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# Pulse oximeter plethysmograph variation and its relationship to the arterial waveform in mechanically ventilated children

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**Abstract** The variations induced by mechanical ventilation in the arterial pulse pressure and pulse oximeter plethysmograph waveforms have been shown to correlate closely and be effective in adults as markers of volume responsiveness. The aims of our study were to investigate: (1) the feasibility of recording plethysmograph indices; and (2) the relationship between pulse pressure variation (ΔPP), plethysmograph variation (ΔPOP) and plethysmograph variability index (PVI) in a diverse group of mechanically ventilated children. A prospective, observational study was performed. Mechanically ventilated children less than 11 years of age, with arterial catheters, were enrolled during the course of their clinical care in the operating room or in the pediatric intensive care unit. Real time monitor waveforms and trend data were recorded. ΔPP and ΔPOP were manually calculated and the relationships between ΔPP, ΔPOP and PVI were compared using Bland–Altman analysis and Pearson correlations. Forty-nine children were recruited; four (8%) subjects were excluded due to poor quality of the plethysmograph waveforms. ΔPP and ΔPOP demonstrated a strong correlation ($r = 0.8439$, $P < 0.0001$) and close agreement (Bias = 1.44 ± 6.4%). PVI was found to correlate strongly with ΔPP ($r = 0.7049$, $P < 0.0001$) and ΔPOP ($r = 0.715$, $P < 0.0001$). This study demonstrates the feasibility of obtaining plethysmographic variability indices in children under various physiological stresses. These data show a similarly strong correlation to that described in adults, between the variations induced by mechanical ventilation in arterial pulse pressure and the pulse oximeter plethysmograph.

**Keywords** Pulse oximeter plethysmograph · Arterial pulse pressure variation · Plethysmograph variation · Plethysmograph variability index

## 1 Introduction

Intravascular volume resuscitation of children is a frequent intervention in the operating room (OR) and in the pediatric intensive care unit (PICU). While appropriate volume administration is beneficial [1], excessive intravenous fluid may lead to peripheral and pulmonary edema. The assessment of intravascular volume status or cardiac preload in children, however, is frequently not guided by robust scientific evidence [2].

Traditional static indicators of cardiac preload, e.g., central venous pressure (CVP), have been shown to be as unreliable in children [3], as they are in adults [4], at predicting a significant cardiac output response to fluid administration or volume responsiveness (VR). Dynamic preload indicators, such as arterial pulse pressure variation (ΔPP), are variables that quantify the effects of mechanical ventilation on cardiac stroke volume, and have been shown in adults to predict VR [5–7]. Pediatric studies examining dynamic preload indicators [8–11] have found that respiratory variations in aortic blood flow predict VR in children.

Truly non-invasive, dynamic markers of volume status derived from the pulse oximeter plethysmograph waveform, the manually calculated pulse oximeter plethysmograph variation (ΔPOP), and the automated plethysmograph variability

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index (PVI) (Masimo® Corporation, Irvine, CA, USA), correlate strongly with ΔPP [12–14] and predict VR [15–17] in adults. In children, where reliable hemodynamic monitoring is challenging to achieve and in whom monitoring tends to be less invasive, these indices may offer significant advantages. Conflicting data exist as to the ability of these indices to predict VR in children. PVI has been found to predict VR in a population of infants with congential cardiac disease [11], however, in a population of children undergoing neurosurgery this predictive ability was not observed [10]. These studies examined children under anesthesia prior to surgery.

The arterial blood pressure and plethysmographic waveform amplitudes are both primarily determined by stroke volume. In addition, the arterial pressure waveform is influenced by arterial compliance [18] whilst the plethysmograph waveform is influenced by vasomotor tone and external light [19]. Physiological differences between adults and children including: altered skin perfusion [20], chest compliance [21], and arterial compliance [22], mean that adult ΔPP, ΔPOP and PVI relationships and predictive characteristics may not apply to children.

Our aims in this study were firstly, to examine the feasibility of measuring dynamic indices from the pulse oximeter plethysmograph in a medically diverse group of mechanically ventilated children, both in the OR and PICU and secondly, to assess the relationship between the ΔPP, ΔPOP and PVI in this population in two separate age groups.

