Stress, strain, ignorance and reinventing the wheel: Understanding central venous pressure

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ABSTRACT
An understanding of the physics, physiology and pathophysiology underpinning the use of the central venous pressure is essential in the effective use thereof. As for any hollow organ, the interaction between intracavity volume and pressure of the container is not linear. Because of this characteristic stress and strain relationship, the central venous pressure cannot be a simple and static indication of the volume inside the container and should neither be used as such nor should across the board comparisons between central venous pressure measurements and other markers of intravascular volume be attempted. Dynamic testing of the system stiffness (elastance) of the container is an effective but still indirect manner to gauge the particular intracavity volume.

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Introduction
Consider a case where a patient with chronic obstructive pulmonary and stable coronary artery disease underwent urgent abdominal aortic aneurysm repair. Postoperatively, information from the central venous pressure and pulmonary artery catheter were downplayed. This approach was extended so that little attention was given to central venous pressure and that the pulmonary artery catheter was removed. Based exclusively on the swing in the arterial pressure trace, intravenous fluid boluses were administered. The patient developed pulmonary oedema necessitating mechanical ventilation and had a protracted stay in the intensive care unit.

This complication would have been prevented if the available information from the monitors had been carefully considered. The significant pulmonary hypertension associated with a septal shift most likely resulted in the swing in systolic pressure. However, the arterial pressure variation was misinterpreted as indicating that intravascular volume replacement was required. This approach did not take into account the real risks associated with fluid loading in the presence of pulmonary hypertension. Intravascular volume expansion probably aggravated right ventricular dilation, right ventricular oxygen consumption[1] and the pre-existing decrease in left ventricular compliance.

The measurement of central venous pressure (CVP) can be a useful tool, provided the practitioner understands both the underlying physical principles and physiology. This article briefly summarises some relevant concepts.

Stress, strain and stiffness
Stress is defined as the force (pressure) per unit cross sectional area of a material[2,3] and strain (volume) change is the deformation which results from the application of the stress.[4]

The stress–strain interaction can be expressed as the chamber stiffness for any container.[5]

The venous vasculature is a container with inherent, albeit variable, stiffness. Upstream from the venous vasculature is the arteriolar bed. This pressure difference acts as a "stopper" for fluid escaping at the capillary end of the venous system. Downstream in the venous system, the right atrium represents a container receiving blood returning to the heart.

The venous-right atrial systems are non-rigid containers. Hence, the relationship between the stress and strain is not linear. This interaction will vary depending on the baseline distension of the venous system.

The equation used to describe the interaction between stress and strain, is[4]:

$$\sigma = \alpha \, (e^{\beta \cdot \varepsilon} - 1) \; \dots\dots\dots\dots\dots\dots\dots\dots \text{ Equation 1}$$

where e = base of the natural logarithm, σ = wall stress, ε = Lagrangian strain, α = coefficient of gain, β = modulus of stiffness.

An alternative equation used to summarise the pressure and volume relationship is[4]:

$$P = A.e^{Kc.V} \; \dots\dots\dots\dots\dots\dots\dots\dots \text{ Equation 2}$$

where P = vessel pressure, A = vessel pressure at zero volume and Kc the modulus of stiffness (chamber stiffness) and V = contained volume.

To intuitively understand the implications described by Equations 1 and 2, consider the effect that small changes in volume will have on empty and full non-rigid closed containers.

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When the container is relatively empty, small volume changes will not cause significant pressure changes. However, small increases in volume will greatly increase the pressure inside a full container. The relationship between pressure and volume is termed stiffness. In a non-rigid closed system, chamber stiffness will therefore fluctuate according to the resting volume of the container. Another method of changing stiffness is to introduce a stiffer container, this latter concept being termed wall stiffness.[6]

This concept is best illustrated by plotting the relationship between volume and pressure of a hollow organ (Figure 1). This relationship also applies to the venous system.

