Review

Functional hemodynamic monitoring

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Abstract

Hemodynamic monitoring is a central component of intensive care. Patterns of hemodynamic variables often suggest cardiogenic, hypovolemic, obstructive, or distributive (septic) etiologies to cardiovascular insufficiency, thus defining the specific treatments required. Monitoring increases in invasiveness, as required, as the risk for cardiovascular instability-induced morbidity increases because of the need to define more accurately the diagnosis and monitor the response to therapy. Monitoring is also context specific: requirements during cardiac surgery will be different from those in the intensive care unit or emergency department. Solitary hemodynamic values are useful as threshold monitors (e.g. hypotension is always pathological, central venous pressure is only elevated in disease). Some hemodynamic values can only be interpreted relative to metabolic demand, whereas others have multiple meanings. Functional hemodynamic monitoring implies a therapeutic application, independent of diagnosis such as a therapeutic trial of fluid challenge to assess preload responsiveness. Newer methods for assessing preload responsiveness include monitoring changes in central venous pressure during spontaneous inspiration, and variations in arterial pulse pressure, systolic pressure, and aortic flow variation in response to vena caval collapse during positive pressure ventilation or passive leg raising. Defining preload responsiveness using these functional measures, coupled to treatment protocols, can improve outcome from critical illness. Potentially, as these and newer, less invasive hemodynamic measures are validated, they could be incorporated into such protocolized care in a cost-effective manner.

Introduction

Hemodynamic monitoring is a cornerstone of care for the hemodynamically unstable patient, but it requires a manifold approach and its use is both context and disease specific. One of the primary goals of hemodynamic monitoring is to alert the health care team to impending cardiovascular crisis before organ injury ensues; it is routinely used in this manner in the operating room during high-risk surgery. Another goal of hemodynamic monitoring is to obtain information specific to the disease processes, which may facilitate diagnosis and treatment and allow one to monitor the response to therapy.

The effectiveness of hemodynamic monitoring depends both on available technology and on our ability to diagnose and effectively treat the disease processes for which it is used. The utility of hemodynamic monitoring has evolved as it has merged with information technology and as our understanding of disease pathophysiology has improved. Within this context, hemodynamic monitoring represents a functional tool that may be used to derive estimates of performance and physiological reserve that may in turn direct treatment. However, no monitoring device can improve patient-centered outcomes useless it is coupled to a treatment that improves outcome. Thus, hemodynamic monitoring must be considered within the context of proven medical therapies, success of which is dependent on the clinical condition, pathophysiological state and ability to reverse the identified disease process.

Rationale for hemodynamic monitoring

A progression of arguments supporting the use of specific monitoring techniques can be proposed. At the basic level, monitoring can be defended on the basis of historical controls. In this regard, prior experience with similar monitoring techniques indicates that they can identify known complications that are undetectable with less invasive means. Clearly, the mechanism by which the benefit is achieved need not be understood or even postulated.

Further support for hemodynamic monitoring comes from an understanding of the pathophysiology of the process being treated, such as heart failure or hypovolemic shock. Weil and Shubin [1] defined circulatory shock as decreased ability of blood flow to meet the metabolic demands of the body. Using their classic approach, four basic groups of circulatory shock can be defined: hypovolemic, cardiogenic, obstructive, and

CVP = central venous pressure; LV = left ventricular; PAC = pulmonary artery catheter; P_{CO_2} = partial carbon dioxide tension; Ppao = pulmonary arterial occlusion pressure; RV = right ventricular; S_{cvO_2} = central venous oxygen saturation; S_{vO_2} = mixed venous oxygen saturation.

distributive. Certain combinations of hemodynamic findings allow the etiology of circulatory shock to be defined using this nosology. Tissue hypoperfusion is common in all forms of shock (with the possible exception of hyperdynamic septic shock). Because specific types of circulatory shock require different therapies and target end-points of resuscitation, defining the cardiovascular state is important in determining both treatment options and their goals. Much of the rationale for hemodynamic monitoring resides at this level. The implied assumption here is that knowledge of how a disease process creates its effect will allow one to prevent the process from altering measured bodily functions, thus preventing disease progression and promoting recovery. This argument may not be valid, primarily because knowledge of the specific process in individual patients is often inadequate. Furthermore, measures of global blood flow and systemic arterial pressure, and changes in them in response to shock and its treatment poorly reflect regional and microcirculatory blood flow [2-4].

