Original Article

Influence of tissue pressure on central venous pressure/peripheral venous pressure correlation: An experimental report

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BACKGROUND: Peripheral venous pressure (PVP) has been shown to correlate with central venous pressure (CVP) in a number of reports. Few studies, however, have explored the relationship between tissue pressure (TP) and PVP/CVP correlation.

METHODS: PVP and CVP were simultaneously recorded in a bench-top model of the venous circulation of the upper limb and in a single human volunteer after undergoing graded manipulation of tissue pressure surrounding the intervening venous conduit. Measures of correlation were determined below and above a point wherein absolute CVP exceeded TP.

RESULTS: Greater correlation was observed between PVP and CVP when CVP exceeded TP in both models. Linear regression slope was 0.975 (95% CI: 0.959-0.990); r^2 0.998 above tissue pressure 10 cmH₂O vs. 0.393 (95% CI: 0.360-0.426); and r^2 0.972 below 10 cmH₂O at a flow rate of 2000 mL/h in the *in vitro* model. Linear regression slope was 0.839 (95% CI: 0.754-0.925); r^2 0.933 above tissue pressure 10 mmHg vs. slope 0.238 (95% CI: -0.052-0.528); and r^2 0.276 in the *en vivo* model.

CONCLUSION: PVP more accurately reflects CVP when absolute CVP values exceed tissue pressure.

KEY WORDS: Peripheral venous pressure; Central venous pressure; Tissue pressure

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INTRODUCTION

Despite limitation, measurement of central venous pressure (CVP) remains valuable when used in concert with clinical examination in guiding manipulation of circulating volume status.^[1] Given the inherent risks associated with central venous catheterization, however, CVP monitoring has largely remained confined to the critically unwell. Recent reports of alternative modalities for obtaining CVP estimation^[2-5] hold promise for utilization of filling pressure estimation in volume state assessment both prior to central line insertion and in those patients in whom central line placement is deemed unnecessary.

Peripherally acquired venous pressure (PVP) has additionally been demonstrated to correlate with CVP in a number of studies in the operating theatre^[6-10] and intensive

care settings.^[11] If demonstrated reliable, utilization of PVP in clinical volume status assessment holds the obvious advantage of widespread potential application as almost all patients admitted to hospital undergo peripheral venous cannulation. To be clinically useful, however, any such estimate of CVP must prove accurate across a breadth of CVP recordings in a wide range of pathologic conditions. Understanding of factors that may influence PVP/CVP correlation during conditions of extreme CVP values (i.e. very low, or very high CVP recordings) is therefore essential as these factors are most likely to result in manipulations of cardiac preload by clinicians.

We have previously demonstrated a greater correlation between PVP and CVP at higher CVP values,^[12] citing a direct influence of the compressive

effect of tissue pressure on the observed relationship between PVP and CVP. Specifically we hypothesized lesser difference between values when intervening conduit resistance was least, affording unimpeded flow. We further postulated this to correspond with an intraluminal pressure above which the propensity for tissue pressure to induce vascular collapse is negated.

The present investigation was therefore conducted to further explore the influence of tissue pressure on the relationship between central and peripherally acquired venous pressure metrics. Both *in vitro* and *en vivo* models were utilized. A bench-top model of the venous circulation of the upper limb was initially interrogated to document the effect of increasing tissue pressure on PVP/CVP correlation. In the second phase of the study CVP/PVP parings were acquired in a solitary human subject undergoing mimicked tissue pressure elevation via external cuff, and Valsalva induced variation of CVP.

METHODS

This investigation utilized both *in vitro* and *en vivo* models of peripheral/central venous pressure correlation to explore the relationship between the two variables. Details of experimental set-up and data acquisition for both methodologies are outlined below.

