

Comparison of Invasive vs. Noninvasive CVP Monitoring in Patients Undergoing Major Intra-Abdominal Surgery: A Prospective Comparative Pilot Study

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Abstract

Background: The primary objective of the study was to compare central venous pressure (CVP) measured invasively to one measured non-invasively (NICVP) by monitoring upper arm blood flow changes in response to externally applied circumferential pressure to the upper arm veins.

Methods: The NICVP monitor (NeuMeDx®) employs impedance plethysmography using 4 electrodes and a blood pressure cuff to determine a person's CVP. Three invasively measured CVP pressure measurements were compared to the NICVP taken during the same time period after induction of anesthesia in 29 patients.

Results: Data from both methods were normally distributed and, in paired tests, were not significantly different ($p=0.255$). Over 95% of the values were within 3.0 mmHg of each other, the threshold estimate for clinical equivalence. The two measurements were highly correlated ($r=0.657$) and a Bland-Altman analysis showed good agreement.

Conclusions: The non-invasive device was accurate and able to mirror the invasive CVP in our study population.

Trial registration: #03705299, Clinical trials.gov

Keywords: Bioimpedance; Central venous pressure; CVP; Plethysmography; Noninvasive CVP

Abbreviations: ASA: American Society of Anesthesiologist; CVP: Central Venous Pressure; IRB: Institutional Review Board; NICVP: Non-Invasive Central Venous Pressure

Introduction

Central Venous Pressure (CVP) monitoring is often used to assess intravascular volume and to guide fluid resuscitation in critically ill patients [1-5]. However, the use of CVP has been disputed recently and it is not the purpose of this investigation to summarize the potential advantages or limitations of CVP measurements [6]. The purpose is to compare the CVP value measured non-invasively by an impedance method to that measured by central vein cannulation.

The standard method of measuring CVP is to insert a catheter into the internal jugular vein or subclavian vein and threading in to the superior vena cava or right atrium of the heart. Access to the central veins is associated with risks and technical difficulties which can lead to several complications such as arterial puncture, pneumothorax, hemothorax, infection, air embolism, bleeding, dysrhythmias and

thoracic duct injury [7]. Because of the associated risks of complications CVP measurement is often impractical and avoided.

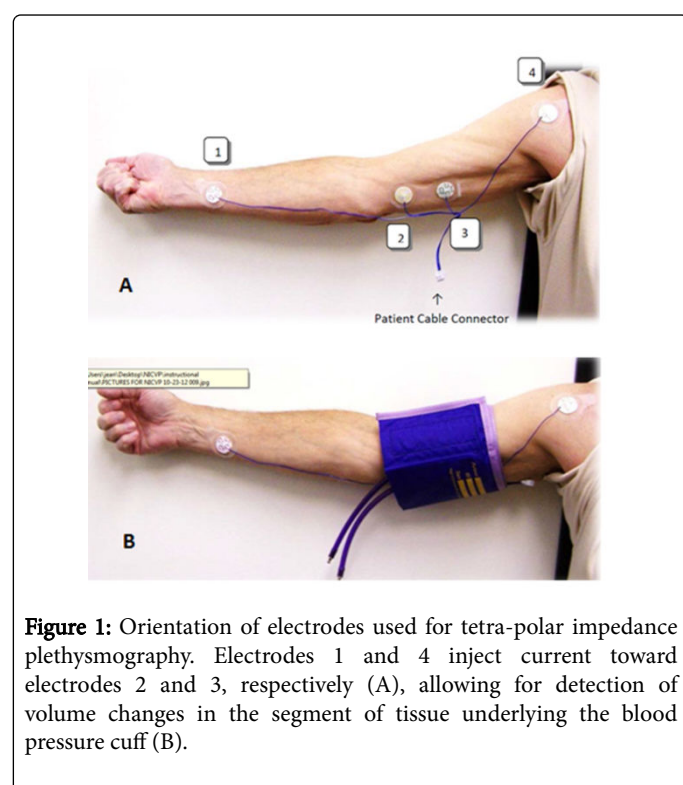
Based on these restrictions, alternate noninvasive devices have been developed, and this prospective study was devised to see if a noninvasive device based on impedance technology can reliably measure the CVP during clinical conditions. The Non-Invasive Central Venous Pressure (NICVP) device utilized in this study is a monitor that employs a form of impedance plethysmography to determine a person's CVP [8,9].

