Comparison of pulse pressure variation and pleth variability index in the prone position in pediatric patients under 2 years old

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* Running title : PPV vs PVI in prone under 2 years old

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Abstract

Background: The assessment of intravascular volume status is very important especially in children during anesthesia. Pulse pressure variation (PPV) and Pleth variability index (PVI) are well known parameters for assessing intravascular volume status and fluid responsiveness. We examined whether there are correlation between PPV and PVI for children under two years old who underwent surgery in the prone position.

Methods: A total of 27 children were enrolled. We measured PPV and PVI at the same limb during surgery before and after changing patients’ position from supine to prone. We then compared PPV and PVI at each period for any correlation.

Results: The bias between PPV and PVI was -2.2% with a 95% confidence interval of -18.8% to 14.5%. Both PPV and PVI showed no significant difference before and after the position change.

Conclusions: The correlation between PVI and PPV was small for children undergoing surgery with position change to prone. Further studies regarding PVI and PPV are needed under measurement of fluid responsiveness and estimation of cardiac output for the population under two years old.
1. Introduction

Respiration-induced arterial pressure variation (RIAPV), which has been shown to be superior to traditional parameters for assessing intravascular volume status, refers to the variation in arterial pressure that occurs during positive-pressure mechanical ventilation and is regarded as an indicator of “fluid responsiveness” [1]. Different parameters have been developed to quantify the RIAPV, represented by pulse pressure variation (PPV) or systolic pressure variation (SPV). Recently, pleth variability index (PVI) has been developed commercially for non-invasive monitoring of plethysmographic variation. Several researches were performed to determine whether PVI is a useful tool for assessing hemodynamics, but the results remain controversial [2-5].

Prior studies evaluating the value of PPV or plethysmographic indices such as PVI to predict fluid responsiveness have been predominantly performed in adult patients undergoing major thoracic or abdominal surgery or under intensive care with a pulmonary artery catheter [6,7]. Some of these studies have indicated that plethysmographic indices are useful for assessing fluid responsiveness [6,8,9]. This is appealing as it allows continuous measurement of fluid responsiveness without invasive methods such as arterial pressure-derived indices.

Two recent studies have examined various parameters for predicting fluid responsiveness in pediatric patients, using aortic blood flow velocity time integral as a gold standard for identifying volume responders. One of these [10] presented only $\Delta V_{\text{peak}}$ (respiratory variation in aortic blood flow velocity) as a predictor of fluid responsiveness, whereas the other [4] showed that both PVI and $\Delta V_{\text{peak}}$ were effective in identifying fluid responders and non-responders, with a recommended cut-off value of 11% for PVI. PPV did not prove to be a predictor of fluid responsiveness, probably because of differences in arterial compliance between adults and children [10,11].

Position change during surgery is believed to be a major factor that can affect hemodynamic stability [12,13]; hence, more thorough monitoring is mandatory. In addition, many studies have
reported that the position of patients can affect the hemodynamics and the data yielded by various monitors [14-16]. However, it is very difficult to make echocardiographic evaluation for patients undergoing surgery in prone position, therefore making $\Delta V_{\text{peak}}$ unobtainable. In this case, anesthesiologists can refer to PVI or PPV as an alternative to $\Delta V_{\text{peak}}$, though not satisfactory. For adult patients, Biais and his colleagues [17] reported that PPV can predict fluid responsiveness in prone position with cut-off value of 15%.

In this study, we evaluated the relationship between PVI and PPV in the supine and prone positions in young children under two years old to evaluate whether there are correlation between those two parameters.
2. Materials and Methods

2.1. Study population

The study was approved by the Institutional Review Board (H-1501-075-641) and registered at http://cris.nih.go.kr (KCT0001613). After obtaining informed consent from the parents or legal guardians, pediatric patients under 2 years old who underwent neurosurgery in the prone position under general anesthesia and invasive blood pressure monitoring were enrolled. The exclusion criteria were a history or presence of peripheral vascular disease, disorders of the cardiovascular or central nervous system, or other conditions deemed inappropriate to the study.

2.2. Study protocol

On the day of surgery, the patients arrived in the operating theater after appropriate fasting and without premedication. Monitoring of lead II of a three-lead electrocardiogram, noninvasive blood pressure at 1 min intervals, peripheral pulse oximetry (SpO₂), end-tidal carbon dioxide and body temperature was applied to patients using a patient monitor (Solar 8000, GE Medical, Milwaukee, WI, USA). Anesthesia was induced in children with intravenous (IV) injection of 5–6 mg/kg of sodium thiopental and 0.6 mg/kg of rocuronium after loss of consciousness. We maintained anesthesia with 100–200 mcg/kg/min of propofol and 0.1–0.5 mcg/kg/min of remifentanil. Arterial cannulation was performed for invasive blood pressure monitoring using a 24-gauge JELCO® IV catheter (Smiths Medical, Dublin, OH, USA). PVI monitoring was started using Masimo rainbow SET® (Masimo, Irvine, CA, USA). PVI and SpO₂ were monitored at the same limb with arterial cannulation. After confirming that the vital signs had stabilized, the patient monitoring data were transmitted to a personal computer using an analog-to-digital converter (DA 149, DATAQ Instruments, Akron, OH, USA) for 1 min without stimulating the patient. After the change in position of the patient to prone, the data were then obtained in the same way after the vital signs had stabilized. During data
transmission, we adjusted the anesthetic depth to maintain the bispectral index between 40 and 60. No specific change to rate of fluid or anesthetics administration were made throughout the periods. The mode of mechanical ventilation was maintained as volume-controlled ventilation with tidal volume of 8-10mL/kg and positive end-expiratory pressure (PEEP) of 0-5 cmH₂O according to clinical need. Both tidal volume and PEEP were kept stationary before and after position change.

