Understanding central venous pressure: not a preload index?

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Purpose of review
Critical care physicians frequently try to manipulate the preload of the heart to optimize cardiac function. There is, however, still debate as to what actually indicates the preload of the heart.

Recent findings
Although central venous pressure (CVP) is commonly used to estimate cardiac filling, it is often argued that it is a poor indicator of preload. This is likely true if one does not understand what preload is, principles of measurement with fluid filled systems, the effect of respiratory efforts on the measurement, the physiological determinants of CVP, and finally which point on the tracing to use as the estimate of the preload of the heart. When these are considered, however, the value of the CVP at the base of the 'c' wave gives a good indication of cardiac preload and a value which can be followed.

Summary
When properly measured CVP can be a useful guide to the filling status of the right ventricle. CVP is especially useful when followed over time and combined with a measurement of cardiac output. Importantly, preload is only one of the factors determining cardiac output and it must be integrated into a comprehensive approach that takes into account changes in cardiac function and the return of blood to the heart. Finally, the specific value of preload does not indicate volume responsiveness.

Keywords
cardiac function, transmural pressure, venous return, z point

INTRODUCTION

Preload is the final force that stretches muscle fibers before the onset of contractions, whether they are cardiac or skeletal muscle fibers. When the heart is considered a whole unit that starts from the right atrium and exits at the aortic valve, preload for this unit can be considered to be the pressure in the right ventricle at the end of diastole just before the onset of isovolumetric contraction. In a normal heart central venous pressure (CVP) is a good estimate of right atrial pressure, which in turn during diastole is the same as right ventricle pressure. CVP thus can be used as an estimate of the diastolic forces distending the right ventricle. CVP has, however, a number of components that have nothing to do with the preload of the heart and only one time point in the cardiac cycle gives the value of the preload. Furthermore, a number of technical aspects of the measurement related to zeroing and leveling of the measuring device can lead to inaccurate measurement of the preload value. If, however, one understands the factors that determine the relation of CVP to right ventricular end-diastolic pressure, CVP can be a good indicator of the state of loading of the right ventricle and thus the heart as a whole [1–3]. CVP is a readily available measurement in any patient who has a central venous line and also can be obtained without any instrumentation in many patients by examining jugular veins. I will begin with the meaning of preload. I then will discuss issues related to measurement of CVP and the factors that determine CVP. Finally, I will give some guidance for its proper use.

COMPONENTS OF CENTRAL VENOUS PRESSURE

CVP, especially when measured in the superior vena cava, has defined components. The 'a' wave is the

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KEY POINTS

- The importance of CVP is that it indicates how the heart is interacting with the return of blood to the heart.
- The CVP value just before the onset of systole is an indication of the preload of the right heart.
- Normal CVP is very low.
- Under normal conditions preload is not a major determinant of cardiac output but rather serves to provide fine tuning of cardiac output.
- CVP values should not be used in isolation but rather in the context of the clinical situation and preferably with a measure of cardiac output.

first positive deflection in the cardiac cycle and is determined by atrial contraction when the rhythm is driven by the sinus node (Fig. 1). The height of this wave depends upon the force of contraction of the atrium and the compliance of the atrium, right ventricle, and upstream veins. The second positive deflection is the 'c' wave which is small and often hard to see. It is produced by buckling of the tricuspid wave back into the atrium during the beginning of right ventricular contraction and also possibly by a reflection wave from the venous return hitting the suddenly closed tricuspid valve. The third positive deflection is the 'v' wave. It is produced by filling of the atrium during ventricular systole.

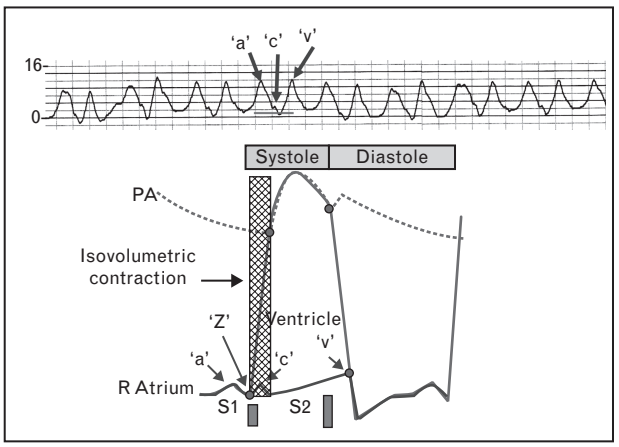

FIGURE 1. The top tracing is a CVP from a patient and the bottom indicates the pressure time curve of the ventricle, pulmonary artery (PA) and right atrium (CVP). The 'a', 'c' and 'v' waves are shown on the CVP tracing and the pressure time curve. The 'z' point marks the final pressure in the ventricle before the onset of systole and thus is the best indicator of cardiac preload. The line on the CVP tracing indicates the proper measuring point for the CVP value that indicates cardiac preload.

