ORIGINAL RESEARCH

The importance of sensor contacting force for predicting fluid responsiveness in children using respiratory variations in pulse oximetry plethysmographic waveform

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Abstract

Predicting fluid responsiveness is crucial for adequate fluid management. Respiratory variations in pulse oximetry plethysmographic waveform amplitude (ΔPOP) are used to predict fluid responsiveness, but show inconsistent results when used for children. Contacting force between the measurement site and sensor can affect the ΔPOP value, thereby hindering its reliability as an indicator. We studied the influence of contacting force on the efficacy of ΔPOP as a fluid responsiveness indicator in children. In total, 43 mechanically ventilated children aged 1 month–5 years were studied. After anesthetic induction, mechanical ventilation began with a tidal volume of 10 ml/kg. ΔPOP was calculated for five different contacting force groups (0–0.3N, 0.3–0.6N, 0.6–0.9N, 0.9–1.2N, and 1.2–1.5N) and individually adjusted contacting force. Pulse pressure variation (PPV), and ΔVpeak were recorded before and after volume expansion. Subjects were considered as fluid responders if volume expansion increased the stroke volume index (SVI) by > 15%. Data from 38 patients were finally analyzed. A significant difference between the responders and non-responders was found only in ΔPOPs at 0.9–1.2N contacting force ($P = 0.002$) and individually adjusted contacting force ($P < 0.000$), while other contacting force groups did not show significant differences. ΔVpeak predicted a 15% increase in SVI ($P = 0.008$), whereas PPV did not. The ability of ΔPOP to predict fluid responsiveness depends on the contacting force in mechanically ventilated children. When contacting force is controlled to an adequate degree, the ability of ΔPOP to predict fluid responsiveness can be improved.

Keywords Fluid responsiveness · Pulse oximetry plethysmography (POP) · Contacting force · Respiratory variations in pulse oximetry plethysmographic waveform (ΔPOP)

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1 Introduction

Adequate fluid management is essential to maintain optimal cardiac output and tissue perfusion pressure, and can reduce the length of hospital stay and mortality [1–3] in patients undergoing major surgery. Traditionally, the assessment of preload is performed using static parameters such as blood pressure, central venous pressure, pulmonary capillary wedge pressure, or left ventricular end-diastolic volume. However, these parameters have shown limited capability in predicting whether cardiac output will increase after fluid administration [4–7].

On the other hand, heart–lung interaction during positive pressure ventilation induces respiratory variations in stroke volume (SVV), pulse pressure (PPV), aortic blood flow peak velocity (ΔVpeak), or inferior vena cava diameter. These dynamic parameters have been proposed as a predictor for fluid responsiveness in mechanically ventilated patients

[7–10]. However, measurement of these parameters is invasive, requires special systems, and is operator dependent.

Plethysmography is a technique that enables visualization of blood volume changes in the microvascular bed within cardiac cycle. A pulse oximeter is a commercial, non-invasive device for calculating peripheral oxygen saturation and displaying a plethysmogram. The respiratory variations in pulse oximetry plethysmographic waveform amplitude (ΔPOP) are known to be correlated with PPV and to predict fluid responsiveness in mechanically ventilated patients, with a cut-off value of 13–15% [6, 11, 12]. Similarly, the pleth variability index (PVI) (Masimo Corp., Irvine, CA, USA), which is automatically calculated ΔPOP on the basis of the perfusion index (ratio of pulsatile and non-pulsatile component) has been used to guide fluid management [13]. However, the ability of ΔPOP to predict fluid responsiveness in children is controversial [14–16].

The amplitude of the pulse oximetry plethysmographic waveform (POP) can be affected by several factors, including the position or level of the measurement site, sympathetic tone, and age [17–20]. Besides, contacting force between the sensor and measurement sites has been shown to greatly affect the amplitude [21]. Since the calculation of ΔPOP is based on the amplitude of POP, different contacting force conditions causing amplitude changes of POP may lead to different ΔPOP values within an individual. Unfortunately, currently available commercial pulse oximeters are mostly of the finger-wrapping type, and do not provide contacting force, which is highly likely to cause one's ΔPOP to be measured in uncontrolled contacting force conditions. Thus, using ΔPOP obtained with commercial pulse oximeters may lack reliability as a fluid responsiveness indicator.

