

# Effect of Inhalational Anesthetics and Positive-pressure Ventilation on Ultrasound Assessment of the Great Vessels

## A Prospective Study at a Children's Hospital

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### ABSTRACT

**Background:** Bedside ultrasound has emerged as a rapid, noninvasive tool for assessment and monitoring of fluid status in children. The inferior vena cava (IVC) varies in size with changes in blood volume and intrathoracic pressure, but the magnitude of change to the IVC with inhalational anesthetic and positive-pressure ventilation (PPV) is unknown.

**Methods:** Prospective observational study of 24 healthy children aged 1 to 12 yr scheduled for elective surgery. Ultrasound images of the IVC and aorta were recorded at five time points: awake; spontaneous ventilation with sevoflurane by mask; intubated with peak inspiratory pressure/positive end-expiratory pressure of 15/0, 20/5, and 25/10 cm H<sub>2</sub>O. A blinded investigator measured IVC/aorta ratios (IVC/Ao) and changes in IVC diameter due to respiratory variation (IVC-RV) from the recorded videos.

**Results:** Inhalational anesthetic decreased IVC/Ao ( $1.1 \pm 0.3$  vs.  $0.6 \pm 0.2$ ;  $P < 0.001$ ) but did not change IVC-RV (median, 43%; interquartile range [IQR], 36 to 58% vs. 46%; IQR, 36 to 66%;  $P > 0.99$ ). The initiation of PPV increased IVC/Ao ( $0.64 \pm 0.21$  vs.  $1.16 \pm 0.27$ ;  $P < 0.001$ ) and decreased IVC-RV (median, 46%; IQR, 36 to 66% vs. 9%; IQR, 4 to 14%;  $P < 0.001$ ). There was no change in either IVC/Ao or IVC-RV with subsequent incremental increases in peak inspiratory pressure/positive end-expiratory pressure ( $P > 0.99$  for both).

**Conclusions:** Addition of inhalational anesthetic affects IVC/Ao but not IVC-RV, and significant changes in IVC/Ao and IVC-RV occur with initiation of PPV in healthy children. Clinicians should be aware of these expected vascular changes when managing patients. Establishing these IVC parameters will enable future studies to better evaluate these measurements as tools for diagnosing hypovolemia or predicting fluid responsiveness. (ANESTHESIOLOGY 2016; 124:870-7)

ACCURATE assessment of intravascular volume in children with acute physiologic perturbations, as frequently encountered in anesthesia and acute care settings, is essential for guiding clinical decisions. If unrecognized and inadequately treated, hypovolemia can lead to inadequate tissue perfusion, end-organ dysfunction, and even death. However, overestimating the degree of hypovolemia with excess volume resuscitation may cause iatrogenic morbidity and mortality.<sup>1,2</sup>

Current methods of volume assessment have limitations. Invasive measurement of central venous pressure, left ventricular end-diastolic volume, and pulmonary artery diastolic pressure imposes procedural risk without demonstrated accuracy or clinical benefit.<sup>3,4</sup> Widely used noninvasive methods also have limited utility. Percent change from baseline weight may be problematic in growing children, and in septic patients, it may be a poor indicator of intravascular volume secondary to third spacing. Furthermore, laboratory values used as surrogate markers for intravascular volume and interpreted within the context of clinical assessment are notoriously unreliable.<sup>5</sup>

#### What We Already Know about This Topic

- Bedside ultrasound has emerged as a rapid, noninvasive tool for assessment and monitoring of fluid status in children.
- This study determined the magnitude of inferior vena cava changes during positive-pressure ventilation in healthy children receiving general anesthesia using ultrasound.

#### What This Article Tells Us That Is New

- Inhalational anesthesia decreased the inferior vena cava (IVC)/aorta ratio but did not change the IVC diameter in response to respiratory variation in healthy children receiving general anesthesia. The initiation of positive-pressure ventilation significantly increased the IVC/aorta ratio and decreased the IVC diameter in response to respiratory variation. There was no change in the IVC/aorta ratio or the IVC diameter in response to respiratory variation with subsequent incremental increases in peak inspiratory pressure or positive end-expiratory pressure.