The magnitude of the 'v' wave is primarily determined by the amount of volume returning to the heart per beat ('stroke return') and the compliance of the right atrium and upstream venous vessels. When the tricuspid valve is insufficient regurgitant flow also contributes to the size of the 'v' wave. Importantly for this discussion of CVP and cardiac preload, CVP only reflects right ventricular diastolic pressure when the tricuspid valve is open. The 'v' wave does not contribute to preload but the magnitude of the 'v' wave can affect upstream structures such as the liver, gastrointestinal tract and kidneys.

WHAT IS PRELOAD?

Muscles are elastic structures. When stretched they develop tension along the muscle fibers (Fig. 2). A basic principle of the function of both skeletal and cardiac muscle is that stretch of the resting length of the muscle increases the peak active tension obtained during contraction until an optimal resting length is reached. This is the basis of the Frank–Starling relationship, which indicates that the greater the resting diastolic volume the greater the peak tension and the greater the stroke volume up to an ideal length (Fig. 3) [4,5]. This length–tension dependence occurs because increased stretch allows more overlap of myosin heads with the active sites on actin and thus increases the force and speed of contraction [4]. Subsequent studies have shown that there are other mechanisms related to increased availability of ionized calcium through geometric, conformational and membrane effects from the increase in muscle fiber length, but the basic principle of increased length leading to increased force during the active contraction is still the same [6▪,7]. The change in active muscle force with a change in preload is studied in isolated cardiac muscle by applying a linear force to stretch the resting muscle (Fig. 3). In Otto Frank's experiments on frog hearts he injected increasing volumes to increase the resting length. Ernest Starling studied relatively intact circulations in dogs and adjusted the volume returning to the heart during the time available for diastole to stretch the walls of the ventricles. Thus in Starling's studies the increase in return of blood to the heart per beat determined the initial loading conditions. The return of blood should not, however, be confused with the preload. Preload has the word 'load' in it which indicates a force. Thus, preload is defined as the force, or pressure, that gives the initial length of the muscle before the onset of contraction. Accordingly, preload should be in pressure units. On the other hand, based on the length–tension relation peak active force produced by muscle is directly related to the initial muscle length

