Advantages and Limitations of Static Parameters of Fluid Loading

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Hemodynamic monitoring is an essential part of managing patients undergoing all types of surgical procedures. It becomes especially relevant in those who are critically ill and hemodynamically unstable, such as those suffering from cardiogenic, septic, or hemorrhagic shock, as it facilitates evaluation and optimization of a patient's physiologic state.

Assessment of hemodynamic variables and parameters often facilitates early diagnosis and treatment of hemodynamic compromise, and assists in assessing a response to therapy.[1] However, no monitoring device or parameter can be used to improve outcome unless the treatment regimen with which it is coupled improves outcome.[2,3] Furthermore, these measurements are only as valuable as they are accurate and valid. Despite this, many studies still show that there is lack of knowledge in interpreting these parameters, understanding the principles behind the measurements, and identifying artifacts associated with them.[4–8]

Although there are many reasons for hemodynamic monitoring, there exists one compelling reason for using specific monitoring as described by Pinsky and Payen.[3] Knowing the effects of a disorder and its progression through specific hemodynamic parameters would assist one in preventing the disease from progressing and inhibiting normal

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organ function.[1,3,9,10] Thus, defining the proper hemodynamic status of the patient would allow correct and adequate treatment. The assumption made, however, is that this assessment is predicated on global circulatory status and is not specific to organ circulation or microcirculation.[1]

Organ dysfunction can occur in the setting of a decreased ability of blood flow to meet metabolic demands.[11] The result is tissue dysoxia owing to a relative lack of oxygen delivery often exacerbated by increased tissue demands and microcirculatory injury.[12,13] Early resuscitation can play an important role in reversing tissue dysoxia and its progression and limiting organ damage. Rivers et al[14] showed that early resuscitation with a goal-directed protocol in patients with septic shock reduced organ dysfunction and improved survival. Other studies have shown that early resuscitation and prevention of initial ischemia is beneficial in high-risk surgical patients.[15–19] Preoptimization protocols with goal-directed fluid loading have shown to decrease morbidity and length of stay[20] and are cost effective.[21] Likewise, postoperative hemodynamic management has shown to improve outcome while being financially feasibile.[2,22,23]

Adequate blood flow to organs often requires a sufficient cardiac output (CO) determined principally by venous return (VR), which itself is a sum of local blood flows from the peripheral circulation.[24] Inadequate circulating intravascular volume, often manifested clinically by a low systemic blood pressure, is frequently due to a decrease in CO as a consequence of inadequate VR. Typically, restoration of ventricular filling through fluid resuscitation allows recovery of CO and ultimately blood pressure. To restore adequate blood pressure and flow, cardiac function, filling of the cardiovasculature (as defined by preload), and vascular tone must all be assessed through various hemodynamic parameters. Therefore, understanding fluid optimization based on fluid loading parameters and what they represent in terms of the pathophysiologic state and response to treatment (ie, a fluid load) is crucial to the overall care of the patient.

Many different hemodynamic parameters are used to aid in diagnosis and guide therapy, and typically they can be classified as either static or dynamic. In terms of organ dysfunction and perfusion, the concept of ''upstream'' or ''downstream'' markers has come to light, whereby these markers help to assess both flow and pressure in the heart, vena cava, pulmonary artery and aorta, or at the end organ/microvasculature level, respectively.[12] They can be continuous, intermittent, invasive, or noninvasive. What defines a static parameter? In a true sense of the word, a static parameter is just that, a variable, whether simple (eg, blood pressure or heart rate) or derived (stroke work), measured at a specific point in time during the dynamic process of filling and pumping of the heart as well as compression and expansion of the vascular beds. Static parameters may measure volumes, such as

end-diastolic volume (EDV) of both ventricles or pressures such as right atrial pressure (RAP) often approximated as central venous pressure (CVP) or pulmonary artery occlusion pressure (PAOP). Traditional static indicators of cardiac preload have included RAP, PAOP, and right ventricular and left ventricular EDVs (RVEDV and LVEDV, respectively). As opposed to dynamic parameters of fluid loading and responsiveness to fluid administration (such as pulse pressure variation, stroke volume variation, and δ RAP as described by Cavallaro et al[25]), these static parameters have been known to be limited in their predictive value of fluid status and of responsiveness to a fluid load. Although other static parameters such as blood pressure and CO can be classically considered in this category, the focus of this review is examination of the physiology of preload and preload responsiveness as well as the utility and limitations of RAP, PAOP, and EDV as static parameters for fluid loading and their affect on CO.