The most important support for hemodynamic monitoring is that, by altering therapy in otherwise unexpected ways, it can improve outcome in terms of survival and quality of life. Few therapies can claim such a benefit, although the trial by Rivers and coworkers [5] represents a notable exception in this regard; those investigators reported that measures of blood flow sufficiency and resuscitation to sustain blood flow improved outcome from septic shock.

Hemodynamic monitoring must also be considered within the context of the patient, pathophysiology, time point in the disease process, and position within the health care delivery system at which it is used. The site where monitoring takes place has a major impact on type of monitoring, and its risks, utility and efficacy. Monitoring outside the hospital and emergency department may be less invasive than in the operating room or intensive care unit. The time point during the course of disease when monitoring is applied will also have profound effects on outcome. For example, preoperative optimization of cardiovascular status [6] and emergency department early goal-directed therapy in septic shock [5] reduces morbidity, whereas the same monitoring and treatment applied after injury in unstable patients with existing shock-induced organ injury does not improve outcome [7-9].

Static hemodynamic monitoring variables

Specific hemodynamic variables are commonly measured and displayed at the bedside, and their values are often used in clinical decision making. However, the utility of each variable as a single absolute value is questionable. Some individual hemodynamic values are useful primarily as threshold monitors. For example, because a primary determinate of organ perfusion is perfusion pressure, systemic hypotension to below a certain threshold is clinically relevant. Furthermore, elevation in central venous pressure (CVP; i.e. >10 mmHg) reflects right ventricular (RV) pressure overload, although this gives no information on the precise etiology involved. Other hemodynamic values can only be interpreted relative to metabolic demand. For example, because blood flow varies to match metabolic requirements, which in turn can vary considerably, there is no one specific value of cardiac output or oxygen delivery that can be defined as 'normal'. These characteristics of blood flow reflect either an ability or an inability to meet the metabolic demands of the body. Finally, other measures are of questionable value in evaluating one parameter but are important in monitoring another. For example, pulmonary arterial occlusion pressure (Ppao) is a poor measure of left ventricular (LV) preload but is a good measure of the back-pressure to pulmonary blood flow and the hydrostatic forces producing pulmonary edema.

Some specific uses for hemodynamic values measured at a single point in time are described in Table 1. Although grouping hemodynamic variables in order to define profiles can improve diagnostic accuracy, there are few reports of improved outcomes resulting from such refinements in data analysis. Nevertheless, in the following discussion we consider the primary hemodynamic measures that are commonly used in critically ill patients.

Blood pressure

Arterial blood pressure is not a single pressure but a range of pressure values from systole and diastole. Mean arterial pressure best approximates the organ perfusion pressure in noncardiac tissues, as long as venous or surrounding pressures are not elevated. Arterial pressure is commonly measured noninvasively on an intermittent basis using a sphygmomanometer [10]. Indwelling arterial catheters permit continuous monitoring of arterial pressure. Because blood pressure is a regulated variable, a normal blood pressure does not necessarily reflect hemodynamic stability [11]. Organ systems also tend to autoregulate their blood flow such that organ-specific blood flow remains constant within a wide range of blood pressures if metabolic rate is unchanged, and varies with changes in local metabolic rate. The lower limit of this flow autoregulation, based on mean arterial pressure, varies between organs, patients (based on their underlying circulatory status, for example essential hypertension or peripheral vascular disease), their disease state, their metabolic activity, and associated vasoactive therapies.

Thus, there is no threshold blood pressure value that defines adequate organ perfusion among organs, between patients, or in the same patient over time [12]. However, because arterial pressure is a primary determinant of organ blood flow, hypotension (mean arterial pressure <65 mmHg) is always pathological.

Central venous pressure

CVP is the back-pressure to systemic venous return. Because CVP is usually very low, defining the appropriate hydrostatic zero level is important in estimating CVP, but

Table 1

Clinical caveats for hemodynamic variables

Type of hemodynamic variable	Parameter	Comments
Solitary	Blood pressure	Hypotension is always pathological
	Central venous pressure (CVP)	CVP is only elevated in disease
	Pulmonary artery occlusion pressure (Ppao)	Ppao is the back-pressure to pulmonary blood flow
	Cardiac output	There is no normal cardiac output, only an adequate or inadequate one
	Mixed venous oxygen saturation (Svo_2)	Decreasing Svo_2 is a sensitive but nonspecific marker of cardiovascular stress
Dynamic	Volume challenge	Positive response defined as an increase in any of blood pressure, CVP, Ppao, cardiac output and/or Svo_2, or a decrease in heart rate
	Echocardiographic analysis of vena cavae collapse during positive pressure inspiration identifies CVP <10 mmHg if it detects	Complete inferior vena caval collapse[a]
		>36% collapse in superior vena cava[a]
	Defining preload responsiveness	≥13% pulse pressure variation during positive pressure ventilation[a]
		>1 mmHg decrease in CVP during spontaneous inspiration[b]

