Comparison of different techniques of central venous pressure measurement in mechanically ventilated critically ill patients

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Abstract

Background. Several techniques exist for measuring central venous pressure (CVP) but little information is available about the accuracy of each method. The aim of this study was to compare different methods of CVP measurements in mechanically ventilated patients.

Methods. CVP was measured in mechanically ventilated patients without spontaneous breathing using four different techniques: 1) end expiratory CVP measurement at the base of the “c” wave (CVP_MEASURED), chosen as the reference method; 2) CVP measurement from the monitor averaging CVP over the cardiac and respiratory cycles (CVP_MONITOR); 3) CVP measurement after a transient withdrawing of mechanical ventilation (CVP_Nadir); 4) CVP measurement corrected for the transmitted respiratory pressure induced by intrinsic PEEP (calculated CVP: CVP_CALCULATED). Bias, precision, limits of agreement, and proportions of outliers (difference > 2 mm Hg) were determined.

Results. Among 61 included patients, 103 CVP assessments were performed. CVP_MONITOR bias [-0.87 (1.06) mm Hg] was significantly different from those of CVP_CALCULATED [1.42 (1.07), P < 0.001 and CVP_Nadir (1.04 (1.29), P < 0.001]. The limits of agreement of CVP_MONITOR [-2.96 to 1.21 mm Hg] were not significantly different to those of CVP_Nadir (-1.49 to 3.57 mm Hg, P = 0.39) and CVP_CALCULATED (-0.68 to 3.53 mm Hg, P = 0.31). The proportion of outliers was not significantly different between CVP_MONITOR (n = 5, 5%) and CVP_Nadir (n = 9, 9%, P = 0.27) but was greater with CVP_CALCULATED (n = 16, 15%, P = 0.01).

Conclusions. In mechanically ventilated patients, CVP_MONITOR is a reliable method for assessing CVP_MEASURED. Taking into account transmitted respiratory pressures, CVP_CALCULATED had a higher proportion of outliers and precision than CVP_Nadir.

Key words: central venous pressure; measurement
Central venous pressure (CVP) measurement remains widely used in the intensive care unit (ICU), especially for guiding fluid management in patients with haemodynamic instability. As it represents the pressure in the right atrium and ventricle at the end of diastole, it is assumed that CVP reflects right ventricular preload and the backpressure to venous return. Because CVP depends on ventricular compliance and cardiopulmonary interactions, measurement technique is important: 1) CVP must be measured in comparison to an arbitrary reference level usually defined as the midpoint of the right atrium and commonly assessed at the mid thoracic position at the level of the fifth rib (Fig. 1); 2) for an optimal assessment of the right atrial pressure at the end of the diastole, CVP should be measured at the base of the “c” wave, which corresponds to the impact of isometric ventricular contraction on right atrial pressure and to the Q wave of the ECG (Fig. 1); 3) to reflect cardiac preload, CVP should be measured at end expiratory time (i.e. when the influence of intra-thoracic pressures surrounding cardiac cavity is minimal). However, even in these conditions, it might be argued that the CVP measured (CVP_MEASURED) at the end of the diastole, does not reflect the trans-mural pressure related to PEEP. This is of particular importance when high PEEP levels are applied or when intrinsic PEEP levels are created in patients with severe chronic obstructive pulmonary disease with pulmonary hyper-inflation. Under these conditions, as reported by Teboul and colleagues CVP could be measured after a transient airway disconnection, called CVP nadir (CVP_NADIR) in order to estimate transmural CVP. The measurement of CVP integrating the influence of the respiratory driving pressure (difference between plateau pressure and the intrinsic positive expiratory pressure (PPLAT – PEEP)) called CVP calculated, (CVP_CALCULATED) is another method to measure transmural CVP. Lastly, the mean reported by modern monitors, (called CVP_MONITOR), averaging CVP over several cardiac and respiratory cycles, could be considered as a reliable estimate of backpressure to venous return.

In daily practice, all these CVP measurements are associated with potential pitfalls, and no previous study has compared their respective accuracy. Therefore, assessing the systematic error associated with these different methods could be of particular interest. A high systematic bias with a narrow limit of agreement could be more useful for clinical decision-making than a small bias with a large limit of agreement. Therefore, the aim of the present study was to compare the bias, limit of agreement, and proportion of outliers of several CVP measurements (CVP_MONITOR, CVP_CALCULATED, and CVP_NADIR) to the reference technique CVP_MEASURED, in mechanically ventilated patients.

