Section 1 Hemodynamic Monitoring in the Perioperative Period

Chapter 1

Overview of the Circulation

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Introduction

Maintaining cardiovascular stability and reserve is fundamental to minimizing complications, morbidity and mortality in surgical patients and those otherwise critically ill. Titration of therapies aimed at supporting the cardiovascular system, respiratory gas exchange and internal homeostasis form the basis for acute care management. Diagnostic approaches, such as therapeutic trials and functional hemodynamic monitoring, or therapies, such as pre-optimization and other goal-directed therapies, are based on data derived from hemodynamic monitoring. Intraoperative clinical trial data documenting hemodynamic monitoring–defined resuscitation efforts that improve patient-centered outcomes were recently described.[1] Thus, the analysis of the cardiovascular status of patients and their response to therapies is tightly linked to physiological monitoring. Invasive hemodynamic monitoring includes arterial, central venous, and pulmonary arterial catheterization, transesophageal echo or ultrasound monitoring, non-invasive pulse oximetry, heart rate, blood pressure and arterial pressure waveform analysis. Similarly, using invasive monitoring one can measure O_2 saturation of central venous or mixed venous (within the pulmonary artery) blood (central venous oxygen saturation, $ScvO_2$, and venous oxygen saturation, SvO_2, respectively). Although specific combinations of hemodynamic variables often reflect certain disease states and their intrinsic physiological adaptive responses, there may be considerable overlap of hemodynamic data sets among markedly different pathological states that often may require different therapies. This diagnostic confusion can be minimized by examining the specific hemodynamic responses of the host to a specific therapy, often referred to as a therapeutic trial. For example, both severe sepsis and acute heart failure in the un-resuscitated patient will present with hypotension, a low cardiac output and SvO_2 and pulmonary artery occlusion pressure (Ppao). However, most patients in septic shock will be fluid responsive, increasing their cardiac output and SvO_2, whereas patients with acute heart failure will tend to increase both Ppao and blood pressure with less of an increase in cardiac output and SvO_2. Why these differences occur is a function of baseline cardiac function and reserve, vascular tone and reactivity, blood flow distribution and the effective circulating blood volume. To a large extent the information needed to identify which of these processes or groups of processes are driving a given pathological state requires hemodynamic monitoring targeted on the specific pathological processes most likely to be operational. Although the cardiovascular system is a tightly integrated system with close inherent and reflex feedback controls at multiple levels, one can artificially separate out the determinants of cardiovascular homeostasis into those that primarily are determined by: 1) ventricular pump function, 2) arterial vasomotor tone and blood flow

distribution and 3) effective circulating blood volume and venous return. Although these processes are discussed further in several of the subsequent chapters in this volume, an overview of these processes is useful to place this massive system within context.

Ventricular Pump Function

Our fundamental understanding of cardiac myocyte contractile performance was initially defined by the pioneering work of Frank and Starling in the 1890s. Subsequently, we have come to realize that systolic and diastolic function can be linked or separated but carry a common determinant in adequate energy stores and delivery, calcium trafficking and structural changes in response to ischemia and either pressure or volume overload. Although most studies of ventricular function revolve around left ventricular (LV) function, right ventricular (RV) function is now getting well-deserved attention as a primary determinant of cardiovascular function. Still, understanding LV physiology is essential to diagnosing and managing critically ill patients. The two ventricles have different roles in sustaining cardiovascular homeostasis. The left ventricle's only role is to sustain a high central arterial pressure by ejecting a reasonable amount of its end-diastolic volume into the aorta with each heart beat without requiring high filling pressures or resulting in cardiac muscle ischemia. The maintenance of a high central arterial pressure allows the circulation to autoregulate blood flow amongst tissue beds relative to their different and often highly varying metabolic demands. The right ventricle's roles are to effectively transfer most of the varying venous return flow into the pulmonary arterial circuit with each beat without causing right atrial pressure (Pra) to increase, thus sustaining a maximal pressure gradient for venous return. Accordingly, LV failure is manifest by increased filling pressure and a low systolic pressure and profound pressure-dependent stroke volumes, whereas RV failure is defined by RV dilation, increased Pra, venous status and low cardiac outputs.