■ Physiologic Concepts to Fluid Loading

Three factors that determine the regulation of CO include the function of the heart itself, the resistance to blood flow in the peripheral circulation, and the amount of filling in the vasculature.[26] Although the heart does supply the CO, the majority of the regulation of CO is from the peripheral circulation as described by Guyton.[24,26,27] The heart itself acts permissively in pumping blood returned to it through the Frank-Starling mechanism. Under normal conditions, it will pump more blood if more blood is returned to it to a limit of about 2 and half times the normal VR before itself becomes the limiting factor.[26]

VR to the heart is regulated in several ways.[27] First, the right atrium, receiving all the VR from the periphery, acts as a backpressure (RAP) to the flow of blood from the vascular circuit. RAP is lowered when the ventricles contract, allowing a greater return to the heart.[28] Second, the degree of filling of the systemic circulation produces a pressure resulting from the elasticity of the peripheral vessels and provides a potential energy for the system. The pressure generated is the mean systemic filling pressure (MSFP) and is determined by the volume and compliance of the vasculature. This pressure is the driving force that powers blood back to the heart. Third is the resistance to blood flow between the peripheral vessels and the atrium, a majority of which is in the veins. Blood flow thus occurs when RAP is relatively lower than MSFP, whereas the heart restores the potential energy in the circuit peripherally by emptying blood back into the vasculature.[24,27,28] Guyton[24] revealed that the return of blood to the heart, or VR, can be described by the equation $VR = (MSFP - RAP)/Rv$, where Rv is the cumulative resistance of the venous circuit. In altered circulatory states such as in shock, VR and cardiac function both change and the interaction between the 2

determines the status of blood flow and identification of potential indications for treatment (Fig. 1).

The way the heart and vasculature respond to a fluid load is variable. Under steady-state conditions, an increase in intravascular volume would elevate MSFP and decrease Rv, thereby increasing VR. By means of the Frank-Starling mechanism, CO would increase owing to the increase in VR to a physiologic limit, then plateau, whereby any further increase in preload would not produce an increase in CO. At this point, the increase in preload would contribute to volume overload causing pulmonary edema or right ventricular dysfunction. This defines whether a patient may be responsive to fluid load. Staying on the vertical aspect of a Frank-Starling curve (CO as a function of RAP) would allow an increase in CO (Fig. 2). Over time, however, the MSFP would return to normal by several mechanisms, and CO would eventually return to its preexisting state.[26]

■ Preload and Preload Responsiveness

In critically ill patients, hemodynamic instability is commonly due to intravascular volume depletion. Ideally, volume-loading parameters must be predictive of responsiveness to volume expansion with an increase in CO. The responsiveness to preload is dependent on where the volume of the heart is located on the Frank-Starling curve and not necessarily on absolute values of pressure or volume. If the heart is on the steep portion of the Frank-Starling curve, then CO should increase in response to a fluid load provided that RAP is less than MSFP. Therefore, it is difficult for an absolute pressure to predict the pattern or response to a fluid load[29]; and CVP or PAOP under various conditions can increase, decrease, or stay the same in response to a fluid challenge.[30,31] In addition, being preload responsive may not necessarily mean that a patient requires resuscitation.[3] A normal person may

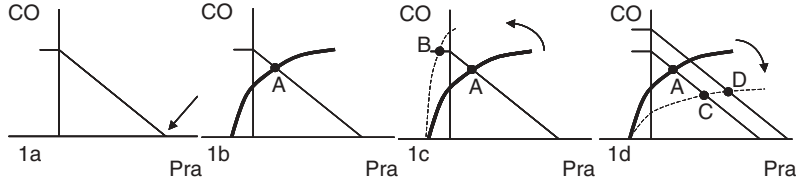

Figure 1. *Schematic of the interaction of the VR and CO curves. 1a, CO is 0 when right atrial pressure (Pra) is equal to mean systemic filling pressure (arrow) on the VR curve. 1b, the interaction of CO and VR at a particular point of physiologic conditions (point A). 1c, maximal VR limits CO (point B); increased cardiac performance (dashed line) does not increase CO. 1d, CO curve (dashed line) showing failure intersects VR curve (point C); point D shows no increase in CO with increased VR, increased vascular resistance, or decreased compliance. CO indicates cardiac output; VR, venous return. Adapted from J Appl Physiol. 2006;101:1523–1525.*

