

## Pulse pressure variation and systolic pressure variation in mechanically ventilated children

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### Abstract

**Background** In mechanically ventilated patients, changes in breathing patterns may affect the preload, causing stroke volume fluctuation. Pulse pressure variation (PPV) and systolic pressure variation (SPV) are dynamic means of the hemodynamic monitoring in ventilated patients. No study on PPV and SPV in children has been reported to date.

**Objective** To study changes in PPV and SPV values in mechanically ventilated children.

**Method** A descriptive cross-sectional study was done at the Pediatric Critical Care Unit (PICU), Cipto Mangunkusumo Hospital, Jakarta. Subjects were mechanically ventilated children aged >12 months. Echocardiography was performed in all patients to determine the cardiac index. Arterial pressure was measured by connecting an arterial line to a vital signs monitor. PPV and SPV were calculated using the standard formulas. Bivariate correlation tests were performed between cardiac index and PPV and between cardiac index and SPV. Receiver-operator characteristic (ROC) curve analysis was done to determine the optimum PPV and SPV cut-off points to predict normal cardiac index ( $\geq 3.5$  L/minute/m<sup>2</sup>).

**Results** Eighteen patients were enrolled in the study, yielding 48 measurements. Mean cardiac index was 2.9 (SD 1-2.6) L/minute/m<sup>2</sup>. Median PPV was 18.9 (4.1-45.5)% and SPV was 12.1 (3.8-18.9)%. We found strong negative correlations between PPV and cardiac index ( $r = -0.7$ ;  $p = 0.001$ ) and SPV and cardiac index ( $r = -0.6$ ;  $p = 0.002$ ). To predict normal cardiac index, the optimum cut-off point was 11.4% for PPV (100% sensitivity, 100% specificity) and 9.45% for SPV (91.7% sensitivity, 100% specificity).

**Conclusion** In mechanically ventilated children, cardiac index is negatively correlated with PPV and SPV. [Paediatr Indones. 2011;51:34-40].

**Keywords:** Pulse pressure variation, systolic pressure variation, hemodynamic monitoring, preload monitoring

Studies on pulse pressure variation (PPV) and systolic pressure variation (SPV) in adult and animals have developed significantly, but studies in children are almost nonexistent. In 1978, Rick and Burke<sup>1</sup> were the first to suggest a link between the volume status of critically ill patients and SPV. Since 1987, Perel's group<sup>2-4</sup> has conducted several animals studies clarifying the physiological determinants of SPV, emphasizing the major role of volume status on its magnitude. However, the clinical use of this physical sign has remained marginal. In 1998, a German survey<sup>5</sup> suggested that only 1% of physicians consider the fluctuation in blood pressure during respiration as part of their decision-making process regarding volume expansion. Presently, as few methods are available to assess ventricular volumes continuously and directly, static pressure measurements such as central venous pressure and echocardiographically-measured ventricular end-diastolic areas are used to monitor cardiovascular filling. Dynamic monitoring by assessment of fluid

This study has been accepted for poster presentation in 6th World Congress on Pediatric Critical Care, 13 - 17 March 2011, Sydney, Australia.

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responsiveness using changes in PPV and SPV induced by positive pressure ventilation has been proposed to replace static measurements.

In mechanically ventilated patients, preload decrease may be influenced by an altered breathing patterns, which indirectly causing stroke volume fluctuation.<sup>6,7</sup> Thus, the emerged arterial pressure wave will fluctuate according to changes in stroke volume. This phenomenon was first described by Adolf Kussmaul as a vanishing pulse on inspiration which reappears on expiration in spite of continuous heart and lung activity in patients with constrictive pericarditis.<sup>8</sup> It was supported by Bilchick *et al*,<sup>8</sup> who noted that blood pressure would decline during inspiration in normal individuals with spontaneous breathing. As the science developed, this phenomenon was recognized as reverse pulsus paradoxus, paradoxical pulsus paradoxus, respirator paradox, or arterial pressure variation, which includes PPV and SPV.<sup>2,9,10</sup> Morgan *et al*.<sup>11</sup> reported changes in pressure of vena cava, pulmonary artery, and aorta during breathing cycles. Indeed, during mechanical ventilation right atrial pressure (RAP) rises secondary to increased intrathoracic pressure, in turn raising pericardial pressure. Intrathoracic pressure increase induces a decrease in venous, causing a decrease in the right-ventricular end-diastolic volume, and a few heartbeats later the left ventricular end-diastolic volume.<sup>12</sup> Under positive pressure ventilation, not only ventricular but also thoracopulmonary compliances and abdominal pressure variations were observed over time. Thus a variable relationship between cardiac pressures and cardiac volumes is often observed.<sup>13</sup>