Methods

This was a single center, prospective, pilot study approved by the Cooper Health System Institutional Review Board. Written informed consent was obtained from patients scheduled for major abdominal surgery requiring CVP monitoring as part of their routine care. Exclusion criteria were medical or surgical contraindications to central vein cannulation. Twenty-nine ($N=29$) adult patients were recruited between October 2009 and July 2013. Patients were between the ages of 23 to 87 years with an American Society of Anesthesiologist (ASA) status class of II to IV. All patients had general anesthesia and were induced by using propofol (2 mg/kg-4 mg/kg) and fentanyl 250 µg. Tracheal intubation was facilitated by the administration of

rocuronium (0.6 mg/kg). Mechanical ventilation was started using a volume controlled ventilator to maintain an adequate saturation and an end- carbon dioxide of 35 mmHg. Inhalational anesthetic (Isoflurane) was added to maintain a BIS of less the 45. Each patient was monitored with a right atrial catheter (triple lumen, 7F Arrow International) inserted through the right internal jugular vein utilizing ultrasound guidance. The CVP catheter was threaded 12 cm into into the right atrium of the heart. The catheter was connected to a continuous flush device pressurized to 300 mmHg. This pressure allows the infusion of about 3 ml of fluid each hour but keeps the line patent. The distal tip of the CVP line was connected to a transducer and the transducer was zeroed at the level of the right atrium (midaxillary line).

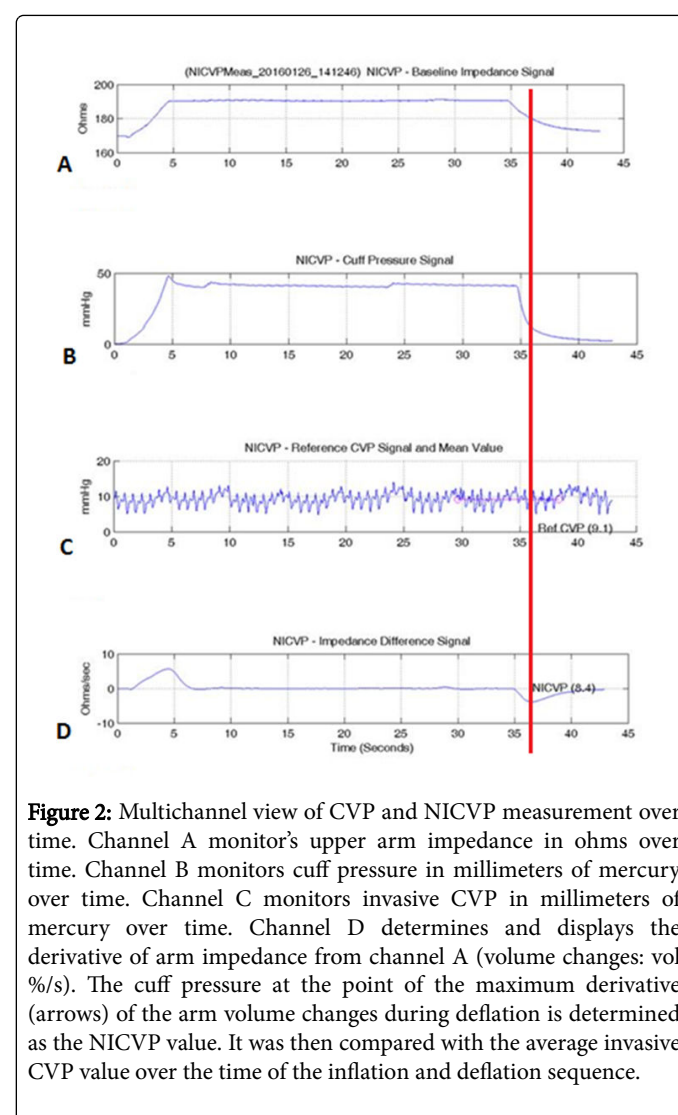
The NICVP device was applied to a prepped arm (clean and shaved if necessary). The choice of arm was at the discretion of the participating anesthesiologist opposite the radial arterial catheter insertion site. Four ECG electrodes are applied to patient's prepped arm (Figure 1A). The blood pressure cuff is applied to the patient's arm covering two electrodes placed at bicep (Figure 1B).