## 2 Methods

A prospective, observational study in the OR and PICU was conducted following approval by The University of British Columbia/Children's and Women's Health Centre of British Columbia Research Ethics Board. Written informed parental consent and subject assent (where possible, in those >7 years old) were obtained for children enrolled in the study. Patients meeting the following criteria were enrolled: in the OR or PICU, patients mechanically ventilated via an endotracheal tube, with an arterial line inserted as part of their management. Patients were stratified into two groups based on age: under 2 years and 2–10 years. Exclusion criteria were: failure to obtain parental consent, spontaneous breathing activity, arrhythmia, known intracardiac shunts, unstable blood pressure, and a location on a hand not available for pulse oximetry monitoring. In the OR data recording took place at either the beginning or end (in the case of cardiac surgery patients) of the surgical case. In the PICU, data recording took place at a time judged suitable by the PICU medical staff.

### 2.1 Data recording procedures

Data were recorded for at least 1 min during which the subject was not stimulated and any drug infusion rates were kept constant. All patients were ventilated with PEEP values of 4-6 $cmH_2O$ and tidal volumes were recorded. The arterial transducer was levelled at the midaxillary line and two extra pulse oximeter probes were placed onto the fingers of one hand and covered to exclude external light. These probes were attached to two oxygen saturation monitors: Novametrix Oxypleth® 520a (Covidien-Nellcor™, Boulder, CO, USA) and Radical 7™ (Masimo® Corporation, Irvine, CA, USA). Patients with inadequate plethysmograph signal quality were defined as those whose perfusion index, a measure of plethysmographic amplitude, as measured by the Radical 7™, was <0.2. The automatic gain control was switched off on the Oxypleth® monitor and real-time raw plethysmograph waveform was extracted via the serial port to a computer using Pulse Oximetry Data Acquisition Viewer (PODAV) software (Convergent Engineering, Gainesville, FL, USA) [23].

Real-time arterial pressure, ECG, end-tidal $CO_2$ waveforms and trend data were downloaded from the Datex-Ohmeda S/5 Anesthesia Monitor (GE Healthcare Technologies, Waukesha, WI, USA) using Datex-Ohmeda PC Collect® software. Real-time waveform data was extracted from the IntelliVue MP70™ (Philips Medical Systems, Andover, MA, USA) PICU monitors via a passive tap into the central network that extracted an exact copy of the raw network data. A custom analyzer (iVUE) used the PCAP (Packet CAPture) [24] application-programming interface running on a customized OpenBSD based operating system to obtain the relevant waveforms. PVI was calculated automatically from the perfusion index (PI), by the Masimo Radical 7™ oximeter using the formula: [13] $PVI = 100 \times [(PImax - PImin)/PImax]$, PVI trend data were downloaded using TrendCom™ software (Masimo).

### 2.2 Data analysis

Waveform data was sampled between 25 and 300 Hz and were exported from the relevant programs as comma separated values or ASCII files. These data were displayed using a custom Matlab® (The Mathworks™, Natick, MA, USA) application, which allowed for time synchronization of the data, displayed the waveforms and allowed relevant data point measurement. Maximum and minimum values of pulse pressure (PP) and pulse oximeter plethysmograph amplitude (POP) were measured over one respiratory cycle (see Fig. 1) and expressed as mmHg and arbitrary units respectively. Plethysmograph output waves represent the quantity of light absorbed by the photo detector and do not have specific units. Neither ΔPP nor ΔPOP were calculated

