Respiratory Variation in Pulse Oximetry:
A Simple Fluid Responsiveness Parameter

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Abstract
Respiratory variation in arterial pulse pressure (ΔPP) has been shown to be the most accurate predictor of fluid responsiveness in mechanically ventilated patients, with a predictive cutoff value of 13%. However, this dynamic parameter is invasive and not widely available. The pulse oximetry plethysmographic (POP) signal resembles the arterial pressure waveform in both shape and amplitude variation. Thus, the respiratory variations in pulse oximetry waveform amplitude (ΔPOP) may be used as a surrogate measure of ΔPP for predicting fluid responsiveness.

The aim of the study was to evaluate the relationship between ΔPP and ΔPOP by using standard monitors. Thirty-six mechanically ventilated patients were enrolled during the course of their clinical care in the medical or cardiothoracic surgical intensive care unit (ICU). The arterial pressure and plethysmographic waveform amplitude were recorded simultaneously. The ΔPP and ΔPOP were manually calculated. The relationship between ΔPP and ΔPOP was compared and analyzed for correlations.

The ΔPOP is well correlated with ΔPP (r = 0.78; P < 0.0001). Our study shows that a ΔPOP value above 15% accurately distinguishes patients with ΔPP above 13% and those with variation of 13% or less with a sensitivity of 93.3% and a specificity of 95.2% (positive predictive value 93.3%).

The results of our study suggest that ΔPOP can be used as a simple and noninvasive predictor of fluid responsiveness in mechanically ventilated patients.
INTRODUCTION

Initial therapy in critically ill patients with circulatory failure is volume therapy. The aim of volume expansion is to increase cardiac output. However, if inappropriate, volume expansion is able to induce side effect such as pulmonary or tissue edema. Therefore, assessment of fluid responsiveness is an important issue in the fluid management. Fluid responsiveness assessment has been studied for many years, and it is now established that static parameters of preload, such as central venous pressure or pulmonary capillary wedge pressure, if not extremely low, fail to predict fluid responsiveness accurately. Dynamic parameters relying on cardiopulmonary interactions in mechanically ventilated patients such as systolic pressure variation ($\Delta SP$) and pulse pressure variation ($\Delta PP$) are the reliable predictors of fluid responsiveness. Among the dynamic measurements, $\Delta PP$ has consistently been shown to be the most accurate predictor of fluid responsiveness. Michard et al previously found that a $\Delta PP$ of 13% had the highest sensitivity and specificity in predicting an increase in cardiac output in response to volume therapy in a study of septic patients. However, these dynamic indices are invasive, operator dependent, not widely available or expensive. Pulse oximeter waveform presents with variation in amplitude that are related to breathing cycles. Respiratory variation in pulse oximetry plethysmographic waveform amplitude ($\Delta POP$) has recently shown its potential interest in predicting fluid responsiveness in mechanically ventilated patients. We conducted a prospective study to evaluate the feasibility of the use in ordinary intensive care unit (ICU) and the relationship between $\Delta PP$ and $\Delta POP$.

Materials and Methods

Patients

We prospectively screened for eligibility in only mechanically ventilated patients admitted to the medical intensive care unit or cardiothoracic surgery intensive care unit, older than 18 years. Criteria for inclusion were as follows: (1) presence of an indwelling radial or arterial catheter placed after the decision of the physician in charge of the patient (2) controlled mechanical ventilation with tidal volume of $\geq 8$ mL/Kg (3) absence of arrhythmia.

We excluded patients in whom pulse oximetry waveform were unreliable measurement (association with noisy waveform). The protocol used in this study was part of routine clinical practice. Although informed consent was waived, the patients or relatives were given clear information about the study.

Measurement

Invasive arterial blood pressure, electrocardiography, pulse oximetry, exhaled tidal volume, respiratory rate, and peak airway pressure were recorded in all patients. Patients were studied in supine position, and zero pressure was measured at the 4th intercostal space in mid-axillary line. A pulse oximeter photoplethysmographic (POP) waveform was obtained by applying the pulse oximeter probe to a finger or a toe. Arterial pressure and POP wave forms were recorded simultaneously from a bedside monitor to a central station monitor and were analyzed by an observer blinded to other hemodynamic data.

Respiratory variations in pulse pressure (PP) analysis

PP was defined as the difference between systolic and diastolic pressure. Maximal (PPmax) and minimal (PPmin) values were determined over the same respiratory cycle (Fig 1). To assess the respiratory changes in PP ($\Delta PP$), the percent change in PP was calculated as described in previous study.
ΔPP (%) = 100 x (PPmax – PPmin) / [(PPmax + PPmin)/2].

