Evaluation of pulse pressure variation validity criteria in critically ill patients: a prospective observational multicentre point-prevalence study†


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Background. Respiratory variation in pulse pressure (ΔPP) is commonly used to predict the fluid responsiveness of critically ill patients. However, some researchers have demonstrated that this measurement has several limitations. The present study was designed to evaluate the proportion of patients satisfying criteria for valid application of ΔPP at a given time-point.

Methods. A 1 day, prospective, observational, point-prevalence study was performed in 26 French intensive care units (ICUs). All patients hospitalized in the ICUs on the day of the study were included. The ΔPP validity criteria were recorded prospectively and defined as follows: (i) mechanical ventilation in the absence of spontaneous respiration; (ii) regular cardiac rhythm; (iii) tidal volume \( \geq 8 \text{ ml kg}^{-1} \) of ideal body weight; (iv) a heart rate/respiratory rate ratio \( > 3.6 \); (v) total respiratory system compliance \( \geq 30 \text{ ml cm H}_2\text{O}^{-1} \); and (vi) tricuspid annular peak systolic velocity \( \geq 0.15 \text{ m s}^{-1} \).

Results. The study included 311 patients with a Simplified Acute Physiology Score II of 41 (39–43). Overall, only six (2%) patients satisfied all validity criteria. Of the 170 patients with an arterial line in place, only five (3%) satisfied the validity criteria. During the 24 h preceding the study time-point, fluid responsiveness was assessed for 79 patients. ΔPP had been used to assess fluid responsiveness in 15 of these cases (19%).

Conclusions. A very low percentage of patients satisfied all criteria for valid use of ΔPP in the evaluation of fluid responsiveness. Physicians must consider limitations to the validity of ΔPP before using this variable.

Keywords: fluid responsiveness; haemodynamic monitoring; pulse pressure variation

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Intravascular volume expansion is important in the treatment modality in hypotensive critically ill patients, but is not always effective, that is, fluid infusion is not always followed by an increase in stroke volume.\(^1\)\(^2\) Given that ineffective volume expansion can even be harmful, it is essential to predict fluid responsiveness in guiding therapy.\(^3\) Several static indices (such as central venous pressure, pulmonary artery occlusion pressure, and ventricular end-diastolic volume) have been studied, but none accurately predicts fluid responsiveness.\(^4\) More recently, a dynamic index [respiratory variation in pulse pressure (ΔPP)] has been described as an accurate tool for predicting fluid responsiveness,\(^5\) and confirmed by several studies over the last decade.\(^5\) Thus, ΔPP and its surrogates (e.g. stroke volume variation) have been implemented in several devices for continuous monitoring of fluid responsiveness.\(^6\) However, there are a number of limitations to this approach.\(^7\)–\(^11\) Unfortunately, the extent to which these limitations are actually encountered in intensive care units (ICUs) has not been evaluated in a large multicentre study. The aim of this prospective study was to evaluate the proportion of critically ill ICU patients meeting all validity criteria for the use of ΔPP (or a surrogate) in the prediction of fluid responsiveness.

Methods

Patients

This was a 1 day point-prevalence study of ΔPP validity criteria in 26 ICUS in 22 French hospitals. General, medical, and surgical ICUs for adults with eight or more beds were included. The independent ethics committee at Amiens University Hospital approved the study’s objectives and procedures and waived the need for informed consent.

Data collection

Data were collected (using two questionnaires) by a clinician nominated as the principal investigator for each centre. A specific form was completed for each patient in each ICU. The investigators had a time window of 3 h in the morning to fill out the forms. Data were then entered into a database at the coordinating centre (Amiens University Hospital). The coordinating centre was available throughout the study to answer queries and provide feedback.

ICU data

The data collected for each ICU were: type of hospital (university or general), type of ICU (general or specialized), whether or not the ICU used a device to automatically calculate ΔPP (or a surrogate), and whether ΔPP was part of a written haemodynamic monitoring protocol.

Patient characteristic data

The patient’s age, BMI, primary diagnosis, Simplified Acute Physiology Score II on admission, and Sequential Organ Failure Assessment score on inclusion were recorded.