Figure 1: The hypothetical change in pressure resulting from the addition of volume to an initially empty container. Initially, as volume is added (A), there is little change in the resulting pressure. Once the chamber compliance has been "used up" the stiffness is activated as further volume is added (B). A, can also be referred to as the "unstressed" volume and B is the "stressed" volume.
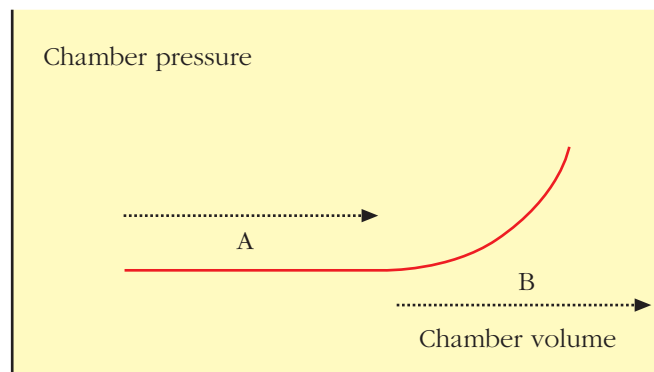
Inspection of Figure 1 reveals that in a non-rigid container, initial increases in volume (A) are accompanied by small changes in pressure. This represents the unstressed volume where the container has not been filled to the point where the "slack" has been occupied. After being filled to the point that chamber stiffness acutely increases (B), additional volume can be referred to as the stressed volume.

The inverse of stiffness is compliance. Compliance is defined as the change in volume (dV) associated with a change in the transmural pressure (dP):

> **Compliance = dV/ dP** …………..……………. Equation 3

It is important to appreciate that the "pressure" referred to in both the compliance and stiffness formulae refers to transmural pressure, the pressure difference between the inside and the outside of the vessel. Transmural pressure should not be seen as only the absolute pressure inside the vessel.

The following points can be deduced from the above discussion.

- The changes in pressure that accompany a fluid challenge of a particular volume are not necessarily comparable because chamber stiffness is affected by the volume in the container. The pressure response to volume administration will depend on whether the venous system is in an unstressed or stressed state.
- Vessel stiffness can and does fluctuate, even in the same patient. Central venous pressure will be affected by such fluctuations in chamber stiffness.
- The above two points indicate that a particular value for central venous pressure cannot be considered "normal" as vessel stiffness and volume status will both vary over time, between patients and following pathology or therapeutic interventions.
- Simply considered, the pressure response to a fluid challenge will provide an indirect indication of the volume inside the chamber.
  - This indirect indication must consider that the practitioner will not have knowledge of the specific stiffness, capacity or baseline volume of the container.
  - This statement is more correct when applied to the stressed (i.e. filled) rather than an unstressed (i.e. relatively under-filled) venous system.

The aim of CVP measurement
CVP measures the pressure in the great veins and right atrium. In the absence of tricuspid valve disease or uncoordinated atrio-ventricular contraction, right atrial pressure at the end of diastole is a good indicator of right ventricular end-diastolic pressure.[6]

Right ventricular end-diastolic pressure has a unique relationship with the right ventricular end-diastolic volume, this relationship also being governed by right ventricular wall stiffness. Right ventricular end-diastolic volume is a significant determinant of right ventricular preload. Hence, the main purpose of central venous pressure is to indirectly gauge right ventricular preload. It should be further noted that if the La Place relationship is considered, right ventricular end-diastolic volume determines wall tension and therefore right ventricular afterload.

Factors affecting venous flow and pressure
The driving pressure governing venous flow from the periphery to the heart is the difference between mean circulatory filling pressure and central venous pressure.[7] Mean circulatory filling pressure, effectively peripheral venous intravascular pressure, is largely determined by the "stressed volume" of blood present in the vasculature. Only after the volume in the venous system exceeds the "unstressed volume", will more volume significantly raise venous pressure. The pressure gradient governing venous return is enhanced by decreases in right atrial pressure that result from both the negative intrapleural pressure and also right ventricular contraction causing forward movement of blood. In dogs, mean circulatory filling pressure is approximately 7–12 mmHg and central venous pressure 2–3 mmHg. Despite this small pressure differential, adequate venous return occurs because the venous resistance is low.