In the present study, we measured the ΔPOP in controlled contacting force conditions and evaluated the influence of contacting force on the ability of ΔPOP to predict fluid responsiveness in children under general anesthesia. Additionally, we attempted to determine the adequate contacting force condition wherein the reliability of ΔPOP is maximized.

2 Materials and methods

This study was approved by the Institutional Review Board of Seoul National University Hospital (H1609-066-791) and registered at ClinicalTrials.gov (NCT 02952651). Written informed consent was obtained from all parents. Children aged between 1 month and 5 years who were scheduled for congenital cardiac surgery or neurosurgery and expected to undergo large fluid shifting were enrolled. Patients with a single ventricle, right heart failure, pulmonary hypertension, any hepatic, renal or pulmonary disease, any cardiac arrhythmia or valvular heart disease, or signs of increased intracranial pressure were excluded.

2.1 Anesthetic protocol

Induction of general anesthesia was performed using 0.02 mg/kg atropine and 5 mg/kg thiopental sodium. Rocuronium (0.6 mg/kg) and (if required) fentanyl (5–10 μg/kg) were used for endotracheal intubation. Mechanical ventilation was controlled to obtain a $PaCO_2$ of 35–40 mmHg, using the volume-controlled mode to maintain a constant tidal volume of 10 mL/kg during surgery.

After induction of anesthesia, a peripheral arterial catheter (Angiocath™, Becton Dickinson, NJ, USA) was placed in the right or left radial artery. A central venous catheter (Arrow Gard Blue, Arrow International Inc., PA, USA) was inserted into the right internal jugular vein under ultrasound guidance. Pressure transducers (Auto Transducer, Ace medical, Korea) were placed on the mid-axillary line and maintained at the atrial level during the study protocol. Anesthetic maintenance was performed at the discretion of the attending anesthesiologist, using inhalational or intravenous anesthetic agents. The anesthetic depth was adjusted to maintain a Bispectral Index value between 40 and 60.

2.2 Experimental protocol and test apparatus

The experiment was performed after the patients were successfully weaned from cardiopulmonary bypass and the sternum was closed during cardiac surgery, or any time when suspicious hypovolemia existed and no active bleeding was seen during neurosurgery. Before the experiment, the anesthesiologists confirmed that there was no residual anatomical defect or abnormality using transthoracic echocardiography (TEE, Philips iE33 system, Philips Healthcare, Andover, MA, USA) in patients undergoing cardiac surgery.

Baseline hemodynamic data including arterial blood pressure (ABP) and central venous pressure (CVP), collected from the patient monitor (Solar™ 8000 patient monitor, GE healthcare, IL, USA), were transferred to a personal computer using data acquisition software (Vital Recorder, VitalDB, Korea). Pulse pressure variation (PPV) was calculated using the following formula: PPV $(\%) = 200 \times (PP_{max} - PP_{min})/(PP_{max} + PP_{min})$ in one respiratory cycle (PP_{max} and PP_{min}; maximum and minimum systolic pressure). The mean value of three consecutive respiratory cycles was used for analysis. Some patients received varying degrees of inotropic support, the vasoactive–inotropic score during the experiment was calculated as follows: dopamine dose (μg/kg/min) + dobutamine dose (μg/kg/min) + (epinephrine dose × 100 [μg/kg/min]) + (milrinone dose × 100 [μg/kg/min]) + (vasopressin dose × 10,000 [U/kg/min]) + (norepinephrine dose × 100 [μg/kg/min]) [22].

