Review article

Rise and fall of CVP

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Abstract

The average blood pressure recorded in the superior vena cava near right atrium represents *'central venous pressure'* (CVP). Traditionally CVP has been used as an indicator for predicting cardiac preload as well as volume responsiveness in critically ill patients. CVP is chiefly dependent on two factors: venous blood volume (venous return) and venous compliance. CVP is not an independent variable in determining cardiac output. Its relationship with cardiac output varies largely with the dynamic changes in the compliance of vascular compartment. The total blood volume in a venous system exists in two forms: Stressed volume (Vs) and Unstressed volume (Vu). The unstressed volume is equivalent to a basal blood volume that occupies the venous system. The stressed volume is the proportion that is dynamic in nature and affects the venous return and cardiac output. In this article, the basic physiology and applications of CVP as well as its limitations when compared to other dynamic parameters in assessing cardiovascular function are discussed.

Keywords: Central venous pressure, stressed volume, venous compliance, venous resistance

Introduction

The term venous pressure denotes average blood pressure recorded in the venous compartment. The average blood pressure recorded in the superior vena cava near right atrium represents *'central venous pressure'* (CVP). Traditionally CVP has been used as an indicator for predicting cardiac preload as well as volume responsiveness in critically ill patients. Of late this application of CVP in predicting fluid responsiveness and cardiac preload has been questioned. In this article, the basic physiology and applications of CVP as well as its limitations when compared to other dynamic parameters in assessing cardiovascular function are discussed.

Basic physiology

CVP is a major determinant factor of right ventricular filling pressure and hence used as a surrogate marker for right ventricular volume (preload) provided there is no tricuspid valve pathology. The right ventricular preload in turn regulates the stroke volume and hence cardiac output through Frank-Starling mechanism.

CVP is chiefly dependent on two factors: venous blood volume (venous return) and venous compliance. Other factors such as intrathoracic pressure, right heart function and myocardial compliance also affect CVP. CVP is not an independent variable in determining cardiac output. Its relationship with cardiac output varies largely with the dynamic changes in the compliance of vascular compartment.

Compliance (Cv), is the change in volume (ΔV) divided by the change in pressure (ΔP) and is given by the formula: Cv= ΔV/ΔP. By rearranging the above formula a change in CVP (ΔCVP) can be determined by the change in volume (ΔV) of blood within the thoracic veins divided by the compliance (Cv) of these veins: ΔCVP=ΔV/ Cv. The venous system is the major blood reservoir accounting for two-thirds of the blood volume and is markedly more compliant than the arterial system. Therefore, an increase in the venous volume or a decrease in venous compliance or both will increase CVP. In the body, venous compliance and venous volume are not

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static, but dynamic, with many factors influencing these two variables.

Under physiologic states, the heart pumps whatever the amount of blood it receives and hence cardiac output is proportional to the venous return. Venous return (VR) is the rate of blood flowing from the systemic veins into the right atrium. There should be a pressure gradient that can drive blood from the systemic veins into the heart. The mean circulatory filling pressure (MCFP), which is the pressure exerted by nonpulsatile blood in the vasculature is the driving force that drives blood into the heart. The normal right atrial pressure at rest is 0 mmHg[1-3] and the mean circulatory filling pressure is approximately 7 mm Hg[1]. The magnitude of this pressure gradient determines the venous return[2] and is given by the formula: VR= (MCFP- CVP)/ Venous Resistance. Hence at the end of myocardial contraction, pressure in the right atrium (CVP) becomes zero and the mean circulatory filling pressure drives the blood into the right atrium.

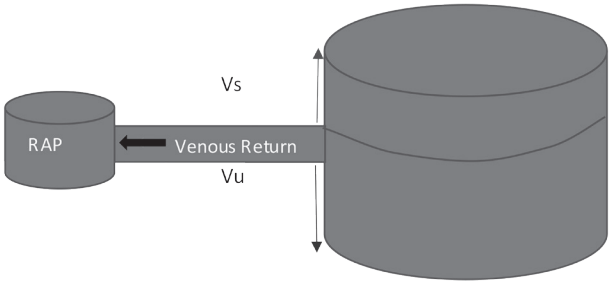

Figure 1: Graphical representation of effect of right atrial pressure (RAP) and venous blood volume on venous return. (Vu: Unstressed volume, Vs: Stressed volume)

The total blood volume in a venous system exists in two forms: **Stressed volume (Vs) and Unstressed volume (Vu)**. The unstressed volume is equivalent to a basal blood volume that occupies the venous system. The stressed volume (about 30% of the total venous volume) is the proportion that is dynamic in nature. The stressed volume increases when there is an increase in blood volume (as happens with volume infusions) for the same volume of venous space. It can also increase when vasopressors are given. The total venous vascular volume reduces consequent to the vasoconstriction. The same blood volume as there was before now occupies a smaller volume, thereby increasing the stressed volume. It is the stressed volume that actually contributes to the mean circulatory filling pressure and participates in the venous return *(Figure 1)*.