Haemodynamic monitoring

The use of haemodynamic monitoring devices (especially arterial lines) and each patient’s arterial pressure and heart rate (HR) values were recorded. Vasopressor use and the volume of fluid received over the previous 24 h were also recorded.

Ventilator settings

In mechanically ventilated patients, the type of ventilation, tidal volume (\(V_t\)), and respiratory rate (RR) were recorded. For patients on controlled mechanical ventilation in the absence of spontaneous breathing, total respiratory system compliance was calculated as \(V_t\) divided by the plateau pressure minus the positive end-expiratory pressure.

ΔPP validity criteria

The following ΔPP validity criteria were defined: regular cardiac rhythm\(^9\) (defined as no arrhythmia or extrasystoles on the monitor screen); controlled mechanical ventilation in the absence of spontaneous breathing;\(^9\) \(^12\) \(V_t \geq 8\) ml kg\(^{-1}\) \(t\); \(0.15\) m s\(^{-1}\);\(^10\) and tricuspid annular peak systolic velocity (S\(_t\)) \(> 0.15\) m s\(^{-1}\).\(^11\)

Fluid infusion

The need for an assessment of fluid responsiveness on inclusion and during the 24 h before the study time-point was recorded for each patient. The methods and parameters used to assess fluid responsiveness were also recorded.

Statistical analysis

Categorical variables were expressed as number (%). Continuous variables were expressed as mean (95% confidence interval, CI) or median (inter-quartile range), depending on their distribution. A Kolmogorov–Smirnov test was performed to assess the normality of distribution. Patients with an arterial line were compared with those without an arterial line. The data for categorical variables were analysed using the \(\chi^2\) test (with Yate’s correction, if necessary) or Fisher’s exact test. Continuous data were analysed in a two-sided t-test or a Mann–Whitney test (depending on the distribution). The threshold for statistical significance was set to \(P<0.05\).

Results

The 26 participating ICUs included a total of 313 patients. Two patients were excluded because of missing data, so the final data set comprised 311 patients. There were 24 university hospital ICUs and two general hospital ICUs. Twelve ICUs admitted both non-surgical and surgical patients, 11 admitted only surgical patients, and three admitted only non-surgical patients. The mean number of beds was 13 (2). Although 23 (88%) of the ICUs were equipped with a device that automatically calculated ΔPP, this variable was a part of a written haemodynamic monitoring protocol in only three (12%) units.
Table 1: Patient characteristics: a comparison of patients with and without arterial lines. BMI, body mass index; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment; ARDS, acute respiratory distress syndrome.