The venous capacity, the inherent vessel "chamber" stiffness and therefore the stressed volume are subject to change by α adrenergic stimulation,[8] pregnancy[9] and drugs such as nitroglycerine.[10]

The splanchnic capacitance vessels are a unique portion of the venous container because of its greater capacitance and its greater reactivity to adrenergic stimulation compared to muscle

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and skin.[11] These differences result in the splanchnic capacitance vessels acting as a reservoir to maintain filling of the mainstream venous container when intravascular volume acutely decreases. This reservoir action maintains the stressed volume, mean circulatory filling and central venous pressures until the splanchnic volume "support" is exhausted. Further intravascular compartment losses will result in precipitous decreases in mean circulatory and central venous pressures.

The right atrium and ventricle have to accept the venous return and pump this into the pulmonary artery. In the event of a mismatch occurring between the elastic properties of the right ventricle and the pulmonary artery, right ventricular end-diastolic volume will increase. The consequence is that right atrial and peripheral venous pressure will be raised in tandem to ensure venous inflow into the heart. If right ventricular stiffness increases, venous pressure will again have to be raised in order to maintain the pressure differential and ensure venous inflow.

The clinical use of central venous pressure

There is an erroneous perception that central venous pressure (and indeed systolic pressure variation) are indications of intravascular volume.[17,18] Central venous pressure cannot reliably indicate intravascular volume if the venous volume does not exceed the stressed volume.[15,16] Only once venous volume exceeds the stressed volume, can a linear relationship between central venous pressure and the venous volume be expected. Studies that do not distinguish whether central venous pressure has been measured at unstressed or stressed volumes will invariably fail to indicate intravascular volume. Nonetheless, even if the above relationships have been considered, factors such as the distribution of volume between the arterial and venous system, the status of the splanchnic reservoir and vessel stiffness will all influence intravascular pressure. Furthermore, the right ventricular end-diastolic volume and pressure relationship is not linear. All these influences emphasise that it always was naïve to expect a particular central venous pressure measurement to indicate what the effective stretching of the ventricle was during diastole or to be an adequate indication of intravascular volume.

What physicians would ideally want to know is the transmural distending pressure and not only the absolute (intraluminal) value of central venous pressure. The transmural pressure is the difference between intra-and extraluminal pressure, the latter being affected by intra-abdominal, intrathoracic or intrapericardial pressures.[12,13,14] Unfortunately, this extraluminal pressure represents yet another, often unknown, factor that the physician needs to take into account when considering the significance of the absolute value of central venous pressure.

There is however no reason to rely on the absolute value of (intraluminal) central venous pressure because of the uncertain significance thereof in a non-rigid system. A dynamic challenge of the stiffness of the system is required to obtain some idea of where on the stressed or unstressed venous volume the patient is at the time of the measurement. To achieve this end, the clinician classically determines the position on the pressure-volume curve in Figure 1 using fluid challenges. This approach will partially circumvent the uncertainty that accompanies extraluminal pressure fluctuations.

Conclusion

Central venous pressure is still an appropriate clinical measurement provided that:

- The user understands the basic concepts that govern the generation of central venous pressure
- It is used as a dynamic tool of preload, venous return and/or intravascular volume
- It is used as an indirect and relative index of right ventricular preload

The main limitations of central venous and indeed pulmonary artery wedge pressure measurement, however, reside in the lack of appreciation of the underlying physical principles and physiology. The fact that novel measurements such as systolic pressure variation are currently under investigation, does invalidate the use of central venous pressure with all its limitations. Not having a sound knowledge does not invalidate a technique; it only disqualifies the practitioner from using these techniques.   **SAJAA**

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