Bedside ultrasound has emerged as a rapid, noninvasive tool for qualitative and quantitative assessment of anatomic structure and function in children.<sup>6</sup> The thin-walled inferior

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vena cava (IVC) is amenable to ultrasound evaluation as it traverses the liver, an organ that readily propagates ultrasound waves. Because IVC and aorta measurements vary with the size and age of a child, the ratio of the diameters of the IVC and the aorta (IVC/Ao) has been used to assess intravascular fluid status in pediatric populations.<sup>7</sup> The IVC varies in size with changes to blood volume and intrathoracic pressure.<sup>8</sup>

In spontaneously breathing patients without positive-pressure ventilation (PPV), decreased intrathoracic pressure during inspiration causes an increase in venous return to the right atrium and a transient decrease in IVC diameter. In patients undergoing PPV, intrathoracic pressure increases with each delivered breath, thus increasing IVC diameter during inspiration. It has been shown in adults that changes in IVC diameter due to respiratory variation (IVC-RV) may serve as an indicator of volume status.<sup>9</sup> However, the effects of initiation and titration of PPV on ultrasound-based measures of the IVC, specifically IVC/Ao, IVC morphology, and IVC-RV, in pediatric populations are not well known.

The first aim of this study is to evaluate the effect of inhalational anesthetic on IVC/Ao, IVC-RV, and IVC morphology in healthy pediatric patients who are undergoing general anesthesia for scheduled surgery. We hypothesized that the addition of inhalational anesthetic would decrease IVC/Ao, increase IVC-RV, and compress IVC morphology. The second aim of this study is to determine the effect of PPV on IVC/Ao, IVC-RV, and IVC morphology in anesthetized patients. We hypothesized that the introduction of PPV would increase IVC/Ao, decrease IVC-RV, and distend IVC morphology and that increasing mean airway pressure would increase IVC/Ao, decrease IVC-RV, and further distend IVC morphology. Describing expected changes for these IVC parameters will enable us in future studies to evaluate these measurements as tools for diagnosing hypovolemia or predicting fluid responsiveness.

## Materials and Methods

### Study Design

This was a prospective observational study conducted from April to May 2014. This study was approved by the local Human Subjects Institutional Review Board at the Children's Hospital of Philadelphia (Philadelphia, Pennsylvania). Written informed consent was obtained by each subject's parent or guardian, and when the child was over the age of 7 yr, assent was obtained.

### Setting and Participants

The study was conducted in the operating room complex of a large academic pediatric hospital. Subjects were healthy children between the ages of 1 to 12 yr old undergoing scheduled extrathoracic/extraabdominal procedures and for whom the attending anesthesiologist planned on using an anesthetic regimen including mask induction, use of neuromuscular blockade, and endotracheal intubation for clinical

care. Exclusion criteria included history of significant pulmonary or cardiac disease (*i.e.*, pulmonary hypertension, tricuspid or pulmonic disease, and right ventricular dysfunction); history of severe sleep apnea (apnea-hypopnea index  $\geq 30$  or use of nighttime continuous or bilevel positive airway pressure); patients with tracheostomy; clinical diagnosis by the clinical team that the patient had moderate-to-severe dehydration; and non-English-speaking parent/guardian.

