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### Comparison between respiratory changes in the inferior vena cava diameter and pulse pressure variation to predict fluid responsiveness in postoperative patients



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#### ARTICLE INFO

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#### ABSTRACT

*Purpose:* The objective of our study was to assess the reliability of the distensibility index of the inferior vena cava (dIVC) as a predictor of fluid responsiveness in postoperative, mechanically ventilated patients and compare its accuracy with that of the pulse pressure variation (PPV) measurement.

*Materials and methods*: We included postoperative mechanically ventilated and sedated patients who underwent volume expansion with 500 mL of crystalloids over 15 minutes. A response to fluid infusion was defined as a 15% increase in the left ventricular outflow tract velocity time integral according to transthoracic echocardiography. The inferior vena cava diameters were recorded by a subcostal view using the M-mode and the PPV by automatic calculation. The receiver operating characteristic (ROC) curves were generated for the baseline dIVC and PPV. *Results*: Twenty patients were included. The area under the ROC curve for dIVC was 0.84 (95% confidence interval, 0.63-1.0), and the best cutoff value was 16% (sensitivity, 67%; specificity, 100%). The area under the ROC curve for Was 0.92 (95% confidence interval, 0.76-1.0), and the best cutoff was 12.4% (sensitivity, 89%; specificity, 100%). A noninferiority test showed that dIVC cannot replace PPV to predict fluid responsiveness (P = .28). *Conclusion*: The individual PPV discriminative properties for predicting fluid responsiveness in postoperative patients seemed superior to those of dIVC.

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#### 1. Introduction

The early recognition and treatment of tissue hypoperfusion in the perioperative period are essential for preventing complications [1–4]. The firstline intervention for the restoration of tissue perfusion is intravascular fluid administration [5]. Ideally, volume expansion should only be indicated for patients in whom the cardiac output is expected to increase. The correct identification of who would benefit from fluid administration allows for hemodynamic optimization and avoids ineffective, or even deleterious, volume expansion [6]. Fluid overload in surgical patients has been associated with increased complications [7–10].

Perioperative patients are usually sedated and under controlled mechanical ventilation. In these conditions, the pulse pressure variation (PPV) is recognized as an accurate predictor of fluid responsiveness [11,12]. Several other minimally invasive methods have been used to determine whether a patient is fluid responsive, including transthoracic echocardiography [13,14]. The changes in the inferior vena cava (IVC)

\* Corresponding author. *E-mail address:* flaviogrf@yahoo.com.br (F.G.R. Freitas). diameter during mechanical ventilation were previously described as a reliable, noninvasive predictor of fluid responsiveness in septic patients [15,16]. However, the accuracy of the distensibility index of the inferior vena cava (dIVC) has been challenged in some recent studies [17,18].

The objective of our study was to assess the reliability of dIVC as a predictor of fluid responsiveness in postoperative, mechanically ventilated patients and then compare it with simultaneous PPV recording.

#### 2. Materials and methods

This study was performed in a 35-bed mixed intensive care unit (ICU) at a Brazilian teaching hospital. The local ethical and research committee (Federal University of São Paulo) approved the protocol under the number 186.785, and written informed consent was obtained from all patients or their relatives.

#### 2.1. Patients

The inclusion criteria were as follows: age older than 18 years, immediate postoperative period (within the first 24 hours), continuous sedation (Ramsay scale 5-6) and mechanical ventilation, instrumentation with indwelling arterial catheter and central venous catheter through the internal jugular vein or subclavian vein, and a clinical requirement for a fluid challenge according to the attending physician. We excluded patients with arrhythmias, spontaneous breathing activity, active bleeding, intraabdominal hypertension, pregnancy, acute cor pulmonale, and surgery around the inferior vena cava. *Acute cor pulmonale* was defined as the association of right ventricular dilatation with a paradoxical septal motion at end-systole [19]. We also excluded those with an inadequate echocardiographic window and those who needed changes in the doses of vasoactive or sedative drugs during data collection. The baseline characteristics and severity scores were collected at the patient's inclusion in the study.

#### 2.2. Study protocol

The selected patients were mechanically ventilated (Vela; Viasys, Palm Springs, CA) using the volume-controlled mode; the tidal volume was adjusted to 8 mL/kg (based on the patient's predicted body weight), with no changes in the other ventilatory parameters. Throughout the study period, the ventilator settings and vasoactive and sedative drugs were held constant. Measurements were performed before and after volume expansion, using 500 mL of crystalloid infused over 15 minutes. We use, as the reference standard, the change in the left ventricular outflow tract velocity time integral (VTI), measured by Doppler echocardiography (SonoAce R7 device; Samsung Medison, Seoul, Korea), equipped with a phased array transthoracic probe (2-4 MHz). "Responders" had a VTI increase of at least 15%, whereas "non-responders" had a VTI increase of less than 15%.

#### 2.3. Hemodynamic measurements

A trained intensivist (OHO) with basic competence on critical care echocardiography performed all echocardiographic assessments [20]. Images were recorded for later off-line measurements. The IVC was examined through a subcostal window in the longitudinal section and measured in M-mode just upstream of the origin of the suprahepatic vein. The dIVC was calculated throughout the same respiratory cycle, as (maximum diameter on inspiration — minimum diameter on expiration)/minimum diameter on expiration and converted to a percentage [15]. The VTI was measured with a pulsed Doppler through the apical 5-chamber window at the end of expiration. Three measurements were obtained and averaged for the dIVC and VTI.