In order to obtain POP with a controlled contacting force, we acquired a photoplethysmogram (PPG) with an in-house developed clip-type PPG sensor integrated with a force sensor, because POP from a commercial device provides a highly filtered or auto-gained signal, which hinders analysis of amplitude changes in the POP [12], and the contacting force information is neither measured nor provided. A pair of light-emitting diodes (LEDs) (SM1206NHC, Bivar Inc., USA) and a silicon photodiode (SFH2430, OSRAM, Germany) were used to measure PPG in reflectance mode. The LED is red in color with a peak wavelength of 625 mm and driven by a continuous current of 20 mA. A force-sensing resistor was used (FSR 408, Interlink Electronics, USA), and placed beneath the optical sensor to measure the contacting force between the optical sensor and measurement site. A force-sensing resistor is a robust thick film-type polymer (PTF) device that exhibits changes in resistance when force is applied to the active area of the sensor. The relation between force and resistance was verified using loads with known weights to guarantee measurement accuracy prior to the study. The varying resistance of the force sensor was calculated by measuring the sensor's output voltage using a simple voltage divider and converted into a force scale. An elastomer was placed on the force sensor so that the force was evenly distributed on the active area of the sensor. The contacting force was controlled by compressing the clip-type housing and maintained using a saw tooth-shaped holder (Fig. 1).

PPG was obtained for 20 respiratory cycles at five contacting force ranges as follows: 0–0.3N, 0.3–0.6N, 0.6–0.9N, 0.9–1.2N, and 1.2–1.5N in these sequence. ΔPOP was calculated from the raw PPG waveform using the following formula: ΔPOP (%) = 200 $\times$ (AMP$_{max}$ − AMP$_{min}$)/(AMP$_{max}$ + AMP$_{min}$) in one respiratory cycle (AMP$_{max}$ and AMP$_{min}$; maximum and minimum amplitude of PPG). The mean of ΔPOP values from three consecutive respiratory cycles was calculated, after which mean ΔPOPs from all sets of three consecutive cycles were averaged again for statistical analysis. After obtaining PPG, 10 mL/kg Volulyte® (6% hydroxyethyl starch 130/0.4) was administered for 20 min.

Following volume administration, hemodynamic and echocardiographic measurements were repeated.

2.3 Echocardiographic measurement

All echocardiographic data were measured by a single expert using TEE or transthoracic echocardiography (TTE) before and after fluid loading.

2.3.1 Stroke volume (SV), stoke volume index (SVI), cardiac output and cardiac index

The aortic annulus diameter (D) was measured during the systolic phase in the mid-esophageal aortic valve long axis view or the parasternal long axis view using TTE. The aortic blood flow waveform at the level of the aortic annulus was obtained using pulsed-wave Doppler in the deep-transgastric long-axis view using TEE or the apical five chamber view using TTE. The mean velocity time integral (VTI) was calculated from three consecutive waves at the end of the expiratory period.

Variables were calculated as follows:

$$SV = VTI \times 3.14 \, (D/2)^2$$

$$\text{Stoke volume index (SVI)} = SV/\text{body surface area}$$

$$\text{Cardiac output} = SV \times \text{heart rate}$$

$$\text{Cardiac index} = \text{Cardiac output/body surface area}$$

2.3.2 ΔVpeak

The maximum and minimum Vpeak during one respiratory cycle were measured at the aortic valve level in the same view for VTI. ΔVpeak was calculated as follows: ΔVpeak (%) = 200 $\times$ (Vpeak$_{max}$ − Vpeak$_{min}$)/(Vpeak$_{max}$ + Vpeak$_{min}$). The mean ΔVpeak was calculated using three consecutive respiratory cycles.