Hence, there are two ways of increasing the MCFP-RAP gradient: one is to add fluid volume into the system that will increase the stressed volume and other is to reduce the vessel wall compliance. The latter is achieved by constricting the veins using vasopressors and thereby mobilising the unstressed blood volume to augment stressed volume and venous return.[4,5] Similarly a rise in right atrial pressure that can occur in certain pathological states or a decrease in MCFP due to volume depletion and venodilatation (*e.g.*, sepsis) can impede venous return.[2,3]

Factors that decrease Central Venous Pressure

1. Decrease in stressed volume (Vs): In initial phases of hypovolaemia, there might not be a decrease in CVP because of compensatory shift of blood from Vu to Vs compartment. However, further loss of blood volume can exhaust Vu and Vs, and the CVP decreases. The second reason for a decrease in Vs is venodilation where the blood volume shifts from Vs to Vu and causes a drop in CVP.
2. Increased venous resistance as seen during forceful inspiration can result in collapse of thoracic veins due to negative pressure and impede venous return.

Factors that increase Central Venous Pressure

1. The main factor that increases CVP is failure in cardiac pump function either because of ineffective myocardial contractility or valvular dysfunction.
2. Positive pressure ventilation as well as application of high PEEP can also result in high CVP values.
3. Venoconstriction (a shift of blood from Vu to Vs) either with the use of venoconstrictors or because of increased sympathetic discharge and/or activation of renin-angiotensin system will raise CVP.

The rise of CVP

Since the Starling's famous "Law of the Heart" experiments on venous return and cardiac output, a number of research papers were published in the earlier part of the century that came out supporting the role and utility of CVP as a surrogate marker for ventricular preload, to predict volume responsiveness in patients and also as a marker for circulatory filling.

The history of CVP dates back to the Starling's original experimental studies which were done about a century ago.[6] Starling emphasised that within physiologic limits, an increase in the venous return raises right atrial pressure and hence cardiac output. However with further increase in venous return that exceeds heart's capacity to respond, right atrial pressure rises without a rise in cardiac output.[6] Forty years after the Starling's experiments, Sarnoff and Berglund echoed similar findings but in a more intact systemic circulation.[7] They emphasised the fact that right atrial pressure is not an independent variable in determining the stroke volume and factors such as juxtacardiac pressures[8] as well as a failing heart secondary to induced coronary ischaemia also affect the stroke volume.

Braunwald *et al* applied Starling's law in human subjects and demonstrated the effects of changes in intrathoracic pressures during respiration on stroke volume variations.[9] All the preceding studies confirmed that heart has an intrinsic ability to contract and increase stroke volume with increasing preload within its physiologic conditions. Increase in right atrial pressure without an increase in stroke volume is seen secondary to a rise in juxtacardiac pressures as in cardiac tamponade, tension pneumothorax, excessive PEEP and positive pressure ventilation.[6,8-10] This can be attributed to the impediment to the venous return because of significant rise in CVP. Elevated CVP can also be seen in right heart failure or in conditions associated with rise in ventricular afterload where the heart cannot accommodate the normal venous return.

Clinical applications

In the 70s and 80s, several papers were published which emphasised maintenance of higher than normal cardiac indices including CVP for improving patient survival.[11-12] CVP measurement gained immense popularity largely because of its ease of measurement. Water filled columns, rigged out of intravenous infusion sets and an ordinary measuring scale were sufficient to measure the CVP. Commercially available water columns also could be used. The late 80's and 90's saw the changeover to pressure transducers, with their advantage of digital display of numbers, waveforms as well as trending capabilities. While the waveforms could provide a lot of information, the numbers were also heavily relied on as a measure of blood volume.

