suprasternal notch

\( \Delta V_{\text{peak}} \) can be measured using transthoracic echocardiography from the suprasternal notch view. This method is useful when access to the chest wall is limited during surgery. A significant relationship between the \( \Delta V_{\text{peak}} \) recorded via the suprasternal notch view and that recorded via the apical 5-chamber view \((r = 0.62, P = 0.003)\) has been previously reported [34].

An ultrasonic cardiac output monitor (USCOM; USCOM Ltd., Australia) is a noninvasive, continuous-wave Doppler monitor that can be used to measure cardiac output via a probe applied to the suprasternal notch. SVV measured with USCOM can be used to predict fluid responsiveness after congenital heart surgery in children [35]. However, the issue of mathematical coupling should be considered because the cardiac output is calculated using the stroke volume obtained from USCOM. Additionally, the accuracy of SVV for predicting fluid responsiveness was reported to be higher among patients with inotropic score > 10 than among those with inotropic score \( \leq 10 \) [35] (Table 1). In addition, in another study, cardiac output measurements using USCOM in children did not reliably represent absolute cardiac output values as compared with measurements using the thermodilution technique with a pulmonary artery catheter [36].

Respiratory variation of carotid artery blood flow peak velocity measured using the transfontanelle approach

\( \Delta V_{\text{peak \ CA}} \) is suggested to be a highly feasible and reliable parameter for predicting fluid responsiveness in mechanically ventilated adult patients undergoing coronary revascularization [37]. In small pediatric patients, the anterior fontanelle remains open, thus providing a ‘window’ for the evaluation of the brain. The blood flow velocity of the internal carotid artery, basilar artery, anterior cerebral artery, pericallosal artery, and middle cerebral artery can be measured using transcranial Doppler. The clinical usefulness of this parameter in pediatric cardiac surgery has been reported [38–40]. \( \Delta V_{\text{peak \ CA}} \) as measured using transfontanelle ultrasound predicts increases in stroke volume in response to fluid, with a similar ability as \( \Delta V_{\text{peak}} \) [4] (Table 1). The transfontanelle approach is a useful method for monitoring because it can provide not only information about fluid responsiveness but also other information such as intracranial abnormality and cerebral blood flow (Fig. 4).

Respiratory variations of inferior vena cava diameter

The \( \Delta IVC \) can be calculated as follows:

\[ \Delta IVC (\%) = 100 \times \frac{IVC \text{ diameter \ max} + IVC \text{ diameter \ min}}{2}. \]

---

**Fig. 3.** Respiratory variation of aortic blood flow peak velocity. Respiratory variation of aortic blood flow peak velocity is measured using transesophageal echocardiography. Sample volume of pulsed wave Doppler is located at just below the aortic annulus. Respiratory variation of aortic blood flow peak velocity \( (\Delta V_{\text{peak}}) \) before (A) and after (B) volume loading in a fluid responder. \( \Delta V_{\text{peak}} \) is calculated as \( 100 \times (V_{\text{max}} - V_{\text{min}}) / \left[ (V_{\text{max}} + V_{\text{min}}) / 2 \right] \).
/ [(IVC diameter max + IVC diameter min) / 2].

In a previous study, the ΔIVC performed moderately well in predicting fluid responsiveness, with a pooled area under the ROC curve of 0.79 in adults [41]. However, in mechanically ventilated children, the results are controversial. ΔIVC was a good predictor of fluid responsiveness in one study [16] (Table 1) but not in other studies [15,42]. The collapsibility of the IVC has also been shown to be a poor predictor of fluid responsiveness in spontaneously ventilating children with sepsis [43].

Positive pressure ventilation has an influence on ΔIVC. In adults with tidal volume ≥ 8 ml/kg and positive end-expiratory pressure (PEEP) < 5 cmH₂O, ΔIVC is a good indicator of fluid responsiveness, but not in patients with a low tidal volume or a PEEP of > 5 cmH₂O [44]. On the other hand, ΔIVC decreases with the initiation of positive pressure ventilation in children (Fig. 5), and the addition of 10 cmH₂O PEEP has been demonstrated to produce no significant change in ΔIVC [45]. These findings should be considered when this variable is used for fluid management in mechanically ventilated children. In addition, measurement errors can easily occur in an IVC with a small diameter.

**Esophageal Doppler indices**

An esophageal Doppler system (CardioQ; Deltex Medical, UK) can measure the blood flow velocity in the descending aorta with the probe placed in the esophagus. Esophageal Doppler peak velocity could be used as an indicator of fluid responsiveness, in which reaching a target value of > 135.5 cm/s is a signal to terminate further fluid challenges in patients aged 1 day to 13 years [8] (Table 1). However, the target value may vary according to age, as the esophageal Doppler peak velocity varies with age. Another study showed that the flow time corrected could predict the stroke volume increase caused by fluid administration in ventilated children in a noncardiac pediatric intensive care unit. However, the same study did not demonstrate any significant predictive value in overall children and in those in a cardiac pediatric intensive care unit [19] (Table 1). There has been little evidence about the usefulness of esophageal Doppler

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**Fig. 4.** Measurement of transcranial Doppler via the transfontanelle approach. Respiratory variation carotid blood flow peak velocity is measured using a sector probe via the anterior fontanelle. (A) Probe application on the anterior fontanelle, (B) Coronal view of the brain and the internal carotid artery, (C) Respiratory variation carotid blood flow peak velocity in a fluid nonresponder, (D) Respiratory variation carotid blood flow peak velocity in a fluid responder.