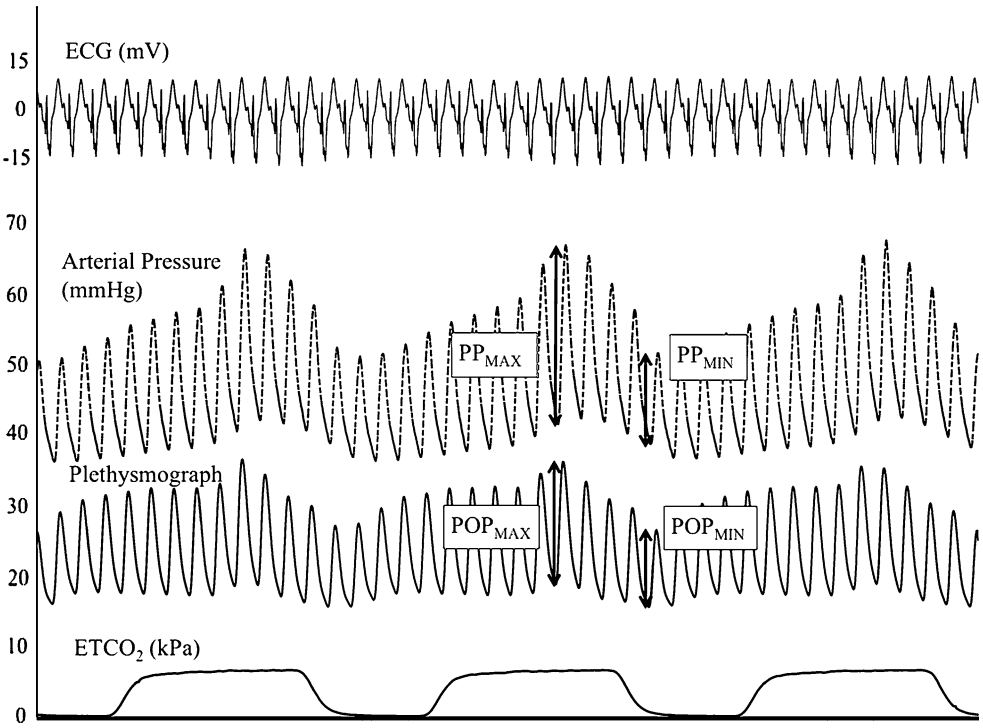


**Fig. 1** Measurement of dynamic indices *ECG* electrocardiogram, *ETCO2* end tidal carbon dioxide, *PP* pulse pressure, *POP* plethysmograph amplitude (arbitrary units)

in real-time; both required post-data collection analysis. ΔPP was calculated from the formula: [6] $\Delta PP(\%) = 100 \times ([PPmax - PPmin]/[(PPmax + PPmin)/2])$. This calculation was repeated for each of three respiratory cycles and averaged. ΔPOP was calculated according to the formula: [12] $\Delta POP\ (\%) = 100 \times ([POPmax - POPmin]/[(POPmax + POPmin)/2])$. This too was repeated for each of three respiratory cycles and averaged.

### 2.3 Statistical analysis

A power analysis demonstrated that for a correlation coefficient of 0.5 at an $\alpha$-value of 0.05 and a $\beta$-value of 0.2, 30 subjects would be required. Demographic data were expressed as ranges and medians for non-parametric data and as means and standard deviations for parametric data. Correlation between ΔPP and ΔPOP were assessed with a Pearson Correlation, and their agreement and bias were compared using a Bland–Altman analysis. The relationship of ΔPP to PVI and ΔPOP to PVI were examined using Pearson Correlations. Statistical significance was defined as $P < 0.05$. Statistical calculations were performed using using MedCalc® (MedCalc Software™, Mariakerke, Belgium, www.medcalc.org) statistical software.

## 3 Results

Of the forty-nine children recruited, sixteen were excluded. Four (8%) were excluded for clinical reasons: two for unrepaired intracardiac shunts, one due to clinical instability and one for spontaneous breaths during data collection. Four (8%) subjects were excluded due to poor plethysmograph waveforms, three following cardiac surgery and one pre-operative craniofacial surgery patient. Eight (16%) were excluded because of software and hardware data collection malfunctions. Therefore, data were analyzed from thirty-three subjects: twenty-nine subjects in the OR and four in PICU (Table 1). Seven subjects (21%) were receiving vasoactive infusions during data collection.

**Table 1** Demographic data

| Variable | Values |
|---|---|
| Age: median (range) | 1.5 years (2 days–10.5 years) |
| Weight: median (range) | 11.5 kg (0.8–43.8 kg) |
| Surgical procedure: n (%) | General: 4 (12.1%) |
| | Plastic: 5 (15.2%) |
| | Cardiac: total: 9 (27.3%) CPB: 8 (24.2%) |
| | Orthopedic: 5 (15.2%) |
| | Neurosurgery: 6 (18.1%) |
| ASA: mode (range) | 3 (1–4) |
| ICU diagnoses: n (%) | Post-op cardiac: 3 (9.1%) |
| | ARDS: 1 (3%) |
| Tidal volume: mean (±SD) | 9.9 ml $kg^{-1}$ (±2.4 ml $kg^{-1}$) |

*ASA* American Society of Anesthesiologists classification, *CPB* Data recorded following cardiopulmonary bypass, *SD* standard deviation