Methods
This prospective study was conducted from November 2013 to April 2014 in a 16-bed ICU of an academic hospital. Because this study was observational and did not change the daily practice, the Institutional Review Board of Nimes University Hospital approved the study and allowed a waiver of informed consent (IRB # 14/05.03). However, the patient next-of-kin was verbally informed and could refuse patient participation. Moreover, the patient, if awake, could opt-out of the study at any time during the study period.

Participants
We included mechanically ventilated patients without spontaneous breaths (recommended tidal volume = 6–8 ml kg⁻¹ ideal body weight, monitoring of plateau pressure <30 cm H₂O, respiratory rate in order to avoid respiratory acidosis with pH < 7.20, inspiratory/expiratory ratio = 1/2) without cardiac arrhythmias and without known or suspected tricuspid regurgitation and in whom a central venous catheter was inserted via subclavian or jugular internal vein approaches as part of their usual care. The tip of the central venous catheter was checked to be in superior vena cava or right atria (standard of care), at the level of carina on a chest radiography. In such patients, CVP monitoring is routinely prescribed every 6 h by the medical staff. After checking the absence of spontaneous breathing of the patient on the screen of the ventilator, CVP was carefully measured by the physician or by a trained nurse under the control of medical staff when necessary. Patients were not included when the CVP tracing showed tricuspid regurgitation (regurgitation on CVP tracing impeding the “x” wave). Finally, patients in whom a transient disconnection of mechanical ventilation could lead to a de-recruitment and deleterious gas exchange impairment (baseline P_O₂/FiO₂ ratio < 200 and FiO₂ > 50%) were not included. Measurements in patients in whom a cardiac arrhythmia occurred were not performed or excluded.

Measurement
CVP measurement was performed according to the usual practices of our ICU. The pressure measurement system was placed on the right or left arm at the level of the mid thoracic position at the level of the fifth rib (Fig. 1). The zero reference was carefully checked and calibrated as required. The pressure line was connected to the monitoring system (Intellivue™, Philips, Eindhoven, The Netherlands) and was alternatively used for the measurements of arterial bp and CVP. Therefore, during CVP measurements, continuous invasive arterial bpmonitoring was transiently interrupted (< 5 min). For the present study, several CVP measurements were assessed (Figs 1 and 2).

CVP_MEASURED
Considered as the reference technique, is the measurement of CVP at the base of “c” wave at the end expiratory phase (Fig. 2C). For this measurement, the research staff (physician or research nurse) froze the screen allowing the measurement of pressure at end expiratory time at the base of the “c” wave.

CVP_MONITOR
Mean CVP value displayed on the monitor after three respiratory cycles without mechanical ventilation interruption and without spontaneous breaths. The pressure measurement system is connected to the distal lumen of the central venous catheter, allowing the measurement of CVP recording the mean CVP value displayed on the screen after three respiratory cycles (Fig. 2C). For each measurement, the operator checked that any
premature atrial or ventricular beats or spontaneous breathing impaired the CVP curve.

\[ \text{CVP}_{\text{NADIR}} \]

CVP at the base of “c” wave measured after a transient disconnection (less than 5 s) of mechanical ventilation (Fig. 2D). This manoeuvre rules out the effect of PEEP just before the increase in venous return related to mechanical ventilation withdrawal.

\[ \text{CVP}_{\text{CALCULATED}} \]

CVP measurement that takes into account the transmitted respiratory pressure according to the following formula (Fig. 2A):\(^6\)

\[
\text{CVP}_{\text{CALCULATED}} = \frac{\text{CVP}_{\text{MEASURED}}}{\left( \frac{\text{PEEP}_i}{\text{ACVP}} \right)}
\]

Where: - PEEP \(_i\) indicates intrinsic PEEP determined by the ventilator (Fig. 2A).

- \(\Delta\text{CVP}\) is the difference between peak-inspiratory CVP and end-expiratory CVP (Fig. 2B).

- (Plateau pressure – PEEP) is the driving pressure (i.e. transmitted pressure induced by the respiratory system).