PPV and SPV are dynamic means of hemodynamic measurement, but PPV and SPV are not the predictors of fluid loss or administered fluid volume.<sup>10</sup> They merely show the hemodynamic states on the Frank-Starling curve. The aim of this study was to describe the changes in PPV and SPV in mechanically ventilated children.

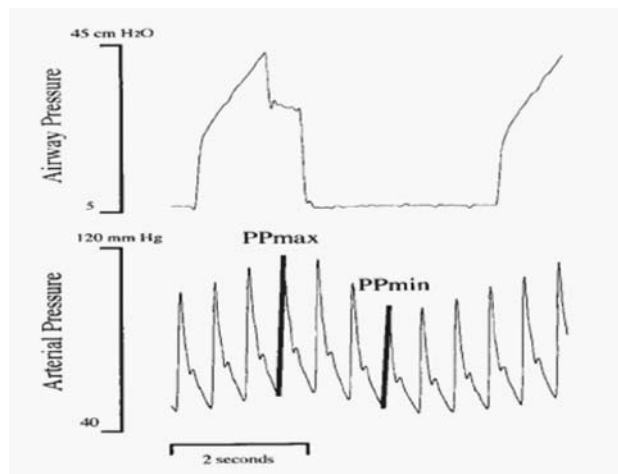
## Methods

We conducted a cross-sectional descriptive study using pediatric patients aged above 12 months who received mechanical ventilation at the pediatric critical care unit (PICU) of Cipto Mangunkusumo Hospital, Jakarta during the period of June 1, 2010 to July 31, 2010. These patients had an arterial line inserted. We excluded patients with cardiac contractility disorder (cardiomyopathies), shunting, congenital heart disease (CHD), hypertension or were clinically unstable. Using the sample size formula for determining correlation coefficient, we estimated that at least 20 measurements were required. The consecutive sampling method was used to obtain subjects. Written parental informed consent was sought and obtained for each subject. Approval for this study was obtained from the Medical/Health Research Ethics Commission.

All subjects were connected to a vital sign monitor (Intellivue MP-60 Philips, Hewlett Packard Str.2., Boeblingen, Germany) through an appropriate transducer. Two-dimensional Doppler echocardiography (Philips, HDIIXE, USA) was



**Figure 1.** Two-dimensional echocardiography showed (a) aortic diameter and (b) velocity time integrated measurements.



**Figure 2.** Breathing and arterial pulse pressure waves were equalized. Pulse Pressure Variation value using the formula of  $PPV\% = [(PP_{maks}-PP_{min}) / (PP_{maks}+PP_{min})/2] \times 100$ , while SPV value was calculated using the formula of  $[(SP_{maks}-SP_{min}) / (SP_{maks}+SP_{min})/2] \times 100$ .

performed by a pediatric cardiology consultant or senior fellow using an S8-3 probe. Aortic diameter ( $D_A$ ) was measured using the left parasternal length in transthoracic axis, while aortic flow or velocity time integrated (VTI) was measured using apical segments of five length axis space. Arterial pressure waves were noted using the wave velocity scale which had been equalized with the breathing pattern wave.

Cross-section area (CSA) was measured using the formula  $CSA = D_A^2 \times 0.785$ .<sup>15</sup> Stroke volume (SV) was determined using the formula  $SV = CSA \times VTI$  (Figure 1), in which VTI is velocity time integral. **Stroke volume index (SVI)** is the stroke volume divided by body surface area (BSA), with the normal range of 30-60 ml/m<sup>2</sup>. **Cardiac Index (CI)**, cardiac output per unit body surface area (BSA), was

calculated as  $[(CSA \times VTI \times HR) / BSA]$  within the normal range value of 3.5-5.5 L/minute/m<sup>2</sup>.<sup>15</sup> **Heart Rate (HR)** is the frequency of heart beat for one minute. **Arterial Pressure** is the magnitude of pulse palpable on the surface of the skin, which is the difference in systolic and diastolic pressures. **Systolic pressure (SP)** is the maximum pressure exerted when the blood is pumped to the arteries during systole. **Diastolic pressure (DP)** is the minimum pressure exerted when blood flows to the periphery blood vessels during diastole.

