

The assessment of intravascular volume

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Introduction

There are numerous reasons for the accurate assessment of intravascular fluid volume status. Some of the most often cited are: concerns regarding urine output, considerations for organ and tissue perfusion or even a desire for optimising fluid status, per se. Most practitioners agree that an underlying theme is the goal of attaining optimal cardiac output, either in the surgical setting or in intensive care. Intravenous fluid loading is often used as first line therapy for patients with hypotension or circulatory failure, but cardiac output responds positively after fluid challenge in only half the patients.¹ For the remainder of patients fluid loading may be associated with adverse consequences.

Measurements of preload have historically been used to help in deciding which patients may benefit from fluid administration. Central venous pressure and pulmonary capillary wedge pressure assessment have played key roles in identifying such patients. Unfortunately, cardiac filling pressures, their surrogates and cardiac end-diastolic parameters have been demonstrated to be of little value in assessing volume responsiveness in the critically ill patient.^{1,2} Research suggests that neither central venous pressure nor capillary wedge pressure have any validity when used to optimize cardiac output or to assess response to fluid administration.³ However, the measurement and response of central venous pressure to fluid administration, continues in many places, to play an apparently crucial role. The following discussion focuses on the validity of the central venous pressure in particular as a means of assessing fluid status and in optimising cardiac output. The arguments proposed are, however, equally applicable to pulmonary capillary wedge pressure.

Historical considerations

As long ago as 1897, in an early treatise on cardiac physiology, Ernest Starling⁴ expressed his misgivings on the validity of the jugular venous pressure as a means of assessing cardiac function. He summarised this saying, "The central veins are so near to the heart that one cannot deduce a general rise of venous pressures from a rise in pressure in these conduits." This was followed by the work of Starr and Rawson⁵ in 1940, who made meticulous observation of the role of central venous pressure in the manipulation of cardiac output.

Starr and Rawson identified that it was not the central venous pressure that was important in influencing cardiac output, but rather the gradient between peripheral venous pressure and central venous pressure that influenced venous return. In other words, the venous pressure gradient regulates and controls the rate of venous return. Central to the application of their work is the understanding that at steady state, venous return and cardiac output are equal, and that factors increasing venous return would enable a greater cardiac output and vice versa. The application of Ohm's law, (Equation 1), where CO is cardiac output and VR venous resistance, holds true.

Equation 1

$$CO = VR = \frac{\text{pressure gradient for venous return}}{\text{venous resistance}}$$

Regarding venous return and the rate of venous flow, this must logically be the difference between some peripheral, driving pressure for venous return, and some central pressure impeding venous return. This is expressed in equation 2, below.

Equation 2

$$VR = \frac{P_{MS} - P_{RA}}{R_v}$$

In physiology the pressure driving venous return is termed "mean systemic pressure" (P_{MS}), not to be confused with mean arterial pressure, and the pressure retarding venous return, right atrial pressure (P_{RA}). The resistance of the venous system is denoted as R_v . Of immediate

concern is the fact that if right atrial pressure impedes venous return, and this is analogous to central venous pressure or CVP, then a higher CVP may be associated with a poorer venous return and hence cardiac output!

Starr and Rawson determined that several permutations might exist regarding the administration of fluid and the response of the cardiovascular system with respect to both venous return and cardiac output. The potential influences of fluid administration on the pressures governing venous return are:

1. An increase in P_{MS} alone, leading to a greater venous return and cardiac output.
2. An increase in both P_{MS} and P_{RA} with the rate of venous return and cardiac output relatively unchanged.
3. An increase in P_{RA} greater than P_{MS} leading to a poorer venous return and hence cardiac output.

In their work the two authors concluded that manipulation of the peripheral circulation is as important to the successful treatment of shock and other altered circulatory states, as is the manipulation of cardiac output.

