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CRITICAL CARE

Predictive value of pulse pressure variation for fluid responsiveness in septic patients using lung-protective ventilation strategies

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Editor's key points

- Changes in cardiac output were measured after fluid challenges in intensive care unit septic patients.
- Pulse pressure variability before and after fluid challenges were measured during 6 and 8 ml kg^{-1} tidal volume ventilation.
- Importantly, pulse pressure variation was a better predictor of fluid responsiveness than the static indicators.

Background. The applicability of pulse pressure variation (ΔPP) to predict fluid responsiveness using lung-protective ventilation strategies is uncertain in clinical practice. We designed this study to evaluate the accuracy of this parameter in predicting the fluid responsiveness of septic patients ventilated with low tidal volumes (TV) (6 ml kg^{-1}).

Methods. Forty patients after the resuscitation phase of severe sepsis and septic shock who were mechanically ventilated with 6 ml kg^{-1} were included. The ΔPP was obtained automatically at baseline and after a standardized fluid challenge (7 ml kg^{-1}). Patients whose cardiac output increased by more than 15% were considered fluid responders. The predictive values of ΔPP and static variables [right atrial pressure (RAP) and pulmonary artery occlusion pressure (PAOP)] were evaluated through a receiver operating characteristic (ROC) curve analysis.

Results. Thirty-four patients had characteristics consistent with acute lung injury or acute respiratory distress syndrome and were ventilated with high levels of PEEP [median (inter-quartile range) 10.0 (10.0–13.5)]. Nineteen patients were considered fluid responders. The RAP and PAOP significantly increased, and ΔPP significantly decreased after volume expansion. The ΔPP performance [ROC curve area: 0.91 (0.82–1.0)] was better than that of the RAP [ROC curve area: 0.73 (0.59–0.90)] and pulmonary artery occlusion pressure [ROC curve area: 0.58 (0.40–0.76)]. The ROC curve analysis revealed that the best cut-off for ΔPP was 6.5%, with a sensitivity of 0.89, specificity of 0.90, positive predictive value of 0.89, and negative predictive value of 0.90.

Conclusions. Automatized ΔPP accurately predicted fluid responsiveness in septic patients ventilated with low TV.

Keywords: fluid therapy; haemodynamics; respiratory distress syndrome, adult; sepsis; tidal volume

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After early sepsis resuscitation, excessive fluid administration may aggravate pulmonary oedema and prolong mechanical ventilation.[1] An accurate prediction of fluid responsiveness may prevent unnecessary fluid loading and detect patients who benefit from volume expansion.[2]

Previous studies demonstrated that pulse pressure variation (ΔPP) is an accurate predictor of fluid responsiveness during mechanical ventilation.[3 4] Almost all patients in these trials were ventilated with tidal volumes (TV) of 8–10 ml kg^{-1}.[5] However, low TV ventilation is commonly used in patients with sepsis because sepsis predisposes patients to acute lung injury/acute respiratory distress syndrome (ALI/ARDS).[6] Ventilation with a low TV is usually considered a limitation for the assessment of functional haemodynamics.[7] The rationale is that a low TV might be insufficient to produce a significant change in the intrathoracic pressure; therefore, ΔPP could indicate a non-responsive status even in 'responders'.[8]

Previous clinical and experimental studies have conflicting results regarding the accuracy of ΔPP measured with a TV below 8 ml kg^{-1}.[9–12] Furthermore, most studies calculated the ΔPP manually using a computer recording or paper printout of the pressure curve, but this form of measurement has been criticized.[13] Thus, the role of automatized ΔPP in this setting is of particular interest.

We designed a prospective study to evaluate the predictive value of automatized ΔPP for fluid responsiveness in patients with sepsis and low TV ventilation.

Methods

The institutional Research and Ethics Committee approved the study. The patients' closest relatives signed the informed consent form to allow the data collection.

This study was performed in a 14-bed mixed intensive care unit at a Brazilian teaching hospital. The inclusion criteria were as follows: age >18 yr, a diagnosis of severe sepsis or septic shock according to the criteria of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference,[14] sedation and mechanical ventilation with a low TV (5.5–6.5 ml kg^{-1} of predicted body weight), instrumentation with indwelling radial or femoral artery and pulmonary artery catheters, a required fluid challenge (as determined by the attending physician), and a signed informed consent. We chose septic patients because they are usually monitored with pulmonary arterial catheter and respiratory dysfunction is often present, leading to ventilation with low TV.