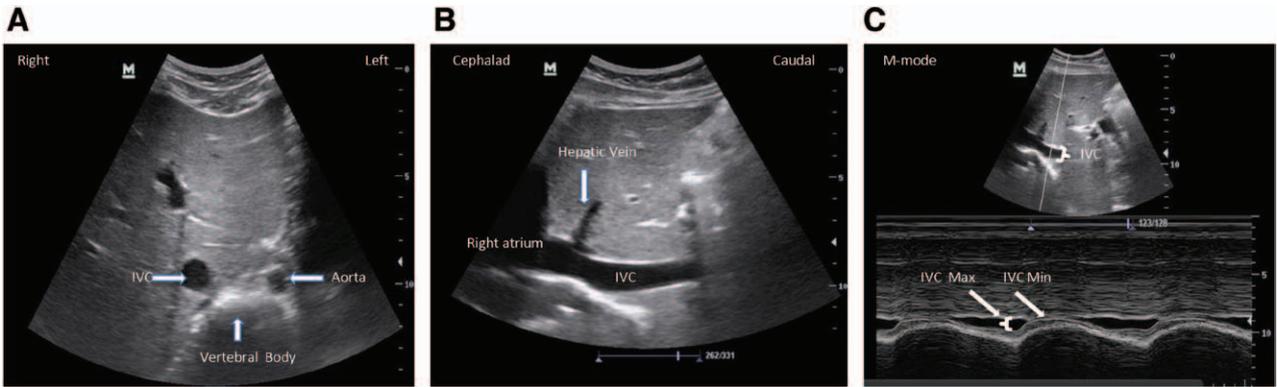
### Ultrasound Protocol

All ultrasound scans were performed by one study investigator (A.E.C.) by using a low-frequency curvilinear array transducer on a Mindray M7 portable ultrasound machine (Mindray Corp, China). This study investigator had prior training in bedside ultrasound with over 1,000 ultrasound scans including cardiac and IVC indications. For each patient, ultrasound images of the IVC and aorta were recorded at five time points with the patient lying supine: awake, spontaneous ventilation with inhalational anesthetic *via* face mask, and postintubation with peak inspiratory pressure (PIP)/positive end-expiratory pressure (PEEP) of 15/0, 20/5, and 25/10 cm H<sub>2</sub>O. For each of the five time points, a 10-s video clip was recorded for each of three measurements: (1) transverse subxiphoid view of the IVC and aorta (fig. 1A); (2) longitudinal subxiphoid view of the IVC (fig. 1B); and (3) longitudinal subxiphoid view of the IVC in M-mode (fig. 1C).

Each of the 15 video clips obtained per patient was assigned a random identification number. A single study investigator (N.P.), blinded to both patient demographics and time point, subsequently performed following measurements on the saved video clips: in the subxiphoid transverse view—(1) measurement of the IVC and aorta in the anterior-posterior plane, from outer wall to outer wall in maximum diameter; and (2) a gross estimate of the IVC morphology in maximum anterior-posterior diameter was categorized as round, elliptical, or flat<sup>10</sup>; in the subxiphoid longitudinal view in M-mode—measurement of the maximal and minimal anterior-posterior IVC diameter approximately 1 cm below the confluence of hepatic veins with the IVC. IVC-RV was calculated with the following formula:  $[(\text{maximum IVC} - \text{minimum IVC})/(\text{maximum IVC}) \times 100]$ .<sup>11</sup>

### Anesthetic Protocol

Subjects received anesthesia based on a standardized clinical anesthetic protocol. End-expired sevoflurane concentration was measured *via* side stream sampling line (Dräger Apollo version 4.10.05, USA). In the preoperative area, each patient received oral midazolam premedication of 0.5 mg/kg to a maximum of 10 mg. In the operating suite, each patient received sevoflurane (vaporizer dial set to 8 vol%) *via* mask to maintain spontaneous unassisted ventilation. An appropriately sized oral pharyngeal airway was placed to minimize upper airway obstruction. A peripheral intravascular catheter was placed after induction of anesthesia. The intravascular catheter was flushed with a small volume of crystalloid fluid



**Fig. 1.** Ultrasound views and measurements used for the study. These images represent the each ultrasound view used for this presented study. (A) An example of a transverse subxiphoid view of the inferior vena cava (IVC) and aorta. (B) An example of a longitudinal subxiphoid view of the IVC. (C) An example of a longitudinal subxiphoid view of the IVC in M-mode. Max = maximum; Min = minimum.

to ensure correct placement and then fluid was administered by gravity; however, additional fluid bolus was not given until the conclusion of the study. After ultrasound measurements were recorded under spontaneous ventilation, neuromuscular paralysis with vecuronium 0.05 mg/kg was given to facilitate intubation. The sevoflurane vaporizer setting was decreased to 2.5 vol% after administration of neuromuscular blockade. No additional medications were given to the subjects until the final ultrasound images were acquired. Ultrasound images were taken 30 s to 1 min after intubation and after each ventilatory setting change to allow for equilibration. The protocol is summarized in figure 2.