PPV was calculated as  $[(PP_{max}-PP_{min}) / (PP_{max}+PP_{min})/2] \times 100$ ,<sup>2,14</sup> in which the maximum pulse pressure ( $PP_{max}$ ) was the highest result of the subtraction of diastolic pressure (DP) from systolic pressure (SP) on each breathing pattern, while minimum pulse pressure ( $PP_{min}$ ) was the smallest result of the same equation. SPV was calculated using the formula  $[(SP_{max}-SP_{min}) / (SP_{max}+SP_{min})/2] \times 100$ . Maximum systolic pressure ( $SP_{max}$ ) was the highest SP obtained during inspiration, while minimum SP ( $SP_{min}$ ) was the lowest.<sup>2,5</sup>

We performed a bivariate correlation test to determine the association between cardiac output changes with PPV and SPV, respectively. We used receiver-operator characteristics (ROC) curve with linear regression analysis to determine optimum PPV and SPV cut-off points to predict a cardiac index above or below 3.5 L/minute/m<sup>2</sup>.

## Results

During the study period, 147 patients were admitted to the PICU, but only 30 were intubated and mechanically ventilated. We included 18/30 patients, yielding a total of 48 measurements. The remaining

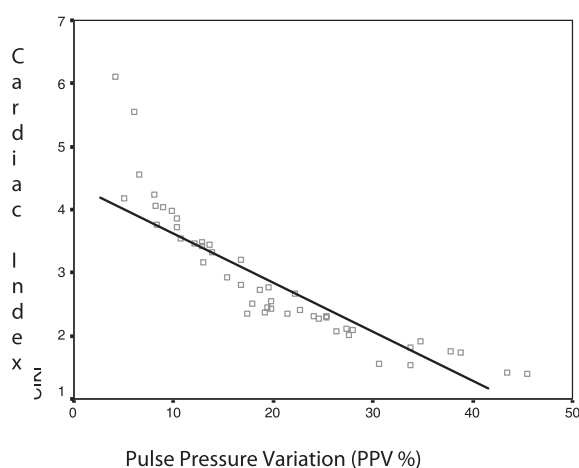
**Table 1.** Mean and standard deviation of the observation factors measurements

	Mean	SD	95% CI		Median
			Low	High	
Heart rate	124.0	27.6	116.2	131.8	125.0
Systolic pressure	105.9	12.1	102.5	109.4	105.0
Diastolic pressure	64.0	13.4	60.2	67.8	67.0
Stroke volume index	24.9	8.4	22.5	27.3	22.5
Cardiac index	2.9	1.0	2.6	3.2	2.4
PPV	19.8	10.3	16.8	22.7	18.9
SPV	11.0	3.4	10.1	12.0	12.1

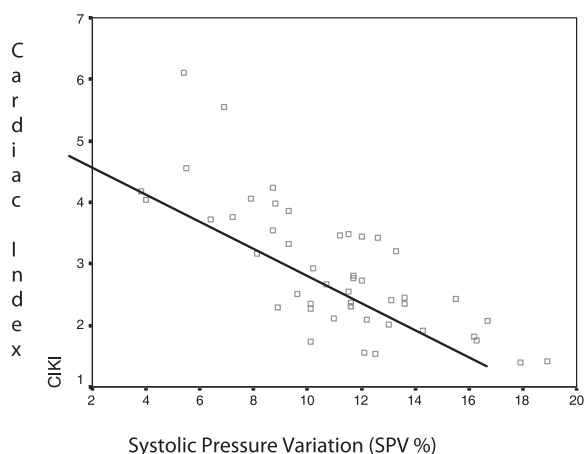
**Table 2.** Correlation of CI with PPV and SPV.

	r*	P**
Heart rate	0.377	0.008
Systolic pressure	- 0.186	0.205
Diastolic pressure	- 0.575	<0.0001
Stroke volume index	0.745	<0.0001
PPV	- 0.892	<0.0001
SPV	- 0.759	<0.0001

\* Correlation is considered strong if  $r > 0.300$ . \*\*p value is significant if  $< 0.05$



