A Novel noninvasive impedance based technique for central venous pressure measurement

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Abstract-- Introduction: Knowledge of central venous pressure (CVP) is considered valuable in the assessment and treatment of various states of critical illness and injury. We tested a noninvasive means of determining CVP (NICVP), by monitoring upper arm blood flow changes in response to externally applied circumferential pressure to the upper arm veins.

Methods: Thirty-six patients who were undergoing CVP monitoring as a part of their care had NICVP determined and compared with CVP. Volume changes were measured in the upper arm using tetrapolar impedance plethysmography underneath a blood pressure cuff. The cuff was inflated over 5 seconds to a pressure above CVP but below diastolic arterial pressure. After 45-60 seconds the cuff was rapidly deflated. NICVP was determined as the cuff pressure noted at the maximum derivative of the volume increase under the cuff during deflation. NICVP was then compared to invasively measured CVP taken during the same period by Bland-Altman analysis.

Results: A total of 108 trials (3 per subject) were performed on 36 patients. Mean bias was -0.26 mm Hg (95% CI -0.67, 0.15). Limits of agreement were -2.7 mmHg and 2.2 mmHg with the 95% CI for the lower limit of agreement (-3.4, -2.0) and (1.5, 2.9) mmHg for the upper limit of agreement. Correlation between CVP and NICVP was 0.95 (95% CI: 0.93 to 0.97; p<0.0001).

Conclusion: NICVP as determined in this study may be a clinically useful substitute for traditional CVP measurement and may offer a valid tool for early diagnosis and treatment of acute states in which knowledge of CVP would be helpful.

Introduction:

Despite limitations, central venous pressure (CVP) is frequently used in clinical practice to assess volume status and cardiac preload. Knowledge of a patient’s CVP can be helpful in the diagnosis and management of a variety of critical illnesses and injuries including trauma, burns, sepsis, congestive heart failure, cardiogenic shock, traumatic brain injury and others.[1-7] This may become increasingly important as the general patient population ages and patients have a variety of pre-existing chronic disease states such as hypertension, heart failure, diabetes, and chronic obstructive pulmonary disease which may make assessment of hemodynamics even more difficult.

The limitations of the physical examination in estimating volume status and CVP has been clearly shown, demonstrating that its accuracy is no better than 50-60%.[5, 8-18] Consequently, patients are at great risk for clinical misdiagnosis and/or institution of either inadequate or frankly contraindicated therapies, which may result in adverse outcomes. Routine placement of central venous catheters for CVP measurement is many times impractical and even when indicated can be associated with significant risks.[19-22] Its use in the outpatient setting, is of course, not an option.

For these reasons, numerous methods have been studied and reported which attempt to measure CVP either noninvasively (NICVP) or in a minimally invasive manner.[23-34] Completely noninvasive methods have not been reported to
have the accuracy and precision necessary for routine use and interchangeability with traditional invasively measured CVP. Minimally invasive methods involving cannulating peripheral limb veins or the internal or external jugular vein followed by transducing venous pressure, have met with mixed results, with some methods demonstrating the potential for substitution with traditional CVP.[24, 25, 32, 33] This study reports on the use of a noninvasive methodology of CVP measurement based on the rate of volume change in the upper extremity in response to low pressure cuff inflation and deflation.

**Methods:**

This study was approved in advance by the Virginia Commonwealth University Institutional Review Board. Patients 18 years of age or older who were having their CVP monitored as a part of their routine care were eligible for enrollment. All central venous access had been obtained from either an internal jugular or subclavian vein site. Correct placement was confirmed by chest X-ray. Informed consent was obtained from patient subjects or their legally authorized representative. Patient enrollment was performed by simple convenience sampling of patients in the various adult intensive care units and the emergency department who had CVP catheters in place. The only exclusion criteria were pregnancy, inability to obtain consent, or inability to access one of the patient’s arms.

A physiologic data acquisition system (AcqKnowledge MP150, Biopac Systems Inc. Goleta, CA) was used to continuously monitor the variables of interest. This included CVP, upper arm impedance changes, and upper arm cuff pressures. CVP was monitored by transiently switching the electronic feed of the patient’s CVP pressure transducer from the bedside monitor into the data acquisition system. The patient’s CVP transducer was zeroed at the level of the right atrium (midaxillary line) with the use of a carpenter’s level (containing a bubble vial). The catheter was flushed and CVP waveforms were visually confirmed using the electronic display. Electrobioimpedance was measured in the upper portion of an upper extremity using an electrobioimpedance amplifier (EBI100C, Biopac System Inc, Goleta, CA). A tetra-polar impedance configuration was used to measure upper arm impedance. A pair of current-injecting electrodes (ECG electrodes, BIO-TAC ULTRA, Tyco Healthcare Group, Mansfield, MA) were placed in positions 1 and 4 and two sensing electrodes were placed in position 2 and 3 as shown in Figure 1 (from the author’s arm KRW).