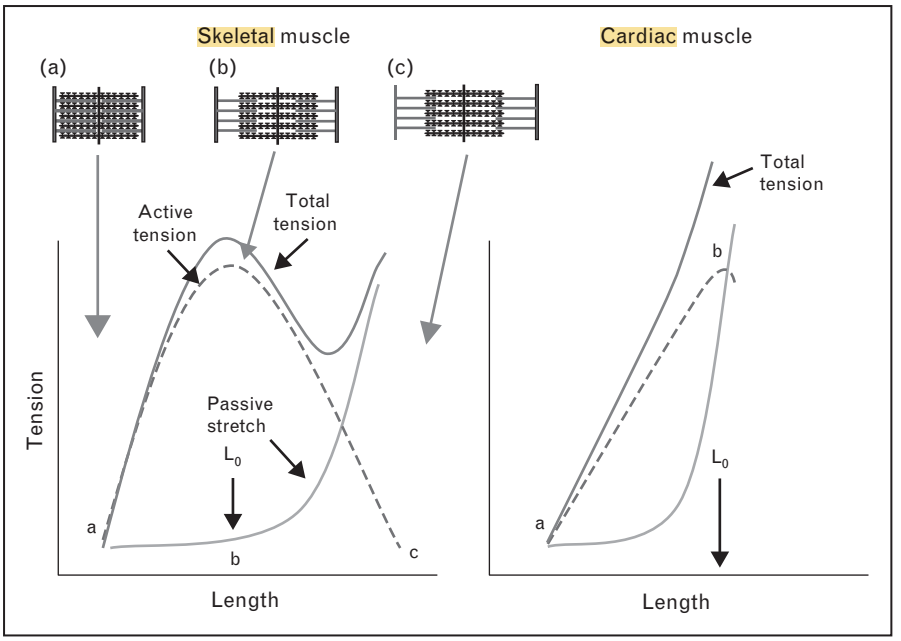

FIGURE 2. Schematic length–tension relations of skeletal muscle (left) and cardiac muscle (right). Sarcomeres are shown above the length–tension curves. Passive stretch produces a resting tension. Stimulation of the muscle produces the active tension. Total tension is the sum of passive and active tension. In skeletal muscle increasing the passive length increases active tension generation until an optimal length is reached (Lo). This occurs when overlap of actin and myosin is optimal. Stretching muscle beyond this point results in a decrease in active force because of a decrease in the optimal overlap. In contrast to skeletal muscle, Lo occurs on the steep part of the passive filling curve which prevents overstretching of the heart and there is no downward component to the length–tension relation.

and not the tension that produced the length, for length at a given tension varies with how stretchy the muscle is. Furthermore, this relation is curvilinear and not linear. In the intact heart

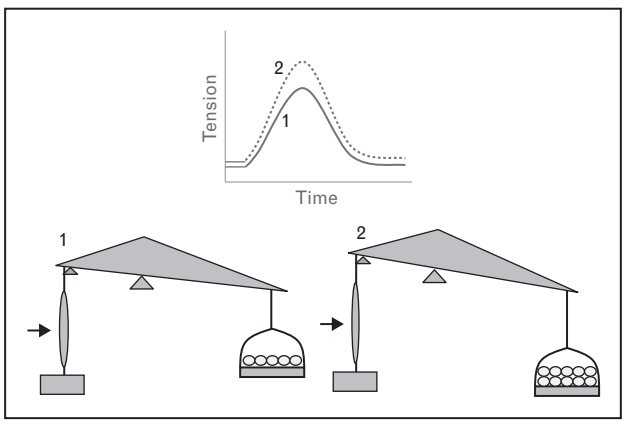

FIGURE 3. Schema for measuring the effect of changes in preload on force production by muscle fibers. A weight is attached to one side of a lever to passively stretch the muscle. The lever is locked (small triangle) so that it will not shorten further. The muscle is then stimulated to contract and produces a transient rise in tension (upper graph #1). When the weight is increased (right side), resting muscle stretch increases as does the active tension (#2).

'stretchiness' is defined by the term elastance or its inverse, one over compliance.

As stroke volume varies directly with initial muscle length, some have argued that end-diastolic volume is the preload [8]. This volume can be assessed by echocardiography, and in the past, by ventricular impedance catheters [9]. In addition to not being correct based on the physiological definition of preload as a tension, there are also, however, practical limitations of the use of volume instead of pressure. First, precise pressure measurements are much easier to obtain than precise volume measurements because volume measurements obtained by imaging techniques are based on measures of the radius and volume which vary with the third power of the radius. Thus, small imprecisions in the measurement of the radius produce large errors in the volume estimate. Second, I have considered preload of the heart as a whole unit to be that of the right ventricle, but the complex geometry of this chamber makes measurement of its volume difficult to quantify. Third, perhaps the most important reason for using pressure rather than volume is that the maximum diastolic volumes of the right and left ventricles cardiac chambers are limited by the pericardium when it is intact and by the cardiac cytoskeleton when there is no

pericardium. When this limit of diastolic filling is reached, further increases in ventricular filling pressure do not change end-diastolic volume. Volume measurements do not detect that this important limit has been reached (Fig. 4).

Under normal circumstances the resistance between the large veins, right atrium and right ventricle during diastole is negligible and CVP gives a good estimate of the right ventricular diastolic pressure. Exceptions are the presence of a stricture between the measurement site and the right atrium or stenosis of the tricuspid valve. Another problem, however, limits use of right ventricular end-diastolic pressure to indicate the preload of the right heart. In all elastic structures, including the heart, stretch of the wall depends upon the difference of pressure inside the structure relative to the pressure outside. Transducers used for hemodynamic measurements are zeroed relative to atmospheric pressure, which then is called the zero value. A CVP of 0 mmHg at sea level is, however, in reality around 760 mmHg, but in Denver or Mexico city it averages around 640 mmHg depending on the weather. The heart, though, is surrounded by pleural pressure which changes relative to atmospheric pressure during the ventilatory cycle. During a spontaneous inspiration pleural pressure falls relative to atmospheric pressure and remains slightly negative relative to atmospheric pressure at the end of expiration. During positive pressure inspiration, pleural pressure rises relative to atmospheric pressure and remains positive during expiration at a value that depends upon the amount of positive end-expiratory pressure and chest wall compliance [10].