Fig. 1 A developed clip-type PPG sensor integrated with a force sensor and layout of its compartments
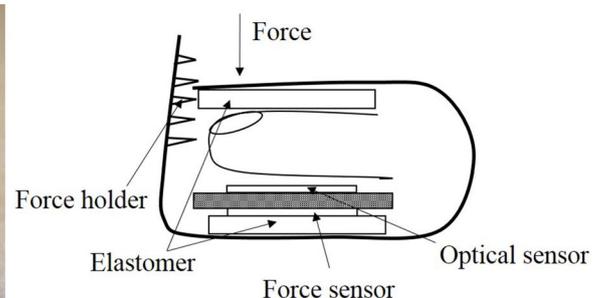
2.4 Statistical analysis

The purpose of this study was to investigate whether the predictive ability of ΔPOP changes according to the change in the contacting force and to find the adequate contacting force for utilizing ΔPOP to guide fluid management in children under general anesthesia. For this, we planned to calculate the area under the receiver operating characteristic (ROC) curve (AUC) of ΔPOP for discriminating fluid responders from non-responders at each level of contact force and to compare the AUCs among different contacting force groups. Furthermore, since ΔPOP is calculated based on the respiratory variation in POP amplitude, a greater POP amplitude may provide better reliability for calculating the ΔPOP. Therefore, we determined an adequate contacting force at which the POP amplitude was maximized for each subject among five different contacting force levels and evaluated the AUC of the ΔPOP at this individually adjusted contacting force.

According to a previous study performed in children, when the ratio between fluid responders and non-responders was approximately 1:1, the AUC for PVI was 0.767 [16]. Therefore, we postulated that the ΔPOP at a certain contacting force would predict fluid responsiveness with an AUC range of 0.7–0.85 and a precision of 0.15 [23]. The ratio of fluid responders and non-responders was set as 1:1. Then, the required sample size was between 38 and 55, depending on the AUC with an estimated attrition rate of 10%. Therefore, 43 patients were finally enrolled in this study.

We divided the patients into two groups following the fluid challenge: the "fluid responder group", comprising patients in whom fluid administration increased the stroke volume index (SVI) by more than 15%, and the "non-responder group", comprising the remaining patients, as described in previous studies [6, 10, 14].

Statistical analyses were performed using SPSS (ver. 22; SPSS, Chicago, IL, USA), MedCalc (ver. 12.7.7;

MedCalc, Ostend, Belgium) software and MATLAB 2014 (The Mathworks, Natick, MA, USA). Student's t-test or the Mann–Whitney U-test was used to evaluate the differences between the responders and non-responders. Paired t-test was used to evaluate the differences in parameters between before and after fluid loading. To determine the ability of ΔPOP to predict fluid responsiveness, an ROC curve was generated for each contact force level. AUCs at different contacting force groups were calculated and compared. A value of $P < 0.05$ was considered to indicate statistical significance. For the contact force level, which shows significant difference between responder group and non-responder group, a threshold value of ΔPOP was determined using Youden's index (J = sensitivity + specificity − 1). In addition, two cutoff values of ΔPOP to represent a gray zone which describes the region providing non-conclusive information were calculated. To acquire two values of ΔPOP for the gray zone, two approaches were used, as described in an earlier study by Cannesson [24]. As first approach, a single threshold was calculated for each bootstrapped population, resulting in a set of 1000 values. Then, the 95% CI of the mean of resulting values was estimated and determined as a gray region. As second approach, a gray zone was defined as ΔPOP values with a sensitivity lower than 90% or specificity lower than 90%. The largest interval between two approaches was defined as the gray zone.

3 Results

This study enrolled a total of 43 patients; 5 were excluded due to limited echocardiographic measurement. Therefore, 38 pediatric patients who had undergone simple cardiac surgery including atrial or ventricular septal defect repair, and neurosurgery were included. Table 1 shows the baseline characteristics of all enrolled patients. There were 20 volume responders and 18 non-responders, and no

Table 1 Baseline characteristics of patients and intraoperative variables

Values	Responder ($n = 20$)	Non-responder ($n = 18$)
Age (years)	3.2 (1.7; range 0.3–5)	3.1 (1.7; range 0.2–5)
ASA physical status (I/II/III/IV/V)	18/2/0/0	17/1/0/0
Height (cm)	95.2 (16.6)	96.8 (17.5)
Weight (kg)	15.9 (6.6)	15.3 (5.1)
Sex (male/female)	8/12	11/7
Operations		
Cardiac surgery	9	8
Neurosurgery	11	10
Body temperature (°C)	36.1 (0.8)	36.2 (0.9)
Vasoactive–inotropic score	3.1 (3.7)	4.0 (4.2)

Values are presented as mean (standard deviation) or number

ASA American society of anesthesiologists

significant between-group difference was observed in clinical characteristics.