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 311)</th>
<th>Patients with an arterial line (n = 170)</th>
<th>Patients without an arterial line (n = 141)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>58 (56–60)</td>
<td>57 (54–59)</td>
<td>59 (58–62)</td>
<td>0.28</td>
</tr>
<tr>
<td>BMI (kg m⁻²)</td>
<td>25 (24–26)</td>
<td>26 (25–27)</td>
<td>25 (24–26)</td>
<td>0.5</td>
</tr>
<tr>
<td>SAPS II</td>
<td>41 (39–43)</td>
<td>44 (39–46)</td>
<td>37 (33–40)</td>
<td>0.02</td>
</tr>
<tr>
<td>SOFA score</td>
<td>4 (3–4)</td>
<td>4 (4–5)</td>
<td>2 (2–3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Patients with ARDS [n (%)]</td>
<td>30 (10)</td>
<td>19 (11)</td>
<td>11 (8)</td>
<td>0.48</td>
</tr>
<tr>
<td>Patients with sepsis [n (%)]</td>
<td>100 (32)</td>
<td>51 (30)</td>
<td>49 (35)</td>
<td>0.41</td>
</tr>
<tr>
<td>Patients with septic shock [n (%)]</td>
<td>32 (10)</td>
<td>32 (19)</td>
<td>0 (0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Patients on vasopressors [n (%)]</td>
<td>42 (14)</td>
<td>42 (25)</td>
<td>0 (0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Patients who received colloid infusions [n (%)]</td>
<td>66 (21)</td>
<td>51 (30)</td>
<td>15 (11)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Volume of colloids received during the previous 24 h (ml kg⁻¹)</td>
<td>8 (6–10)</td>
<td>8 (6–10)</td>
<td>8 (6–15)</td>
<td>0.21</td>
</tr>
<tr>
<td>Patients who received crystalloid infusions [n (%)]</td>
<td>288 (93)</td>
<td>157 (92)</td>
<td>131 (93)</td>
<td>0.9</td>
</tr>
<tr>
<td>Volume of crystalloids received during the previous 24 h (ml kg⁻¹)</td>
<td>23 (21–26)</td>
<td>23 (20–26)</td>
<td>24 (19–29)</td>
<td>0.2</td>
</tr>
<tr>
<td>Patients who satisfied all ΔPP validity criteria [n (%)]</td>
<td>6 (2)</td>
<td>5 (3)</td>
<td>1 (0.7)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Characteristics of the study population are shown in Table 1. Only six (2%) patients satisfied all ΔPP validity criteria (Fig. 1). Of the 170 (54%) patients with an arterial line, only five (3%) satisfied all ΔPP validity criteria (Table 1). One hundred and fifteen (37%) of the patients with an arterial line also received mechanical ventilation; of these, only five (4%) satisfied all ΔPP validity criteria.

During the 24 h immediately preceding the study time-point, fluid responsiveness was assessed for 79 patients (with 69 of the latter receiving fluids). Methods used to assess fluid responsiveness were as follows: ΔPP: n=15 patients (19%); clinical examination: n=30; fluid challenge: n=24; passive leg raising manoeuvre: n=21; central venous pressure: n=1; respiratory variations of the inferior vena cava: n=8; other echocardiographic parameters: n=5; a combination of two or more of these methods: n=25.

On inclusion, fluid responsiveness was assessed in 23 (7%) patients. Only one (4%) of these patients satisfied all six of the defined ΔPP validity criteria.

When comparing patients with and without arterial lines, we found that patients with an arterial line had higher severity scores and were more likely to have received vasopressors and colloids (Table 1).

**Discussion**

To the best of our knowledge, this is the first multicentre study to evaluate ΔPP validity criteria in a mixed ICU population. Our results show that of the 170 ICU patients who had an arterial line in place, only 3% satisfied all ΔPP validity criteria. When considering the ICU study population as a whole (n=311), only 2% satisfied all ΔPP validity criteria.

In 2000, Michard and colleagues reported the value of ΔPP for prediction of fluid responsiveness. In a population of 40 patients, they showed that a cut-off of 13% was able to discriminate between responders and non-responders with a sensitivity of 94% and a specificity of 96%. This was a significant step forward in fluid management of the critically ill. Since then, several studies have confirmed these results in various settings. Although ΔPP can only be used in patients on mechanical ventilation with no spontaneous breathing activity and no arrhythmia, several research reports have shown...
that this parameter has other limitations in this situation. When studying 60 mechanically ventilated ICU patients with no spontaneous breathing or cardiac arrhythmia, De Backer and colleagues showed that ΔPP was not a reliable predictor of fluid responsiveness in patients with $V_t < 8\,\text{ml kg}^{-1}$ of IBW. These results were subsequently confirmed. Mechanical ventilation with low $V_t$ (<6 ml kg$^{-1}$) for acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) has been shown to decrease mortality. For patients free of ALI/ARDS, some studies have suggested that the use of $V_t > 7\,\text{ml kg}^{-1}$ was an independent risk factor for developing ARDS. The use of low $V_t$ in ICUs has therefore become common practice and some researchers recommend using low $V_t$ for the majority of patients. In the present study, only 12 of 44 mechanically ventilated patients without spontaneous breathing or arrhythmia had $V_t \geq 8\,\text{ml kg}^{-1}$.