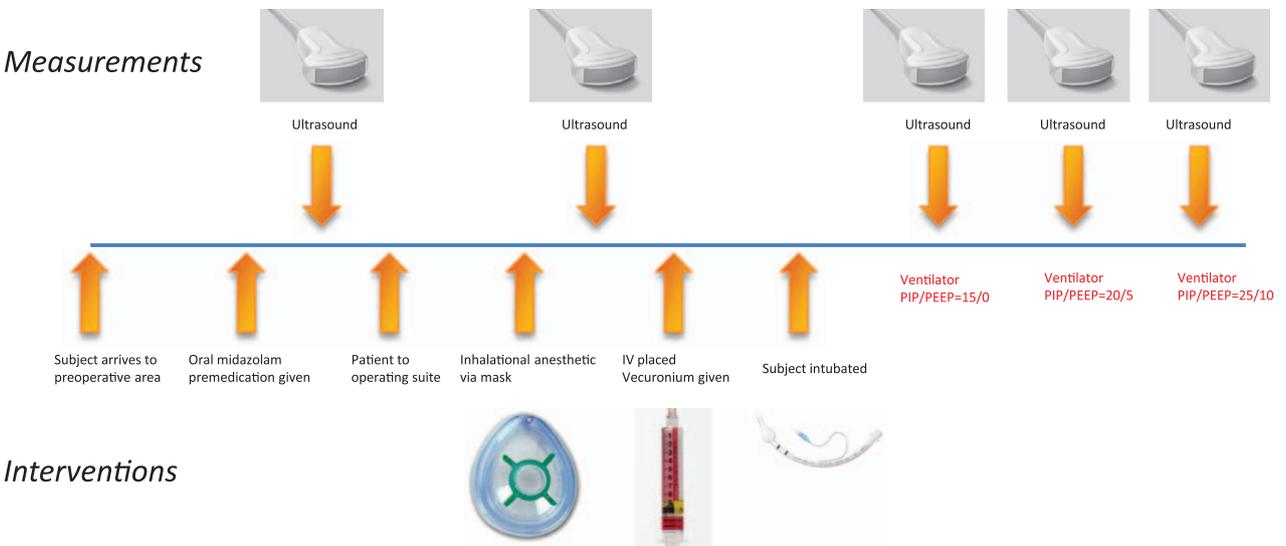
**Sample Size Calculation**

Sample size calculations were made based on change in IVC/Ao with the addition of PPV. Baseline IVC/Ao was estimated at 1.2 based on prior studies.<sup>12,13</sup> We estimated the IVC/Ao would increase to 1.6 (increase of 33%) after

initiation of PPV based on our preliminary observations in anesthetized children and from extrapolating from adult studies that showed an IVC diameter of 12 mm in spontaneously breathing healthy subjects<sup>14</sup> and 18.7 mm in intubated septic patients<sup>15</sup> (increase of 50%). A sample size of 24 was calculated with two-sided  $\alpha = 0.05$  and  $\beta = 0.1$ .

**Statistical Analysis**

Statistical analysis was performed by using STATA 11.2 (StataCorp, USA). Summary statistics were described by using means and SD for parametric variables and medians with interquartile ranges (IQRs) for nonparametric variables. Distribution of variables was evaluated by skewness/kurtosis tests for normality.<sup>16</sup> Outcomes were plotted in box-whisker plot. For univariate analyses, repeated measure of ANOVA for parametric outcome variables (IVC/Ao) and Friedman test for nonparametric outcome variables (IVC-RV) were used. For variables that do not meet tests of normality, Friedman test



**Fig. 2.** Study protocol timeline. Study protocol timeline to display the association of clinical intervention and ultrasound-based measurements. PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure.

was used. A *post hoc* pairwise comparison was performed with Bonferroni or Dunn correction, as appropriate. IVC morphology under different PPV condition was assessed by test for trend across order groups. Finally, a multivariable longitudinal model was constructed for the primary outcome using a random-effect model to account for repeated measures within each subject and baseline differences between subjects. Mean airway pressure was calculated for each respiratory setting and used as a continuous variable. We *a priori* chose to include up to a second power of mean airway pressure as a polynomial term. Sevoflurane concentration (% volume) was included as a continuous variable. Potential confounding variables were evaluated in association with outcomes and included in a multivariable model if *P* value was less than 0.1. A *P* value less than 0.05 was considered statistically significant.