Before volume expansion, the responder group showed a significant lower cardiac index, SVI, and ΔVpeak than the non-responder group ($P = 0.03$, 0.008, and 0.015, respectively). Volume expansion reduced heart rate and increased central venous pressure in both groups, while the cardiac index, SVI, and ΔVpeak were significantly changed in only the responder group (all $P < 0.001$) (Table 2). No significant complications such as pulmonary edema or cardiac dysfunction associated with volume expansion were observed in both groups.

The AUC values predicting an increase in SVI ($> 15\%$) for heart rate, central venous pressure, PPV, and ΔVpeak were 0.512 [95% confidence interval (CI) 0.345–0.678], 0.506 (95% CI 0.301–0.710), 0.621 (95% CI 0.433–0.786) and 0.726 (95% CI 0.557–0.858), respectively.

Table 3 shows ΔPOP values for fluid responders and non-responders at each contacting force level. For some subjects, specific force levels could not be measured, resulting in different number of subjects for each contacting force level. Significant difference was found in ΔPOP between the responders and non-responders at 0.9–1.2N contacting force ($P = 0.002$), while ΔPOP in the other

Table 2 Hemodynamic variables before and after volume expansion

Variable	Responder ($n = 20$)		Non-responder ($n = 18$)	
	Before VE	After VE	Before VE	After VE
Heart rate (beats/min)	116.9 (4.4)	112.3 (17.8)*	115.9 (21.9)	105.3 (25.8)*
Systolic arterial pressure (mmHg)	95.3 (13.2)	98.0 (17.8)*	93.0 (15.7)	97.9 (15.6)
Diastolic arterial pressure (mmHg)	47.5 (7.7)	53.7 (7.0)*	52.6 (9.9)	55.1 (11.3)
Mean arterial pressure (mmHg)	62.8 (9.9)	70.3 (10.6)*	67.2 (11.9)	69.7 (13.6)
Central venous pressure (mmHg)	7.0 (2.7)	9.0 (2.4)*	6.9 (3.2)	8.9 (3.0)*
Peak airway pressure (cm H_2O)	15.7 (2.9)	16.2 (3.5)	14.3 (1.3)	14.8 (1.7)
Cardiac index (L/min/m^2)†	2.5 (0.6)	3.2 (0.9)*	3.2 (1.3)	3.1 (1.5)
SVI (mL/m^2)†	22.4 (5.7)	28.8 (7.4)*	27.7 (11.2)	29.2 (11.10)
Pulse pressure variation (%)	15.3 (5.1)	14.7 (5.7)	15.0 (6.6)	13.2 (4.6)
ΔVpeak (%)†	14.7 (3.6)	9.5 (4.3)*	11.3 (3.4)	9.8 (4.0)

Variables are expressed as mean (SD)

VE volume expansion

*$P < 0.05$ before VE versus after VE

†$P < 0.05$ between responders and non-responders before VE

Table 3 The ΔPOP values of fluid responders and non-responders at different contacting force levels

Contacting force	ΔPOP of responders	ΔPOP of non-responders	P value*	AUC (95% CI)
0–0.3N	14.9 (13.2–22.8) (n = 11)	11.0 (7.5–13.9) (n = 7)	0.151	0.714 (0.451–0.978)
0.3–0.6N	16.5 (12.9–26.1) (n = 15)	10.6 (9.1–15.1) (n = 11)	0.121	0.685 (0.465–0.904)
0.6–0.9N	14.7 (11.7–24.3) (n = 16)	10.4 (8.3–15.6) (n = 17)	0.094	0.673 (0.486–0.860)
0.9–1.2N	21.7 (13.5–35.3) (n = 18)	11.0 (7.7–15.1) (n = 18)	0.001	0.815 (0.674–0.956)‡
1.2–1.5N	23.4 (16.5–24.4) (n = 6)	9.4 (7.5–30.6) (n = 9)	0.328	0.667 (0.373–0.960)
Individually adjusted†	14.8 (11.6–18.5) (n = 19)	8.4 (6.1–9.8) (n = 19)	0.000	0.847 (0.716–0.978)‡