The underlying theory involves a well-founded and studied method incorporating impedance plethysmography. Specifically, a small amount of current, 400 μ A @ 28 kHz sine wave is applied to the patient's arm through standard ECG electrodes. A blood pressure cuff on the patient's arm is inflated to ~40 mm Hg, blocking venous return but below diastolic arterial pressure. After 45-60 sec, the pressure is rapidly deflated for a period of approximately 30 sec and the impedance is measured by the processing unit while simultaneously measuring the pressure in the cuff. Changes in bioimpedance, resulting from the changes in volume and velocity of blood in the arm are directly related to the pressure within the large veins of the upper arm. Pressures in these veins are essentially the same as pressures in the large central veins in which they empty into. Maximum blood volume

changes in the upper arm detected by impedance are matched to the pressure in the blood pressure cuff during deflation. The pressure in the blood pressure cuff at this time is pressure within the large vein in the upper arm and this pressure is substituted for CVP.

The NICVP device measures impedance in ohms over time (Figure 2A). The initial change in impedance seen in Figure 2A is due to the arm filling with blood when venous return is impeded by the cuff. The change in impedance over time is calculated by the processing unit and a waveform is generated (Figure 2D). This waveform of the rate of change in impedance over time is an indirect measurement of blood flow under the blood pressure cuff. The cuff pressure, graphed in (Figure 2B), that is observed at the minimum point in this delta-impedance waveform (see red vertical line in Figure 2) has been found to correlate to the patient's CVP, as measured with a catheter. The cuff pressure reading is reported as the NICVP parameter value by the device. The invasive CVP waveform is also captured simultaneously (Figure 2C).



Invasive measurement of CVP was carefully calibrated using the mid-axillary line as the zero reference while patients were all in the horizontal plane. Three pressure measurements were simultaneously

made through both devices over a 10 min period after the induction of general anesthesia and intubation.

Demographic and clinical characteristics of the patients were summarized using means and standard deviations for continuous variables and frequencies and percents for categorical variables. Data from both CVP and NICVP measurements were examined to ensure that each method did not depart significantly from the normal distribution using the Shapiro-Wilk test. Paired Student's t-tests were used to compare overall differences between methods and to examine differences controlling for patients (patients had between 3 and 5 observations each). To compare the two methods, Bland-Altman plots with corresponding correlation coefficients and Pitman test results were constructed comparing CVP with NICVP. With a significance level of 5% and a power of 80%, a sample size of 29 patients is sufficient to estimate a maximum difference between pressure measurements of 5 mmHg and the precision of this difference no more than 8 mmHg. No dropouts or complications were seen in the trial from this noninvasive procedure. All statistical analyses were performed using Stata v15.1 (College Station, TX).

Results

Patient characteristics are presented in Table 1. A total of 96 comparative data points were obtained to compare the two measurements of CVP. There were at least 3 data points per patient, taken over 10 min range of time with 7 patients having 4 data points and 2 patients with 5 data points. All data are included in the study.

	Mean (min, max)	Std. Deviation
Age (Years)	65.65 (23, 87)	13.69
Height (meters)	1.71 (1.52, 1.88)	0.11
Weight (Kg)	72.45 (36.11, 100.90)	15.17
	Frequency	Percent
Gender: Male	10	43.5
ASA Score: 2	6	26.1
3	15	65.2
4	2	8.7
Smoker: Former	6	26.1
Nonsmoker	13	56.5
Current	3	13
Comorbidities		
Diabetes Mellitus	8	34.8
Hypertension	12	52.2
Hyperlipidemia	6	26.1
Cardiac Artery Disease	2	8.7
CABG	2	8.7
PCI	1	4.3
MI	1	4.3

Afib	3	13
PVD	2	8.7
Cirrhosis	1	4.3
CVA	1	4.3
CKD	2	8.7
Obesity	1	4.3
OSA	2	8.7
COPD	4	17.4

Table 1: Patient demographics & Clinical characteristics.