**Results**

**Demographics**

A total of 24 subjects were enrolled, with a mean (±SD) age of 5.9±3.5 yr. Mean weight was 26±16 kg and mean body mass index was 18.0±3.2, shown in table 1. Mean *nil per os* (NPO) time was 9.6±4.6 h. Surgeries included urologic, ophthalmologic, plastics, dental, and orthopedic procedures. All patients were given an oral premedication of midazolam, and sevoflurane concentrations were highest at induction (5.0±0.7 vol%) and then decreased to 3.3±0.5, 2.7±0.5, and 2.7±0.3 at airway pressures of 15/0, 20/5, and 25/5 cm H<sub>2</sub>O, respectively. Mean volume of IV fluid (lactated Ringer’s solution) given over the duration of the study was 4.5±1.7 ml/kg. One subject did not have evaluable images due to image quality for IVC-RV during the awake and PIP/PEEP 20/5 time points. All other subjects had evaluable ultrasound images at all five time points.

**Table 1.** Patient Characteristics

Demographic	
Age, yr	5.8±3.5
Sex (% female)	7 female and 17 male (29% female)
Weight (kg)	25.8±16.0
Body mass index	18.1±3.3
Race	
Caucasian	10 (42%)
African American	8 (33%)
Other	2 (8%)
Unidentified	4 (17%)
Anesthesia and Procedural Characteristics	
<i>Nil per os</i> time (h)	9.6±4.6
IV fluids (cc/kg)	4.5±1.7
Type of surgery	
Ophthalmology	8 (33%)
Urology	9 (38%)
Plastic surgery	4 (17%)
Dental	2 (8%)
Orthopedics	1 (4%)

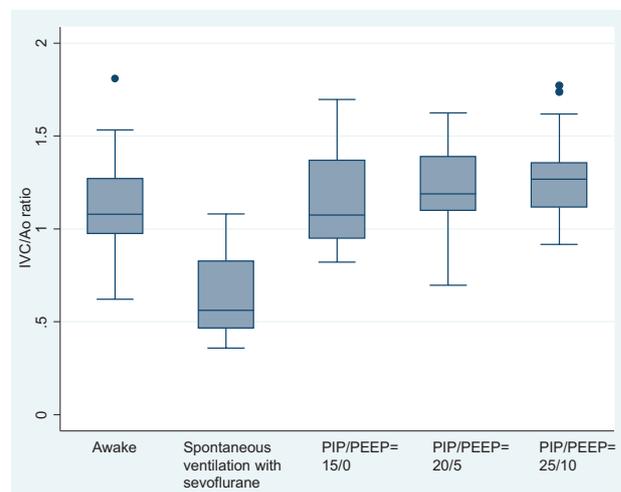
Mean ± SD was reported for age, weight, body mass index, *nil per os* time, and IV fluids.

**Effect of Inhalational Anesthetic**

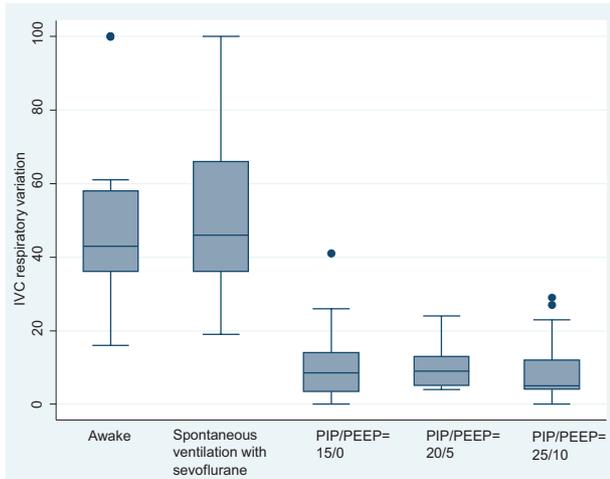
The IVC maximum diameter decreased with addition of inhalational anesthetic under spontaneous unassisted ventilation (8.4±2.5 mm *vs.* 5.1±2.1 mm; *P* < 0.001). In contrast, the aorta diameter did not change (7.6±1.4 mm *vs.* 7.8±1.4 mm; *P* = 0.59). The IVC/Ao decreased with inhalational anesthetic (1.1±0.3 *vs.* 0.6±0.2; *P* < 0.001) (fig. 3). The IVC-RV did not change with inhalational anesthetic (median, 43%; IQR, 36 to 58% *vs.* median, 46%; IQR, 36 to 66%; *P* > 0.99 after adjustment for multiple comparison; fig. 4). The IVC-RV had substantial variability among subjects at baseline and during spontaneous ventilation with sevoflurane (fig. 4). This variability was larger in children with lighter weight. IVC compressed toward elliptical and flat morphology (fig. 5).