2.3. Calculation of parameters

PP is the difference between systolic pressure (SP) and diastolic pressure (DP); that is,

\[ PP = SP - DP \]

PPV is defined as the difference between the maximum and minimum PP over a single respiratory cycle. It is calculated as follows:

\[ PPV = \frac{[PP_{max} - PP_{min}]/PP_{mean}}{PP_{mean}} \times 100\% \]

Perfusion index (PI) is the ratio of the pulsatile signal to non-pulsatile signal obtained from the pulse plethysmograph. It is calculated as follows:

\[ PI = \frac{AC}{DC} \times 100 \]

where AC indicates a variable amount of light absorbed by the pulsatile arterial flow and DC is a constant amount of light from the pulse oximeter. To reflect respiratory variations in PI, PVI is calculated as follows:

\[ PVI = 100 \times \frac{PI_{max} - PI_{min}}{PI_{max}} \]

2.4. Data analysis

PPV data based on arterial blood pressure were obtained for 1 minute at 10-s interval after induction of anesthesia with supine position (period 1) and 1 minute after the change in position to prone (period 2). PPV was calculated for each period automatically, using a computer software (Vital
recorder, VitalDB team, Seoul National University College of Medicine, Seoul, Republic of Korea) [18] that automatically records patients’ vital sign and provides calculation of parameters. Calculations were made for six explicit sub-period of 10 seconds without overlap. PPV values were averaged for each period before being regarded as final. PVI data were recorded at the end of each period.

2. 5. Sample size calculation

In the pilot study, the mean of difference was 32.6% with standard deviation of 30.4% with upper limit of 195.8 and lower limit of -130.7. With these data, and $\alpha=0.05$, $\beta=0.2$, the required sample size was 6 pairs. The required size being considerably small, we enrolled patients based on previous similar study [3].

2. 6. Statistical analysis

After excluding the effect of artifacts, mean values of PPV were calculated for each period. To identify artifacts, fast-flush test [19] was performed to identify and remove cases with overdamped arterial waveform. As there are some limited evidence that PVI can predict fluid responsiveness, we regarded PVI as gold standard, since there were no better alternatives. PPV and PVI were compared using Bland–Altman plot and the correlation coefficient between PPV and PVI was calculated.

Each parameter before and after the change in position from supine to prone (periods 1 and 2) was compared using paired $t$-test. Statistical analyses were performed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA) and MedCalc® version 17.2 (MedCalc Software, Ostend, Belgium). P–values of <0.05 were considered statistically significant.
3. Results

A total of 34 patients were screened, and 31 patients completed the study; 27 datasets were collected, with four cases discarded because of incomplete data. Demographic data are shown in Table 1.

In supine position, the correlation coefficient between PPV and PVI was 0.130 with p-value of 0.518. The bias between PPV and PVI was -2.0%, with 95% limits of agreement of -15.5% to 11.5%. In prone position, the correlation coefficient between PPV and PVI was -0.371 with p-value of 0.062. The bias between PPV and PVI was -2.3%, with 95% limits of agreement of -21.9% to 17.3%. Altogether, the correlation coefficient between PPV and PVI was -0.131 with p-value of 0.350. The bias between PPV and PVI was -2.2%, with 95% limits of agreement of -18.8% to 14.5% (Figure 1). With paired t-test, both PPV and PVI showed no statistically significant difference before and after the position change from supine to prone (P = 0.245, 0.535, respectively). There was no statistically significant difference in PEEP and peak inspiratory pressure before and after the change in position to prone (P = 0.064, 0.162, respectively). Heart rate showed statistically significant difference following the position change, while mean blood pressure did not (P = 0.000, 0.879, respectively) (Table 2).
4. Discussions

The correlation between PPV and PVI was insignificant in each position or altogether, so that one cannot replace the other. The bias seems acceptable, but the range of 95% limits of agreement in the supine and prone position is unacceptably high in each position or altogether.

A previous study [3] on children undergoing spinal fusion showed similar findings with the present study and reported that PVI is not a surrogate for PPV, and that PVI measurements were not affected by the change in position from supine to prone, therefore may be useful in patients undergoing spine surgery. We obtained similar results with younger population.