MEASUREMENT BASICS

As preload is a pressure it is essential to understand the basics of making pressure measurements. Three general types of energy determine vascular pressures: elastic, kinetic, and gravitational energy. Preload is determined primarily by elastic energy but gravitational energy provides an important confounding factor. Errors in measurement of the CVP can be because of errors in leveling, errors in identification of changes in pressure related to changes in pleural pressure (incorrect estimates of transmural pressure), and errors in choosing the proper place on the tracing to measure the CVP value that estimates preload. The range of CVP measurements before right heart filling becomes limited normally only is from 0 to 12 mmHg. Thus, errors in measurement can have very important clinical implications.

Zeroing and leveling

Pressure measurement must be related to a reference value. As we are surrounded by atmospheric pressure, the first step is to adjust the measuring device so that the baseline force or 'neutral value' is atmospheric pressure. We call this 'zero' and measure pressure deviations from this value. If this is not done we would have to check with the weather

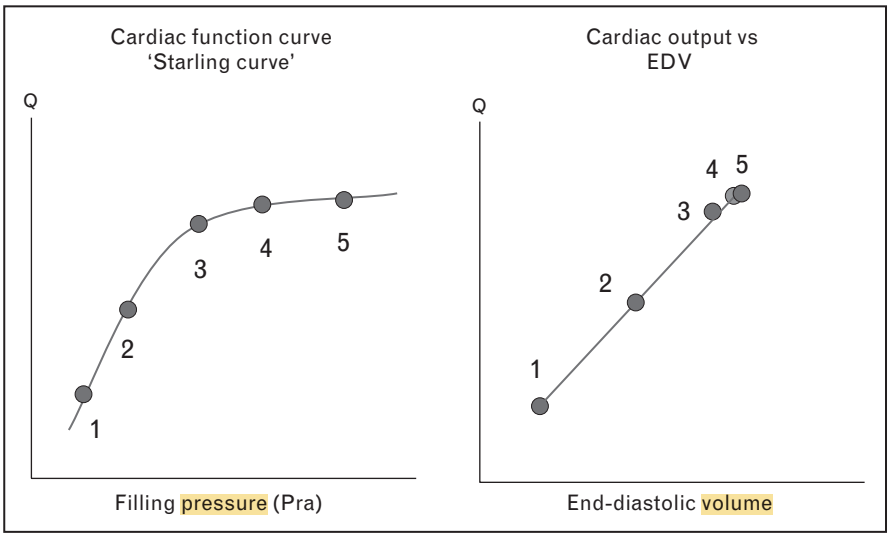

FIGURE 4. Cardiac output plotted against right atrial pressure (Pra) (left) and against end-diastolic volume (EDV) (right). The plot of cardiac output against pressure in the classic Starling curve is curvilinear. The plot of cardiac output against end-diastolic volume is linear which would seem to make this the more useful plot. The Starling plot can, however, identify the plateau of cardiac function when the limit of passive stretch is reached but on the plot of cardiac output against end-diastolic volume the points just cluster in this range and it is hard to identify the limit.

office before interpreting any measurements! Measurements of pressure become more complicated when they are made with a fluid filled device as is the case in standard hemodynamic studies. This is because the height of the fluid in the measuring device adds an additional force because of the acceleration of the fluid mass by gravity. This is not a problem with air-filled catheters used for most respiratory studies. Because of the gravitational effect the bottom of the measuring device which is called the zero value must be set at the level which is considered to be the physiological reference level in the body. For example, if the transducer for measuring CVP in a patient lying in bed is put on the floor, the pressure would be around 80 mmHg! Furthermore, the actual pressure distending vessels in a supine patient is higher in posterior vessels than anterior vessels because of the hydrostatic gradient between them. The higher value would be measured if the transducer was leveled to the bottom of the back and the smaller anterior value would be obtained if the transducer was at that level. It thus is necessary to have a standard reference position so that pressures can be compared among different people [2]. In physiological studies the consensus reference level is the mid-point of the right atrium, which is around the tricuspid annulus. On physical examination, this level can be approximated by identifying a level 5 cm below the sternal angle, which is where the second rib attaches to the sternum and produces a slight palpable bump [11]. This works because the right atrium is a relatively round anterior structure and is up against the sternum. The mid-point of the right atrium rotates around this value with the person sitting up to about a 60° angle. The precise position will, however, vary with body size and chest size in particular. On the basis of computed tomographic studies, it has been argued that one-third of the vertical distance of the thoracic anterior–posterior diameter more accurately estimates the zero reference line [12▪]. The authors, however, did not make their measurements at the sternal angle. When this is done, at least in the supine position, 5-cm vertical distance from the sternal angle is a good estimate of the mid-right atrium [13▪▪]. Furthermore, calculation of one-third of the anterior–posterior diameter adds the potential for more errors and is more time consuming than simply identifying the sternal angle and 5 cm below it. Most commonly, transducers are leveled to the mid-thoracic position which gives a pressure of approximately 3 mmHg greater than the sternal angle-based measurement (because it is lower). This method does not require a leveling device but also has less rigor and is subject to greater variability among operators. The key point is to have a standardized approach that can be used by all the members of the treating team and easily verified on a regular basis.