**Table 2** Monitored variables

| Variable | Mean (SD) | Range |
|---|---|---|
| HR | 119 (29) | 71–186 |
| RR | 17 (5) | 10–30 |
| $SaO_2$ (%) | 99 | 97–100 |
| SBP (mmHg) | 80 (17) | 35–117 |
| MBP (mmHg) | 55 (11) | 26–80 |
| DBP (mmHg) | 42 (10) | 21–66 |
| ΔPP (%) | 13 (12) | 3–62 |
| ΔPOP (%) | 12 (9) | 1–43 |
| PI (%) | 3.8 (2.3) | 0.32–10 |
| PVI (%) | 15 (8) | 4–41 |

*DBP* diastolic blood pressure, *HR* heart rate, *MBP* mean blood pressure, *PI* perfusion index, *PVI* plethysmograph variability index, *RR* respiratory rate, $SaO_2$ oxygen saturations, *SBP* systolic blood pressure, *ΔPP* pulse pressure variation, *ΔPOP* plethysmograph variation

The hemodynamic variables displayed a wide range of values, as expected across the patient population studied. The data recorded from the various patient monitors are shown in Table 2. As displayed in Table 3, ΔPP and ΔPOP demonstrated a strong correlation ($r = 0.8439$, $P < 0.0001$, Fig. 2). The Bland–Altman analysis of ΔPP and ΔPOP exhibited a small bias with close agreement (Bias = 1.44 ± 6.4%, Fig. 3). ΔPP was also strongly correlated with the automated index PVI ($r = 0.7049$, $P < 0.0001$, Fig. 4). Similarly, the two measures of plethysmograph variability, calculated from data recorded from two different oxygen saturation monitors, ΔPOP and PVI were strongly correlated ($r = 0.715$, $P < 0.0001$, Fig. 5). The correlation between ΔPP and ΔPOP remained strong and demonstrated little variation when analyzed across each of the two age groups (0–2 years & 2–10 years, Table 3).

**Table 3** Correlation between hemodynamic indices

| Relationship | r-value | 95% CI for r | *P*-value |
|---|---|---|---|
| PI versus PVI | −0.286 | −0.5732 to 0.0634 | =0.1065 |
| ΔPP versus ΔPOP | 0.8439 | 0.704–0.9205 | <0.0001 |
| ΔPP versus PVI | 0.7049 | 0.4771–0.844 | <0.0001 |
| ΔPOP versus PVI | 0.715 | 0.4926–0.8497 | <0.0001 |
| ΔPP versus ΔPOP (0–2) n = 18 | 0.8687 | 0.6761–0.9502 | <0.0001 |
| ΔPP versus ΔPOP (2–10) n = 15 | 0.7086 | 0.3082–0.8957 | =0.0031 |

*PI* perfusion index, *PVI* plethysmograph variability index, *ΔPP* pulse pressure variation, *ΔPOP* plethysmograph variation, (0–2) age group less than 2 years, (2–10) age group 2–10 years