**Figure 3.** Scatter chart of the correlation between CI of 3.5 L/minute/m<sup>2</sup> and PPV.

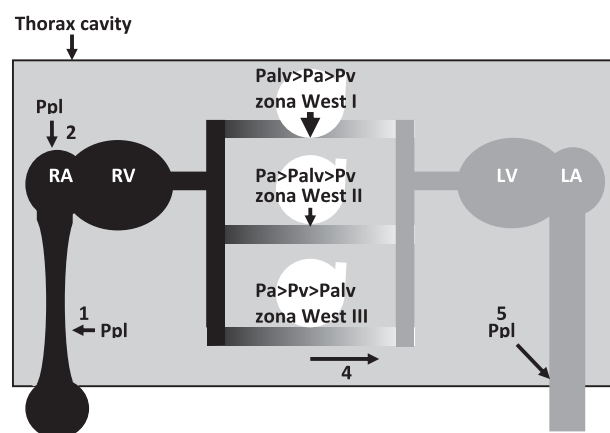


**Figure 4.** Scatter chart of the correlation between CI of 3.5 L/minute/m<sup>2</sup> and SPV.

12/30 patients were excluded because they were aged  $< 12$  months, private patients, had heart diseases (eg. cardiomyopathy or shunt), had been extubated before measurements were made or because placement of an arterial line was unsuccessful. Of the 48 measurements, we performed 30 on subjects receiving resuscitation fluids, 8 on patients with arterial pressure changes on the vital sign monitor, and 10 re-performed in other cases.

The majority of subjects in this study were female at a ratio of 2:1. The median age of subjects was 5 years (1-13 years old). Further observation showed that 15/48 measurements were made when the subject was receiving inotropic drugs such as dopamine, dobutamine, or norepinephrine with varying doses. The same amount of measurements were also obtained in subjects with CI values below normal range, each subject received resuscitation fluid up to 10 ml/kgBW normal saline.

Mean heart rate, blood pressure, stroke volume, cardiac index, PPV and SPV are shown in Table 1.



**Figure 5.** Physiologic effects of mechanical ventilation in hemodynamic circulation. 1. Vena cava superior compression due to increase in pleural pressure leads to decreased right ventricular preload. 2. An increase in intramural right atrial pressure due to increment of pleural pressure. 3. In West zones I ( $P_a < P_{alv}$ ) and II ( $P_v < P_{alv}$ ), right ventricular afterload increases because pulmonary capillaries are compressed. 4. In West zones III ( $P_{alv} < P_v$ ), the increase in alveolar pressure squeezes out the blood contained in the capillaries toward the left side of the heart. 5. The increase in pleural pressure induces a decrease in left ventricular afterload. LA (left atrium); LV (left ventricle); Palv (alveolar pressure); Ppl (pleural)

The median PPV was 18.9% (4-46%) and the median SPV was 12.1% (4-19%). Bivariate analysis revealed a strong correlation between increment of CI and decrement of SPV ( $r = -0.759$  and  $p < 0.0001$ ). Using linear regression, we found a regression equation of [cardiac index =  $5.475 - 0.234 \times \text{SPV}$ ] (Figure 4). A very strong correlation was found between the increment of cardiac index and the decrement of PPV ( $r = -0.892$ ;  $p < 0.0001$ ) (Table 2). Forty-eight measurements were utilized to assess the correlation between cardiac index and changes in PPV. Regression analysis of this correlation resulted in a negative linear regression line with the regression equation [cardiac index =  $4.664 - 0.090 \times \text{PPV}$ ] (Figure 3). By setting the lowest normal cardiac index value at 3.5 L/minute/ $\text{m}^2$  on the ROC curve, we obtained a PPV cut-off point of 11.4% with sensitivity and specificity of 100% and an SPV cut-off point of 9.45% with sensitivity of 91.7% and specificity of 100%.