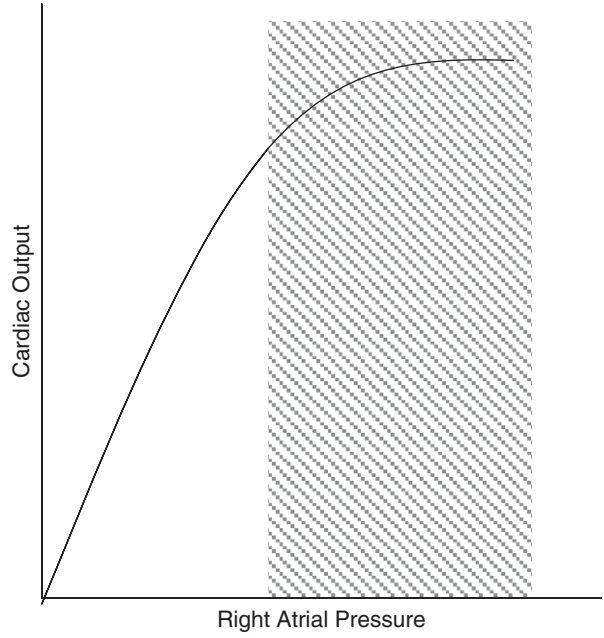

Figure 2. *Schematic of the Frank-Starling curve. CO as a function of Pra. CO increases as a function of Pra to a point (dashed area) where any further increase in Pra does not increase CO but produces signs and symptoms of congestion. CO indicates cardiac output; Pra, right atrial pressure.*

have a CO of 5 L/min with a normal RAP of 0 mm Hg and may be responsive, but not necessarily require resuscitation. In addition, evidence is lacking to support the concept that static measurements can be used to avoid tissue underperfusion,[29] as it is known that despite normal systemic and filling pressures, hypovolemia or hypervolemia may be present.[32] Thus, the question lies in whether the absolute static values of RAP, PAOP, and RVEDV or LVEDV actually predict preload status, and whether they can be predictive of changes in CO and stroke volume in hemodynamically unstable patients when administered a fluid load.[33]

Static parameters may not be able to predict volume status and fluid load responsiveness during dynamic changes in critically ill patients under nonsteady state conditions. The most common scenario is in critically ill patients who are mechanically ventilated. Traditional means of assessing fluid status have been by checking whether a fluid challenge results in an increase in CO. This may be time consuming and detrimental, potentially causing respiratory, renal, or cardiac failure and congestion of other organs.[34] Alternatively, a passive leg raise allows for an efficient assessment of fluid responsiveness as it transiently increases VR in patients who are preload responsive.[35–37] However, the ability to assess an increased hemodynamic response with absolute values may be problematic and ambiguous.

■ CVP

CVP is the pressure in the large central veins entering the right atrium relative to atmospheric pressure. It is an estimate of RAP provided there is no vena caval obstruction.[38] CVP is easily assessed in any patient noninvasively by inspection of the jugular veins. This is a basic bedside skill taught to all medical students.[39] Venous distention above the midthoracic level in a patient semireclined reflects CVP. In addition, it can be estimated on echocardiography by observing the changes in inferior vena cava diameter proximal to the right atrium during respiration.[40] CVP can be conveniently monitored when central venous access is used for the purpose of fluid resuscitation, infusion of vasoactive and inotropic drugs, and hyperalimentation either through a central venous catheter or pulmonary artery catheter (PAC) having a central venous port.

Technical Considerations

An important precept when measuring CVP is that CVP reflects the variable transmural pressure during different phases of ventilation. Transmural pressure is the difference between the pressure inside the heart and that on the outside. Intrathoracic vascular structures such as the heart are not surrounded by atmospheric pressure, which is the 0 reference point where pressures are measured, but surrounded by the pleural pressure, which varies with the respiratory cycle. Because of its variation during breathing, pleural pressure is difficult to measure and it is easier to measure pressures of vascular structures in the chest when pleural pressure is close to 0. At end-expiration, the pressure around the heart is roughly -2 to -3 cm H_2O and not very different from atmospheric pressure.[6] Therefore, measurements of CVP are typically taken at end-expiration.