**Fig. 5.** Changes in the inferior vena cava (IVC) diameter during mechanical ventilation. The M-mode of IVC shows no significant change induced by the respiratory phase during mechanical ventilation in a 5-month-old infant. RA: right atrium.
for the prediction of fluid responsiveness in pediatric patients. In addition, cardiac output values measured with CardioQ in children do not well correlate with the cardiac output values measured using the thermodilution technique [46].

**Others**

**Abdominal compression-induced blood pressure change**

Increase in diastolic blood pressure induced by liver compression can be used to predict fluid responsiveness in mechanically ventilated children after cardiac surgery [6] (Table 1). This method uses the redistribution of blood volume into the central part of the body. Liver compression can increase the preload by pushing the blood volume to the heart, possibly increasing the stroke volume (Fig. 6). This finding is consistent with that of a study showing that an increase in the stroke volume index during a calibrated abdominal compression of 22–26 mmHg was able to predict fluid responsiveness regardless of the ventilation status in children aged < 8 years [42] (Table 1).

**Passive leg raising**

Concomitant measurements in cardiac index changes after the passive leg raising maneuver can be helpful in identifying patients whose cardiac index might increase with subsequent fluid resuscitation [47] (Table 1). The passive leg raising test may be helpful in assessing the volume status in children aged > 5 years, but not in those < 5 years old [48]. The blood volume shift to the central part during passive leg raising may be less in small children owing to the relatively less blood volume in the lower extremity. Accordingly, this method does not seem to be useful for the prediction of fluid responsiveness in small children.

**Parameters derived from noninvasive cardiac output monitoring**

The stroke volume index and SVV based on bioreactance measured using noninvasive cardiac output monitoring (NICOM; Cheetah Medical Inc., USA) have been found to have ability to predict fluid responsiveness in sedated and mechanically ventilated children after craniosynostosis repair [7] (Table 1). In addition, SVV measured using NICOM has been found to predict fluid responsiveness with optimal cutoff values of 10% during mechanical ventilation of children after ventricular septal defect repair [32] (Table 1). However, another study reported that the SVV measured using NICOM could not predict fluid responsiveness in pediatric patients aged < 5 years during cardiac surgery [33]. In addition, the study found no correlation between the cardiac index obtained using NICOM and that measured using echocardiography [33].

**Differences between the Pediatric and Adult Populations**

Studies have shown that fluid responsiveness in the pediatric population is different from that in adults. Pressure-based parameters such as PPV and SPV seem to be poor indicators of volume management in children. In addition, the results of studies on plethysmography-derived parameters in children were different from those of studies in adult patients. These differences can be explained by the physiologic and anatomic characteristics of the pediatric population.

First, the characteristics and compliance of blood vessels differ according to age. With increasing age, the arterial vessel wall thickness and collagen fiber quantity change [49], and both peripheral resistance and aortic resistance decrease with different rates [50,51]. Blood vessels become stiff with age because of calcification. Consequently, both peripheral and proximal arterial wall distensibility decrease with increasing age [50], which affects the relationship between SVV and parameters derived from peripheral arterial blood pressure such as PPV and SPV. In addition, there are inherent differences in vascular properties among various pediatric cardiac pathologies [52].

Second, the overall respiratory compliance of children can be larger than that of adults. Therefore, the change in the intrathoracic pressure transmitted to the vascular system may be less when applying the same tidal volume per weight to the pediatric population.

Third, cardiac ventricular compliance is decreased in the neonatal heart after cardiopulmonary bypass and in the pres-

**Fig. 6. Abdominal compression-induced blood pressure change.** Arterial blood pressure waveforms are displayed in the Frank-Starling curve. The arrow indicates the start of liver compression. Notice the difference of blood pressure change during liver compression between a fluid responder (left bottom of the curve) and a nonresponder (right top of the curve).
Considerations for Research on Fluid Responsiveness in the Pediatric Population

First, the most difficult part of the investigation on fluid responsiveness in the pediatric population is obtaining the cardiac output, the reference value. It is difficult to measure cardiac output in children. Many pediatric studies have used cardiac echocardiography to obtain the cardiac output value. The velocity time integral and the diameter at the level of the aortic annulus or left ventricular outflow tract are used to calculate the stroke volume (Fig. 7). However, inter-observer and intra-observer variability should be considered during echocardiographic measurements [53]. A more accurate method is placement of a perivascular flow probe around the aorta [54]. However, the application of this method is highly limited.

Second, various definitions of fluid responsiveness have been provided by different studies (Table 1). Considering the Frank-Starling curve, the change in the stroke volume index may be a reasonable indicator of fluid responsiveness. However, considering overall perfusion and oxygen delivery, evaluation of cardiac output increase may be more appropriate. The heart rate can change after fluid loading. Fluid responders might change to nonresponders according to which parameter is used to determine fluid responsiveness. Accordingly, the definition of fluid responsiveness should be reconsidered.

Third, a patient’s cardiac condition and use of inotropic and vasoconstrictor agents should be considered [55]. Patients with poor baseline contractility need more fluid to increase stroke volume. The clinical implications are important for patients with reduced contractility, who will require increased volume administra-
Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Ji-Hyun Lee (Writing–original draft)
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