Respiratory variations in POP waveform amplitude analysis

POP waveform amplitude was measured as the vertical distance between peak and preceding valley trough in the waveform. Maximal POP (POPmax) and minimal POP (POPmin) were determined over the same respiratory cycle (Fig. 1). ΔPOP was calculated using the following formulae:

ΔPOP (%) = 100 x (POPmax – POPmin) / [(POPmax + POPmin)/2].

Fluid responsiveness

Patients were divided into 2 groups of fluid responders (FR) and fluid nonresponders (FN). In accordance with previous studies, we used the ΔPP of 13% as the cut-off value to differentiate FR from FN.

Figure 1. Simultaneous record of arterial pressure and plethysmographic waveform in a representative patient.

Respiratory parameters

All patients were mechanically ventilated in a volume-controlled mode with a tidal volume of > 8 ml/kg ideal body weight. Ventilatory variables such as respiratory rate, the inspiratory to expiratory ratio (I:E) and Positive End Expiratory Pressure (PEEP) were set according to the attending physician.

Statistical Analysis

We calculated that 30 subjects would be needed to detect a correlation coefficient of 0.5 at the significance level of 5% (α-value of 0.05) and power 80% (β-value of 0.2). Correlation between ΔPP and ΔPOP were assessed with a Pearson Correlation. Statistical significance was defined as P <0.05. Statistical analysis was performed using Stata Statistical Software version 11.0.

Results

Of the 39 patients recruited from July 2014 to December 2014, 3 subjects (8%) were excluded from analysis due to poor plethysmograph waveforms. Therefore, data were analyzed from 36 subjects: 25 subjects in the cardiothoracic ICU and eleven in medical ICU (Table 1). This group consisted of 16 men and 20
women aged between 19 and 84 year (mean age, 56±16 years). The demographic, hemodynamic data and mechanical ventilator setting were shown in table 1.

<table>
<thead>
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<td>PEEP, cmH₂O</td>
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SpO₂ = oxygen saturation measurement determined by pulse oximeter.
PEEP = Positive End Expiratory Pressure.

There was a significant correlation ($r = 0.78; P < 0.0001$) between $\Delta$PP and $\Delta$POP, as shown in Fig 2.

Figure 2. Correlation between pulse pressure variation ($\Delta$PP) and plethysmograph variation ($\Delta$POP).

Overall, 14 patients were classified as fluid responders, and 22 patients were classified as fluid nonresponders. The $\Delta$POP threshold value of 15% discriminated fluid responders from nonresponders with sensitivity of 93.3% and specificity of 95.2%, positive predictive value (PPV) of 93.3 and negative predictive value (NPV) of 95.2%. The area under the ROC curve was 0.952 (Fig 3).

Figure 3. Receiver operating characteristic (ROC) curves describing the ability of $\Delta$POP to discriminate fluid responders (FR, $\Delta$PP > 13%) and fluid nonresponders (FN, $\Delta$PP ≤13%).
**Discussion**

In mechanically ventilated patients, dynamic parameters have consistently been shown to be more accurate predictors of fluid responsiveness than static parameters. These indices rely on the respiratory induced variations in stroke volume or its surrogates induced by positive pressure ventilation. The concept behind these indices is based on the change in stroke volume along the steep (fluid responders) or the flat (fluid nonresponders) portion of the Frank-Starling curve (Figure 4). Among the dynamic measurements, ΔPP was the best predictor of fluid responsiveness⁴. High ΔPP indicates that the patient is on the steep part of the Frank-Starling curve. Low ΔPP indicates that the patient is on the plateau part.

![Figure 4. Representation of Frank-Starling curve with corresponding respiratory variations in the arterial pressure waveform.](image)

The ΔPP measurement is invasive, operator-dependent, and not widely available. The pulse oximetry plethysmographic signal resembles the peripheral arterial pressure waveform and the degree of respiratory variation in the pulse oximetry wave is close to the degree of respiratory arterial pulse pressure variation. The use of pulse oximetry as a noninvasive indicator of volume status was firstly suggested by Partridge⁵ in 1987. Recently, variation in the pulse oximeter plethysmograph (ΔPOP) was shown to be a reliable noninvasive surrogate for ΔPP because both parameters are dependent on stroke volume.⁶⁻⁹

Pulse oximeter is applicable on most patient categories and is noninvasive, simple and widely available. The present study showed that analyzing the ΔPOP is feasible (successful measurement in 98% of patients in our study) in the ordinary ICU. However, the quality of the plethysmographic signal is critically dependent on peripheral perfusion, which may be significantly reduced by factors such as hypothermia, low cardiac output, and drug-induced vasoconstriction. In particular, norepinephrine, by increasing the peripheral vascular tone, may reduce the pulsatile component and accuracy of plethysmographic wave.¹⁰

ΔPP is considered to be a good predictor of fluid responsiveness⁴. Thus, other variables should correlate with ΔPP. We were able to demonstrate a significant correlation (r = 0.78; P < 0.0001) between ΔPOP and ΔPP in critically ill patients. The correlation between the respiratory variations in arterial pulse pressure and plethysmograph amplitude found in our study is in keeping with previous studies. Cannesson et al⁶ and Natalini et al¹¹ found correlations between ΔPP and ΔPOP of $r^2 = 0.89$ and $r = 0.62$ respectively.