Positive end expiratory pressure (PEEP) is also important as it creates a pressure around the heart greater than atmospheric, giving a minor overestimation of the transmural pressure of about 1 to 2 mm Hg in normal lungs.[6] During the use of high values of PEEP, however, these pressures can create large errors. In addition, CVP does not always change with PEEP and cannot be used for assessing the effect of PEEP on CO.[41] Not surprisingly, these high pressures do affect venous flow back to the heart, creating higher backpressures to venous flow from outside the chest.[6]

Another consideration in measuring CVP is proper placement of a reference level. Incorrect placement of a reference point can have considerable variation in the measured pressure. Although there is wide variability in placement of a reference level among health care providers,[42] one commonly accepted reference point for CVP measurements is the

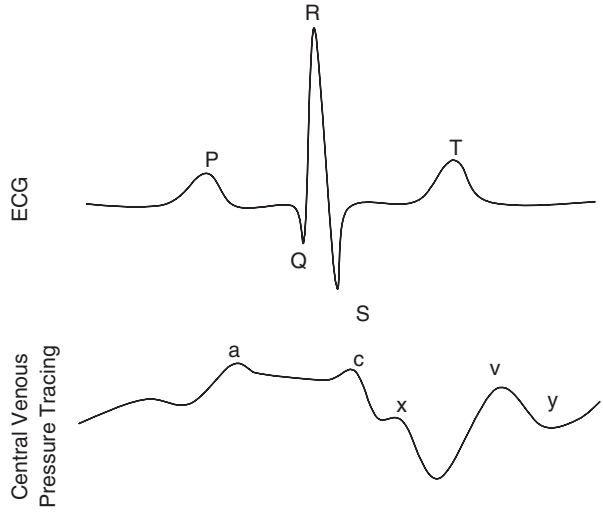

Figure 3. *Schematic of a central venous pressure waveform and corresponding ECG trace. The c-wave is caused by elevation of the tricuspid valve and follows the ECG R-wave. ECG indicates electrocardiogram.*

midpoint of the right atrium, as this is where the blood returns to the heart and is the backpressure to VR. This is identified anatomically at a vertical distance of 5 cm below the sternal angle. This distance remains at the level of the midpoint of the right atrium whether the patient is supine or sitting at an angle of 60 degrees, as the right atrium is a relatively round structure just below the sternum.

One last principle is where to take the measurement of CVP on the CVP tracing. In estimating cardiac preload, the best estimate is the pressure at the base of the "c" wave as that is the last atrial pressure before ventricular systole and is the backpressure to VR. As atrial pressure decreases following the "a" wave, the atrium relaxes and is interrupted by the c wave at the beginning of ventricular mechanical systole.[6,43] This represents isovolemic right ventricular contraction, which closes the atrioventricular (tricuspid) valve and causes it to bow back toward the atrium producing an increase in atrial pressure.[44–46] Alternatively, when the c wave is not evident, the base of the a wave can give a good approximation (Fig. 3).

Determinants of CVP

CVP is determined by the interaction of cardiac function and VR as already discussed. It acts as a backpressure to the flow of blood from the vascular circuit and is minimized as CO increases. Therefore, the value of CVP by itself has little meaning without knowing the relationship between CO and VR. The classic example is in a normal person with a

normal volume and normal cardiac function whose CVP is usually less than 0 in the upright position.[47] However, a low CVP can also exist in one with hypovolemia or in someone who is hypervolemic with a hyperdynamic heart.[48] Conversely, it may be high in someone with hypervolemia and a normal cardiac function or in someone with normal volume and depressed function.[48] CVP must be correlated to CO to have any useful meaning.

Utility of CVP

CVP is widely used in the critical care setting and operating rooms as a monitor of central blood volume and guide to fluid therapy, and is incorporated in some protocols endorsed by professional societies.[14,49,50] Unfortunately, the value of this single variable has undergone much debate in terms of its ability to help in predicting volume status and preload.[51] Few clinical studies have actually shown any benefit in the use of CVP as a means of guiding fluid therapy. A study by Jellinek et al[52] found that patients with acute lung injury had a significantly decreased cardiac index if RAP was ≤ 10 mm Hg when they were subjected to a transient apneic hold maneuver to an airway pressure of 30 cm H_2O. In those with RAP >10 mm Hg, the cardiac index did not decrease significantly and showed a variable response when patients were subjected to the same intervention. This may suggest that values of RAP above 10 mm Hg may not be reliable to predict appropriate filling and response to VR.[9] Another study showed a benefit of using CVP to guide fluid therapy in patients undergoing proximal femoral fracture repair.[53] Although CVP-guided fluid administration did not make a difference in major morbidity or mortality, it did make a difference in shortening the time to being medically fit for discharge compared with conventional intraoperative fluid management. Another study showed a benefit of CVP-guided fluid replacement in renal transplant patients.[54] The number of kidneys with delayed function was reduced in those whose fluid replacement was guided by CVP.[54]