Bearing this crucial work and its important implications in mind, one must ask why there is still so much emphasis placed on the measurement of central venous pressure and its assessment following fluid administration. It has to be accepted that measurement of the central venous pressure alone, cannot discern the permutations of P_{MS} and P_{RA} , and that fluid loading may indeed be associated with a worsening venous return and cardiac output.

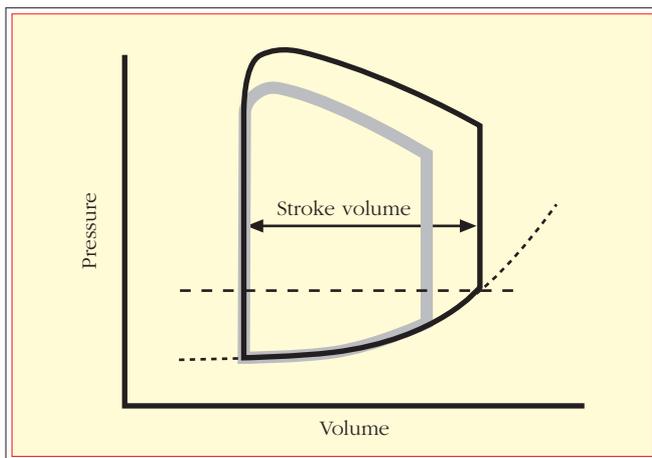
Assessing central venous pressure in response to fluid administration

Many practitioners feel that following a trend in CVP with respect

to fluid administration is still a valid means of optimising fluid status. This practise warrants further investigation.

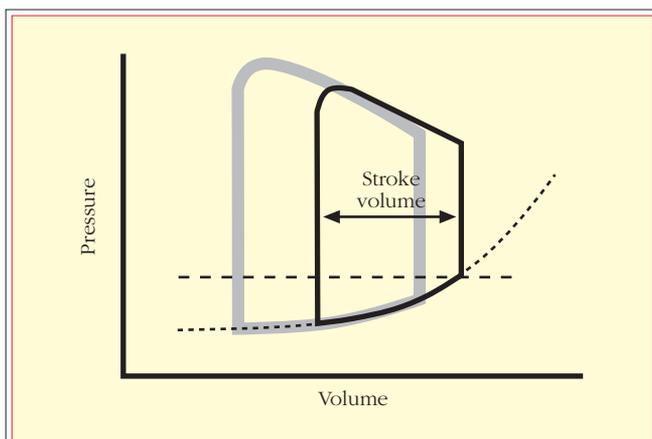
Best represented by pressure-volume curves, the potential effects of fluid administration can be appreciated in the diagrams that follow. Figure 1 shows the most desirable effect of fluid administration. Fluid administration shifts the end-diastolic volume rightward along the ventricular elastance curve and a greater end-diastolic volume is associated with a raised end-diastolic pressure. Ideally a greater stroke volume follows intravascular loading and there is little change in end-systolic volume.

Figure 1: The ideal effect of fluid administration. The dark pressure volume loop shows a greater end-diastolic volume with corresponding increase in end-diastolic pressure. The ultimate effect is an enhanced stroke volume and the possibility of greater cardiac output.



Unfortunately the effects of fluid administration are not necessarily those depicted in figure 1. There are important assumptions that have been made: central venous pressure, or pulmonary capillary wedge pressure, are not necessarily representative of end diastolic pressure, and an improved stroke volume is not necessarily the end result of fluid loading. An equally probable result is depicted in figure 2. Here it is seen that end-systolic volume has increased.

Figure 2: An unwanted effect of fluid administration. The darker loop shows a greater end-diastolic pressure with corresponding increase in end-diastolic pressure. There is however a smaller stroke volume and the potential of a lesser cardiac output.



Two possibilities exist: the stroke volume remains unchanged despite a greater end-diastolic volume; the stroke volume decreases with a greater end-diastolic volume.