In this study, we also assessed if ΔPOP could identify those patients likely to respond to intravascular fluid administration. We found that a ΔPOP value above 15% allowed discrimination between patients with ΔPP above 13% and those with variation of 13% or less (positive predictive value 93.3%) with good
sensitivity (93.3%) and specificity (95.2%). Therefore, the non-invasive ΔPOP measurement could potentially be used for the prediction of fluid responsiveness in patients with circulatory failure, especially if they are treated in general ward or ICU that could not be instrumented with an arterial catheter. Application includes preliminary evaluation of unexpected circulatory failure in hospitalized patients.

The limitation of this work is that, this index cannot be used in spontaneously breathing patients, patients with irregular heart rhythm and patients ventilated with tidal volume < 8 ml/Kg. However, this index may be used to predict preload responsiveness in a ventilated patient if the ventilated patient is temporarily paralyzed and tidal volume is temporarily increased for a couple of minutes to 8 mL/kg (if plateau pressure remains < 30 cmH₂O).

**Conclusion**

This study shows the feasibility of recording and calculating ΔPOP in ordinary ICU and a significant correlation between ΔPOP and ΔPP. Since ΔPOP, obtained from non-invasive technique, could identify those patients likely to respond to intravascular fluid administration, we concluded that ΔPOP may be an attractive method to detect fluid responsiveness in critically ill patients in a similar manner as invasive arterial line pulse pressure variation.

**References**

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วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างค่าเปลี่ยนแปลงตามการหายใจของความแตกต่างระหว่างความดันเลือดสูงสุดและความดันเลือดต่ำสุดและค่าเปลี่ยนแปลงตามการหายใจของกราฟจากเครื่องวัดระดับออกซิเจนในเลือดและศึกษาความเป็นไปได้ในการใช้การวัดค่าการเปลี่ยนแปลงตามการหายใจของกราฟจากเครื่องวัดระดับออกซิเจนในเลือดในหอผู้ป่วยวิกฤติ

วิธีการศึกษา: ผู้วิจัยได้ทำการศึกษาผู้ป่วยที่ใช้เครื่องช่วยหายใจและใส่สายสวนเส้นเลือดแดงเพื่อวัดความดันโลหิตแบบต่อเนื่องที่มีความผิดปกติของระบบไหลเวียนเลือดในหอผู้ป่วยหนังสาหร่ายและหอผู้ป่วยหนักอาการทางโรคทางกายภาพและโรควิทยาศาสตร์ และครอบคลุมโรงพยาบาลนครราชสีมา ระหว่างวันที่ 1 กรกฎาคม ถึง 30 พฤศจิกายน พ.ศ. 2557 สถิติที่ใช้ในการวิเคราะห์ข้อมูลได้แก่ค่าคะแนนเฉลี่ย ค่าความเบี่ยงเบนมาตรฐาน ค่าสัมประสิทธิ์สหสัมพันธ์ตามวิธีของเพียร์สัน

ผลการศึกษา: พบความสัมพันธ์ของค่าการเปลี่ยนแปลงตามการหายใจของความแตกต่างระหว่างความดันเลือดสูงสุดและความดันเลือดต่ำสุดและค่าเปลี่ยนแปลงตามการหายใจของกราฟจากเครื่องวัดระดับออกซิเจนในเลือด โดยค่าสัมประสิทธิ์สหสัมพันธ์เท่ากับ 0.78

สรุป: ค่าการเปลี่ยนแปลงตามการหายใจของกราฟจากเครื่องวัดระดับออกซิเจนในเลือดและค่าเปลี่ยนแปลงตามการหายใจของความแตกต่างระหว่างความดันเลือดสูงสุดและความดันเลือดต่ำสุดมีความสัมพันธ์อย่างมีนัยสำคัญและสามารถทำได้โดยง่ายในหอผู้ป่วยหนักทั่วไปโดยไม่จำเป็นต้องทำการทดสอบการที่อยู่มากหรืออาจมีอันตรายต่อผู้ป่วย