The second major issue is the assessment of transmural pressure, which, as already noted, is the measure of the elastic energy that distends the walls of the cardiac chambers. The problem is pressure outside the heart is pleural pressure and it varies during the ventilator cycle relative to the atmospheric pressure, which was used to 'zero' the transducer. A solution would be to have the transducer in the chest or to have a catheter in the chest to measure the change in pleural pressure and subtract this value from the vascular pressure measured relative to atmospheric pressure. Neither of these is practical. To minimize this error vascular pressures are made at end-expiration, which is when pleural pressure is closest to atmospheric pressure. With spontaneous ventilation, pleural pressure is slightly negative at end-expiration and transmural pressure is slightly underestimated, whereas pleural pressure usually is positive in someone with positive pressure ventilation and positive-end-expiratory pressure in which case transmural cardiac pressure is overestimated. The higher the positive-end-expiratory pressure the greater the error. There is no simple way around this problem when measuring the CVP, although there are some techniques that can be used for measurements of pulmonary artery occlusion [14]. Disconnecting the ventilator is not recommended for this will change the hemodynamics. One must simply keep in mind this artifact of the measurement and make the mental adjustment.

An important exception to making CVP measurements at end-expiration occurs in patients who have recruitment of expiratory muscles and 'forced-expiration' for this raises pleural pressure at end-expiration. Forced-expirations can be of two types. We have called type A the conditions under which the patient pushes maximally at the beginning of expiration and the expiratory effort decreases during expiration [15]. This usually produces a small alteration of CVP and the problem is minimized by picking the CVP value at end-expiration in the longest cycles. The second type, which we call type B, is much more problematic and can result in a large error in the measurement of CVP. These patients increase their expiratory effort throughout the expiratory period so that CVP on the monitor progressively increases during expiration and, in all likelihood, the transmural CVP is actually falling. When this pattern is present the clinician needs to identify a period in some breaths at the beginning of expiration before the patient begins to push. It is also necessary to look at many

breaths and to identify some breaths in which the patient does not recruit expiratory muscles.

CVPs often have large 'a' and 'v' waves (Fig. 1) and very different values are obtained depending upon where on the waveform the measurement is taken. When CVP is used to estimate preload the measurement should be made at the base of the 'c' wave which is called the 'z' point for this point indicates the last pressure in the right heart before the onset of systole. If the 'c' wave cannot be identified the base of the 'a' gives a reasonable estimate. The timing of the onset of systole also can be made by drawing a vertical line from the end of the QRS wave of the electrocardiogram. If this value is reported as the CVP measurement, this CVP value gives a good estimate of preload.

DETERMINANTS OF CENTRAL VENOUS PRESSURE

Use of CVP as an estimate of cardiac preload requires an understanding of its determinants. If a heart is studied in isolation, as was the case in Otto Frank's studies, CVP gives a clear estimate of the preload of the heart. In the intact circulation CVP is determined by the interaction of two functions – cardiac function and return function [3]. An increase in cardiac function can be considered to be the ability of the heart to have a higher cardiac output with the same right atrial pressure and thus the same preload. Factors that increase cardiac function are an increase heart rate, increase in contractility, and a decrease in afterload [4]. As cardiac output generally matches metabolic needs, an increase in cardiac function usually results in a decrease in CVP and indicates a decrease in preload. This can occur because the heart does not require as much stretch to obtain the same output. The opposite occurs with a decrease in cardiac function. This matching of cardiac output and return of blood is well seen during exercise in which there is as much as a five-fold increase in cardiac output with little change in CVP and thus little change in preload. On the other hand, an increase in the return function by itself results in an increase in cardiac output through the Starling mechanism, which means that CVP and preload increase. Under normal conditions increases in venous return and increases in cardiac function occur together so that little change in CVP and preload occur.