The fluid challenge test was based on the initial CVP and its response to varying amount of volumes (chosen on the basis of initial CVP). This was called the 5-2 rule. The baseline CVP was recorded. If it was <8 cm H_2O, a bolus of 200 ml of fluid was given over 10 minutes. If CVP was > 8 and < 14 cm H_2O, 100 ml bolus was given and if the baseline CVP was ≥ 14 cm H_2O, 50 ml of fluid was given. If any time during the infusion, the CVP rose by >5 cm H_2O, the infusion was stopped immediately. If the rise was absent or < 2 cmH_2O, the infusion could be continued. If the rise was between 2 and 5 cm H_2O, the infusion was stopped, and after 10 minutes of waiting restarted if the CVP came back to baseline.[13] If there was a pulmonary artery catheter in place, a 7-3 rule using the pulmonary capillary wedge pressure (PCWP), similar to the 5-2 rule for CVP could be used. This was a commonly adopted strategy and integral part of assessment of fluid responsiveness until recently.

In a study done by Rivers *et al*, early goal directed therapy (EGDT) was compared with standard therapy in ED for treating severe sepsis and septic shock.[14] Patients in both the groups had a CVC in place and CVP was targeted in the range of 8-12 mm Hg. Further the study had supported the use of CVP as a guide in the initial resuscitation of patients presenting with severe sepsis and septic shock.[14] The 2012 Surviving Sepsis Campaign guidelines too recommended the target CVP values in the range of 8-12 mm Hg for nonventilated patients and still higher values for ventilated patients.[15]

The fall of CVP

Several clinical studies have shown that CVP alone is not an ideal index for predicting right ventricular preload. CVP has been shown to correlate poorly with cardiac index[16] and also with stroke volume index.[17-20] It does not correlate well with other more reliable indices of cardiac preload such as the intrathoracic blood volume index, left ventricular end diastolic volume index[21] and right ventricular end diastolic volume index.[22,23]

Contrary to Rivers *et al* study, three randomised control studies namely, Protocol-based Care for Early Septic Shock (PROCESS),[24] Australasian Resuscitation in Sepsis Evaluation (ARISE),[25] and Protocolised Management in Sepsis (ProMISe)[26] that were done across the continents between 2014 and 2015 no longer recommended routine insertion of CVC just for the sake of monitoring the $ScvO_2$ and CVP. These series of studies compared EGDT with the usual care for the treatment of patients in sepsis and have stated that if the patients are recognised early as having sepsis and aggressively treated with intravenous fluids and early antibiotics, EGDT did not provide significant improvement over patients treated with usual care.

In 2008, Marik *et al* performed a systematic review of 24 studies reviewing the benefits of CVP in the management of fluid therapy.[27] The correlation coefficient between intravascular volume and CVP in patients with sepsis and postoperative patients was 0.16, and change in cardiac index and CVD was 0.18 and the area under the receiver operating characteristic curve was 0.56, illustrating that there is only a poor correlation between CVP and circulating blood volume.

A systematic review of literature was done by Marik *et al* in 2009 compared the dynamic indicators of fluid responsiveness such as arterial pressure waveform variation with respiration and the static indicators.[27] They concluded that in patients receiving mechanical ventilation the dynamic indicators are highly accurate in predicting volume responsiveness in critically ill patients as compared to traditional static indices of volume responsiveness. In 2013, Marik *et al* re-reviewed all existing data and conducted a meta-analysis of the literature which included 43 articles. They concluded that there were no data to support the use of CVP to guide fluid therapy, and both papers concluded that CVP should not be used for fluid resuscitation *(Table 1)*.[28,29]

Table 1: Predictive value of various techniques used to determine fluid responsiveness

Method	Technology	AUC*
Pulse pressure variation	Arterial waveform	0.94 (0.93–0.95)
Systolic pressure variation	Arterial waveform	0.86 (0.82–0.90)
Stroke volume variation	Pulse contour analysis	0.84 (0.78–0.88)
Left ventricular end-diastolic area	Echocardiography	0.64 (0.53–0.74)
Global end-diastolic volume	Transpulmonary thermodilution	0.56 (0.37–0.67)
Central venous pressure	Central venous catheter	0.55 (0.18–0.62)

*AUC = area under the curve with 95% confidence intervals.

Surviving Sepsis Campaign guidelines (2016) states that wherever available, dynamic parameters should be used to predict fluid responsiveness over static parameters such as CVP.

Conclusion

CVP is determined by the interaction between venous return and cardiac output. Static recordings of CVP had enjoyed tremendous popularity as an indicator of fluid responsiveness for many decades. It is now recognised that it may not be of much use in assessing cardiac function and fluid responsiveness, rather serial monitoring of CVP over time may provide useful information regarding intravascular fluid changes. With the availability of techniques for accurate assessment of dynamic parameters such as Stroke Volume Variation, Pulse Pressure Variation, Pleth Variability Index and imaging techniques such as echocardiography, the role of CVP has further diminished.

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