All patients were included after the first 6 h of resuscitation as in this late phase, fluid responsiveness assessment is more relevant.[15] The absence of spontaneous respiratory movements was identified upon clinical examination, and the respiratory curves were examined using the ventilator and capnographic signal on the bedside monitor. Patients received neuromuscular block if needed.

The exclusion criteria were as follows: cardiac arrhythmias and previously known significant valvular disease or intracardiac shunt, acute bleeding (suspected or confirmed), air leakage through chest drains, an urgently required fluid challenge, abdominal compartment syndrome, and pregnancy.

Baseline and sepsis-related characteristics, and also the Acute Physiological and Chronic Health Evaluation (APACHE II) and Sequential Organ Failure Assessment (SOFA) severity scores, were collected at the patient's inclusion.

Study protocol

The selected patients were mechanically ventilated (Vela, Viasys, Palm Springs, CA, USA) using the volume-controlled mode; the patients' TV was adjusted to 6 ml kg^{-1} (based on the patient's predicted body weight), with no changes in the other ventilatory parameters. The predicted body weight of male patients was calculated as equal to 50+0.91 (centimetres of height−152.4); that of female patients was calculated as equal to 45.5+0.91 (centimetres of height−152.4).[16] The static compliance of the respiratory system was calculated as follows: TV/(plateau pressure−PEEP). The plateau pressure was measured after an inspiratory pause of 2 s.

Throughout the study period, the doses of the sedative, inotropic, and vasopressor medications remained constant. Each patient was observed for 20 min before the fluid challenge to assure that there were no significant variations in haemodynamic parameters. If the heart rate (HR), ΔPP, arterial pressure, right atrial pressure (RAP), pulmonary arterial occlusion pressure (PAOP), or cardiac output (CO) varied by more than 20% during this period of observation, the experiment was interrupted. At the end of 20 min (baseline), we obtained a complete set of haemodynamic and respiratory measurements, including arterial and mixed-venous blood gases, haemoglobin, and arterial lactate levels. At this time, the ΔPP was measured in patients ventilated with a TV of 6 ml kg^{-1} and was recorded as ΔPP6.

To assess the correlation and the agreement between the ΔPP measured during low TV ventilation (6 ml kg^{-1}) and during 'standard' TV ventilation (8 ml kg^{-1}), we increased the TV to 8 ml kg^{-1} of predicted body weight. After 5 min, the haemodynamic and respiratory measurements were repeated. The ΔPP measured at this time was recorded as ΔPP8. No fluids were given at this step.

After this manoeuvre, the patients were again ventilated with a TV of 6 ml kg^{-1} and given a standardized fluid challenge with 7 ml kg^{-1} (actual body weight) of hydroxylethyl starch 130/0.4 (up to 500 ml), which was infused over 30 min. At the end of the fluid challenge, another set of haemodynamic and respiratory measurements was obtained.

Considering the CO obtained with a TV of 6 ml kg^{-1}, we classified the patients into two groups according to their per cent increase in CO in response to the fluid challenge. 'Responders' had a CO increase of at least 15%, whereas 'non-responders' had a CO increase of <15%.[3 17] The CO was determined by a semicontinuous thermodilution technique that considered the average value of four consecutive measurements from the STAT mode screen of the Vigilance® monitor (Edwards, Irvine, CA, USA). The ΔPP was measured with a multiparameter bedside monitor (DX 2020, Dixtal, São Paulo, Brazil) using an automatic calculation and real-time monitoring of ΔPP. The monitor uses specific software allowing the recognition of respiratory cycles (capnographic signal) and the automatic calculation of ΔPP over each respiratory cycle. The mean value of ΔPP is calculated over three consecutive periods of 10 respiratory cycles (from cycles 1 to 10, 2 to 11, and 3 to 12); the median value of this triple determination is displayed on the bedside monitor. This automatic real-time monitoring of ΔPP was validated previously in patients using TV of 8 ml kg^{-1} and a PEEP of 5 cm H_2O.[18] All pressures were determined at the end-expiration with the zero reference level settled at 4th–5th intercostal space along the mid-axillary line. The head of the bed was elevated at ∼30°.

Statistical analysis

Categorical variables were compared using the Pearson χ^2 test. The distribution of continuous variables was assessed by a Shapiro–Wilk test, and variance homogeneity was assessed with a Bartlett test. The data that were normally distributed and had a homogenous variance were expressed by means [standard deviations (SD)]. Non-parametric variables were described as medians and inter-quartile ranges (IQR). The effects of intravascular volume expansion on