In vitro model—experimental set-up

A mechanical model was constructed mimicking the venous circulation from the antecubital fossa to the confluence of the subclavian and internal jugular veins of the upper limb. In brief, this consisted of a 45 cm length of 7.5 mm internal diameter thin walled deformable latex tubing as a surrogate for the venous conduit, supported within a rigid water-filled transparent bath mimicking surrounding soft tissues. The "vein" was manufactured to include two internal one-way "fish-mouth" valves positioned at equal intervals as per human anatomy. The apparatus was "perfused" with two automated flow generators (IPX1 infusion pump, Cardinal Health, Rolle, Switzerland) connected in parallel and capable of providing from 0 to 2000 mL/h continuous flow. Luminal pressure at both ends of the apparatus with a 35 cm water manometer connected by 3-way tap to the distal (nominally PVP) and proximal (nominally CVP) ends of the tubing respectively. Adjustment of the height (H) of the perfusate outflow served to provide varying CVP pressures. Pressure within the surrounding water-bath (nominally tissue pressure[TP]) was controlled via graded injection of fluid, and assessed by an identical

water filled manometer attached to the bath. A schematic of the experimental set-up is presented in Figure 1.

Data collection

The experimental apparatus was perfused with 0.9% saline solution at constant rate (1000 mL/h and 2000 mL/h) during phase one and two of acquisition of study metrics respectively. For both flow rates, CVP/PVP parings were obtained at three differing tissue pressure settings (0 cmH₂O, 10 cmH₂O, and 20 cmH₂O). Each venous pressure recording was made two minutes after adjustment of CVP height. Pressure metrics were recorded to the nearest one mm. All data-points were obtained in triplicate and mean values reported.

En vivo model—experimental set-up

Ethical approval for the *en vivo* model was sought and gained from the Northern Y division of the New Zealand Health and Disability Ethics Committees. A single volunteer (MH) underwent venous cannulation of the antecubital fossa vein (PVP) and external jugular vein (CVP) with 18G intravascular cannulae (Becton Dickinson Infusion Therapy Systems Inc, Utah, USA) on the right. These were connected via Truwave pressure transducers (Edwards Lifesciences, Irvine, CA, USA) to a Phillips IntelliVue MP50 (Boehringer, Germany) and a bedside monitor for assessment of venous pressure metrics. The pressure transducers were room air zero-calibrated with reference to the mid thorax. The subject remained in supine, with the arm in the mid-thoracic position, for the duration of the experimental protocol.

Following instillation of 1 mL 1% lignocaine solution, one 22G needle was inserted to a depth of 1.5 cm overlying the central biceps on the right for assessment of tissue pressure. One mL of 0.9% saline solution was injected, and the needle connected via an identical pressure

Figure 1. Schematic of *in vitro* experimental set-up.

transducer to the monitoring system. This transducer was likewise room air zero-calibrated with reference to the mid thorax. Following taping, a standard sphygmomanometer blood pressure cuff was centred over the sampling needle and applied. Tissue pressure was thereby able to be manipulated by inflating the blood pressure cuff to a predefined tissue pressure, and clamping the attached pneumatic tubing. A thirty-minute stabilization was afforded before acquisition of study parameters.

Data collection

While positioned in supine, the subject performed graded Valsalva manouevres (against closed glottis only) to a constant CVP value. Repeated paired CVP/PVP recordings were obtained following maintenance of a stable CVP for a period of 10 seconds across a range of CVP levels. Acquisition of venous pressure recordings was repeated at three different tissue pressure settings (native[cuff deflated], 10 mmHg, and 20 mmHg). Pressure metrics was taken as a time-weighted average of venous pressure waves as per the manufacturer software. All pressures were recorded to the nearest mmHg.

Statistical analysis

Statistical analysis of all variables was conducted using GraphPad Prism (version 5.0, La Jolla, CA, USA). Simple linear regression was used to observe the relationship between PVP and CVP values for both models. In each case (*in vitro/en vivo* models, and for individual flow rates in the *in vitro* model) the slope of linear regression was compared for grouped venous pressure values below (and inclusive) and above the nominated tissue pressure level. Goodness of fit for each was assessed using the r^2 statistics. Bland-Altman plots were constructed to assess limits of agreement between PVP and CVP for the *en vivo* model.