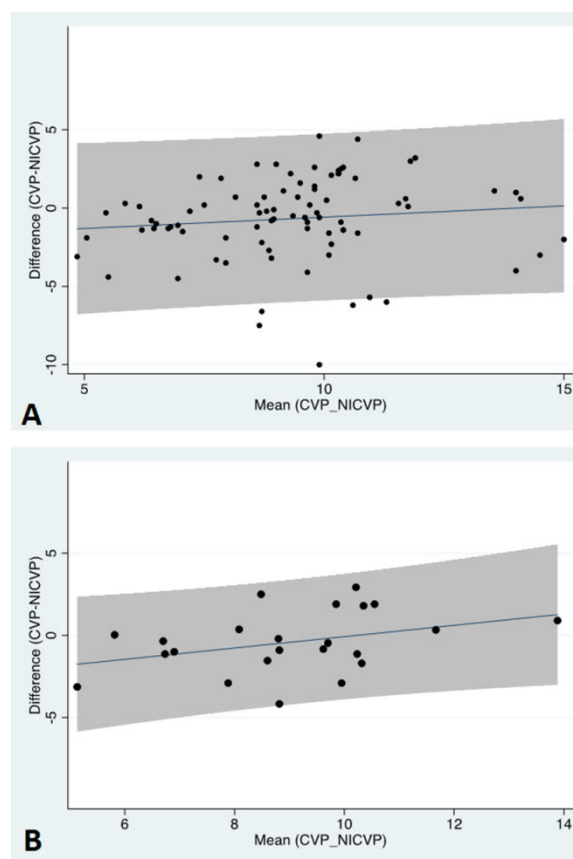


Figure 3: Bland-Altman plots showing close agreement between CVP and NICVP over all measurement values (A) and values controlling for patient (B).

Prior to analysis, the Shapiro-Wilk test was used to ensure that the distributions of NICVP and CVP were normally distributed and not significantly different ($p=0.255$). The mean difference between measurements was -0.282 mmHg with 95% confidence bounds from -0.773 to 0.209 mmHg. Over 95% of the paired values were within 3 mmHg of each other. The NICVP measurements showed good correlation ($r=0.657$, $p<0.001$) with the CVP values. The overall Bland-Altman plot (Figure 3A) shows the difference between the NICVP and invasive CVP. The Pitman test of the difference in variance was not

significant ($p=0.089$) and the plot shows very little trend in the mean difference value as the average value increases giving a very small bias $=0.677$ mmHg. The shaded area indicates two standard deviations around the mean difference of 4.15 mmHg. The plot shows good agreement between the NICVP and invasive CVP values overall. An examination of the agreement between methods by patient rather than overall measurements showed similar results with a mean difference between CVP and NICVP of 0.421 ($p=0.292$). The Bland-Altman plot controlling for patients is given in Figure 3B (Pitman test $p=0.094$). Figure 4 shows the overall agreement between the two methods.

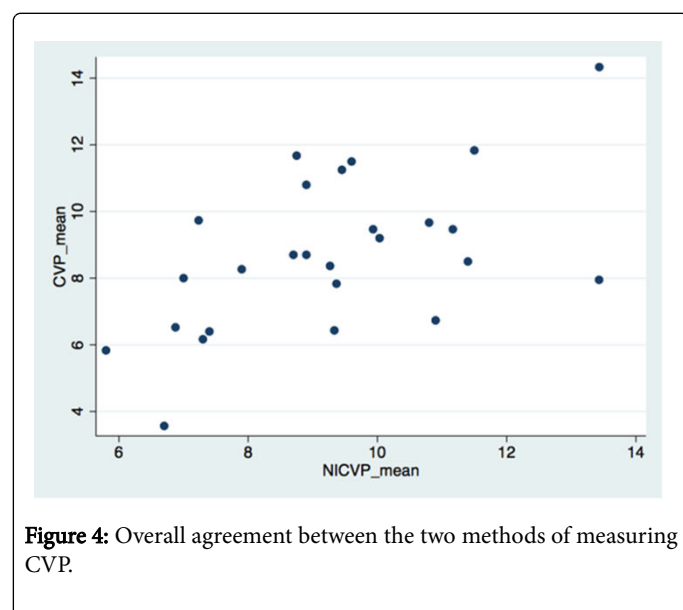


Figure 4: Overall agreement between the two methods of measuring CVP.

Discussion

While advancements in dynamic indices such as stroke volume variation (SVV) and pulse pressure variation (PPV) are now included in recent guidelines [10,11]. Limitations to PPV and SVV exist in that these indices require patients to be mechanically ventilated, sedated and without arrhythmias. In this setting knowledge of the CVP is considered valuable and can provide useful information about the risks associated with fluid administration in the critically ill patient.