The PPV was measured with a multiparameter bedside monitor (DX 2020; Dixtal, São Paulo, Brazil) using an automatic calculation [21]. We also registered other hemodynamic variables, such as the arterial pressure, heart rate, and central venous pressure. All pressures were determined at the end-expiration with the zero reference level set at fourth intercostal space along the midaxillary line.

#### 2.4. Statistical analysis

We hypothesized that the discriminating power of the PPV and dIVC would be significantly different, with an estimated area under the receiver operator characteristic (ROC) curve of 0.95 and 0.70, respectively, and a rank correlation between them of 0.75. Using the 2-sided test with a 5% level of significance and an 80% power, the calculated sample size was 20 patients.

Data are expressed as numbers (%), means  $\pm$  SD, or medians and interquartile ranges (25th to 75th percentile). The distribution of continuous variables was assessed by the Shapiro-Wilk test. The effects of the intravascular volume expansion on hemodynamic variables were assessed using a Wilcoxon rank sum test or paired *t* test, as appropriate. The linear correlation between the baseline PPV, baseline dIVC, and changes in VTI were tested using the Spearman correlation test.

We constructed ROC curves to evaluate the capacity of the PPV and dIVC to predict fluid responsiveness. The best cutoff values were also calculated (Youden method). We used DeLong test to compare the areas under the ROC curves. We also tested if the area under ROC curve for dIVC was noninferior to the area under ROC curve for PPV to predict fluid responsiveness [22], considering a margin of noninferiority of 15%.

We used SPSS software version 17.0 (SPSS, Inc, Chicago, IL), Stata software version 12.0 (StataCorp, College Station, TX), and MedCalc software 14.12.0 (MedCalc Software bvba, Ostend, Belgium) for Windows. The results with P values less than .05 were considered significant.

#### 3. Results

From February 2013 to September 2014, 30 patients were eligible for our study, and 20 of these were included. We excluded 3 patients because of poor acoustic windows, and 1 patient submitted to surgery around the IVC. The other reasons for exclusion were changes in vasoactive drugs (n = 3), arrhythmia (n = 2), and declined consent (n = 1). Most patients (65%) were admitted to ICU after neurosurgical procedures because this type of surgery very often requires sedation in the immediate postoperative period. Baseline characteristics are shown in Table 1.

The main reasons for fluid infusion were hyperlactatemia (40%), hypotension (15%), attempt to reduce vasopressors (15%), and oliguria (15%). The volume expansion impacts in the hemodynamic variables are available in Table 2. None of the patients who underwent abdominal surgery had a high intraabdominal pressure. Nine patients had an increase in the VTI of 15% or more after volume expansion. There was a strong correlation between the VTI changes and baseline PPV (r = 0.70; P < .001) and a moderate correlation between the VTI changes and baseline dIVC (r = 0.66; P = .001).

The area under the ROC curve for PPV was  $0.92 \pm 0.08$  (0.76-1.0), and the best cutoff was 12.4% (sensitivity, 88.89%; specificity, 100%). The area under the ROC curve for dIVC was  $0.84 \pm 0.10$  (0.63-1.0), and the best cutoff was 16% (sensitivity, 66.67%; specificity, 100%; Fig. 1). There was no significant difference between the areas under ROC curves (P = .49). Of note, the area under the ROC curve for the central venous pressure was  $0.65 \pm 0.13$  (0.40-0.84), and the best cutoff was 10 mm Hg (sensitivity, 54.55%; specificity, 77.78%). The difference between the areas under ROC curves was 0.081 (confidence interval)

| Ta | ble 1 |  |
|----|-------|--|
| -  |       |  |

| Baseline chai | racteristics |
|---------------|--------------|
|---------------|--------------|

| Variable                                      | n                |
|---|------------------|
| Age (y)                                       | 50 ± 17.6        |
| Male sex                                      | 8 (40)           |
| Types of surgery                              |                  |
| Neurosurgery                                  | 13 (65)          |
| Major abdominal procedure                     | 3 (15)           |
| Others  | 4 (20)           |
| Parameters used to guide fluid administration |                  |
| Hyperlactatemia                               | 8 (40)           |
| Oliguria                                      | 3 (15)           |
| Hypotension                                   | 3 (15)           |
| Use of vasopressors                           | 3 (15)           |
| Others  | 3 (15)           |
| PEEP (cm $H_2O$ )                             | 5 (5-6)          |
| Tidal volume (mL/kg)                          | 8.0 (8.0-8.1)    |
| Static compliance (mL/cm H <sub>2</sub> O)    | 46.2 (39.2-56.1) |
| Norepinephrine use                            | 11 (55)          |
| Norepinephrine dose ( $\mu$ g/kg/min)         | 0.22 (0.08-0.24) |
| SOFA  | $6 \pm 3.2$      |
| SAPS 3  | $45.6 \pm 11.1$  |
| Charlson Index                                | 1 (0-2)          |

PEEP indicates positive end-expiratory pressure; SOFA, Sequential Organ Failure Assessment; SAPS 3, Simplified Acute Physiology Score 3. The results are expressed as the median (25%-75%) or mean  $\pm$  SD or number (%).

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