RESULTS

Venous pressure correlation and PVP/CVP differential according to tissue pressure for flow rates 1000 mL/h and 2000 mL/h in the *in vitro* model are presented graphically in Figure 2. Linear regression slopes for this model and goodness of fit are presented in Table 1 (0 cm water grouping not differentiated).

Venous pressure correlation and PVP/CVP differential according to tissue pressure for the *en vivo* model are presented graphically in Figure 3. Bland-Altman plots of the *en vivo* data are presented in Figure 4. Linear regression slopes for this model and goodness of fit are presented in Table 2 (6 mmHg grouping not differentiated).

Figure 2. PVP and PVP-CVP vs. CVP, *in vitro* model.

DISCUSSION

In the *in vitro* model we found a good correlation, with linear regression slope approximating 1.0, for PVP/CVP parings above a point wherein CVP exceeds tissue pressure. Conversely, while correlation remained good, the slope of linear regression was significantly lesser and PVP-CVP differential greater, for CVP values below tissue pressure. The former findings were replicated in the *en vivo* model with good correlation and slope approaching 1.0 for CVP values exceeding tissue pressure. Peripheral venous pressure/CVP correlation was, however, poor and PVP-CVP differential large for measured CVP values acquired with tissue pressure exceeding CVP. These findings support the forwarded hypothesis of greater PVP/

Table 1. Linear regression slope below and above tissue pressure according to flow rate for *in vitro* data.

Tissue pressure (TP)	Slope ($\leq$ TP)	Slope ($>$ TP)	Goodness of fit [r^2] ($\leq$ TP & $>$ TP)
0 cmH ₂ O (1000 mL/h)	0.994 (0.986 to 1.003)		0.999
10 cmH ₂ O (1000 mL/h)	0.556 (0.489 to 0.623)	0.975 (0.959 to 0.990)	0.972 & 0.999
20 cmH ₂ O (1000 mL/h)	0.430 (0.402 to 0.458)	0.873 (0.813 to 0.933)	0.982 & 0.993
0 cmH ₂ O (2000 mL/h)	0.945 (0.922 to 0.969)		0.999
10 cmH ₂ O (2000 mL/h)	0.393 (0.360 to 0.426)	0.975 (0.959 to 0.990)	0.972 & 0.998
20 cmH ₂ O (2000 mL/h)	0.299 (0.267 to 0.330)	0.873 (0.813 to 0.933)	0.982 & 0.996

Data presented as mean (95% confidence interval)

Table 2. Linear regression slope below and above tissue pressure for *en vivo* data.

Tissue pressure (TP)	Slope ($\leq$ TP)	Slope ($>$ TP)	Goodness of fit [r^2] ($\leq$ TP & $>$ TP)
Native (6 mmHg)	0.821 (0.779 to 0.863)		0.978
10 mmHg	0.238 (-0.052 to 0.528)	0.839 (0.754 to 0.925)	0.276 & 0.933
20 mmHg	0.272 (0.094 to 0.449)	0.776 (0.532 to 1.021)	0.338 & 0.870

Data presented as mean (95% confidence interval)

Figure 3. PVP and PVP-CVP vs. CVP, *en vivo* model. **Figure 4.** Bland-Altman plot of *en vivo* data.

CVP correlation at CVP values exceeding that of tissue pressure, where the propensity for vascular collapse in thin walled veins is negated.

