Cephalic Versus Digital Plethysmographic Variability Index Measurement: A Comparative Pilot Study in Cardiac Surgery Patients

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Objectives: **Noninvasive measurement of digital plethysmographic variability index ($PVI_{digital}$) has been proposed to predict fluid responsiveness, with conflicting results. The authors tested the hypothesis that cephalic sites of PVI measurement (namely PVI_{ear} and $PVI_{forehead}$) could be more discriminant than $PVI_{digital}$ to predict fluid responsiveness after cardiac surgery.**

Design: **A prospective observational study.**

Setting: **A cardiac surgical intensive care unit of a university hospital.**

Participants: **Fifty adult patients.**

Interventions: **Investigation before and after fluid challenge.**

Measurement and Main Results: **Patients were prospectively included within the first 6-hour postoperative period and investigated before and after fluid challenge. A positive response to fluid challenge was defined as a 15% increase in cardiac index. $PVI_{digital}$, PVI_{ear}, $PVI_{forehead}$, and invasive arterial pulse-pressure variation (PPV) measurements were recorded simultaneously, and receiver operating characteristic (ROC) curves were built. Forty-one (82%) patients were responders and 9 (18%) patients were nonresponders to fluid challenge. ROC_{AUC} were 0.74 (95% confidence interval [95% CI]: 0.60-0.86), 0.81 (95% CI: 0.68-0.91), 0.88 (95% CI: 0.75-0.95) and 0.87 (95% CI: 0.75-0.95) for $PVI_{digital}$, PVI_{ear}, $PVI_{forehead}$, and PPV, respectively. Significant differences were observed between $PVI_{forehead}$ and $PVI_{digital}$ (absolute difference in ROC_{AUC} = 0.134 [95% CI: 0.003-0.265], p = 0.045) and between PPV and $PVI_{digital}$ (absolute difference in ROC_{AUC} = 0.129 [95% CI: 0.011-0.247], p = 0.033). The percentage of patients within the inconclusive class of response was 46%, 70%, 44%, and 26% for $PVI_{digital}$, PVI_{ear}, $PVI_{forehead}$, and PPV, respectively.**

Conclusions: **$PVI_{forehead}$ was more discriminant than $PVI_{digital}$ and could be a valuable alternative to arterial PPV in predicting fluid responsiveness.**

KEY WORDS: fluid challenge, plethysmographic variability index, plethysmography, fluid responsiveness, pulse-pressure variation

THE PLETHYSMOGRAPHIC VARIABILITY INDEX (PVI) (Masimo Corp., Irvine, CA) is a noninvasive and continuous dynamic parameter resulting from the cardiopulmonary interaction in mechanically ventilated patients, which has been developed as an alternative to the invasive arterial pulse-pressure variation (PPV).[1] Initial proof-of-concept studies conducted in the operating room reported encouraging results.[2,3] Recently, an early goal-directed therapy strategy showed the use of PVI decreased perioperative blood lactate levels, suggesting a potential clinical method to reduce postoperative morbidity in the surgical setting.[4] More contrasting results have been reported in the settings of critical care and cardiac surgery.[5–7] In those patients, a high vasomotor tone and the frequent infusion of norepinephrine have been found to markedly alter the accuracy of PVI measurement at the digital site,[8–10] prompting the search for alternative anatomic sites to assess the effects of mechanical ventilation on the pulse oximeter waveform.[11] Cephalic sites (namely the ear and the forehead) could be more appropriate in critically ill and/or high-risk surgical patients. To date, a single study conducted in anesthetized patients suggested cephalic sites could be of clinical value for measurement of PVI.[12] Thus, additional phase-II validation studies conducted in different subgroups of high-risk patients clearly are needed to address this lack of data before recommending a wider use of cephalic sites at the bedside.

Therefore, the present observational study aimed to assess the clinical utility of both forehead and ear PVI measurements when compared with digital PVI to predict fluid responsiveness after cardiac surgery. The authors tested the hypothesis that $PVI_{forehead}$ and/or PVI_{ear} could be more effective than $PVI_{digital}$ in predicting fluid responsiveness in this subgroup of high-risk patients.

