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Pleth variability index is a weak predictor of fluid responsiveness in patients receiving norepinephrine

X. Monnet[1,2]*, L. Guérin[1,2], M. Jozwiak[1,2], A. Bataille[1,2], F. Julien[1,2], C. Richard[1,2] and J.-L. Teboul[1,2]

[1] Hôpitaux universitaires Paris-Sud, Hôpital de Bicêtre, service de réanimation médicale, 78, rue du Général Leclerc, Le Kremlin-Bicêtre F-94270, France

[2] Univ Paris-Sud, Faculté de médecine Paris-Sud, EA 4533, Le Kremlin-Bicêtre F-94270, France

* Corresponding author. E-mail: xavier.monnet@bct.aphp.fr

Editor's key points

- Respiratory variations in the amplitude of plethysmography traces may correlate with fluid responsiveness in surgical patients.
- However, the effect of vasoconstrictor drugs on the quality and accuracy of plethysmography indices is unclear.
- This study of critically ill patients found that the plethysmography variability index did not reflect fluid responsiveness.
- Plethysmography variability was less useful than other indices of stroke volume.

Background. In patients receiving an infusion of norepinephrine, the relationship between the amplitude of the oximeter plethysmographic waveform and stroke volume may be variable and quality of the waveform might be reduced, compared with patients not receiving norepinephrine. We assessed the reliability of the pleth variability index (PVI), an automatic measurement of the respiratory variation of the plethysmographic waveform, for predicting fluid responsiveness in patients receiving norepinephrine infusions.

Methods. We measured the response of cardiac index (transpulmonary thermodilution) to i.v. fluid administration in 42 critically ill patients receiving norepinephrine. Patients with arrhythmias, spontaneous breathing, tidal volume <8 ml kg^{-1}, and respiratory system compliance <30 ml cm H_2O^{-1} were excluded. Before fluid administration, we recorded the arterial pulse pressure variation (PPV) and pulse contour analysis-derived stroke volume variation (SVV, PiCCO2) and PVI (Masimo Radical-7).

Results. In seven patients, the plethysmographic signal could not be obtained. Among the 35 remaining patients [mean SAPS II score=77 (SD=17)], i.v. fluid increased cardiac index $\geq$15% in 15 'responders'. A baseline PVI $\geq$16% predicted fluid responsiveness with a sensitivity of 47 (inter-quartile range=21–73)% and a specificity of 90 (68–99)%. The area under the receiver operating characteristic curve was significantly lower for PVI [0.68 (0.09)] than for PPV and SVV [0.93 (0.06) and 0.89 (0.07), respectively]. Considering all pairs of measurements, PVI was correlated with PPV (r^2=0.27). The fluid-induced changes in PVI and PPV were not significantly correlated.

Conclusions. PVI was less reliable than PPV and SVV for predicting fluid responsiveness in critically ill patients receiving norepinephrine. In addition, PVI could not be measured in a significant proportion of patients. This suggests that PVI is not useful in patients receiving norepinephrine.

Keywords: cardiorespiratory system, responses; cardiovascular system; equipment; fluid therapy; measurement techniques; pulse oximetry; responses

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Among the different indices that have been developed for predicting fluid responsiveness, the respiratory variation of stroke volume and surrogates has generated a large amount of evidence.[1] Schematically, insufflations during mechanical ventilation in the control mode induce cyclic regular decreases in the left ventricular preload. This can be used as a test for assessing the effects of preload changes on stroke volume and cardiac output, that is, for diagnosing preload dependence. At the bedside, the key question is to know on which surrogate of stroke volume one can rely for assessing the haemodynamic effects of mechanical ventilation and predicting fluid responsiveness. Initially, the arterial pulse pressure has been proposed for this purpose[2] and it is now well demonstrated that pulse pressure variation (PPV) allows a reliable prediction of fluid responsiveness.[3] This is also the case for the respiratory variation of stroke volume estimated from pulse contour analysis (SVV).[1]

As a non-invasive alternative to arterial pulse pressure and pulse contour analysis-derived stroke volume, some authors proposed to use the amplitude of the oximeter plethysmographic signal as a surrogate of stroke volume. The respiratory variation of the 'pulse' of the plethysmographic signal was found to be correlated with PPV.[4] It was demonstrated to predict fluid responsiveness with reliability.[5–7] More recently, a commercial device has been developed for providing an automatic calculation of the respiratory variation of the plethysmographic signal through a 'pleth

variability index' (PVI).[8] This index was found to reliably predict fluid responsiveness.[8–11]