The observation that filling pressure cannot discern a change in stroke volume as depicted in figures 1 and 2 is not surprising. Filling pressure is a function of ventricular elastance in diastole, while stroke volume is a function of systole. A rise in central venous pressure, or pulmonary capillary wedge pressure cannot automatically be linked to an increase in ejection fraction. The measurement of these surrogate values for filling pressure may then have questionable benefits on the optimisation of cardiac output. The error made is not in the validity of the pressures measured, but rather in the deduction of what the changes in the pressure represent. At no point can it be assumed that a greater filling pressure is associated with a greater stroke volume or cardiac output, a greater filling pressure is only indicative of the ventricle's diastolic performance on its elastance curve.

Filling pressures as a guide to optimisation of cardiac output

In terms of optimisation of cardiac output, (one of the ultimate goals of fluid management), it would seem senseless to load with fluid if stroke volume is to be impacted negatively. We have seen that both central venous pressure and pulmonary capillary wedge pressure may be non-intuitive guides to the magnitude of change in stroke volume. Nevertheless both are frequently relied upon in the clinical setting for precisely this purpose. It has to be appreciated that the assessment of stroke volume or cardiac output directly, are the only means by which these important variables can be manipulated.

In addition, it must be remembered that both central venous pressure and pulmonary capillary wedge pressure are dramatically influenced by overall intrathoracic pressure. This is particularly so, in the patient receiving positive pressure ventilation, and even more so, where large amounts of positive end expiratory pressure (PEEP) are used. The poorer a patients' lung compliance and the higher the mean airway pressure, the more difficult it becomes to interpret the surrogates of cardiac filling pressure. Both central venous and pulmonary capillary wedge pressures may therefore become more a function of ventilation than of cardiac status.

Critical assessment of central venous and pulmonary capillary wedge pressure

Numerous authors have studied the validity of both central venous and pulmonary capillary wedge pressure for assessing fluid status, and also the impact of fluid loading on cardiac output. A recent meta analysis has addressed this issue.¹ No threshold value discriminates responders and non-responders, and static parameters should not be used to predict fluid responsiveness. Several papers have considered both variables in the intensive care setting and uniformly agree that neither is of value in the optimisation of cardiac output and hence oxygen delivery. Specific patient population groups assessed have been those with sepsis,^{6,8} trauma,⁹ burn injury,¹⁰ acute respiratory failure,^{3,6,11} critical illness,^{6,11,12} and surgery requiring cardiopulmonary bypass.^{13,14} There would appear to be little correlation between changes in central venous pressure and cardiac output when these are followed with time.¹⁵ A major criticism has been that the studies addressing the issue of filling pressure assessment and cardiac output have investigated critically ill patients, or those with other potential reasons for confounding variables. Many practitioners, particularly in anaesthesia, justifiably argue

that the apparent pitfalls in the interpretation of filling pressure may not apply in settings of normal cardiovascular physiology. Argument hinges on the fact that in all situations investigated above, there may be varying amounts of ventricular dysfunction and this leads to no conclusion other than that central venous and pulmonary capillary pressure are poor surrogates in these specific situations.

The value of central venous pressure assessment in healthy individuals

Despite concerns regarding the validity of central venous pressure as a measure of preload as outlined above, many clinicians have continued with its use. A recent publication has specifically questioned the correlation of both central venous pressure and pulmonary capillary wedge pressure in healthy individuals.¹⁶ The objective of this study was to assess the relationship between pressure estimates of ventricular preload (pulmonary artery occlusion pressure, central venous pressure) and end-diastolic ventricular volumes/cardiac performance in healthy volunteers. The subjects in the study were not ventilated; eliminating any potential interaction with raised intrathoracic pressure, and had no underlying heart disease or disturbance of contractility. This questions the validity of the concerns raised in the previous section. Normal healthy volunteers demonstrate no correlation between central venous pressure and pulmonary artery occlusion pressure, and both end-diastolic ventricular volume indices and stroke volume index. Similar results were found with respect to changes in these variables following volume infusion. Study data suggest that the lack of correlation of these variables in specific patient groups described in other studies, represents a more universal phenomenon that includes normal subjects. Neither central venous pressure nor pulmonary artery occlusion pressure appear to be useful predictors of ventricular preload with respect to optimizing cardiac performance.