MATERIALS AND METHODS

All consecutive adult patients admitted to the surgical intensive care unit (ICU) after conventional cardiac surgery (coronary artery bypass grafting, aortic and/or mitral valve replacement or repair, and combined cardiac surgery) with cardiopulmonary bypass (CPB) and requiring cardiac output monitoring using transpulmonary thermodilution from May 2012 to July 2013 were screened for the study. Institutional approval was obtained from the local ethics committee. Because data were collected during routine care that conformed to standard procedures currently used in this institution, authorization was granted to waive written informed consent. Verbal consent was obtained, however, from all study participants before surgery. They were enrolled if they received a fluid challenge during the initial postoperative 6-hour period in the ICU according to the decision of the attending anesthesiologist. This decision followed institutional standards and was based on the presence of at least one of the postoperative criteria: Cardiac index $\leq$2.2 L/minute/m^2, systolic arterial pressure $<$90 mmHg or norepinephrine requirement, urinary output $<$0.5 mL/kg/hour for at least 2 hours, and skin mottling. Patients with echocardiographic evidence of right ventricular dysfunction, abnormalities in postoperative cardiac rhythm (paced rhythm, extra-systoles), ventilatory abnormalities (spontaneous ventilation, tidal volume $<$7 mL/kg, thoracic compliance $<$30 mL cm/H_2O), a heart rate/respiratory rate ratio $<$3.6, and with a clinical context of abdominal hypertension

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were not included in the study.[7,13–17] Patients with missing data were excluded from the study.

General anesthesia and postoperative management followed institutional standards. Intraoperative and postoperative fluid management were left to the discretion of the attending anesthesiologist (not involved in the study protocol). All patients were admitted postoperatively to the ICU. At the time of the study, they were intubated, ventilated (volume-controlled regimen), and sedated with propofol and remifentanil to maintain the Ramsay score above 5. All patients underwent a Doppler echocardiographic examination upon arrival in the ICU. The examination was performed using a standard transthoracic probe (S5-1, Philips Healthcare, Bothell, WA) and a dedicated unit (CX Cart 50, Philips Healthcare, Bothell, WA) by an echocardiographic expert (A.P.) who classified patients according to the presence or the absence of right ventricular dysfunction (RVD).[18] For each eligible patient, a femoral 5F thermistor-tipped arterial catheter (Pulsiocath Thermodilution Catheter PV2015L20N [Pulsion France sarl, La Montagne, France]) and a jugular central venous catheter were inserted in the operating room after induction of general anesthesia. The Pulsiocath thermodilution catheter was connected to a stand-alone PiCCO2 computer PC8500 version 3.1 (Pulsion Medical Systems, Munich, Germany). All pressure monitors were zeroed at the mid-axillary line. Cardiac index (CI) and indexed global end-diastolic volume (GEDVI) were performed by a triplicate 15-mL ice-cold normal saline injection through the central venous catheter at arrival in the ICU and before and after fluid challenge.[19] Three pulse oximeter probes were connected at three different anatomic sites: On the second/third finger of the nondominant hand via a finger clip (LNOP DC-12, Masimo Corp., Irvine, CA); on the right ear lobe via an ear clip (LNOP TC-I, Masimo Corp., Irvine, CA); and on the forehead just above the eyebrow via a headband (LNOP TF-I, Masimo Corp., Irvine, CA). Each probe was connected to a Masimo SET Radical-7 Pulse Co-oximeter (Masimo Corp., Irvine, CA) using the PVI Software version 7.6.0.1.

Arterial PPV induced by positive pressure ventilation was derived from the femoral arterial catheter and automatically calculated by the $PiCCO_2$ device as $PPV = ([PP_{max} - PP_{min}]/[(PP_{max} + PP_{min})/2]) \times 100$. PPV was averaged over a floating period of 30 seconds.

PVI was a measure of the dynamic changes in perfusion index (PI) during mechanical ventilation. A constant amount of light (direct current [DC]) from the pulse oximeter is absorbed by tissues and nonpulsatile blood flow. A variable amount of light (alternating current [AC]) is absorbed by the pulsating arterial flow. To calculate the PI, the infrared pulsatile signal is indexed against the nonpulsatile infrared signal and expressed as a percentage ($PI = [AC/DC] \times 100$). PVI then was calculated as $PVI = ([PI_{max} - PI_{min}]/PI_{max}) \times 100$.[3] PVI was displayed continuously and averaged over a 2-minute period. Measurements began after stabilization of both PVI and PPV values (ie, when values remained unchanged or varied for a maximum of 1% over a 5–minute period.