The sequence of CVP measurements was designed as follows for avoiding the influence of one measurement on another. First, \(\text{CVP}_{\text{MONITOR}}\) was assessed. Second, the measurement of \(\Delta\text{CVP}\) was performed. Thirdly, \(\text{CVP}_{\text{MEASURED}}\) was performed allowing calculating \(\text{CVP}_{\text{CALCULATED}}\). Fourthly, \(\text{CVP}_{\text{NADIR}}\) was finally measured, as it needs a transient disconnection from the mechanical ventilation.

For each patient sex, age, height, weight, main diagnosis and the New Simplified Acute Physiology Score II (SAPS II) at admission were collected.\(^{13}\) For each CVP assessment (measurement of \(\text{CVP}_{\text{MEASURED}}, \text{CVP}_{\text{MONITOR}}, \text{CVP}_{\text{CALCULATED}}, \text{and CVP}_{\text{NADIR}}\)), the concomitant Sequential Organ Failure Assessment (SOFA) score was calculated.\(^{14}\) Moreover, Richmond Agitation Sedation Scale (RASS),\(^{15, 16}\) mean arterial bp (MAP), heart rate (HR), tidal volume, respiratory rate (RR), plateau pressure, extrinsic PEEP were collected. The ventilator (Evita II Dura or Evita XL, Drager, Lübeck Germany) automatically measures intrinsic PEEP. Finally, \(\text{CVP}_{\text{MEASURED}}, \text{CVP}_{\text{MONITOR}}, \Delta\text{CVP}, \text{CVP}_{\text{CALCULATED}}, \text{and CVP}_{\text{NADIR}}\) were collected. Each series of data collection for CVP assessment did not last more than 5 min. No more than two CVP assessments were performed per included patient, with at least a 6 h interval and no more than 48 h between two different assessments.

**Endpoints**

The aim of the present study was not to determine which method of measurement gives the most accurate or “real” value of CVP rather it is a comparison of differing measurement techniques. The main objective was to compare \(\text{CVP}_{\text{MONITOR}}, \text{CVP}_{\text{CALCULATED}}\) and \(\text{CVP}_{\text{NADIR}}\) to \(\text{CVP}_{\text{MEASURED}}\) defined as the reference method. The primary endpoint was to compare the limits of agreement between the different methods. Secondary endpoints were the comparison of the bias, precision, and proportion of outliers. A difference of 2 mm Hg in CVP can be considered clinically relevant as such a difference could lead to erroneous clinical decisions.\(^{17-19}\) Therefore, a difference of \(\text{CVP}_{\text{MEASURED}} > 2\) mm Hg was defined as an outlier.

**Statistical analysis**

We tested the hypothesis that the limit of agreement of \(\text{CVP}_{\text{MONITOR}}\) was equal to those of \(\text{CVP}_{\text{CALCULATED}}\) and \(\text{CVP}_{\text{NADIR}}\). The Pitman-Morgan’s test for paired data was used to compare the variances. To estimate the number of patients needed, we assumed a minimal variance ratio of 1.5. With an alpha risk of
1% (taking into account multiple comparisons of variances between each technique for CVP measurement) and a power of 90%, at least 50 patients were required (number of measurements was estimated according to simulation performed with R version 3.1.0, http://cran.r-project.org).

Data are expressed as mean (SD) or median [25-75 interquartile, IQ] for non-Gaussian variables (assessed with Shapiro-Wilk test), or number (percentages). For comparing biases and precisions, paired Wilcoxon and Student’s t-tests were used. For comparing outliers, χ²-test was used. To determine Bland and Altman limits of agreement we used the correction for repeated measurements.20

All P values were two tailed and a P value of less than 0.05 was considered significant.