PRELOAD AND VOLUME

The criticism has been made that CVP is not useful because it does not represent blood volume [16], but why would one consider this in the first place? First, under resting conditions only about 30% of total blood volume produces the venous elastic recoil that drives blood back to the heart [3,17]. The rest of the blood volume simply rounds out vessels and does not stretch vascular walls. This is called unstressed volume. Changes in the proportion of stressed to unstressed volume can change venous return and thus change CVP without a change in total blood volume. The consequent increase in preload, though, increases cardiac output if the right heart is not volume limited. Second, the elastic recoil from the veins passes through a resistance in downstream veins. Changes in this resistance will alter the relation of total blood volume to CVP. Finally, as discussed above, CVP is determined by the interaction of cardiac function and return function so that if a change occurs in cardiac function at the same time as a change in return function from a change in blood volume, the relation of CVP to blood volume also will change. The same arguments relate to the use of mean systemic filling pressure as a guide to 'filling' of the heart.

USE OF CENTRAL VENOUS PRESSURE

When all the technical factors discussed above are considered, CVP as measured at the base of the 'c' wave can be a good guide to the force filling the heart (Fig. 1). This should not be confused with volume responsiveness for once the flat part of the cardiac function curve is reached an increase in preload, as indicated by an increase in cardiac filling pressure, does not increase cardiac output.

Under normal physiological conditions CVP is very low and even below zero when sitting quietly [18]. As noted above, even with the markedly elevated levels of cardiac output during exercise CVP remains at relatively low levels. Thus, a marked rise in CVP indicates that the heart is not handling the venous return the way it normally should. For example, patients who have had heart transplants have much higher CVPs during exercise than normal study participants because the heart does not receive the normal rapid changes in sympathetic input to increase contractility and heart rate [18]. Under normal physiological conditions, preload is not a major determinant of cardiac output, but rather acts by 'fine-tuning' cardiac output so that inflow matches outflow. It is very helpful clinically that many patients respond to an increase in preload with an increase in cardiac output, but a normal cardiovascular system should not need this increase in blood volume.

Although actual values of CVP do not indicate cardiac status, important clinical information can be obtained by considering high and low values. For

example, cardiac tamponade, pulmonary embolism or right heart dysfunction are unlikely explanations for a low blood pressure and low cardiac output if the CVP is close to zero. These still are possible diagnoses, but there must be something else going on such as a simultaneous gastrointestinal bleed, over diuresis or a loss of vascular tone due to sepsis. Conversely hypovolemia is very unlikely to be the only cause of shock if the CVP is high unless pleural pressure is high and the transmural right atrial pressure is actually low, or there is confounding right ventricular dysfunction, or the right heart is being strategically compressed by something resulting in a low transmural pressure.

CVP is used most effectively by following trends, especially if there is a concomitant measurement of cardiac output. On the basis of Starling's law, a fluid bolus increases cardiac output by increasing preload. If the bolus fails to increase cardiac output the next question should be did the CVP rise? I use a value of an increase of 2 mmHg to indicate an adequate rise to test Starling's law because that is a change in value that I feel I can recognize confidently on a monitor. If CVP rises by 2 mmHg and the cardiac output or clinical parameters being followed do not improve, more volume will not solve the problem. If cardiac output, however, does not change and CVP increased by less than 2 mmHg cardiac preload responsiveness has not been ruled out and more fluid needs to be given until the CVP is increased by 2 mmHg. The faster the fluid is given, the less the amount of fluid needed.

The same reasoning works diagnostically. If cardiac output falls with a rise in CVP, this is indicative of a primary decrease in cardiac function. If cardiac output falls with a fall in CVP, this is indicative of a primary decrease in return function and there is likely a decrease in volume [3].

CONCLUSION

The clinical range of CVP values is small and thus the measurement must be made carefully and consistently, especially leveling. This is essential when CVP is trended over time. CVP may not give a precise measure of the preload of the heart and in isolation does not give much information but a high CVP always is abnormal. When taken in the context of the whole clinical picture, CVP can be very helpful diagnostically. It is most helpful when it is used to follow patients over time, especially when there is simultaneous measurement of cardiac output, for this allows one to determine whether the primary change is because of a change in cardiac function or of a change in return function. Direct measurement of CVP is readily available in many patients, and an approximate value is available from almost all patients by physical examination. It seems a waste not to understand the determinants of this value.

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Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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