Data were presented as median (interquartile ranges)

POP pulse oximetry plethysmography

*P value from comparison between responders and non-responders using Mann–Whitney U test
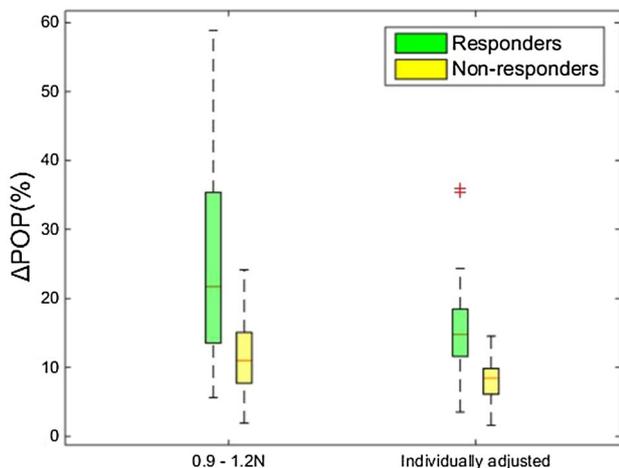
†Individually adjusted contacting force was defined as the contacting force where the maximal POP amplitude was derived in each patient
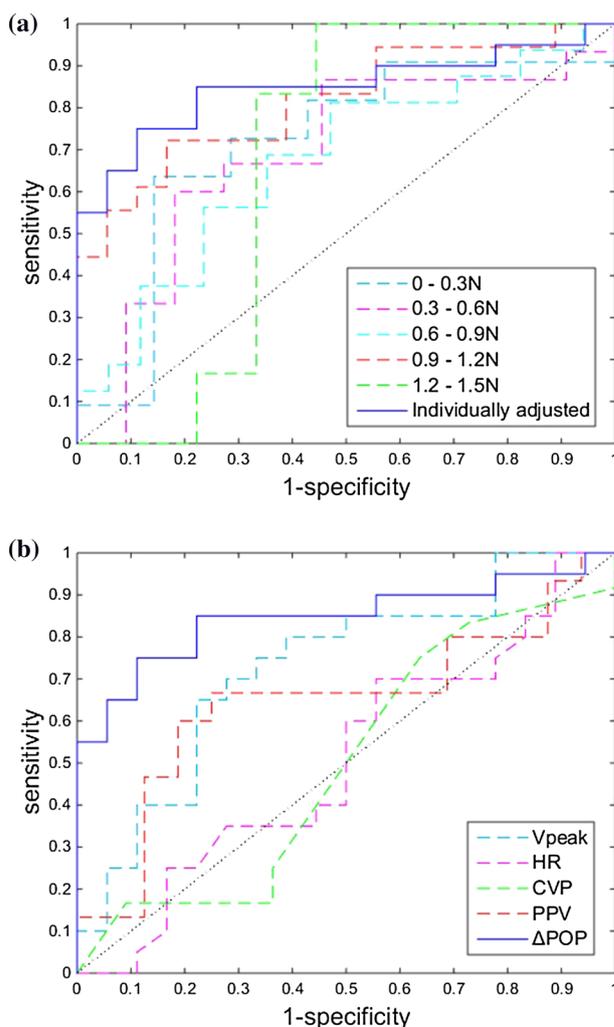
‡$P < 0.05$ for ROC curve analysis

contacting force groups did not show significant differences between the responder and non-responder group.