Several other factors can influence the value of CVP as an indicator for volume status and responsiveness, including tricuspid valve disease, cardiac rhythm, right ventricular failure, and intrathoracic pressure such as in mechanical ventilation.[10] Right ventricular dysfunction occurs on the plateau of the Frank-Starling curve and creates a limit to the amount of output that can be generated with increasing RAP. This is important, as any fluid loading beyond that point only increases CVP and not CO. This may result in congestion and potential failure. Therefore, knowing the position on the cardiac function curve could tailor therapy to improve pump function, not return function.[48] In most patients, however, CO measurements are not easily accessible, so creating a threshold of CVP above which an infusion of volume would

prove ineffective in improving CO would be advantageous. In a study by Magder and Bafaqeeh,[38] volume responsiveness was evaluated in postsurgical patients over a range of CVP values. They found that patients failed to respond (increase in cardiac index by 300 mL/min/m^2) to volume (volume to increase CVP by 2 mm Hg) at all CVP values; even 25% of those whose initial CVP was <5 mm Hg failed to respond to fluid administration. In addition, CVP values >10 mm Hg indicated a low probability of improving CO with volume administration. The study demonstrates that there may be no uniform threshold CVP applicable to a wide range of patients. In patients with pulmonary hypertension, elevated pleural pressures, ventricular hypertrophy, or restrictive cardiomyopathy, volume responsiveness could occur even at high CVP.[38]

It is evident that a major limitation to CVP is its inability to assist in predicting changes in CO with volume infusion. In a meta-analysis by Michard and Teboul[55] that studied the predictive factors of fluid responsiveness in intensive care unit (ICU) patients, a RAP threshold could not be identified among the studies to discriminate responders, defined as an increase in CO or stroke volume, and nonresponders before fluid was administered. In addition, there was no difference in baseline values of RAP to distinguish a responder from a nonresponder, and there was no relationship between cardiac filling pressures before infusion and the hemodynamic response after volume expansion. This was owing to the numerous factors that could have contributed to the hemodynamic response including a high venous capacitance, poor ventricular function, or low ventricular compliance. However, one study did suggest that the lower the RAP or PAOP before volume expansion, the greater the increase in stroke volume in response to fluid infusion.[56] Furthermore, it has been shown that a fluid infusion can increase CO in some patients with elevated CVP >15 mm Hg.[30] Michard et al[57] also revealed that CVP and PAOP did not correlate with the change in cardiac index after a volume expansion in septic patients who were mechanically ventilated. Prevolume expansion values of CVP and PAOP were not significantly different between responders ($\geq$15% increase in cardiac index) and nonresponders. In addition, measuring these parameters in ascertaining fluid responsiveness was no better than flipping a coin. Two other studies have shown no correlation between CVP and changes in cardiac index in response to fluid resuscitation in critically ill patients.[58,59] Finally, in a literature review, Marik et al[60] showed a very poor relationship between CVP and blood volume and response to a fluid challenge in ICU and surgical patients. Overall, there was a poor correlation between CVP and measured blood volume [0.16 with 95% confidence interval (CI) 0.03-0.38], baseline CVP and change in stroke index or cardiac index (0.18 with 95% CI 0.51-0.61), and a change in CVP and change in stroke index or cardiac index (0.11 with

95% CI 0.015-0.21). In addition, there was no significant difference in baseline CVP in the responders versus nonresponders.

These studies show that CVP should not be used as a marker of intravascular volume or ventricular preload, and is limited in its value as an approximation of RAP. This is important, as RAP (or CVP) is a major factor in determining CO. VR is regulated by RAP and the role of the heart is to minimize this backpressure to allow better return of blood from the compliant vascular circuit. The lack of ability of CVP to be a good predictor of fluid responsiveness is multifactorial and is due to a variable compliant vasculature, ventricular compliance, and ventricular function, itself having a plateau that limits output with increased RAP from a fluid load. It is known that this plateau occurs at a RAP of 6 to 12 mm Hg in most individuals.[61] CVP values >10 mm Hg only represent a low probability of increasing CO with a fluid load alone and probably indicate a disease process already occurring.