While the finding of accurate PVP/CVP correlation was reported in numerous series,^[6-10] few investigators have sought to quantify factors associated with lesser agreement between these variables. Greater PVP-CVP differential at low absolute CVP values has been reported by Hoftman et al^[6] in nine patients undergoing orthotopic liver transplantation. Similarly we have found a greater PVP/CVP correlation in high CVP values, with increased PVP/CVP divergence at lower absolute CVP values in 34 adult patients undergoing elective cardiac surgery.^[12] The explanation forwarded by both authors to explain this phenomenon was collapse of peripheral venous conduits during the period of low intraluminal pressure, thereby obscuring an intact fluid column from central to peripheral monitoring sites. Such a classic "vascular waterfall" effect may in large part explain the results of the current study. Notably, 'vessel' collapse was observed to occur visually in the *in vitro* model during investigation at higher tissue pressures, with complete 'vessel' expansion noted following CVP elevation above tissue pressure in all instances of data acquisition.

The implications of these findings are of potential clinical relevance. Any utilization of PVP in volume state assessment must include consideration for tissue pressure elevation to effect elevated and erroneous PVP recordings relative to true CVP. Given greatest PVP-CVP differential has been observed at low CVP values, and with higher tissue pressures, greatest potential for clinical inaccuracy exists in patients with genuine hypovolaemia (and therefore reduced cardiac filling pressures). Unfortunately, this population represents a subgroup of patients wherein accurate knowledge of CVP might conceivably result in appropriate clinician directed action to undertake preload enhancement with infusion of circulatory volume expanders.

The clinician undertaking PVP assessment as a surrogate for CVP must therefore ensure all practical steps are taken to minimize the effect of external pressure (limb positioning, constricting gowns, leaning surgeons) on the limb between the sites of peripheral cannulation and the thorax. Additionally, while likely to remain unmeasured, consideration of the likelihood of elevated tissue pressure (peripheral edema, traumatic insult, ischemia) may assist in interpretation of acquired PVP metrics. Notably, early investigators reported subcutaneous tissue pressures between zero and eight cmH₂O in the forearm and leg for normal individuals,

and exceeding 20 cmH₂O in edematous patients.^[13]

The framework in which these results are viewed may additionally provide insights into the management of the circulation. CVP is often used in assessment of the volume state. That (venous pressure – tissue pressure) rather than venous pressure alone is the determinant of venous volume may in part explain the variability in usefulness of this measure. Additionally, the role of tissue pressure in impeding venous return may be underappreciated clinically. The venous return equation is as follows: Cardiac output = (mean systemic filling pressure – CVP/resistance of the average circulatory element). Much of the circulatory volume exists in the veins, increasing the contribution of this compartment to resistance of the average element. Venous collapse secondary to tissue pressures within the range caused by edema could impede venous return. A "vicious circle" of overfilling leading to edema leading the need for more fluid could be hypothesized.

This study has a number of methodologic limitations inherent to the interrogated models utilized in this work. The *in vitro* model utilized presents a 'static' representation of the dynamic human circulation. Variability in venous return secondary to alteration in vascular tone, cardiac index, and the respiratory cycle has not been replicated. Furthermore, the model was perfused with 0.9% saline solution, rather than a fluid more accurately mimicking the flow dynamics of human blood. While the presented results nevertheless demonstrate a good approximation of those observed in the *en vivo* model, we are unable to comment on the potential for differing patterns of flow associated with more viscous fluids to alter observed pressure metrics. Interpretation of the results of the *en vivo* model are constrained by the use of external jugular pressure as a surrogate for true CVP. While there is some evidence suggesting that external jugular pressure is correlated well with centrally acquired venous pressure,^[14,15] we have failed to include central venous cannulation and true CVP estimation in this protocol. The risks associated with central venous cannulation were, however, considered in excess of those appropriate for such a volunteer study. The *en vivo* model furthermore contained no measure of venous flow rate in the studied limb. Data from the *in vitro* model would nevertheless suggest a similar relationship between the two variables irrespective of blood velocity.

A greater correlation between peripherally acquired venous pressure and central venous pressure was demonstrated when absolute CVP exceeded tissue pressure in the *in vitro* and *en vivo* models utilized in

this study. Clinical utilization of PVP in volume status assessment must depend upon the potential for elevated tissue pressure to obscure accurate PVP estimation of CVP, at low absolute CVP values.

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