Interchangeability between Respiratory Variations of Subclavian Vein and Pulse Pressure Variation in Ventilated Patients in the Operating Room

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Abstract

Objective: For mechanically ventilated patients, the best predictors of fluid responsiveness are dynamic parameters. Many methods that reflect cardiopulmonary interactions have been proposed to evaluate the preload dependency. In this study, we describe the interchangeability between respiratory variations of the subclavian (ΔSCV) vein and pulse pressure variation (PPV) in sedated and mechanically ventilated patients benefiting from kidney transplantation.

Methods: The ΔSCV via infraclavicular transthoracic echocardiography and PPV measurements were recorded simultaneously by a single operator. The Bland–Altman method assessed the interchangeability between ΔSCV and PPV.

Results: A total of 27 patients were prospectively included in the study. The Bland–Altman analysis showed a bias of +1.6% for ΔSCV measurements vs. PPV. The limit of agreements was, respectively, −4% and 8%. The agreement between PPV >13% and ΔSCV >13% was 100%, and the agreement between PPV <9% and ΔSCV <9% was 58%. No misclassification (PPV <9% [0%] and PPV >13% [0%]) was observed.

Conclusion: ΔSCV and PPV are interchangeable when assessing preload dependency in mechanically ventilated patients benefiting from kidney transplantation. ΔSCV appears to be a suitable tool because it is non-invasive, simple, easy and almost always available.

Keywords: Echography, interchangeability, pulse pressure variation, subclavian vena

Introduction

In the operating room (OR), haemodynamic optimisation is a daily consideration of physicians who strive to improve the outcome. It is one of the key elements of perioperative goal-directed therapy strategies and enhanced recovery after surgery protocols (1). Haemodynamic optimisation is associated with a lower mortality rate for acute severe medical and/or surgical patients (2-5).

To improve haemodynamic, preload dependency, assessment is one of the utmost important parameters to choose between fluid expansion and norepinephrine infusion. Previous studies reported that fluid responsiveness dynamic tools overperform clinical signs or static predictors to assess preload dependency (6-9). Yet, in the OR and in the emergency department, only a few patients are managed using an invasive haemodynamic monitoring. Otherwise, in the OR, it has been reported that unnoticed hypotension events are frequent and result in an increase of post-operative cardiac events such as myocardial infarction (10). Therefore, the use of invasive dynamic tools to assess the preload dependency tends to be limited to a small portion of the perioperative population. Nonetheless, most patients would likely benefit from the fluid loading optimisation (11) to avoid unnoticed cardiovascular events and their effects (10). A non-invasive evaluation of the preload dependency may reduce discrepancies between a time- and cost-consuming approach and its benefits.
In this study, we aimed to conduct and evaluate a non-invasive, easy-to-perform assessment of the variability of the subclavian vein diameter during mechanical ventilation and to examine its interchangeability with PPV in patients benefiting from kidney transplantation.

Methods

Study population
From December 2015 to November 2017, consecutive adult patients who were mechanically ventilated benefiting from kidney transplantation in the OR were prospectively included in the study.

Patients with cardiac arrhythmia, tachycardia >120 beats per minute, or a tidal volume <8 mL kg\(^{-1}\) were not included. Demographical characteristics (age, gender, size, body weight, and ideal body weight were calculated from the Lorentz formula), cardiovascular disability, haemodynamic measurements (systolic, diastolic, mean blood pressure, and heart rate), vasopressor support and ventilatory settings (respiratory rate, inspired fraction of oxygen, tidal volume) and airway pressures (peak and plateau) were recorded.

The institutional review board, Comité de Protection des Personnes Paris-Ile de France 2 (Number ID-RCB: 2012-A01289-34), approved the study with a waived consent form.

Assessment methods
All measurements were obtained during the stable period, with no change in the anaesthetic protocol or ventilator settings. All patients were deeply sedated (Ramsay score of 6) prior to receiving a muscle relaxant (atracurium) during the protocol. Invasive blood pressure monitoring was performed with a 3- or 5-French catheter radial or femoral (Vigileo, Edwards Lifesciences, Irvine, CA) allowing the continuous PPV measurement. The pressure transducer was levelled at the midaxillary line and kept on the atrial level during measurement. A single operator performed simultaneously PPV and sonography measurements using a linear ultrasound probe. ∆SCV measurements were made on both sides unless a central venous line was inserted in the SCV.