[a]Requires a fixed tidal volume of 6–8 ml/kg and complete adaptation to the ventilator. [b]Requires a spontaneous inspiratory effort greater than −2 mmHg to be valid.

such physiological zeroing can be difficult. Few absolutes can be stated regarding static measures of CVP. If CVP is 10 mmHg or less then cardiac output will uniformly decrease when 10 cmH_2O positive end-expiratory pressure is given to ventilator-dependent patients [13], whereas a CVP above 10 mmHg has no predictive value. Demonstration, using echocardiographic techniques, of more than 36% superior vena caval collapse during positive-pressure inspiration [14] or complete inferior vena caval collapse [15,16] identifies individuals whose CVP is below 10 mmHg. However, there is no threshold value of CVP that identifies patients whose cardiac output will increase in response to fluid resuscitation [17]. Importantly, CVP is only elevated in disease, but the clinical utility of CVP as a guide to diagnosis or therapy has not been demonstrated.

Pulmonary artery catheter

The pulmonary artery catheter (PAC) permits LV filling pressures to be estimated by measuring Ppao [18,19]. However, Ppao values do not correlate with LV end-diastolic volume, and neither do they predict preload responsiveness [20]. Nevertheless, Ppao is the back-pressure to pulmonary blood flow, and it can be used to identify the presence of a hydrostatic component to pulmonary edema and to assess pulmonary vascular resistance. Using a rapid response thermistor, the PAC can be used to monitor RV end-diastolic volume based on measures of residual thermal signal. Measures of changes in RV end-diastolic volume are useful in cardiac surgery when trying to identify right-sided cardiac failure. If RV end-diastolic volume increases as cardiac output decreases, then the patient has cor pulmonale [21]. Using a transthoracic measure of thermal decay, one can estimate intrathoracic blood volume, global cardiac volume, and lung water. Of these three measures, intrathoracic blood volume is presently the most widely used technique, although intrathoracic lung water measures may be of interest in the management of patients with acute lung injury. Intrathoracic blood volume and its changes in response to fluid challenge reflect LV preload and changes in LV preload better than do more conventional measures, such as CVP or Ppao [17,22]. However, the utility of any of these measures as static single-point values in predicting preload responsiveness or in improving outcome in unstable patients has not been documented.

Indicator dilution techniques using thermal, indocyanine green, and lithium can measure blood flow from both central venous and PAC [23]. LV stroke volume can be estimated using a beat-to-beat based, algorithmic analysis of arterial pulse pressure [24]. Several monitoring techniques use subtle variations in this concept to calculate stroke volume and cardiac output. The overall accuracy of these techniques varies. Esophageal Doppler techniques can be used to measure descending aortic flow [25-27] and to estimate both stroke volume and cardiac output. Because accurate measurement of cardiac output is less important than accurate documentation of trends in flow, these measures may have profound clinical utility if they are accurate and stable over time.

Recall that there is no normal cardiac output; because cardiac output varies with metabolic demand, it is either able

or unable to meet these demands. Measures of mixed venous oxygen saturation ($Sv{O_2}$) may reflect better the adequacy of oxygen delivery. The normal value for $Sv{O_2}$ is 75–70%. Exercise, anemia, hypoxemia, and decreased cardiac output all independently decrease $Sv{O_2}$. Although $Sv{O_2}$ above 70% does not necessarily reflect adequate tissue oxygenation, a persistently low $Sv{O_2}$ (>30%) is associated with tissue ischemia [28]. Measures of central venous oxygen saturation ($Scv{O_2}$) tend to track $Sv{O_2}$. However, $Scv{O_2}$ and $Sv{O_2}$ are not equal, and so use of $Scv{O_2}$ to define thresholds of resuscitation requires one to give special attention to related clinical variables [29]. Splanchnic oxygen consumption can be estimated from hepatic venous oxygen saturation and hepatic venous blood flow measures [30]. However, this measure has not been shown to be superior to less invasive techniques in directing resuscitation or in improving outcome.