**Effect of PPV**

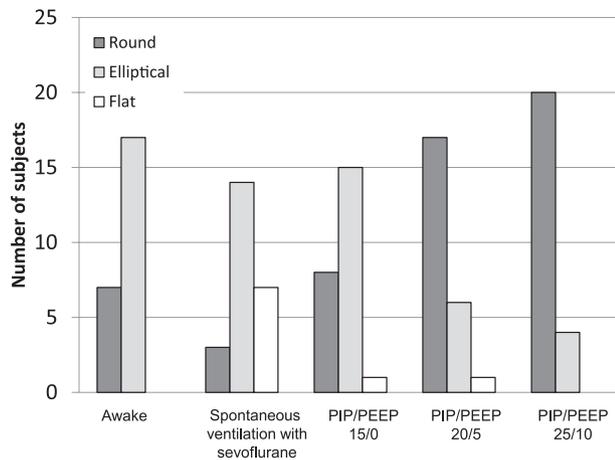
The IVC maximum diameter increased with initiation of PPV in PIP/PEEP = 15/0 *via* an endotracheal tube (5.1±2.1 mm *vs.* 8.3±2.2 mm; *P* < 0.001). The aorta diameter did not change (7.8±1.4 mm *vs.* 7.3±1.9; *P* = 0.28). The IVC/Ao increased with PPV (0.64±0.21 *vs.* 1.16±0.27; *P* < 0.001) (fig. 3). There was no significant change with subsequent incremental increases in PIP/PEEP from 15/0 to 25/10 cm H<sub>2</sub>O (*P* = 0.83). The IVC-RV decreased with initiation of PPV 15/0 (median, 46%; IQR, 36 to 66% *vs.* median, 9%; IQR, 4 to 14%; *P* < 0.001 after adjustment for multiple comparison). However, there was no significant change with subsequent incremental increases in PIP/PEEP from 15/0 to 25/10 (median 9% with IQR 4 to 14% at PIP/PEEP = 15/0, median 9% with IQR 5 to 13% at PIP/PEEP = 20/5, and median 5% with IQR 4 to 12% at PIP/PEEP = 25/10; *P* > 0.99), shown in figure 4. IVC distended toward round morphology as PPV was initiated and PEEP was increased (*P* < 0.01) (fig. 5).



**Fig. 3.** Inferior vena cava to aorta ratio (IVC/Ao) on different respiratory settings. IVC/Ao on five different respiratory settings. PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure.



**Fig. 4.** Inferior vena cava respiratory variation (IVC-RV) on different respiratory settings. IVC-RV at five different settings. IVC-RV was calculated with the following formula: (maximum IVC – minimum IVC)/maximum IVC × 100. PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure.



**Fig. 5.** Inferior vena cava (IVC) morphology on different respiratory settings. Morphology of IVC changes at different respiratory settings. Note that IVC becomes more round with increase in mean airway pressure. *P* value less than 0.001 for chi-square test for trend (this analysis excluded awake condition). PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure.

**Multivariable Analysis for IVC/Ao**

A mixed-effect model with random intercept was developed to model IVC/Ao to evaluate the impact of mean airway pressure and sevoflurane simultaneously. None of patient demographic variables (height, weight, and age), NPO time, or given IV fluid volume were independently associated with IVC/Ao and therefore were not included in the model. Mean airway pressure was positively but nonlinearly associated with IVC/Ao ratio (table 2). Sevoflurane concentration was negatively associated with IVC/Ao ratio (*P* < 0.001). Based on this model, after adjusting for sevoflurane effect, the conversion from spontaneous ventilation to PPV at PIP/PEEP = 15/0 (mean airway pressure = 4 cm H<sub>2</sub>O) will increase IVC/Ao by

**Table 2.** Multivariable Analysis for Inferior Vena Cava/Aorta Ratio with Mean Airway Pressure and Sevoflurane

	Coefficient (95% CI)	<i>P</i> Value
Mean airway pressure	0.080 (0.053 to 0.107)	< 0.001
Mean airway pressure <sup>2</sup>	-0.004 (-0.006 to -0.002)	< 0.001
Sevoflurane (% volume)	-0.083 (-0.107 to -0.059)	< 0.001
Baseline (constant)	1.098 (1.000 to 1.196)	< 0.001

Dependent variable = inferior vena cava/aorta ratio (IVC/Ao). Random intercept longitudinal model including second power of mean airway pressure as a polynomial variable. The model was significant overall (*P* < 0.001). Subject baseline variable (height) was neither associated with IVC/Ao in univariate analysis nor as an independent variable in the multivariate model; therefore, final model did not include the term. Mean airway pressure<sup>2</sup> denotes the second power of mean airway pressure. Note that mean airway pressure was calculated from each ventilator setting.