If there is no evidence for central venous and pulmonary capillary wedge pressure as reliable guides to the manipulation of stroke volume and cardiac output, we have to question a fundamental cornerstone of our clinical practice.¹⁷ One study has indicated that only a central venous pressure of less than 2 mmHg is of any value in assessing intravascular fluid status.¹⁸

Alternative means of assessing response to fluid administration

If the arguments and evidence presented above are accepted, or if it is acknowledged that there are serious flaws in the current use of central and pulmonary capillary wedge pressures, an important question follows. Is there a better more reliable means of assessing intravascular fluid status and the potential response to fluid administration?

There is a growing interest in the clinical value of the observed variations in blood pressure and cardiac output that result from the interactions between the heart and lungs during ventilation.¹⁹ It is not uncommon to observe a rise and fall of the blood pressure on an arterial line trace, or the variations detected by plethysmography, coinciding with ventilatory rhythm. This is known as systolic pressure variation and represents a potentially powerful tool in the assessment and manipulation of fluid status. It has recently been established that several analogous derivatives also provide valuable clinical information on a continuous basis including pulse pressure variation, pulse volume variation and pulse velocity variation.²⁰⁻²²

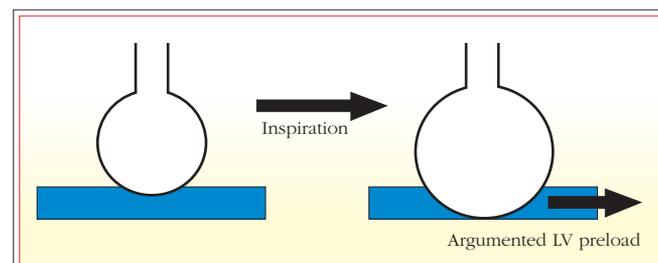
The physiologic basis of systolic pressure variation

The fluctuations of the arterial pressure waveform during intermittent positive pressure ventilation are familiar, and the 'swing' of the pressure trace during inspiration and expiration are easily seen on a standard monitor display. These changes are largely the consequence of alterations in instantaneous preload to the ventricle. To facilitate understanding of the physiologic processes involved it is convenient to consider changes in inspiration and exhalation separately.

The inspiratory phase

During inspiration alveolar volume increases. Early in inspiration distending alveoli impinge on the pulmonary capillary beds, decreasing capillary volume and driving pulmonary capillary blood forward through the lung to the left atrium and ventricle (Figure 3). This represents positive inspiratory pulmonary venous flow and augments left ventricular preload and hence stroke volume. The phenomenon occurs mostly in West zone 3 regions of the lung where alveolar capillaries are distended with blood. The increase in stroke volume and consequent increase in arterial pressure is denoted Δ up and is particularly prominent in the setting of hypervolaemia and conversely almost absent in hypovolaemic states.

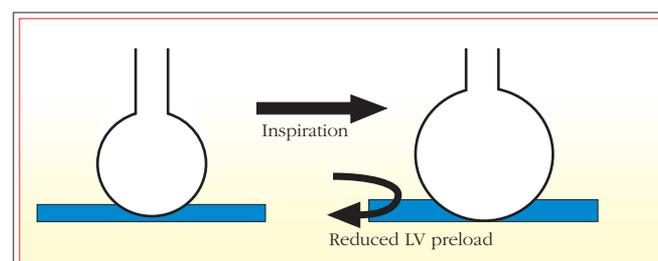
Figure 3: Augmented left ventricular preload as a result of inspiratory alveolar distension. Pulmonary capillary blood is pushed forward to the left ventricle as alveoli compress the pulmonary capillaries.