Hypoperfusion initially decreases blood flow but not oxidative phosphorylation; thus, tissue partial carbon dioxide tension ($P{CO_2}$) reflects both local metabolism and regional blood flow. If blood flow decreases then tissue $P{CO_2}$ will increase relative to arterial $P{CO_2}$. Measurement of this $P{CO_2}$ gap could allow one to assess whether tissue blood flow is effective. Measures of gastric [31] and sublingual [32,33] $P{CO_2}$ gaps identify tissue hypoperfusion. Gastric tonometry is useful in guiding resuscitation in critically ill patients [31], and sublingual $P{CO_2}$ measures may have similar utility.

Functional hemodynamic monitoring: defining response to therapy

Although one may use hemodynamic monitoring to identify cardiovascular insufficiency before it results in clinical hypoperfusion or as a prognostic indicator of survival, its greatest potential role is in directing application of cardiovascular therapies that are of proven efficacy. Monitoring conducted to evaluated the effect of treatment can be referred to as functional monitoring, because it implies a therapeutic application. Although trends in specific variables over time are useful in defining hemodynamic stability, their rapid change in response to application of a therapy has greater clinical utility. Some examples of functional monitoring variables are given in Table 1. The most common example of functional monitoring is in a therapeutic trial. Below we list the various types of functional monitoring presently validated.

Volume challenge

The time-honored method of assessing preload responsiveness is to administer a relatively small intravascular volume bolus rapidly and observe the subsequent hemodynamic response in terms of blood pressure, pulse, cardiac output, $Sv{O_2}$ and related measures. There is little agreement regarding what absolute volume and infusion rate defines an adequate fluid challenge. In a volume challenge trial estimates of improved circulatory status (e.g. increasing blood pressure and decreasing heart rate) and improved effective blood flow (e.g. increasing $Sv{O_2}$ and decreasing blood lactate) are used to document a beneficial response. The primary factor addressed by a fluid challenge is preload responsiveness; specifically, will cardiac output increase with fluid loading? Importantly, being preload responsive does not equate to requiring fluid resuscitation. Normal individuals are preload responsive but do not require resuscitation. Thus, a fluid challenge must be conducted within the context of known or suspected tissue hypoperfusion [34]. Furthermore, a volume challenge is not fluid resuscitation; it is merely a test to identify those who are preload responsive [35]. Volume responders can then be given additional fluid resuscitation with minimal risk for worsening cor pulmonale or inducing pulmonary edema.

However, a volume change, as a primary diagnostic approach in hemodynamically unstable patients, has important clinical drawbacks. First, only half of all hemodynamically unstable patients are preload responsive [36]. Second, it delays primary therapy in a setting where delayed appropriate treatment has consequences for survival. Finally, a volume challenge in an unresponsive patient may worsen or precipitate pulmonary edema or cor pulmonale. Therefore, several surrogate methods of creating reversible or transient volume challenges, including breathing and passive leg raising, have been advocated.

Passive leg raising

Passive leg raising to 30° transiently increases venous return [37] in patients who are preload responsive. Leg raising only transiently increases cardiac output in responders, and so it is not a treatment for hypovolemia. When coupled with measures of aortic flow, patients exhibiting a sustained (15 s) increase in mean aortic flow 30 s after leg raising were found to be preload responsive [38]. The advantages of this approach are that it is easy perform, induces only a transient and reversible volume challenge, yields volume challenges proportional to individual body size, and can be repeated as needed to reassess preload responsiveness. Limitations of the technique are that, presently, only measures of mean aortic flow, using esophageal Doppler, can assess preload responsiveness and that the blood volume mobilized by leg raising is dependent on total blood volume and so could be small in severely hypovolemic patients [39].

Changes in central venous pressure during spontaneous breathing

With spontaneous inspiration, venous return normally increases in association with the decrease in intrathoracic pressure [40]. If the right ventricle can transfer this transient bolus of blood into the pulmonary circulation, then CVP will correlate with intrathoracic pressure, decreasing with each spontaneous inspiratory effort. An inspiratory decrease in CVP of more than 1 mmHg in the setting of an intrathoracic pressure decrease of more than 2 mmHg accurately predicts preload responsiveness, whereas those patients whose CVP does not decrease do not increase their cardiac output in

response to fluid challenge [41]. This simple approach requires central venous catheterization, and one must give close attention to CVP waveform analysis. During positive pressure ventilation, the interpretation of CVP as reflected by changes in inferior vena cava diameter is complex and of minimal diagnostic utility.