Results

From November 2013 to April 2014, among 298 patients admitted into our ICU, 102 patients were eligible, and 61 were included (Fig. 3). One hundred and three CVP assessments were performed (two CVP assessments in 42 patients, a single one in 19 patients). Concomitant conditions of CVP measurement are shown in Table 1. The values of CVP measured with the different techniques are shown in Table 2. The bias, precision, limits of agreement, and proportion of outliers of the different CVP techniques are also shown in Table 2. Figure 4 depicts Bland and Altman diagrams. The limits of agreement (primary endpoint) of CVPMONITOR, CVP NADIR, and CVP CALCULATED were not significantly different. The bias of CVPMONITOR was significantly different from those of CVP CALCULATED and CVP NADIR (P < 0.05). The precision of CVPMONITOR was not significantly different from the precision of CVP ADJUST but was lower than the precision of CVP MEASURED (Table 2). The proportion of outliers was not significantly different between CVPMONITOR and CVP NADIR (5 vs 9%, P = 0.27) but was significantly different between CVPMONITOR and CVP CALCULATED (5 vs 15%, P = 0.01) (Table 2). The values of CVPMONITOR were greater than those of CVPMODEL in 94/103 CVP assessments (91%). In 14 CVP measurements performed with PEEP ≥ 10 cm H₂O (8 patients), the associated median transmitted pressure (ΔCVP) was 2 mm Hg [range(1-6)] vs 2 mm Hg [range(1-6)] in 89 CVP measurements with PEEP < 10 cm H₂O.
298 admitted patients during study period

171 (57%) patients with subclavian or internal jugular catheter

102 eligible patients

42 non-included patients
  - Spontaneously breathing patients = 30
  - Physician non available = 12

61 included patients

- 34 female (56%)
- Age (yr) 60 (17)
- Body weight (kg) 82 (23)
- Ideal body weight (kg) 63 (8)
- SAPS II score at admission 50 (20)
- ICU mortality rate 17 (28%)

Diagnosis

- Septic shock 17
- Acute respiratory failure 13
- Haemorrhagic shock 7
- Trauma brain injury 6
- Polytrauma 5
- Stroke and status epilepticus 4
- Cardiac arrest 3
- Others 6

Fig 3 Flow chart of the study.
Discussion

The present study comparing three different techniques of CVP measurement (CVP\textsubscript{MONITOR}, CVP\textsubscript{NADIR}, CVP\textsubscript{CALCULATED}), to a reference method defined a priori, CVP\textsubscript{MEASURED}, shows that the limits of agreement and bias of CVP\textsubscript{MONITOR} displayed on the monitor screen are acceptable. This method can be used to accurately estimate CVP\textsubscript{MEASURED}. When considering transmural CVP measurements, the limits of agreement of CVP\textsubscript{CALCULATED} and CVP\textsubscript{NADIR} were similar; however, CVP\textsubscript{CALCULATED} had a higher proportion of outliers and precision.

Even though the ability of CVP to predict fluid responsiveness has been challenged over the last decade,\textsuperscript{24-26} its measurement is still recommended for haemodynamic monitoring of critically ill patients\textsuperscript{3} and a low value of CVP (<7 mm Hg) is predictive of fluid responsiveness.\textsuperscript{26,27} In the setting of anaesthesia, Venn and colleagues\textsuperscript{18} showed that fluid administration guided by CVP decreases the number of per-anesthetic hypotensive episodes and also duration of hospital stay. In ICU patients with septic shock, Lin and colleagues\textsuperscript{28} showed that an algorithm including a CVP target decreases mortality. Magder and colleagues\textsuperscript{29} reported that after cardiac surgery, an algorithm based on the measurement of CVP and cardiac output, could decrease the vasopressor requirement.

However, the method to measure CVP may widely vary and potential errors in measurement can occur.\textsuperscript{5} CVP\textsubscript{MEASURED} was considered as the reference measurement in the present study as it is the most commonly used and simplest technique for measuring CVP.\textsuperscript{5}

Some of the monitors currently used in the ICU can display values of CVP continuously recorded (CVP\textsubscript{MONITOR}). These values take into account the variations of CVP during the respiratory cycle and could better reflect the influence of ventilation on venous return. However, the concordance of this method of measurement has never been assessed. In the present study, the limit of agreement of CVP\textsubscript{MONITOR} was considered acceptable (-2.96 to 1.21 mm Hg). Indeed, Blot and colleagues\textsuperscript{30} compared the measurement of right atrial pressure using a pulmonary artery catheter and a central venous catheter. Even if these techniques measured a pressure in the same cardiac cavity, the authors reported limits of agreement of -3.78 to 3.00 mm Hg, which are wider than those reported for CVP\textsubscript{MONITOR} in the present study.