![Figure 1: Orientation of electrodes used for tetrapolar impedance plethysmography. Electrodes 1 and 4 inject current towards electrodes 2 and 3 respectively allowing for detection of volume changes in the segment of tissue underlying the blood pressure cuff. The author’s arm (KRW) was used for the photograph.](image-url)

A constant current source (1 mA, 100 kHz) was sent through the current electrode and the voltage drop between the two sensing electrodes was amplified. This allows measurement of impedance in the upper arm between the two sensing electrodes. The predominant determinant of impedance in the limbs is blood volume. The sensing electrodes were placed where a traditional blood pressure cuff would be positioned. This is also the area overlying the brachial-axillary vein system.

The blood pressure cuff (RX120, Biopac System Inc, Goleta, CA) was positioned over the two sensing electrodes (Figure 1). The data acquisition system was connected to a portable computer (Inspiron 7500 Dell notebook, Dell Inc. Dallas TX) to record the measurements, and store the data for future analysis.
Measurement Sequence

The data acquisition software acquired three analog channels (cuff pressure in mm Hg, invasively measured CVP in mm Hg, and upper arm impedance in ohms) via an analog to digital board and calculated one channel (the real-time filtered derivative of the impedance). The open port of the CVP transducer (RX104A, Biopac System Inc, Goleta, CA) was placed at the midaxillary line as the zero reference port.[35] The mid upper arm (surrounded by the cuff) was positioned at approximately the same level. After the setup and calibrating the pressure transducer (0 to 100 mmHg against a mercury manometer) the measurement was started.

For all patients, the cuff pressure was quickly inflated to a value higher than central venous pressure but lower than the diastolic arterial pressure (40 mm Hg) and kept at that pressure for 45-60 seconds. At this pressure arterial blood continues to flow into the arm but venous return is interrupted. During this period the patient’s upper arm underneath the blood pressure cuff was monitored for volume changes via the impedance monitor. As blood is a good conductor of electricity, the displacement in blood volume from under the cuff due to cuff inflation increases impedance which generally approaches a plateau before cuff deflation. At the end of the inflation hold period, the cuff pressure valve was opened to atmosphere to allow rapid self-deflation. Measurements were repeated 3 times in each subject. The sampling rate of all signals was 200 Hz.

NICVP was determined as the cuff pressure noted at the maximum slope of the impedance change during deflation. This was determined by creating a separate channel that determined the derivative of the impedance changes in real-time. The channel utilized a low pass digital infinite impulse response filter (frequency of 0.25 Hz, Q of 0.7070). NICVP was then compared to average invasively measured mean CVP taken at the same 45-60 second time period. Figure 2 provides an example of the data recorded from a subject.

Body fat was determined using a body fat caliper (ACCU-Measure Fitness 2000, Accu-Measure LLC. Englewood, CO). Determinations were made as directed by the manufacturer on the supra-iliac skin fold. This method has been demonstrated to be accurate in determining the percentage of body fat.[36]

Statistical Analysis:

Correlation between CVP and NICVP were determined using Pearson’s correlation. We assessed agreement between the two methods of measuring CVP using the methods described by Bland and Altman.[37-40] Bias was estimated from the differences between paired measurements. The limits of agreement were defined as the mean bias ± 1.96 SD of the differences. The variance for single differences between pairs of measurements on different subject was estimated from the sum of the between-subjects and within-subjects variances. Within-subject variance was estimated from one-way ANOVA on subject with the differences between matched pairs as the dependent variable;
the between-subjects effect (heterogeneity) was estimated from the difference between mean squares for subjects and the residual mean square, divided by the number of observations per subject. Repeatability was assessed by calculating the mean and SD of differences on repeated measurements for each subject. We checked the assumption that the variance of the repeated measurements for each subject by each method is independent of their mean by plotting the within-subject SD against the mean of each subject; this check determines if there was systematic variation of measurement error over the range of measurements.

Descriptive data are presented as means ± SD. An alpha level of ≤ 0.05 was considered statistically significant. Data was analyzed using GraphPad Prism v4.03 (GraphPad Software Inc. San Diego, CA).