0.26 (95% CI, 0.18 to 0.34). The conversion from spontaneous ventilation to PPV at PIP/PEEP = 20/5 (mean airway pressure = 14 cm H<sub>2</sub>O) will increase IVC/Ao by 0.42 (95% CI, 0.32 to 0.52).

**Discussion**

We demonstrated that IVC/Ao, IVC-RV, and IVC morphology changed with addition of inhalational anesthetic and initiation of PPV. Specifically, the IVC/Ao decreased with addition of inhalational anesthetic and increased after initiation of PPV. The IVC-RV, another often-used volume indicator, did not change after addition of inhalational anesthetic but substantially decreased after initiation of PPV. The IVC morphology became more elliptical or flat with addition of inhalational anesthetic and changed toward round after initiation of PPV.

We hypothesized that inhalational anesthetic would increase venous capacitance, resulting in decreased IVC/Ao and a more compressible IVC with greater IVC-RV. Interestingly, in our study, IVC-RV did not change between awake to anesthetized state. Because IVC-RV measures the changes in the IVC diameter directly related to respiration, this measurement might be more affected by changes in intrathoracic pressure than changes in venous capacitance.<sup>17</sup>

As expected, in our study, the IVC/Ao increased with introduction of PPV. This result is thought to be from increased intrathoracic pressure transmitted to right atrial pressure, which impedes venous return. Therefore, not only did IVC/Ao change, but also the IVC morphology changed to round after initiation of PPV. The IVC/Ao was initially used by researchers to noninvasively determine dry weight in pediatric patients undergoing dialysis.<sup>13</sup> Its application has extended to the acute care setting as a surrogate marker for intravascular volume. Emergency medicine providers in both rural and urban settings have found the IVC/Ao correlates with standard clinical definitions of dehydration in pediatric populations.<sup>18-20</sup> The IVC/Ao reported in this study is consistent with previously published numbers. Chen *et al.*<sup>12</sup> reported a baseline IVC/Ao of 1.01 in nondehydrated children. In the dehydrated children, IVC/Ao increased

from 0.75 to 1.09 after IV hydration, demonstrating an association between IVC/Ao, clinical dehydration, and fluid responsiveness. Although the measure held great promise in the quest for a noninvasive means of evaluating intravascular volume, meta-analysis of both adult and pediatric studies demonstrate that static parameters (point-in-time measures), including IVC/Ao, were poor predictors of fluid responsiveness compared with dynamic parameters (changes-in-time), including IVC-RV.<sup>15,21,22</sup>

The decrease in IVC-RV with the initiation of PPV was dramatic in our study. Although we were not able to identify studies that evaluated the initiation of PPV on this measurement, our finding was consistent with adult studies that demonstrated decreased IVC-RV in patients receiving mechanical ventilation. Although 40% IVC-RV has been associated with fluid responsiveness in spontaneously breathing patients,<sup>23,24</sup> an 18% IVC-RV is seen in fluid responsive patients on PPV.<sup>25,26</sup> Increases in mean airway pressure resulted in a positive but nonlinear increase in IVC/Ao. This study demonstrates a potential range of change that can be used when assessing IVC/Ao in patients undergoing PPV independent of inhalational anesthetic in future studies or clinical scenarios. Additional research is needed to determine whether these study findings are generalizable to the critically ill population.

Studying fluid responsiveness was beyond the scope of this study. What can be extracted from our study result is that care must be taken to consider impact of anesthetic and PPV when we assess surrogate markers of volume status. Inhalational anesthetic resulted in a significant decrease in IVC/Ao from baseline and no change in IVC-RV. IVC-RV significantly decreased when positive pressure was introduced while IVC/Ao returned to preanesthesia measurements. IVC/Ao changes were significantly influenced by sevoflurane administration as demonstrated in multivariable analysis. Clearly, IVC/Ao and IVC-RV are not synonymous. Fluid boluses were not provided to patients and thus the variability is unlikely to have any association with changes in intravascular volume. Again we are confronted with the realization that surrogate markers of physiologic variables have their limitations and that we need to understand these limitations when such markers may guide clinical decisions.