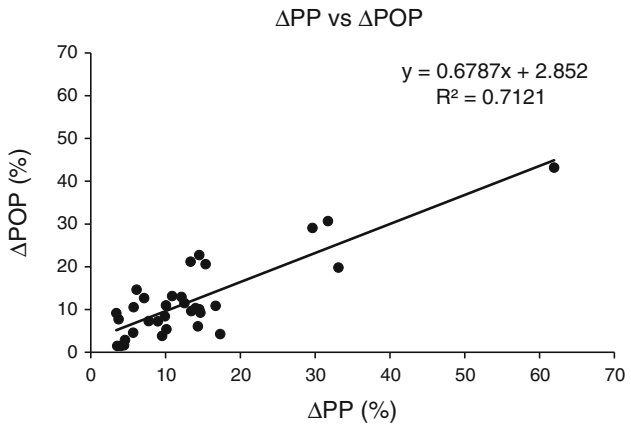


**Fig. 2** Correlation between pulse pressure variation (ΔPP) and plethysmograph variation (ΔPOP)

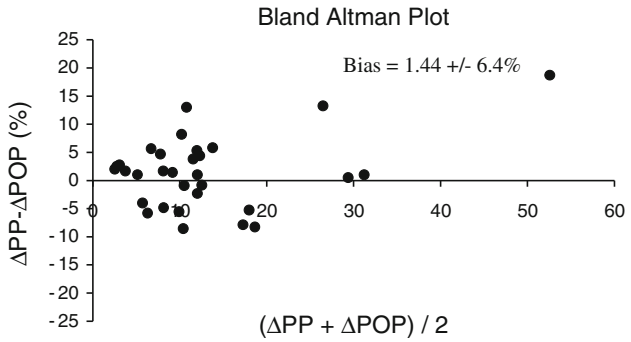


**Fig. 3** Bland-Altman plot of pulse pressure variation (ΔPP) versus plethysmographic variation (ΔPOP)

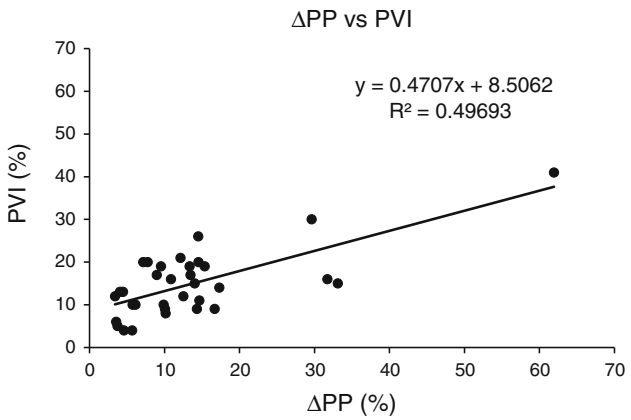


**Fig. 4** Correlation between pulse pressure variability (ΔPP) and plethysmograph variability index (PVI)

## 4 Discussion

This study demonstrates the feasibility of recording and analysing plethysmographic data from children in the OR and PICU. Our data demonstrate a strong correlation

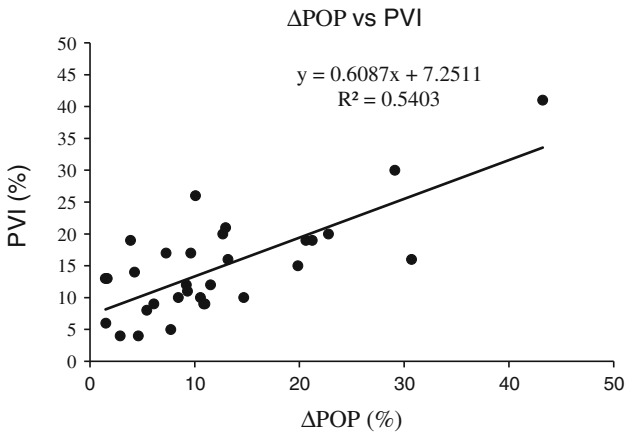


**Fig. 5** Correlation between plethysmograph variation (ΔPOP) and plethysmograph variability index (PVI)

between ΔPP and ΔPOP with close agreement. Strong correlations also exist between PVI and both ΔPP and ΔPOP: these relationships were largely unchanged across the two age groups. Despite encompassing a medically diverse group of mechanically ventilated children, in a variety of physiological states and spanning a considerable range of ages, our exclusion rate for poor plethysmographic waveforms (8%) was similar to some adult studies [13, 25], demonstrating that plethysmograph waveforms in children are as amenable to collection and analysis as in adults.

Dynamic preload indicators are those, which demonstrate the changes induced in left ventricular stroke volume by positive pressure ventilation. These changes are mainly produced by the reduction in venous return and therefore right ventricular stroke volume with each positive pressure breath, and the subsequent transmission of this effect to the left ventricle as decreased preload causing a reduction in left ventricular stroke volume [26]. Adults capable of producing a cardiac output response to volume expansion, i.e., those patients on the steep portion of the starling curve, show a larger variation in stroke volume than those incapable of producing such a response. Methods of quantifying this variation, or downstream manifestations of this effect, including: stroke volume variation, arterial pulse pressure variation, aortic flow velocity variation and plethysmograph variation [5, 6, 17, 27] have been demonstrated in adults to predict VR.

The plethysmograph signal is produced by the changes in light absorbency caused by alterations in blood flow to the finger during each cardiac cycle, as detected by the oximeter probe [28]. This flow is dependant on the vasomotor tone and the stroke volume. External light detected by the probe may also be a source of signal variation. If one assumes that the vasomotor tone remains unchanged during each respiratory cycle and external light is excluded, the variation in amplitude of the plethysmograph waveform is primarily dependant on the variation of the stroke volume [12].