■ PAOP

PAOP is the pressure obtained when the balloon at the tip of a PAC is inflated. The theoretical value is an approximation of left ventricular end-diastolic pressure (LVEDP), which, according to the Frank-Starling mechanism, is directly related to LVEDV for a given ventricular compliance.[62] In this regard, PAOP can be considered a measure and true determinant of preload.[63,64] After inflation of the balloon, a continuous column of blood is established distally from the medium-sized pulmonary artery to the reconnection of arterial branches approximately 1.5 cm before entering the left atrium (LA). The pulmonary venous pressure at this juncture is the PAOP.[65] As the vasculature is more compliant than the tip of the catheter, the vascular pressure signals dampen, giving the characteristic signature of the PAOP waveform and a value less than pulmonary artery diastolic pressure.[8,10] PAOP monitoring can aid in the assessment of the etiology of pulmonary edema (hydrostatic vs. nonhydrostatic causes), pulmonary vascular tone to detect lung or cardiac causes of pulmonary hypertension, left ventricle (LV) filling (preload), and LV function.[10,66]

Technical Considerations

A consideration in using the PAOP measurement is that pulmonary artery occlusion may not always make a continuous column of blood in some cases. This occurs when the catheter tip is in West zone 1 or 2 where the increase in alveolar pressure interrupts the blood column. As a result, the occlusion pressure reflects airway pressure more than pulmonary venous pressure and is higher than both end-diastolic pulmonary artery pressure and pulmonary venous pressure.[67,68] The catheter tip, therefore, must be in West zone 3 to prevent this occurrence.[67]

Similar to CVP measurements, PAOP measurements are also influenced by ventilatory swings in pleural pressures. As such, PAOP readings are also taken at end-expiration to minimize the influence of pleural pressure on PAOP, although end-expiration may be challenging to define.[69] Any elevation in pleural pressure, whether due to hyperinflation, air trapping, or varying degrees of PEEP (as alveolar pressure is transmitted partially to pleural pressure), is due to the compliance of the lung and chest wall that can vary in the same patient or among different patients.[8,66] Unfortunately, this gives an overestimation of PAOP in patients who are mechanically ventilated with PEEP, and techniques for estimating PAOP in that setting have been described.[70,71]

The effectiveness of a PAOP measurement is also dictated by left heart valvular pathology. In mitral valve disease, PAOP reflects increases in left atrial pressure and not necessarily LVEDP. The characteristic a- wave in mitral stenosis and v- wave in mitral regurgitation are indicative of altered left atrial pressure, and are not representative of LV volume. In mitral stenosis, a diastolic gradient is established between the LA and the LV. In mitral regurgitation, the transmission of systolic pressure back to the LA results in mean LA pressures that are higher than diastolic LA pressures and are above LVEDP.

Another major consideration deals with changes in LV compliance defined as the LVEDP/LVEDV relationship whereby PAOP estimation of preload is unreliable. Myocardial ischemia or failure, myocardial hypertrophy or dilation, pericardial disease, aortic disease, or shock can all influence the relationship between pressure and volume in the ventricle.[67] Furthermore, these changes in compliance can occur rapidly. There are several factors that diminish PAOP values from predicting LVEDV and stem from the relationship of ventricular compliance and function.[66,72] The relationship between LVEDP (PAOP) and LVEDV is curvilinear, and a measure of LVEDP can represent different states of filling based on compliance. Thus, a change in PAOP may represent a change in compliance without a change in filling or it may represent a true change in filling along the same compliance curve.[72] In addition, the distending pressure to LV filling is not represented by PAOP as it poorly accounts for the late rise in diastolic filling from atrial contraction and does not account for the influence of pericardial pressure on LV filling.[66] Therefore, PAOP, being an internal pressure in pulmonary veins proximal to the LA, is a value that cannot define absolute EDVs or volume changes to filling.

Utility

Despite its limitations, PAOP can be used to assess the functional status of the heart to the extent that PAOP can reflect LVEDV. Used with cardiac index values, PAOP can assist in assessing the etiology of heart failure.[73] High values of PAOP (>18 mm Hg) with high cardiac indexes

(>2.2 L/min/m^2) or low cardiac index (<2.2 L/min/m^2) are indicative of volume overload or primary heart failure, respectively. Those with low PAOP (<18 mm Hg) and high or low cardiac indexes are indicative of increased sympathetic tone or hypovolemia, respectively. In addition, finding a threshold gradient between diastolic pulmonary artery pressure and PAOP (>7 to 8 mm Hg) is suggestive of increased pulmonary artery or capillary resistance and primary pulmonary hypertension.[67] Conversely, a gradient <7 to 8 mm Hg is suggestive of increased pulmonary venous resistance and etiologies may include myocardial ischemia, failure, or mitral disease, all of which change ventricular compliance.[67]

In terms of assessing fluid status and response to fluid resuscitation, few studies have shown PAOP to be of any benefit.[56,74,75] In a study of cardiac surgical patients, Bennett-Guerro et al[76] found that PAOP was a better predictor of responsiveness to a fluid bolus than systolic pressure variation or transesophageal echocardiographic (TEE)-derived LV end-diastolic area. A PAOP value <10 mm Hg predicted an increase in stroke volume by 10% to a fluid bolus with a sensitivity of 68% and specificity of 79%. It has also been shown that using PAOP values in context of patient characteristics (eg, decreased ventricular compliance) may have some benefit.[77]