The mean and standard deviation of individually adjusted contacting forces that produce maximum amplitude of POP was 0.9 ± 0.3 N. When ΔPOP was used at the individually adjusted contacting force, the responder group were more clearly discriminated against the non-responder group than when using ΔPOP at the same contacting force for all subjects (Fig. 2). According to the ROC curve analysis, the AUCs of ΔPOP at the contacting force of 0.9–1.2N and individually adjusted contacting force were 0.815 (95% CI 0.674–0.956; $P = 0.001$) and 0.847 (95% CI 0.716–0.978; $P < 0.001$), respectively (Fig. 3a; Table 3). For the contacting force group of 0.9–1.2N, a single threshold predicting a 15% increase in SVI was determined as 15% of ΔPOP value, and the gray zone spreading from 9.1 to 24.2% of ΔPOP value was calculated considering two aforementioned approaches. A threshold for the individually adjusted contacting force group was 11% of ΔPOP value, and the gray zone of this group spread from 8.9 to 14.5%.

When hemodynamic and respiratory variables were compared in terms of AUC, ΔPOP at both individually adjusted contacting force and 0.9–1.2N range was better than any other variables including ΔVpeak in discriminating the responder from the non-responder group (Fig. 3b).

Fig. 3 Comparison of the predictive ability of ΔPOP at the individually adjusted contacting force **a** with ΔPOP at the five contacting force levels, and **b** with other hemodynamic and respiratory variables using areas under receiver operating characteristic curves

4 Discussion

In this study, we found that the ability to predict fluid responsiveness of ΔPOP was affected by the contacting force between the sensor and measurement site; among five contacting force levels, the fluid responsiveness was predicted with statistical significance only for 0.9–1.2N. In addition, we found that the ΔPOP at the individually adjusted contacting force level that produced the maximal POP amplitude showed the best ability in fluid responsiveness prediction in children under mechanical ventilation.

The ΔPOP are suggested as a promising dynamic indicator of fluid responsiveness as it is easily accessible in clinical situations and is non-invasive, compared to PPV and ΔVpeak, both of which are invasive or not easily available [6, 11]. Despite its advantages, several previous studies using

Fig. 2 Box plots of the ΔPOP values for fluid responders and non-responders at the contacting force of 0.9–1.2N and the individually adjusted contacting force. Significant difference between the responders and non-responders was found in both groups. When contacting force was individually adjusted, the responder group were more clearly discriminated against the non-responder group than when using ΔPOP at the same contacting force for all subjects. Cross symbol represents extreme values

plethysmography have shown conflicting results regarding the ability of ΔPOP to predict the preload status during surgery in mechanically ventilated children [14–16]. Pereira de Souza Neto et al. [14] found that neither ΔPOP nor PVI could predict a response to volume expansion in children undergoing neurosurgery. However, Renner et al. [15] and Byon et al. [16] reported that PVI is a useful parameter to predict fluid responsiveness in children undergoing neurosurgery and cardiac surgery. On the contrary, we observed both positive and negative ability of ΔPOP in discriminating the responder from non-responder group depending on the contacting force which is inevitably exerted between the finger and the sensor. According to our results, ΔPOP is only reliable and becomes a valid indicator when contacting force is controlled, which is possibly the reason why other previous studies have shown the negative ability of ΔPOP as a fluid responsiveness predicting indicator.

In the present study, we showed that ΔPOP at the contacting force individually adjusted to produce maximized POP amplitude has best ability to predict fluid responsiveness, suggesting that POP amplitude modulated by contacting force substantially affects the ability of ΔPOP for predicting fluid responsiveness. Variations in POP are created by blood volume changes in arterial and venous vessels under the measurement site. The blood volume changes in vessels are largely affected by the vessel compliance, which changes with the external contacting force [25]. At the high vessel compliance created by manipulation of the external force, small vessel variations such as the respiratory variation can be intensified and reflected to a greater degree in the POP amplitude, which may explain the effect of contacting force on the predictive ability of ΔPOP. Our result can be considered to be in accord with the earlier study by Broch et al. [26] who reported that the accuracy of PVI was improved in a high perfusion index (> 4%), and argued that the PVI has to be used with caution depending on the perfusion index because a greater POP amplitude produced by adequate contacting force corresponds to increased perfusion index.