There are several limitations to this study. It was not possible to study the pure effect of initiation of PPV because anesthesia was necessary to allow for intubation. Furthermore, due to the nature of mask induction and the need to maintain a relatively high level of anesthesia before intubation to reduce the incidence of complications such as laryngospasm, the sevoflurane level was not consistent across all time points. Thus, the multivariable model was created to determine the effect of and adjust for this confounder on IVC/Ao and IVC-RV. Even after adjusting for sevoflurane concentration, mean airway pressure has an independent effect on IVC/Ao and IVC-RV. Although both IVC/Ao and IVC-RV measures may be incorporated into routine

clinical practice in the future, these measurements cannot be obtained during upper abdominal surgery. We also have no data on how laparotomy affects these IVC/Ao and IVC-RV measures. This is an area for future investigation.

We used a smaller than standard intubating dose of vecuronium based on our clinical practice. This may have decreased the potential vasodilatory effect of vecuronium in our IVC/Ao measurement. It was beyond the scope of this study to address the potential impact of a higher dose of neuromuscular blockade. Furthermore, we had a 30- to 60-s delay between changes in ventilator settings and ultrasound measurements to allow for some degree of equilibrium within a patient with each new ventilator setting. With a pressure-controlled ventilator mode and a respiratory rate set at 20 breaths/min, this resulted in 10 to 20 breaths after a change in ventilator settings. Although this is likely adequate to reach a new equilibrium in tidal volumes, it may not be sufficient to reach a new equilibrium in depth of anesthesia and venous carbon dioxide levels. Because these factors affect pulmonary artery and right atrial pressure, this potentially inadequate transition time may have introduced additional variabilities in IVC measurements in response to ventilator mode change.

The mean airway pressure was not directly measured in this study but rather calculated based on the PIP and PEEP set on the ventilator. In healthy children with normal lungs and airway, the calculated values should be close to actual mean airway pressure when patients are ventilated with pressure-preset ventilation. Furthermore, for safety and ethical reasons, the range of mean airway pressure studied was relatively narrow. It is possible that at higher PEEPs, as is often required in sick ventilated patients in the intensive care unit, incremental increase in mean airway pressure may have an effect on IVC/Ao and IVC-RV.

All children in this study were appropriately NPO for their surgery with a mean NPO time of 9.6 h. Although NPO time could certainly cause some degree of dehydration, it was not thought to be clinically significant as healthy children tolerate being NPO overnight while sleeping for greater than 10 h. In our study, NPO time was not associated with either IVC/Ao or IVC-RV. Furthermore, the baseline IVC/Ao of 1.1 in awake status measured in our study is similar to the reported IVC/Ao values of 1.01 in control pediatric subjects and 1.09 in rehydrated pediatric subjects as reported by Chen *et al.*<sup>7</sup> Therefore, we speculated that NPO time did not alter our study findings. In addition, it was not possible for us to quantify intravascular volume status at the start of the study protocol and thus we cannot assume that all subjects started with the same intravascular volume status. Undetected differences in volume status could potentially confound the observed responses to sevoflurane and PPV.

It was beyond the scope of this study to evaluate IVC/Ao and IVC-RV in the context of a fluid responsiveness. During the study, IV fluids were minimized to decrease confounding, with a mean of 4.5 ml/kg crystalloid (lactated Ringer's

solution) throughout the course of the study. From our study result, it is not possible to determine whether IVC/Ao or IVC-RV has diagnostic capability for fluid responsiveness after volume resuscitation.

## Conclusion and Future Directions

Current methods of intravascular volume assessment have limitations when used in clinical practice. IVC-based measurements using bedside ultrasound are easy to perform, quick, and amenable to serial measurements during clinical care. Our study found patterns in pediatric IVC-based measurements due to inhalational anesthetic and initiation of PPV, consistent with underlying physiology. Due to the inherent limitations of these measurements, clinicians should be cautious when using these measurements to guide management of patients. These findings may pave the way for future studies assessing volume status in pediatric patients with both static (IVC/Ao) and dynamic (IVC-RV) measures.

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## Competing Interests

The authors declare no competing interests.

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