Changes in left ventricular output during positive pressure ventilation

If changes in both right and left ventricles induce changes in output, then one can use positive pressure ventilation to assess the dynamic and necessarily cyclic effect of ventilation on venous return by assessing dynamic swings in LV output. The greater the increase in tidal volume for the same lung compliance, the greater is the transient decrease in venous return and subsequently greater decrease in LV output [42]. Changes in systolic arterial pressure during a programmed series of increasing tidal breaths quantify the degree of preload responsiveness [43]. Furthermore, during fixed tidal volume positive pressure ventilation, variations in systolic pressure [44], pulse pressure [45], LV stroke volume [46], and aortic flow [47] are robust measures of preload responsiveness. Michard and coworkers [45] found that a systolic pressure or a pulse pressure variation of 13% or more in septic patients breathing with a tidal volume of 8 ml/kg is highly sensitive and specific for preload responsiveness. In contrast, no threshold values for either Ppao or CVP could be identified that were better than random chance in predicting preload responsiveness.

One can estimate LV stroke volume based on the arterial pressure pulse contour. Several studies conducted in patients undergoing surgery have documented a good relation between this measure of pulse contour derived stroke volume variation and preload responsiveness [48]. Unfortunately, the accuracy of the pulse contour algorithm used to calculate stroke volume is proprietary and has changed on commercially available devices since these validation studies were preformed [49]. Thus, the extent to which these measures accurately track real stroke volume fluctuations is unclear. Furthermore, because these various devices calculate stoke volume differently, the threshold values for each parameter in predicting preload responsiveness may be different between devices, and may exhibit different degrees of robustness under varying clinical conditions. Changes in vasomotor tone [50] will also alter the observed changes in each parameter and may do so to proportionally different degrees. Thus, more clinical validation work must be done on these measures before they may become standard measures in most intensive care units.

Standardization of care

The application of evidence-based guidelines to clinical practice is rational. This approach often reduces health care costs by reducing practice variations, medical errors, and length of stay [51]. Fluid optimization as an end-point of resuscitation reduces length of hospital stay and important complications in patients undergoing a variety of major surgical procedures that routinely require postoperative resuscitation, but the degree of this effect varies among patients [52-54]. Cost-effectiveness analyses of specific types of treatment directed by hemodynamic monitoring, namely SvO_2 monitoring to identify adequacy of treatment for hemodynamic instability [55] and preoptimization in high-risk surgery patients [56], have demonstrated benefit. These studies underscore the importance of examining the utility of monitoring systems within the context of a specific disease process coupled to effective treatment protocols.

Conclusion

Fundamentally, one may ask just three questions regarding the cardiovascular system during resuscitation from shock [57]: will blood flow to the body increase with fluid resuscitation?; is arterial hypotension due to inadequate blood flow or loss of vasomotor tone, or both?; and is the heart capable of maintaining effective blood flow without going into failure? If the answer to the first question is 'yes', then treatment must include volume expansion. However, if the patient is also hypotensive and has reduced vasomotor tone, then vasopressor therapy may be started simultaneously because arterial pressure will not increase with volume expansion alone, even though cardiac output will increase. If the patient is not preload responsive but has reduced vasomotor tone associated with hypotension, then a vasopressor alone is indicated. If the patient is neither preload responsive nor exhibiting reduced vasomotor tone and hypotension, then the problem is the heart, and both diagnostic and therapeutic actions must be taken to address these specific problems (e.g. echocardiography, dobutamine). Protocolized cardiovascular management based on functional hemodynamic monitoring has the added advantages of being intuitively obvious (facilitating buy-in by stakeholders), pleuripotential (many different monitoring devices can all drive the same protocol) and scalable (alter intensity of resuscitation), and lends itself to automation.

Competing interests

The following text details the potential conflicts of interest for the participants of the Roundtable Meeting (see Acknowledgement): David Bennett: speaker's fees from LiDCO; Joachim Boldt: none listed; Jacques Creteur: received support for studies from Arrow International, Edwards LifeScience, Hutchinson, LiDCO, Marquet, and Pulsion; Daniel DeBacker: received support for studies from Arrow International, Edwards LifeScience, Hutchinson, LiDCO, Marquet, and Pulsion; Phillip Dellinger: Edwards Lifescience Speaker's Bureau and Ortho-Biotech Educational Consultant; Luciano Gattinoni: none listed; Alwin Goetz: Pulsion Medical Advisory Board; Johan Groenveld: none listed; Jessie Hall; none listed; Can Ince: Chief Science Officer, Microvision Medical, and received support for studies from Baxter and Edwards LifeScience; Jos Jansen: Arrow

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