Dynamic indicators of preload have begun to be investigated in children in recent years. Both pressure related and flow related surrogates of stroke volume variation have been studied. Two studies have found that ΔPP does not predict VR in patients in the PICU [8] and in the OR [10]. The same studies did find, and have been supported by two further studies [11, 29], that aortic flow variation (ΔVpeak) is useful to predict VR in children. In contrast to all these previous studies, Renner et al. [30] recently published results from a study that demonstrated that an automated index of pulse pressure variation (PPV) predicts VR in infants with congenital cardiac lesions. The same study did not find any predictive value for stroke volume variation (SVV) as derived from the same arterial pressure waveform. These conflicting results may be due to one or both of: different study populations and different monitor systems. ΔVpeak is a central flow-related index of stroke volume variation and whilst it predicts VR, the cut off values calculated vary widely between studies from 7 to 20%. The pulse oximeter plethysmograph waveform amplitude is also primarily flow related and two studies have examined the ability of its respiratory variations to predict VR in children. Pereira de Souza Neto et al. [10], examined both automated and manually calculated plethysmograph indices, PVI and ΔPOP. Their findings suggest that neither predicted VR in a population of children, between the ages of 5.5 months and 14 years, anaesthetized prior neurosurgical procedures. In contrast, Renner et al. [11] found that in anaesthetized infants about to undergo cardiac surgery with intracardiac shunts, PVI had a significant ability to predict VR.

The results of this study demonstrate significantly closer correlations between the indices of arterial and plethysmograph variation in children than was reported by Pereira de Souza Neto et al. [10], they found correlations between: ΔPOP and PVI ($r = 0.39$), ΔPP and ΔPOP ($r = 0.48$) in comparison to our results: $r = 0.7049$, and $r = 0.8439$ respectively. These differences may be explained by the differences in study populations and is discussed below. Renner et al. did not measure other peripheral measures of respiratory variation to allow comparison. The close association between the respiratory variations in arterial pulse pressure and plethysmograph amplitude found in our study are more in keeping with previous adult studies. Cannesson et al. [12] and Natalini et al. [14] found correlations between ΔPP and ΔPOP of $r = 0.91$ and $r = 0.62$ respectively (in this study $r = 0.8439$). Cannesson et al. [13] in a separate study, calculated a correlation coefficient between ΔPP and PVI of 0.72 (in this study $r = 0.7049$).

The pulse oximeter is a potentially appealing hemodynamic monitor for pediatric patients both in the OR and in

the PICU, as it is almost universally used in these clinical areas. Pediatric patients are also less likely than adult patients to be monitored with an arterial line, due to technical difficulties with placement. The conflicting results reported in Renner et al. [11] and Pereira de Souza Neto et al. [10] may be explained by the presence of intracardiac shunts in all patients in the former study. Pereira de Souza Neto et al. suggest that the reduced arterial compliance in the child when compared to the adult is to blame for the inability of ΔPP, ΔPOP and PVI to predict VR. A possible mechanism by which intracardiac shunts may affect plethysmograph variation may be due to sympathetic up-regulation and a consequently a raised peripheral vascular resistance and a reduced arterial compliance in these children. The different relationships of peripheral indicators of respiratory variation found in this study when compared to Pereira de Souza Neto may be explained by inclusion of children the post-operative period with up-regulated sympathetic systems, altered volume status and, in some cases, receiving vasoactive infusions. Perhaps the correlation values, similar to those found in adults, found in this study population are indicative of a reduced arterial compliance, it may be that in such a population of children that respiratory variations in the pulse oximeter plethysmograph may predict VR.

### 4.1 Study limitations

Being a simple observational study this study cannot assess the ability of plethysmographic indices to predict volume responsiveness. Further studies examining this relationship in children are necessary. The calculation of ΔPOP is done in an artificial fashion i.e., offline and with the gain control turned off. To use this index clinically would require an automated method of calculation, similar to PVI. We chose to compare the plethysmographic indices with ΔPP. This marker has not been shown to predict volume responsiveness in children. The close relationship seen in this study between ΔPP and ΔPOP may be a marker of decreased arterial compliance, however, further study of VR in the intensive care setting would be necessary to examine if this is the case and to assess if this reduction is sufficient to change the ability of plethysmographic indices to predict VR.

## 5 Conclusion

This study demonstrates the feasibility of recording and calculating plethysmographic variability indices in children 10 years of age and younger, with a variety of medical and surgical diagnoses, in the OR and the PICU. These data show a strong correlation between the variations induced by mechanical ventilation in arterial pulse pressure and the pulse oximeter plethysmograph. This study suggests that analysis of the pulse oximeter plethysmograph waveform is worthy of further investigation towards a non-invasive marker of volume responsiveness in sick children.

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**Conflict of Interest** The authors declare that they have no conflict of interest.

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