De Backer and colleagues also demonstrated that ΔPP was unreliable when the HR/RR ratio was <3.6, a value that is frequently encountered in the ICU (especially in ARDS patients). For example, the mean RR in the ARDS Net study was around 30 bpm, such that the HR/RR ratio will be <3.6 if HR is <108 beats min$^{-1}$. Another limitation of ΔPP relates to low chest wall compliance. In a study of 54 patients with circulatory shock, Monnet and colleagues demonstrated that the area under the receiver operating characteristic (ROC) curve of ΔPP for predicting fluid responsiveness was low (0.69 (0.10)) for patients with total respiratory system compliance below 30 ml cm H$_2$O$^{-1}$. Lastly, right ventricular failure (as assessed by Doppler tissue imaging) can be responsible for false-positive ΔPP values. Unfortunately, tissue Doppler imaging requires a level of expertise that might not be available in all ICUs.

All these limitations must be taken into account when using ΔPP to predict fluid responsiveness. The present study shows that when these limitations are taken into account, this index can only be correctly applied in a very low proportion of patients (2%). We found that patients with an arterial line had higher severity scores and were more likely to be on vasopressors. Even when only patients with an arterial line in place were taken into account, the percentage of patients satisfying all ΔPP validity criteria was just 3%.

This percentage of ICU patients meeting criteria for ΔPP monitoring is much lower than that observed in an anaesthesia setting. In a single-centre retrospective study of 12 308 procedures, Maguire and colleagues found that 38.9% of patients satisfied ΔPP validity criteria. However, in this general anaesthesia study, patients were more heavily sedated (only 13% showed spontaneous breathing), ventilated with a higher $V_t$ (41% had $V_t > 8\,\text{ml kg}^{-1}$), and had a lower prevalence of ARDS and cardiac arrhythmia. Moreover, Maguire and colleagues did not use the same validity criteria, since neither $C_{\text{TR}}S$ nor $S_t$ was assessed.

Our findings do not appear to agree with the conclusions of Mark and colleagues’ systematic review of the literature on dynamic changes in arterial waveform variables. These researchers found that ΔPP is highly accurate for predicting fluid responsiveness in the ICU [with an area under the ROC curve of 0.95 (0.93–0.96)]. However, their analysis encompassed six studies of highly selected patient populations (heavily sedated patients under mechanical ventilation, with no arrhythmia and $V_t > 7\,\text{ml kg}^{-1}$). Other validity criteria (HR/RR, respiratory system compliance, and $S_t$) were published after this systematic review and thus were not studied. However, the last three validity criteria have not been extensively studied and are subject to debate. In contrast, mechanical ventilation without spontaneous breathing or arrhythmia and $V_t > 7\,\text{ml kg}^{-1}$ are well accepted. Nevertheless, only 12 (4%) of our patients satisfied these three well-accepted validity criteria.

We also found that although ΔPP was part of a written protocol in just one ICU, this parameter was used in 19% of fluid responsiveness assessments. Moreover, we observed that despite its known poor reliability, clinical examination alone was the most frequently used technique for evaluating fluid responsiveness.

This study has a number of limitations. As this was a 1 day study based on a snapshot at a given time-point, results might have been different at other time-points. Secondly, our study took place primarily in tertiary hospitals in a single country (France). This might represent a source of selection bias that would have to be addressed in larger, international studies. Thirdly, some of the validity criteria studied here are still subject to debate. Nevertheless, all these criteria have been previously studied in ICUs in this context. Fourthly, other criteria that limit the applicability of ΔPP have been described and need to be investigated further: vasopressors appear to decrease ΔPP, whereas intra-abdominal hypertension appears to increase ΔPP. Lastly, the study’s design prevented us from investigating the sensitivity and specificity of a ΔPP cut-off value in the assessment of fluid responsiveness in patients who satisfied all validity criteria. Further studies are needed to investigate this issue.

In conclusion, a very small proportion of ICU patients satisfied all validity criteria for the use of ΔPP. Caution is therefore advised when using ΔPP to assess fluid responsiveness.

**Authors’ contributions**


**Acknowledgements**

De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL. Pulse pressure variation validity criteria in intensive care

References