Unfortunately, numerous studies have shown the inability of PAOP to predict fluid responsiveness.[57,59,78–85] Michard and Teboul[55] found, similarly to CVP findings, no threshold value of PAOP to predict responders from nonresponders of fluid administration despite the fact that some studies did show a significant difference in baseline values between the 2 groups. Michard et al[57] found that measuring PAOP to asses fluid responsiveness was no better than chance with a receiver operating characteristic of 0.40 ± 0.09. Osman et al[37] also found that a CVP <8 mm Hg and PAOP <12 mm Hg, values suggested by guidelines for hemodynamic management of severe sepsis,[49,86] were poor predictors of fluid responsiveness in septic patients with only a positive predictive value of 47% and 54% and receiver operating characteristic values of 0.63 and 0.58, respectively. Not only in critically ill patients, but also in normal subjects, these 2 parameters seem to be poor predictors of preload as described by Kumar et al.[33] It is evident that, even if PAOP measurements are measured accurately and actions are taken to make the measurement more applicable to the circumstance, PAOP values whether at baseline or in response to fluid therapy are unpredictive of hemodynamic status in many clinically relevant scenarios.

■ EDVs

Ventricular volumes have been estimated by a variety of methods including radionuclide angiography, cineangiocardiography, thermodilution, echocardiography, and modified flow-directed pulmonary

artery catheterization in the assessment of fluid status and responsiveness to a fluid load. EDV as a parameter for fluid loading responsiveness has been considered superior to the pressure indices as preload, the degree of stretch of myocardial fibers just before contraction, or EDV, is the independent variable that directly relates to CO. Interference of ventricular compliance such as from myocardial ischemia, inotropic support, or changing intrathoracic pressures is minimized.[87]

PAC-derived RVEDV

The volumetric PAC is a unique device that determines right ventricle ejection fraction (RVEF) which is used to calculate the RVEDV by the equation RVEDV = CO/(heart rate/RVEF) where the heart rate is in beats per minute.[67] Newer models of the volumetric PAC can measure both the RVEF and RVEDV (continuous EDV), eliminating any error in volume assessment due to mathematical coupling between CO and RVEDV. This is because RVEDV index is calculated from stroke volume (stroke volume/RVEF). Nevertheless, inconsistencies exist in studies evaluating RVEDV as a reliable indicator of preload. These may be owing to errors in measurement of CO during mechanical ventilation, low flow states, or tricuspid regurgitation.[67,88–92]

Many reports have shown RVEDV to be an unreliable predictor of fluid responsiveness.[56,84,93] The study by Wagner and Leatherman[56] actually revealed that RVEDV index was not a reliable predictor of the response to fluid, and that PAOP was superior to RVEDV index as a predictor of fluid responsiveness. Jellinek et al[52] revealed that apneic positive airway pressure decreased CO mainly by reducing VR and that RVEDV index was the least sensitive in predicting a hemodynamic response. Finally, the lack of ability of RVEDV index to predict fluid responsiveness was demonstrated in cardiac surgical patients where continuous EDV was used.[94]

There have been studies, however, which have found a value of RVEDV index that was significantly lower before a fluid bolus than before. Reuse et al[59] found that in critically ill patients fluid resuscitation was more effective at increasing CO if the RVEDV index was less than 140 mL/m^2. Diebel et al[80,81] in 2 studies found that patients with a RVEDV index above 138 mL/m^2 did not respond with an increase in CO to a fluid bolus, whereas there was a significant percentage of those with a value <90 mL/m^2 who responded. Values of RVEDV index between 90 and 139 mL/m^2 were equivocal. In two other studies, RVEDV correlated well with cardiac index in mechanically ventilated patients.[95,96]

It is evident that these studies bring about many salient points about the dynamics associated with ventricular filling and output. The complex relationship of VR, heart function, and vascular filling can be

oversimplified with a single optimal value. Association with RVEF may be necessary to place in context the responsiveness to a fluid challenge.