The medial part of the SCV was evaluated via infraclavicular longitudinal approach (Figure 1) to avoid manual compression by the probe. Bi-dimensional echography (2D), time movement echography (TM), and colour Doppler echography were successively used to confirm the absence of pulsatility of the subclavian vena vs the artery (Figure 2). The diameter of SCV was measured at the end of the expiration (SCV max diameter) and insufflation (SCV min diameter). ∆SCV is equivalent to the distensibility index (12) and corresponds...
to the variation between the maximum SCV and minimum SCV diameter (Figure 3) as follows:

\[ \Delta SCV = \frac{SCV \text{ max diameter} - SCV \text{ min diameter}}{SCV \text{ max diameter}} \]

The result was expressed in the percentage to get rid of the absolute value variations depending on the size and ethnicity (13).

**Predefinition of the acceptable limit of agreement**

We pre-specified that a difference of up to 4% between PPV and ΔSCV would be acceptable for a clinically acceptable conclusion. The choice of the previous value was based on the ‘grey zone’ concept described for PPV values (14, 15).

**Statistical analysis**

This was a pilot, prospective and observational study. No prior power calculation and no sample size were performed. The correlation between PPV and ΔSCV was based on the Pearson correlation coefficient (r²). Because correlation does not mean interchangeability, the Bland–Altman graphical agreement method (16) was used to estimate the interchangeability between PPV and ΔSCV. We compared the bias-corrected evaluation of the ΔSCV (exact ΔSCV±bias) with PPV. The result of bias was expressed using the mean±limits of agreement (LOA).

The interchangeability between ΔSCV and PPV was evaluated by clinical decision-making rules used in practice (14, 17): PPV was <9%, i.e., ‘non-responders,’ PPV was >13%, i.e., ‘responders’ fluid expansion and when 9%<PPV<13%, i.e. ‘inconclusive’ (14).

A statistical analysis was performed using the R software version 3.4.2 (www.R-project.org; the R Foundation for Statistical Computing, Vienna, Austria).

**Results**

A total of 27 patients who benefited from kidney transplantation were included in the study.

Demographic characteristics, cardiovascular and haemodynamic measurements, vasopressor support and ventilator settings are summarised in Table 1.

No patient had cardiac arrhythmia. One patient had a subclavian central venous line.

A total of 162 measurements were performed and analysed. The mean overall PPV was 11±6%, and the mean overall ΔSCV was 9±6%. We found a good correlation (r²=0.75, p<10⁻⁴) between ΔSCV and PPV. The graphical correlation between PPV and ΔSCV is presented in Figure 4.

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**Table 1. Demographic, respiratory and haemodynamic characteristics**

| Demographic characteristics          | 56±15 | 75±11 | 66±5 | 172±6 |
|--------------------------------------|-------|-------|------|-------|
| Age (year)                           |       |       |      |       |
| Body weight (kg)                     |       |       |      |       |
| Ideal body weight (kg)               |       |       |      |       |
| Size (cm)                            |       |       |      |       |
| Respiratory parameters               |       |       |      |       |
| Tidal volume indexed on body weight (mL kg⁻¹) | 7±1   |       |      |       |
| Respiratory rate (min)               | 12±1  |       |      |       |
| Oxygen fraction inspired (%)         | 51±19 |       |      |       |
| Peak pressure (cmH₂O)                | 33±10 |       |      |       |
| Plateau pressure (cmH₂O)             | 23±4  |       |      |       |
| End tidal CO₂ (mmHg)                | 32±5  |       |      |       |
| Haemodynamic parameters              |       |       |      |       |
| Systolic blood pressure (mmHg)       | 98±17 |       |      |       |
| Diastolic blood pressure (mmHg)      | 54±12 |       |      |       |
| Mean blood pressure (mmHg)           | 69±12 |       |      |       |
| Heart rate (beats per minute)        | 86±17 |       |      |       |
| Pulse pressure variation (%)         | 1126  |       |      |       |
| ΔSCV (%)                             | 9±6   |       |      |       |

ΔSCV: respiratory variation of subclavian vein

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**Figure 4. Graphical evaluation of correlation between PPV and ΔSCV measurements**
According to the Bland–Altman graphical representation (Figure 5), the average bias value was 1.6 %, with a minimal LOA extending from −4% to a maximal LOA of 8%. The agreement between PPV and ∆SCV adjusted (ΔSCV+bias) is summarised in Table 2. Using the practice clinical decision-making rules for PPV, we observed the following:

- No misclassification between PPV and ΔSCV: with a PPV < 9 %, ΔSCV was never > 13% (n=0), and with a PPV > 13 %, ΔSCV was never < 9% (n=0).