Moreover, the proportion of outliers in the CVP\textsubscript{MONITOR} group was low (5%). As previously reported by Coquin and colleagues\textsuperscript{31} when comparing methods for haemoglobin measurement, the outliers are considered as values that could lead to erroneous decisions in patient management. This method should help physician decision-making.\textsuperscript{32} In the present study, the difference between CVP\textsubscript{MONITOR} and CVP\textsubscript{MEASURED} was >2 mm Hg in only five assessments. These findings support that CVP\textsubscript{MONITOR} is a reliable surrogate of CVP\textsubscript{MEASURED}. Another advantage is that CVP\textsubscript{MONITOR} could be easily assessed at bedside.

When CVP measurement is used to determine cardiac preload, the pressure surrounding the heart should be a determinant of CVP measurement. However, the methods of transmural CVP determination can also suffer from measurement errors.\textsuperscript{5} In the present study, CVP\textsubscript{NADIR} and CVP\textsubscript{CALCULATED} were the two methods of measurement involving transmural pressure. Even if the limits of agreement of CVP\textsubscript{NADIR} or CVP\textsubscript{CALCULATED} were in the same range (figure 3), the precision of CVP\textsubscript{CALCULATED} was higher than those of CVP\textsubscript{MONITOR} and CVP\textsubscript{NADIR}. Moreover, the proportion of outliers was significantly higher when using CVP\textsubscript{CALCULATED}.

The reason for this disagreement is probably related to the definition and the calculation of CVP\textsubscript{CALCULATED}. High values of PEEP,
and/or ΔCVP lead to a greater difference between CVP_MEASURED and CVP_CALCULATED. In contrast, the difference between CVP_MEASURED and CVP_NADIR is probably lower in view of lung compliance being different when performing insufflation as compared with the withdrawal of mechanical ventilation and PEEP. However, CVP_NADIR can suffer from overestimating filling pressures in COPD patients with remaining hyperinflation during the withdrawal of mechanical ventilation. Therefore, assessing the actual cardiac preload remains associated with many potential pitfalls (calculation formula for CVP_CALCULATED and potential hyperinflation for

Fig 4 Comparison of central venous pressure (CVP) techniques using the Bland and Altman diagrams. CVP_MEASURED (CVP_MEAS) was taken as the reference technique. Diagrams assess CVP_MONITOR (CVP_MON) (Panel A), CVP_CALCULATED (CVP_CALC) (Panel B), and CVP_NADIR (CVP_NAD) (Panel C) (See text for explanation). The full lines depict the bias and the dotted lines the limits of agreement.
CVP_{NADIR}. The actual trans-pulmonary pressure method (using an oesophageal probe) to measure transmural CVP, probably remains potentially the only accurate technique to assess right ventricle preload. However, this technique is invasive and time consuming and its impact on clinical management and patient outcome has never been assessed.

In contrast, right ventricle preload assessment by CVP_{MEASURED} leads to a greater error.

The present study has some limitations. First, we did not calculate CVP with the actual trans-pulmonary pressure as suggested by Talmor and colleagues \(^\text{34}\) in patients with acute respiratory distress syndrome. However, this technique requires an oesophageal probe that is not used in daily practice. Second, even if CVP_{MONITOR} was greater than CVP_{CALCULATED} of CVP_{NADIR} in 94/103 CVP assessments (91%), the tracing of CVP on the monitor should be checked for diagnosing a potential anomaly. \(^\text{7}\) Tricuspid regurgitation or a deeper insertion with intra-ventricular pressure could indeed impair the value of CVP_{MONITOR}. \(^\text{12}\) Third, the extrapolation of the present study into patients with severe acute respiratory distress syndrome should be taken with caution. Indeed, patients in whom a transient withdrawal of mechanical ventilation could lead to a de-recruitment and deleterious gas exchange impairment were not included in our study. However, the transmitted pressure (ACVP) seems to be similar whatever the level of PEEP (<10 or ≥10 cm H\(_2\)O) is. Fourth, the present findings cannot be extrapolated into patients with spontaneous breathing patterns (with or without mechanical ventilation).

**Conclusion**

In clinical practice, CVP_{MONITOR} can be rapidly measured and gives an estimation of CVP_{MEASURED} with acceptable limits of agreement and bias. Therefore, CVP_{MONITOR} should be proposed as an alternative to CVP_{MEASURED}.

**Authors’ contributions**


Study conduct: C.R., L.M., B.L., H.K., J.-Y.L.


Revising paper: all authors

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**Declaration of interest**

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