Echocardiography-derived RVEDV

Because of the irregular shape of the right ventricle (RV), multiple echocardiographic images must be acquired to define its shape and size. Many techniques have been described to measure RV volume.[97–104] Most commonly, the RV size is determined with TEE using the midesophageal 4-chamber view or apical 4-chamber with transthoracic echocardiography.[105,106] Unfortunately, with the difficult and inaccurate results in these methods, assessment of RV volume is rarely used clinically, and no study has been performed to evaluate the RV chamber size or volume as a predictor of fluid responsiveness.[88] However, the evolution of 3 dimensional-TEE may offer insights into the management RV function and volume assessment.[107]

Echocardiography-derived LVEDV

Echocardiography provides a qualitative and quantitative estimate of LV preload. One of the most widely used views is the short-axis view in detection of hypovolemia in a hyperdynamic heart without inotropic support.[108] However, to derive a true volume, more than one imaging plane is needed. Moreover, volumetric calculations are based on assumptions that the LV is of a particular shape. Assessment of LV volume is performed by detection of the end-diastolic endocardial border either traced manually or detected automatically. The modified Simpson's method to assess LV volume has been compared with other methods of detecting volume, and has shown to correlate the closest to ventricular angiography, although it may underestimate diastolic and systolic volumes due to ventricular apical foreshortening.[109]

As a surrogate for cardiac preload assessment, LVEDA in the transgastric midpapillary short-axis view has been shown to have good correlation to LVEDV. Clements et al[110] used this view to evaluate LVEDA and end systolic area in patients undergoing open abdominal aortic aneurysm repair. They found that LVEDA correlated well ($r = 0.86$) with ventricular volumes taken from radionuclide imaging. LVEDA was used in a study by Cheung et al[111] to detect hypovolemia. In that study, LVEDA detected changes in LV function caused by blood loss by $0.3\,cm^2/1.0\%$ estimated blood volume deficit. Konstadt et al[112] showed TEE -obtained LVEDA correlated well ($r = 0.88$) with epicardial echocardiographic-derived LVEDA in patients having coronary revascularization. Finally, Hofer et al[113] showed strong correlations of LVEDA index and LVEDV index by the modified Simpson's method with measurements of global EDV index and stroke volume index in cardiac surgery patients during a fluid challenge. It is not surprising, then, that

changes in LVEDA can reflect changes in stroke volume and preload. Approximately 90% of LV stroke volume is based on radial shortening at the midpapillary level.[114] This makes for easy reproducibility in the assessment of preload. Unfortunately, LVEDA as an indicator of preload is limited. The presence of regional wall motion abnormalities, especially at the apex, may preclude the use of this parameter for filling status.[87]

Studies examining LVEDV or LVEDA to predict fluid responsiveness are conflicting. Two studies[82,83] have reported that baseline LVEDA was significantly lower before a fluid load in those who responded with an increase in stroke volume compared with those who did not. Conversely, 2 other studies[76,115] have shown no significant difference in baseline LVEDA between responders and nonresponders to a fluid load. Greim et al[116] revealed that stroke volume correlated with LVEDA in post surgical patients mechanically ventilated in the ICU when cardiac index was normal or high, but the association weakened if the cardiac index was low. Belloni et al[85] also found no difference in baseline values of LVEDA or LVEDV in off-pump coronary bypass patients who responded and did not respond to a fluid load. However, baseline LVEDA and LVEDV did correlate significantly (correlation index = -0.834, $P = 0.0002$ and -0.712, $P = 0.001$, respectively) to increases in cardiac index after fluid was administered. Finally, Reuter and Goetz[117] demonstrated baseline LVEDA index had a better correlation to fluid responsiveness (increase in cardiac index) than baseline CVP and PAOP.

These studies show that although LVEDV in theory should be a better predictor of preload, results are inconsistent. The dynamics of volume change and the trends in preload supplant any absolute value obtained through echocardiography.

■ Conclusions

Optimization of preload for adequate CO is necessary to prevent organ dysfunction due to ineffective circulating intravascular volume. Selection of patients who might benefit from volume expansion through a fluid load and who might be harmed or unaffected by volume expansion must be ascertained and differentiated through specific parameters as a guide to fluid therapy. Unfortunately, the utility of the static parameters such as CVP, PAOP, and RVEDV and LVEDV is limited in predicting changes in CO with a fluid load. One reason for the limitation is that CO depends on the interplay between the preload and the nonlinear Frank-Starling curve.[114] Another reason is that the static parameters poorly reflect the preload.

CVP and PAOP have been found to have little to no correlation with CO and are unreliable in predicting responsiveness to a fluid challenge. Volumetric parameters LVEDV and LVEDA through TEE eliminate interference of ventricular compliance in estimation of volume from

pressures and have been more useful in quantifying intravascular volume, but not in predicting fluid responsiveness. These static parameters have limited applications in estimating vascular volume, and even more in fluid responsiveness.

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