Later in the inspiratory phase, or if the pulmonary capillary bed is relatively underfilled, the distending alveoli present an obstruction to pulmonary capillary flow (figure 4). This leads to a state of poor pulmonary venous flow and relative underfilling of the left ventricle, as well as a reduction in preload. This is appreciated as a reduction in stroke volume and a decrement in arterial pressure, denoted Δ down. Δ down is prominent in states of hypovolaemia and dynamic hyperinflation.

Figure 4: Reduction in left ventricular preload as alveoli distend and compress the pulmonary capillary bed.

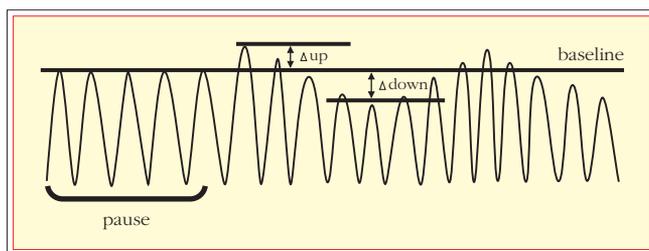
Alveoli may reduce pulmonary venous flow and reduce filling of the left ventricle.



The expiratory phase

During exhalation, the above phenomena cease to occur and pulmonary venous flow returns to baseline state. A steady state of ventricular filling occurs and stroke volume approaches baseline. The net physiologic effect of the interactions described above can be observed in figure 5 below. An inspiratory pause is effected in order to appreciate baseline conditions of pulmonary venous return and consequent stroke volume. Both Δup and Δdown can now be appreciated.

Figure 5: The effect of an inspiratory pause on systolic pressure variation. The identification of up and down becomes possible. In figures 3, 4 and 5 the physiologic consequences and the derivation of up and down are illustrated. In an analogous fashion, stroke volume variation, pulse pressure variation and pulse velocity variation can be derived.



The utility of systolic pressure variation

Substantial amounts of literature have confirmed the utility of the analysis of systolic pressure variation in the assessment of fluid status.^{21,23} Excessive “swing” of the trace can be identified as being either predominantly Δup or Δdown . Where the “swing” is predominantly Δdown , hypovolaemia may be identified and a positive result of fluid administration expected. In effect the administration of fluid can be predicted from the net effect of the small variations in preload or “fluid administration” to the ventricle resulting from the normal cardiopulmonary interaction. down has been shown repeatedly to be a sensitive predictor of preload.²⁰ In a sepsis study down predicts the response of cardiac output to volume load better than either pulmonary capillary wedge pressure or left ventricular end-diastolic area as determined by echocardiography.²² This is astounding evidence, bearing in mind that both variables have traditionally been regarded as clinical gold standards for the assessment of fluid status with regard to the manipulation of cardiac output.

Conclusion

Over a period of almost twenty years numerous authors have progressively and systematically researched and reviewed the utility of filling pressures and their surrogates as tools for fluid assessment and optimisation of cardiac output. Recent publications^{1,2,6,9,14} on the validity of central venous and pulmonary capillary wedge pressures only bear out concerns expressed almost seventy years ago⁵ and first hinted at over a century ago.⁴ The overwhelming consensus is that central venous pressure and pulmonary capillary wedge pressure measurement and interpretation are of little value in the management of fluid status and cardiac output. Newer dynamic means, such as systolic pressure variation, stroke volume variation, pulse pressure variation and pulse velocity variation, all seem to hold much in store for clinical practice. Already these new derivatives appear set to displace our old stalwarts from the clinical arena. Monitoring systolic pressure variation enables real time prediction and monitoring of the left ventricular response to preload

enhancement. It also aids in guiding fluid therapy.²¹ Even the haemodynamic response to passive leg raising would appear to a promising index of fluid responsiveness. One study has interpreted the consequences of passive leg raising within the context of systolic pressure variation.²⁴

If nothing else, the assessment of intravascular fluid status remains the identification of a syndrome complex.¹⁸ Peripheral perfusion, acid-base status, urine output, lactate and fluid balance remain as important discriminators, but central venous and pulmonary capillary wedge pressure probably do not!

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