ΔPOP at the 0.9–1.2N of contacting force also could predict fluid responsiveness. Considering the mean of individually adjusted contacting forces was 0.9N, 0.9–1.2N of controlled contacting force may have also induced high vessel compliance for many subjects, causing ΔPOP to be able to predict fluid responsiveness unlike ΔPOP at other contacting force groups. But, possibly due to high standard deviation of contacting forces that produced maximized POP for an individual, ΔPOP at the individually adjusted condition showed better ability of predicting fluid responsiveness than ΔPOP at the 0.9–1.2N of contacting force.

Along with ΔPOP, PPV has been suggested as a predictor for increase in cardiac output after volume expansion in adults [6, 27]. However in children group, ΔVpeak is shown to be a superior predictive parameter with cut-off values

ranging from 7 to 20% compared to PPV [14–16, 28]. In agreement with the previous studies, ΔVpeak could predict fluid responsiveness in the present study with a cut-off value of 11.3%, while PPV could not. The ability of ΔVpeak as an indicator may be explained by the fact that the ΔVpeak was measured at the aortic valve level, at which the blood flow passes a relatively larger area and the diameter was unchanged. Due to this, the velocity might be correlated directly to the amount of stroke volume.

The study has several limitations that need to be mentioned. First, we did not measure the perfusion index, which had to be maintained at a stable level while obtaining the POP signal. However, since the duration of data acquisition was short and with no acute bleeding, significant changes in hemodynamics and anesthetic depth were not observed during measurement of POP. Second, as a wide range of age of subjects were involved in the study, finger dimension of the subjects greatly varied. As a result, for some subjects, specific force levels could not be measured due to limitation of hardware structure, which resulted in different number of subjects for each contacting force level. Particularly, for extreme force levels (0–0.3N, and 1.2–1.5N), data from less than half the subject population was acquired, which lowers statistical power for these groups. However, assuming the contacting area between the sensor and fingertip as a circular area with 5 mm of radius, median pressure of each group is approximately converted to 14, 128 mmHg for 0–0.3N, 1.2–1.5N group, respectively, which is hardly the case in clinical practice with a finger-wrapping type sensor. In addition, considering the purpose of the study, demonstration of differences of the predictive ability of ΔPOP between contacting force conditions, we think the lack of data in extreme force levels does not degrade the overall result of the study. Third, it can be viewed impractical in clinical situations to measure the contacting force and to find out the adequate contacting force for the maximum amplitude of POP prior to volume expansion. However, if the adequate contacting force is automatically set within a short period of time using an automatic feedback system consisting of a pulse oximeter sensor and a contacting force controller, more reliable prediction with ΔPOP can be achieved in a practical way. This needs to be dealt with in a future study. Fourth, the force sensor we employed in this study does not exhibit highly accurate measurement. It is also reported to entail possible hysteresis and drift over time, which might affect the accuracy of the force measurement. However, as we classified contacting force into five different levels and compared predictive ability of ΔPOP among force levels, the result of the study is not likely to be affected by accuracy of the sensor. And finally, as we measured the force, not the pressure which is the force per area, the contacting force range of 0.9–1.2N obtained in this study may not be applicable to older children or adolescents who have larger fingers. However, if ΔPOP is

measured at individually adjusted contacting force, even in other subject groups, ΔPOP can be utilized for prediction of preload status, and better hemodynamic management.

In conclusion, the present study demonstrates that the ability of ΔPOP to predict fluid responsiveness depends on the contacting force exerted between the sensor and measurement site in mechanically ventilated children. In the condition where the contacting force is controlled to maximize the POP amplitude, ΔPOP becomes a valid and reliable indicator to predict fluid responsiveness. Furthermore, if the contacting force is adjusted individually to produce the maximum amplitude of POP, the ability of ΔPOP to predict fluid responsiveness can be improved.

Compliance with ethical standards

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

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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