Results:

A total of 36 subjects were studied (30 males, 6 females). Average age was 57 ± 13 years (range 26 to 84 years) and the average weight was 82 ± 16 kg. The average upper arm circumference was 29 ± 3.2 cm and average body fat was 28 ± 5%. Twenty patients were mechanically ventilated. The reasons for CVP monitoring included cardiogenic shock (4), post heart transplant (4), post coronary artery bypass graft surgery (13), severe sepsis (7), trauma (4), and surgical catastrophes (4). Fifteen subjects had NICVP measured using the right arm with twenty-one having the measure made using the left arm. The choice of arm was dictated by such factors as ease of access for placement of equipment and presence of an AV-fistula.

A total of 108 measurement trials were performed on the 36 subjects (3 per subject). CVP values ranged from 2.7 mmHg to 20.3 mmHg. Figure 3 shows the correlation and Bland-Altman plots between CVP and NICVP using all measures. There was no systematic variation in measurement error over the range of measurements obtained for either method (r = 0.23, p = 0.17; r = 0.25, p = 0.14 for CVP and NICVP respectively).

![Bland-Altman plot of all 108 measures in 36 subjects (three measures per subject). Mean bias was -0.26 mm Hg (95% CI -0.67, 0.15). Limits of agreement were -2.7 mmHg and 2.2 mmHg with the 95% CI for the lower limit of agreement (-3.4, -2.0) and (1.5, 2.9) mmHg for the upper limit of agreement.](image)

There was no relation between the difference in methods and the magnitude of the measurements (r = 0.16, p = 0.35). Mean bias was -0.26 mm Hg (95% CI -0.67, 0.15). Limits of agreement were -2.7 mmHg and 2.2 mmHg with the 95% CI for the lower limit of agreement (-3.4, -2.0) and (1.5, 2.9) mmHg for the upper limit of agreement.

![Pearson’s Correlation of all 108 measures of ICVP with CVP. The correlation was 0.95 (95% CI: 0.93 – 0.97) and was statistically significant (p < 0.0001).](image)

The correlation between CVP and NICVP (Figure 4) was 0.95 (95% CI: 0.93 – 0.97) and statistically significant (p < 0.0001).
Discussion:

Although controversy exists as to the value of using cardiac filling pressures such as CVP or pulmonary artery wedge pressure as indicators of cardiac preload or circulating volume status, CVP is a frequently used invasive measure in clinical practice to understand and follow a patient’s hemodynamic status for diagnostic and treatment purposes. Its true value will not be debated in this report, but as indicated earlier, the physical examination has been demonstrated to perform extremely poorly as a tool to estimate CVP. Unfortunately, it is likely that the physical examination continues to be used more often than it should. Development of a noninvasive technique to measure CVP would assist in removing many of the barriers associated with CVP monitoring such as time, expense, and the potential for complications. Use of such a measure in the emergency setting, especially when coupled with a noninvasive measure of end-organ perfusion is enticing as a potential noninvasive goal-directed diagnostic and therapeutic monitoring system since it would lend itself to rapid screening and treatment implementation.[1, 3]

When developing a new monitoring method to replace another, it must be determined what differences are clinically acceptable. As argued by Bland and Altman, correlations are not adequate to answer this.[38] The limits of agreement using the technique of Bland and Altman are defined as the mean difference ± 1.96 SD of the difference. The results of the current study demonstrate that NICVP as determined by measuring impedance based volume changes in the upper arm may have sufficiently small bias and limits of agreement to serve as a surrogate or replacement measure for traditionally measured invasive CVP. The high correlation values also indicate that the directional change and magnitude of changes are highly congruent between the techniques. However, clinicians and regulatory agencies will be the final arbiters in deciding if the differences between the two techniques are such that management of the patients would change.

The methodology developed and used in this study is based on several previous findings. The first is that the pressure within the cephalic, basilic, and brachial veins are very close (normally within the measurement error of commonly used commercial transducers) to those of the superior vena cava, due to the low resistance to venous return.[33] The second is that cuff pressure is transmitted to intraluminal vein pressure with very high fidelity.[41, 42] In other words, a pressure cuff inflated to 40 mmHg will produce an underlying intravenous pressure very close to 40 mmHg. Thus the potential to determine the pressure in veins in the upper half of the upper extremity (and hence CVP) would be possible if there was an additional variable that could be monitored simultaneously to cuff pressure that was coupled to venous pressure. In this study, that variable was the maximal change in upper arm volume under the cuff or more specifically maximum upper arm venous outflow.

Upper arm volume and flow changes were measured using tetrapolar impedance plethysmography. This is a well known and studied technique used to study vascular compliance and has been used clinically as a means to diagnose deep venous thrombosis (venous occlusion plethysmography).[43-48] We previously reported a method of noninvasive CVP measurement using the mercury-in-silastic strain gauge technique to measure volume change in the forearm in response to upper arm cuff inflation and deflation.[49] While this technique worked very well giving essentially the same results as the current study, we felt that wide spread use of the mercury-in-silastic strain gauge apparatus would be problematic because of the potential hazards associated with mercury. Use of the impedance technique provides for a more robust method.