As the difference in PPV following position change is not statistically significant, we can infer that increased intrathoracic pressure in the prone position does not substantially affect PPV in young children. Further, RIAPV does not seem to increase much in this circumstance [20].

This study has several limitations. First, automatic recording of PPV carries a risk of artifacts at any time, especially immediately after the position change. Although we attempted to exclude the effect of these artifacts as mentioned in the methods section, we admit that our efforts could be imperfect and subjective. On the contrary, PVI was recorded manually only once at the end of each period. Like PPV, it would have been better if we recorded PVI for multiple times for each period.

Second, light absorption can be affected by many factors such as site of measurement, structure of peripheral vasculature and degree of peripheral vasoconstriction. The site for PVI measurement is diverse in small children. For example, PVI can be measured at the digits in some large children, whereas it can be measured at the palm in some smaller infants. This can lower the reliability of PVI in small children. A recent study showed that PVI measurements in neonates are poorly reproducible, even within a single limb [21].
Third, we could not assess fluid responsiveness in children in this study owing to the position of the patients. To assess fluid responsiveness, we need some additional means of measurement to directly or indirectly estimate the cardiac output. In a previous study from our institution, transthoracic echocardiography was used to indirectly assess volume status and thus fluid responsiveness [4], which is impossible in patients in the prone position. Otherwise, we should have used arterial pressure waveform analysis [22] or pulmonary artery catheterization for the real-time measurement of cardiac output, which are both unsuitable in children under 2 years old. If the measurement of fluid responsiveness was possible, we would have divided the children into responder and non-responder groups. We might also be able to evaluate the correctness of PPV and PVI measurements with a gold standard.

Finally, we did not strictly control ventilatory profile for each patient. Dynamic parameters such as PPV and PVI can be affected by intrathoracic pressure, especially during positive-pressure ventilation. Although our study mainly focused on comparison of PPV and PVI at the same time, it would have been better if we controlled the tidal volume and PEEP and evaluate effect of ventilatory profile by subgroup analysis.

In conclusion, the results of our study suggest that there is little correspondence between PVI and PPV for children under two years of age undergoing position change from supine to prone. Neither PPV nor PVI showed significant change following position change from supine to prone. Further study comparing PPV and PVI with respect to fluid responsiveness via adequate cardiac output estimation is encouraged to improve our strategy for fluid administration management in young children under two years of age.
References


8. Yang SY, Shim JK, Song Y, Seo SJ, Kwak YL. Validation of pulse pressure variation and corrected flow time as predictors of fluid responsiveness in patients in the prone position. Br


Table 1. Demographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>mean ± SD</th>
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<tbody>
<tr>
<td>Age (mo)</td>
<td>7.2 ± 4.7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>70.0 ± 6.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>8.6 ± 1.6</td>
</tr>
<tr>
<td>Anesthesia time (min)</td>
<td>271.2 ± 115.4</td>
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<tr>
<td>M:F</td>
<td>17:10</td>
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SD : standard deviation
Table 2. Comparison of period 1 (supine) and period 2 (prone) for pulse pressure variability, pleth variability index, heart rate and mean blood pressure.

<table>
<thead>
<tr>
<th></th>
<th>Supine</th>
<th>Prone</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV Mean (%)</td>
<td>12.63</td>
<td>13.97</td>
<td>0.245</td>
</tr>
<tr>
<td>PPV SD</td>
<td>4.51</td>
<td>5.42</td>
<td></td>
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<tr>
<td>PPV SD/Mean</td>
<td>0.36</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td>PVI Mean (%)</td>
<td>10.1</td>
<td>10.88</td>
<td>0.535</td>
</tr>
<tr>
<td>PVI SD</td>
<td>5.64</td>
<td>7.06</td>
<td></td>
</tr>
<tr>
<td>PVI SD/Mean</td>
<td>0.56</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>PIP Mean (cmH₂O)</td>
<td>19.81</td>
<td>20.52</td>
<td>0.162</td>
</tr>
<tr>
<td>PIP SD</td>
<td>3.52</td>
<td>3.07</td>
<td></td>
</tr>
<tr>
<td>HR Mean (beats/min)</td>
<td>154.81</td>
<td>145.71</td>
<td>0.000*</td>
</tr>
<tr>
<td>HR SD</td>
<td>16.81</td>
<td>19.02</td>
<td></td>
</tr>
<tr>
<td>MBP Mean (mmHg)</td>
<td>64.04</td>
<td>63.52</td>
<td>0.879</td>
</tr>
<tr>
<td>MBP SD</td>
<td>9.10</td>
<td>18.60</td>
<td></td>
</tr>
</tbody>
</table>

PPV: pulse pressure variation, PVI: pleth variability index, PIP: peak inspiratory pressure, HR: heart rate, MBP: mean blood pressure, SD: standard deviation

* P < 0.05
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Figure 1. Bland–Altman plot comparing pulse pressure variation and pleth variability index. PPV and PVI were compared for supine position (A), prone position (B) and altogether (C).