However, the majority of studies validating the respiratory variation of the plethysmographic pulse or PVI as markers of fluid responsiveness were conducted in the perioperative setting in patients with a stable haemodynamic condition.[6–10] Altered sympathetic tone, induced either by circulatory failure or by vasoactive drugs, might alter the amplitude of the plethysmographic curve by modifying the distensibility of the small vessels where the plethysmographic curve is recorded and the proximal venous pressure. In such conditions, the plethysmographic pulse may not be related to stroke volume and its respiratory variation could fail to predict the haemodynamic response to fluid loading. In addition, vasoconstriction might alter the quality of the plethysmographic signal and impair the correct calculation of PVI. To date, available data are conflicting. Loupec and colleagues[11] found that PVI was a reliable predictor of fluid responsiveness in a population of patients receiving norepinephrine. In contrast, Biais and colleagues[12] found that the relationship between PVI and PPV was poorer in surgical patients receiving norepinephrine compared with patients who did not. However, since no volume challenge was performed, this study did not test whether the prediction of fluid responsiveness by PVI was impaired by norepinephrine administration. Thus, it is unclear whether PVI can predict fluid responsiveness in patients receiving norepinephrine.

The aims of this present study were to assess whether PVI can be recorded in patients with circulatory failure receiving norepinephrine and to test the ability of PVI to predict fluid responsiveness. We also aimed at comparing PVI with well-established indicators of fluid responsiveness, namely PPV and SVV.

Methods

Patients

After approval by the institutional review board of our institution (comité pour la protection des personnes Ile-de-France 7), patients' relatives were informed about the study at the time the patient was included and asked to provide assent. After assent and inclusion in the study, patients were informed as soon as their mental status enabled it and they were given the option to withdraw their participation to the study. Patients were prospectively included if they received norepinephrine and if they presented an acute circulatory failure for which the attending physician had decided to administer fluid. This decision was based on inadequate tissue perfusion defined by the presence of at least one of the following signs:[13–15] (i) systolic arterial pressure $<$90 mm Hg (or a decrease $>$50 mm Hg in previously hypertensive patients), (ii) urine output $<$0.5 ml kg^{-1} h^{-1} for at least 2 h, (iii) tachycardia $>$100 beats min^{-1}, (iv) skin mottling, or (v) blood lactate concentration $>$2 mmol litre^{-1}. Patients were excluded if they presented cardiac arrhythmias (atrial fibrillation and flutter, atrial and ventricular extrasystoles, and ventricular tachycardia), spontaneous triggering of the ventilator, as assessed by visual observation of the pressure curve of the ventilator by investigators (L.G., A.B., M.J., F.J.). They were also excluded if their lungs were being ventilated with a tidal volume $<$8 ml kg^{-1} of predicted body weight[16] and if the compliance of respiratory system was $\leq$30 cm H_2O,[17] since these two conditions preclude using the respiratory variation of stroke volume to assess fluid responsiveness. Patients' lungs were ventilated with an Evita 4 (Dräger Medical Systems, Telford, PA, USA) in the volume-controlled mode. Tidal volume was not changed for the purpose of the study. All patients received sedation.

Assessment of the haemodynamic status

All patients had an internal jugular vein catheter and a thermistor-tipped arterial catheter (PV2024 Pulsion Medical Systems, Munich, Germany) in the femoral artery connected to the $PiCCO_2$ device (Pulsion Medical Systems). This device estimates global end-diastolic volume indexed for body surface and cardiac index by transpulmonary thermodilution. For this purpose, three cold boluses (15 ml saline at 6°C) were injected in the internal vein catheter. The average of three values was taken into account.[18] The $PiCCO_2$ device also measures PPV and SVV. Systemic vascular resistance index was calculated as the ratio of mean arterial pressure over cardiac index. A pulse oximeter probe (LNOPw Adt, Masimo Corp., Irvine, CA, USA) was placed on a finger of one hand and connected to a Masimo Radical-7 device (Masimo Corp.). This device measures a perfusion index, which is the ratio of the infrared pulsatile signal over the infrared non-pulsatile signal expressed as a percentage. PVI is calculated as the difference between maximal and minimal perfusion index over the maximal value.[8] The perfusion index is an indicator of the amplitude of the PVI signal. If the plethysmographic signal and PVI signal were not obtained from a finger, another finger was used until a signal could be obtained. If no signal could be obtained from any finger, efforts were made for rewarming the hand before all fingers were tested again. If the Masimo Radical-7 device did not eventually display any plethysmographic signal and PVI values, it was recorded that PVI 'was not obtainable'.

Study design

At baseline, we recorded heart rate, PPV, SVV, and PVI, and transpulmonary cardiac index was estimated by thermodilution. Immediately after, volume expansion was performed by infusing saline 500 ml over 30 min.[19] At the end of volume expansion, we again recorded heart rate, PPV, SVV, PVI, and transpulmonary thermodilution cardiac index.

Statistical analysis

Data normality was tested by the Kolmogorov–Smirnov test and are expressed as mean (SD) or as median (inter-quartile range), as appropriate. Data before and after fluid challenge were compared using a paired Student's *t*-test. The comparison of data between different groups of patients was performed using a two-sample Student's *t*-test or a