Invasive procedures are not without risk and may lead to a variety of complications and noninvasive techniques are being increasingly recognized as potential replacements. While the gold standard continues to be the CVP measured with a pressure transducer, ultrasound guided CVP assessment as recommended by the American Society of Echo has been suggested as an acceptable substitute [12]. Despite the low risk associated with the ultrasound technique it requires expertise and the cost of the equipment is significant. For a device to be clinically useful its application should require minimal training, be relatively inexpensive and the results should yield sufficient accuracy and precision as that of the reference standard [10].

In the past decade goal directed fluid therapy and non-invasive devices have been integrated into daily anesthesia practice. The development of impedance monitoring to estimate cardiac output and stroke volume in anesthetized or critically ill patients has become increasing routine. The movement away from invasive catheters (both arterial and central) is most likely secondary to the reduced rate of adverse events and ease of monitoring that is afforded by the

introduction of new novel non-invasive devices. These newer methods of monitoring display an active feedback process displaying hemodynamic parameters in response to fluid therapy. For these newer devices, estimates are used in place of actual CVP measurements due to the invasive nature of the gold standard. The utilization of a non-inferior, non-invasive CVP monitor to provide accurate CVP values at the start and duration of the case would lead to increased accuracy of goal directed fluid therapy and possible improvements in outcomes. The movement to suitable alternatives for invasive monitoring will continue.

The results of our study on this limited patient population showed that impedance-based methodology has a sufficiently small bias and limits of agreement to potentially replace the invasive technique. The device has clinically relevant accuracy and precision in intubated mechanically ventilated patients under general anesthesia. It is user friendly and free of user bias. No external calibration is required.

Limitations to this preliminary study are the relatively small sample size and short duration of monitoring. As with any CVP study the accuracy of the actual value of the intracardiac pressure depends on the placement of the transducer and the external reference point that represents the right atrium especially when the measured parameters have small normal values. The small sample size and relatively stable hemodynamics limits conclusions about the application in unstable or septic patients. Future studies would include a larger number of patients, and would include increased manipulation of the CVP (i.e. leg raise, fluid challenge). Other disease groups may be stratified in further studies to observe accuracy in septic patients or patient requiring vasopressors. All subjects were mechanically ventilated via volume control using 6 ml/Kg and no other mode of mechanical ventilation was utilized. All patients were in sinus rhythm, so it will be necessary to test the technique on patients who have dysrhythmias to determine if it is capable of accurately measuring CVP in this setting. Furthermore, we did not record cardiac output in patients where cardiac output was measured. In the future, it will be necessary to understand if the technique has limitations in the setting of a low cardiac output.

An investigation recruiting a more varied and larger patient population will help to determine if there is a subset of patients where the technique would not be accurate by over or underestimating the actual CVP. The monitoring period for each of our patients was rather short and a revised study with multiple determinations over a longer period would help to validate this technique. In addition, the technique should be evaluated to see if it is capable of rapidly detecting changes in CVP induced by acute volume resuscitation, diuresis, or the use of inotropic agents. However, despite these limitations the bias and limits of agreement of the technique seem to be clinically acceptable coupled with the high correlation would indicate that it should be possible to rapidly track changes within an individual in response to treatment.

Conclusion

The noninvasive CVP device may provide the clinician an alternate technique to measure CVP via a noninvasive approach. The trend to noninvasive monitoring will continue and any device that can accurately replace an invasive one is a welcome addition. While this is still a preliminary study the device has potential and further validation in different clinical settings are required to understand the application and limitations of this promising method.

Declarations

Ethics approval and consent to participate

The protocol was approved by Cooper University Hospital Institutional Review Board (IRB), study number 12-121. Informed consent was obtained from all subjects.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare they have no competing interests.

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Authors' contributions

IG participated in study conception, design of the study protocol, data acquisition, data interpretation, and manuscript draft preparation. VK participated in data acquisition and patient selection. FS participated in study design and data interpretation. SJ supervised the study, contributed to study design, patient selection, and data acquisition. EA and JS participated in study design and data and statistical analysis. ED participated in study design. All authors read and approved the final manuscript.

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