- A good agreement between PPV and ΔSCV: with a PPV > 13 %, ΔSCV was in accordance in 100% (n=32) and with a PPV < 13%, ΔSCV was in accordance in 58% (n=37) measurements.

Fifty-three percent (n=35) of ΔSCV measurements were in the ’grey zone.’

**Discussion**

In this study, we observed the interchangeability between ΔSCV with the PPV measurements for mechanically ventilated patients benefiting from kidney transplantation. The interchangeability was characterised by a lack of damaging misclassification. The thresholds used for PPV are interchangeable with those used for ΔSCV.

Haemodynamic optimisation of recovery following surgery and patient’s outcome has been recognized (1, 18) in anaesthesia, which makes the haemodynamic optimisation assessment a daily issue in the OR. Several dynamic parameters, invasive and non-invasive, have been described to assess the preload dependency in order to choose between the fluid expansion and norepinephrine infusion. Deleterious effects of the lack or undue fluid volume expansion has been established, and for this reason, a personalised clinical decision making to optimise haemodynamics is needed. For this purpose, the use of tools should be quick and safe. Echographic parameters, based on inferior and superior vena cava diameter variations, appear to overperform, less invasive and faster than the invasive pulse pressure assessment.

The medial part of the SCV was chosen because SCV is submitted to the same pressure variations regimen as the superior vena cava induced by mechanical ventilation, so that ΔSCV reflects cardiopulmonary interactions (14, 19). During insufflation, due to an increase in the airway pressure, the diameter of intrathoracic venae decreases, whereas during expiration, it increases (19, 20). The variations are especially marked in preload dependent situations, that is, on the slope of the Franck–Starling curve (6). To correctly measure the diameter of the SCV, we choose the infraclavicular vs supraclavicular approach to avoid the SCV compression by the probe and a false evaluation, which were observed for the internal jugular vena (21, 22).

**Limitations and strengths**

This was a mono-centric study with a small sample size. We did not examine the accuracy of ΔSCV to evaluate the cardiac output, but only compared the interchangeability with a validated method evaluating preload dependency. Otherwise, the study was not designed to determine thresholds for ΔSCV.
for preload dependency evaluation. As described with PPV, a grey zone exists with ∆SCV as well (14, 15); thus, we must keep in mind that the ∆SCV approach shows the same limitations. Conversely, the bias value was acceptable for PPV values. The low bias value with a restricted LOA range allows assuming that these thresholds should be pretty close to PPV thresholds.

The ∆SCV evaluation allows a quick, easy and non-invasive evaluation of preload dependency, making this tool very interesting in the OR for daily clinical practice. This non-invasive method does not require any arterial catheterisation. The approach is useful during abdominal surgery or elevated intra-abdominal pressure (23), where the inferior cava vena is not accessible. Furthermore, ∆SCV evaluation does not require a long learning phase as for trans-oesophageal echography. Implications for anaesthesia and critical care research.

Because it is interchangeable with PPV, ∆SCV would probably allow reducing the post-operative incidence of cardiovascular events by a better and faster intraoperative haemodynamic management available for all patients. Use of a cheap, non-invasive, easy and quickly available tool interchangeable with PPV would probably be more interesting, especially for non-cardiac patients where invasive monitoring is not required (10).

**Conclusion**

In this study, we found a reliable and adequate interchangeability between PPV and ∆SCV. ∆SCV is an attractive, safe, non-invasive, easy, fast and almost always available tool.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Paris-Ile de France 2 (Number ID-RCB: 2012-A01289-34).

**Informed Consent:** Written informed consent was obtained from patients and or patients’ parents who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – R.J.; Supervision – R.J., B.V.; Data Collection and/or Processing – V.N., B.P.L., R.J.; Analysis and/or Interpretation – V.N., B.P.L., R.J.; Literature Search – R.J., B.V.; Writing Manuscript – V.N., B.P.L., R.J., B.V.; Critical Review – V.N., B.P.L., R.J., B.V.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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