The changes in impedance (as an indicator of volume) over time (vol%/sec) as measured in our study, represents flow. Specifically, this represents venous outflow since the cuff was not inflated above diastolic blood pressure. By tracking the slope of the change of this flow it was possible to determine the point of maximum flow.
In this study, we found that cuff pressure at the point of maximum venous outflow is very close to CVP presumably because it is close to the venous pressure within the basilic, cephalic, and brachial veins, which form the major outflow tracks of the upper extremity. Preliminary data in our laboratory (not shown) using vascular ultrasound appears to confirm that flow through these veins is maximum at this time.

It might be expected that NICVP would be the cuff pressure at the point where upper arm volume immediately decreased after beginning cuff deflation. NICVP determined at this point would grossly overestimate CVP (Figure 2) likely because of the high peripheral venous pressure that has developed distal to the inflated cuff prior to cuff deflation. Others have attempted to use the principles of Laplace’s law to determine CVP by applying pressure to veins and measuring indices of vein closure such as visualization of vein closure via ultrasound but have produced variable success.[23, 31, 34] Although we initially tried our technique by increasing cuff pressure and then comparing cuff pressure at the time of forearm volume increase, the data for this method were unsatisfactory and may be due to the fact that we had no way of slowly and precisely stepping up pressures at very small increments in a controlled fashion. Doing this might allow the determination of NICVP during cuff inflation as opposed to cuff deflation. However, it seems that less control is required in our method since we made no effort to precisely step down cuff pressure during deflation.

Body weight and arm circumference was widely varied and again, did not appear to be a significant issue in the measure of NICVP. While we attempted to document body fat with the use of skin fold calipers and understand its potential implications, the true accuracy of this technique in the critically ill and injured where interstitial edema may be present is unknown. Although many patients were mechanically ventilated, mechanical ventilation itself does not appear to adversely affect the techniques ability to determine CVP. This may have to do with the potential robust relationship between flow and pressure in this setting.

**Limitations:**

There are several limitations to this study. First, this preliminary study used simple convenience sampling for enrollment and no attempt was made to control for CVP level, rhythm type, or cardiovascular status. Thus unintended bias cannot be excluded since a relatively small number of patients were studied. In addition, no one disease group contained a significant number of patients to understand if the technique might be disease limited. This includes a relatively small number of mechanically ventilated patients on various modes of mechanical ventilation. 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. Only a larger study will help determine if there are subgroups of patients where the technique would significantly over or underestimate true CVP. Secondly, we did not monitor each patient over an extended length of time to understand if the technique is capable of rapidly detecting changes in CVP induced by volume resuscitation, diuresis, or the use of inotropic agents. Studies will need to be undertaken to understand the performance of the technique in these settings. However, the fact that the bias and limits of agreement of the technique appear to be clinically acceptable coupled with the high correlation values over such a wide range of CVP values would indicate that it should be possible to rapidly track changes within an individual in response to treatment.

The use of dynamic CVP response to treatment is perhaps a better means of utilizing CVP. While, the technique in its present or future form lends itself to automation and measures could
possibly be taken as often as every 1-2 minutes, this will need to be tested in the future to understand if performance deteriorates, if dynamic changes can be measured and tracked, and if it is well tolerated by patients. As a result of convenience sampling and perhaps because of patient specific pathology and treatment only 4 patients had CVP’s less than 5 mmHg. Future studies will require more patients with lower CVP values to understand if the technique has limitations at this low range.

We also did not subject any of the raw signals to advanced signal filtering and processing. Doing such might slightly improve the accuracy and precision of the measurement. In addition, using contact pressure measurements (between the cuff and skin) as opposed to intracuff pressures as a reflection of intravenous pressure may also improve the performance of the NICVP measurement. Lastly, additional consideration will need to be given in regards to determining the best position for the upper arm to be in for a zero reference point. It may simply be fortuitous that the outflow veins of the upper arm will are normally positioned near the midaxillary line of the chest, which is presumed to be at, or near the level of the right atrium.

The use of other monitoring sites might also be possible. Studies have shown that iliac vein pressures are clinically acceptable substitutes for supradiaphragmatic measurement of CVP even in mechanically ventilated patients.[50, 51] Although not studied with our technique, it may be possible to obtain CVP noninvasively by using our method in the lower extremity.

**Conclusion:**

The noninvasive determination of CVP performed in this study, may provide clinically acceptable values that may potentially be used in place of invasively measured CVP. More study is needed to understand the application and limitations of this promising method.

**References:**


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