The patient was enrolled within the first 6 postoperative hours by the investigator (M.O.F.) after the decision by the attending anesthesiologist to administer a fluid challenge (500 mL of hydroxyethyl starch 130/0.4, 6% over 15 minutes). Two consecutive sets of measurements of cardiac index were recorded for each patient: Immediately before and 10 minutes after the fluid challenge. CI was averaged on 3 consecutive bolus thermodilution measurements performed at any time during the respiratory cycle. Patients who experienced an increase in CI of at least 15% after fluid challenge were classified as responders while others were classified as non-responders.[19] At each step, all hemodynamic parameters (including PPV and PVI) were recorded simultaneously by the investigator. During the short observation period, ventilator settings, sedation, and vasoactive drugs remained unchanged.

The number of patients was fixed empirically at 50. The primary endpoint was the comparative discriminations of $PVI_{forehead}$, PVI_{ear}, and $PVI_{digital}$ in predicting fluid responsiveness. Data are expressed as mean (SD) or median (25th-75th percentile) for non-normally distributed variables (Kolmogorov-Smirnov test) or number and percentage, as appropriate. Continuous variables were analyzed with the unpaired Mann-Whitney U test. Categoric variables were analyzed with the Fisher exact test or the χ^2 test, as appropriate. Changes in hemodynamic parameters after fluid challenge were compared using the paired Wilcoxon test. Relationships between dynamic indices (PPV, $PVI_{digital}$, PVI_{ear}, and $PVI_{forehead}$) and changes in CI (ΔCI) were determined by linear regression. To assess the discrimination of PPV, $PVI_{digital}$, PVI_{ear}, and $PVI_{forehead}$ in predicting fluid responsiveness, the empiric receiver operating characteristic (ROC) curves were determined and the areas under the ROC curves (ROC_{AUC}) and their 95% confidence intervals (95% CI) were calculated. Comparison of ROC_{AUC} was performed using a nonparametric paired technique, as previously described.[20] The ROC curves also were used to determine the best thresholds for PPV, $PVI_{digital}$, PVI_{ear}, and $PVI_{forehead}$ in predicting fluid responsiveness. The best threshold was the one that maximized the Youden index.[21] Assessment of the diagnostic accuracy of an increased PPV, $PVI_{digital}$, PVI_{ear}, and $PVI_{forehead}$ above the threshold value in predicting fluid responsiveness was performed by calculating the sensitivity, specificity, positive and negative predictive values, and their 95% confidence intervals. Finally, the ROC curves were used to describe the clinical utility of PPV, $PVI_{digital}$, PVI_{ear}, and $PVI_{forehead}$ by defining 3 classes of response: Negative, inconclusive, and positive. Inconclusive responses were defined by values with sensitivity and specificity lower than 90% (tolerance of 10%).[22]

A p value of less than 0.05 was considered to be statistically significant, and all p values were two-tailed. Statistical analyses were performed using MedCalc Software bvba version 12.4.0. (Mariakerke, Belgium).

RESULTS

One hundred thirty consecutive adult patients were screened from May 2012 to July 2013. Among them, 85 received a fluid challenge and subsequently were enrolled. Thirty-one patients were not included and 4 patients were excluded from the study. Finally, 50 patients had a full set of data and were analyzed. The complete flow chart of the study is depicted in Fig 1. The perioperative characteristics for the remaining 50 patients are reported in Table 1. Forty-one (82%) patients were classified as responders according to the primary definition and 9 (18%) patients were nonresponders. Responders more often were treated chronically with statins and more often needed postoperative dobutamine than nonresponders (Table 1).

Hemodynamic data before and after fluid challenge in responders and nonresponders are presented in Table 2. The increase in CI after fluid challenge was significantly higher in responders than in nonresponders: 31% ± 14% [95% CI: 26-35] versus 8% ± 4% [95% CI: 5-11], $p < 0.001$. At baseline, PPV, $PVI_{digital}$, PVI_{ear}, and $PVI_{forehead}$ were significantly higher in responders than in nonresponders and systematically decreased in responders after fluid challenge (Table 2).

The discriminations, the threshold values, the diagnostic performances, and the clinical utility of $PVI_{digital}$, PVI_{ear}, $PVI_{forehead}$, and PPV in predicting fluid responsiveness are reported in Table 3. Comparisons of ROC curves are depicted in Fig 2. Significant differences were observed between PPV and $PVI_{digital}$ (absolute difference in $ROC_{AUC} = 0.129$ [95%