## Discussion

Previous studies have suggested a PPV cutoff point of 12-13% and a SPV cutoff point of 10-6%<sup>5,10,14,16-21</sup>. This data was obtained from studies in animals and adult human patients in varied situations. Similarly, we found a PPV cutoff point of 11.4%, with sensitivity and specificity of 100%, and a SPV cutoff point of 9.45%, with sensitivity 91.7% and specificity 100%, on a CI value of 3.5 L/minute/ $\text{m}^2$ . The similarity in the pediatric and adult patient results may be due to similar mean arterial pressure (MAP) levels of children above 1 year old and adults.<sup>22</sup> In children who received mechanical ventilation with PPV and SPV values  $< 11.4\%$  and  $> 9.45\%$ , there is a possibility that patients might be developing hypovolemia, but further studies should be conducted to prove the efficacy and safety of the patient with more specific condition since our study was a descriptive, cross-sectional and observational nature not the diagnostic study.

Ideally, echocardiography should be performed by a cardiologist who is always available; however, this was very difficult to achieve. Instead, echocardiographic examinations in this study were performed by an external cardiologist whose measurements were subjected to interobserver tests with a cardiology fellow in our institution. A dedicated arterial pressure

monitor was initially unavailable, but a study by Auler et al<sup>16</sup> showed that measurement of arterial pressure variations using real-time monitoring (direct monitoring through a vital signs monitor) produced accurate results.

We found the median PPV was 18.9% (4-46%) and median SPV was 12.1% (4-19%). Mean cardiac index was 2.9 (SD 1.0) L/minutes/ $\text{m}^2$ . The cardiac output of the subjects were slightly below normal. Cardiac output is the stroke volume in one minute, or in other words, the amount of blood pumped out of the heart for each beat in one minute. Cardiac output is usually reported as cardiac index, which is formulated as  $[(\text{CSA} \times \text{VTI} \times \text{HR}) / \text{BSA}]$  in L/minute/ $\text{m}^2$ . Previous studies on adult patients and animals reported that every decrease in cardiac index would be accompanied with an increase in PPV and SPV, or vice versa.<sup>2,5</sup> This may be caused by changes in intrathoracic pressure, which is influenced by positive end-expiratory pressure (PEEP) volume,<sup>3,10</sup> causing changes in venous return (preload) or as a result of mechanical ventilation pressure.

Statistical analysis showed a strong correlation in cardiac index and SPV ( $r = -0.759$ ;  $P < 0.0001$ ). We also found a very strong correlation between cardiac index and PPV ( $r = -0.892$ ;  $P < 0.0001$ ). In accordance to the Frank-Starling law, a decrement in preload will cause decreased left ventricular cardiac output. This declining preload is the result of vena cava compression by pleural pressure and transmission of pleural pressure leading to an increased right atrial pressure. Other factors which explain the decrease in left ventricular cardiac output is the compression of pulmonary blood vessels on West I and II zones (alveolar pressure higher than the pulmonary arterial pressure), thus increasing afterload of the right ventricle during inspiration. The compensation mechanism will try to squeeze the pulmonary blood vessels to the left ventricle, but prolonged transit time ( $\pm 2$  seconds) on the existing pulmonary blood vessels will cause a decrease in left ventricular stroke volume (Figure 5).<sup>9,10,13,23</sup>

Previous researchs on animals and adult humans have suggested cutoff points for PPV and SPV of 12-13% and 10-6%, respectively.<sup>5,10,14,16-21</sup> In this study, we obtained a PPV cutoff point of 11.4%, with sensitivity and specificity of 100%. In addition, using a cardiac index value of 3.5 L/minute/ $\text{m}^2$ , we found

an SPV cutoff point of 9.45%, with sensitivity 91.7% and specificity 100%. Our results were similar to those in studies on adult patients, possibly because children age above 1 year and adults have similar mean arterial pressure (MAP).<sup>22</sup> Mechanically ventilated children with PPV and SPV value above the cut-off point might be developing hypovolemia, but further studies in specific conditions should be conducted to explore the utility of these two measures to determine volume status, since our study was merely descriptive, observational, and cross-sectional in nature, and not a full diagnostic test study.

In conclusion, to predict a normal cardiac index ( $>3.5$  L/minute/m<sup>2</sup>) regardless of the hemodynamic status, the optimum PPV cut-off point is 11.4%, with sensitivity and specificity of 100%, and the optimum SPV cut-off point is 9.45%, with a sensitivity of 91.7% and a specificity of 100%. In mechanically ventilated children, significant negative correlations are noted between cardiac index and PPV and SPV, respectively. Further investigation is needed in patients with more specific conditions and to assess the utility of PPV and SPV to determine a patient's response to fluid resuscitation.

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