Frank, a German physiologist, noted that unlike skeletal muscle strips, when cardiac muscle strips were stretched above their resting length this increased their force of contraction. Starling reasoned that since the LV cavity approximated a sphere, increases in LV end-diastolic volume (EDV) should proportionally increase LV myocardial fiber stretch. Thus, he modified Frank's observations to say that force of LV contraction was related to LV EDV. According to this rule, increasing LV EDV when LV function is normal will increase LV stroke volume, and for a constant heart rate, cardiac output will increase as well. If LV pump function is impaired, then for the same increase in LV EDV stroke volume will increase much less (Fig. 1.1). This concept is central to most diagnostic and therapeutic protocols used to assess cardiac function.[2] The immediate treatment of acute cardiovascular insufficiency and arterial hypotension is to increase intravascular volume with the goal of increasing LV stroke volume via the Frank–Starling mechanism. If LV stroke volume increases, then the subject is said to be "preload-responsive," and the presumptive diagnosis of hypovolemia is made. The relation between LV EDV and either stroke volume or cardiac output is referred to as the Frank–Starling relationship. Still, focusing on the Frank–Starling mechanism to augment cardiac output when treating patients with presumed hypovolemia and preserved ventricular pump function is misleading and potentially dangerous. The Frank–Starling mechanism is primarily in place to match the varying outputs of the right and left ventricles over relatively short time intervals (e.g., 5–10 seconds) as venous return to the right ventricle varies with ventilation and subsequently varies to the left ventricle two to three beats later. In essence, it is an intrinsic process keeping the outputs of the two

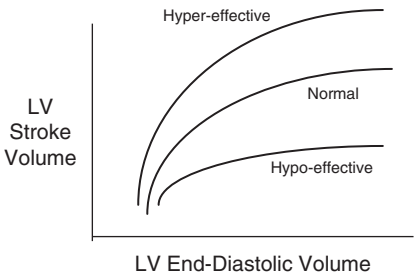

Figure 1.1 Graphic representation of the Frank–Starling relationship defining left ventricular (LV) function showing the relation between LV end-diastolic volume and stroke volume for normal, hyper- and hypo-functioning ventricles.

ventricles similar to prevent either pulmonary vascular congestion/edema or intrathoracic hypovolemia developing as either venous return or LV afterload are varied.

Importantly, it is difficult to document a sustained increase in LV EDV in an otherwise healthy subject following volume loading or exercise. Amazingly, with exercise or artificially increased venous return due to opening an arterio-venous fistula or rapid volume infusion, one sees a transient increase in both LV EDV and stroke volume. But after about 20 seconds, LV EDV returns to baseline values, although stroke volume remains elevated. The interpretation of these data must be that intrinsic contractility has increased. Indeed, this phenomenon, referred to as the Anrep effect or homeometric autoregulation, can be demonstrated in isolated perfused hearts, showing that it is intrinsic to the myocardium. [3] Presumably, increased myocardial wall stress increases local calcium flux by phosphorylation of the calcium channels, causing increased contractility. In fact, we can define patients as having systolic heart failure if they can only increase their LV stroke volume through the Starling mechanism.

However, with either the Frank–Starling or Anrep mechanisms in play, we still model the left ventricle as a pump, the work done is to create a stroke volume under pressure. The mechanical correlate of volumes moved under pressure is work, or stroke work. LV stroke volume will vary inversely with outflow pressure (arterial pressure) for a constant LV EDV and LV contractility. To account for this important influence, LV stroke work, rather than stroke volume, is often used to assess LV functional status. If stroke work is less for the same LV EDV, then LV contractility is also said to be less under this condition as well (Fig. 1.2). The measure of LV function used to assess cardiovascular status is highly dependent on the question being asked. If the clinician is wishing to assess the adequacy of LV output to meet the metabolic demands of the body, the cardiac output is most important, because it reflects blood flow. On the other hand, if the clinician wishes to understand the level of myocardial contractile reserve, independent of the level of blood flow, then the change in LV stroke work relative to the change in LV EDV is a better index.

Unfortunately, the Frank–Starling relationship is only a superficial description of the mechanical quality of ventricular ejection. The actual mechanical properties of the contracting ventricle are better characterized by the rate of increase in myocardial wall stiffness or elastance over systole, described as time-varying elastance.[4] Graphically, this distinction is better illustrated by displaying LV performance as a hydraulic pump plotting the relation between LV pressure and volume during the cardiac cycle.

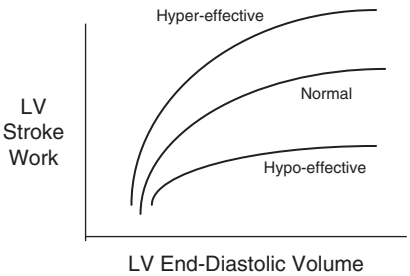

Figure 1.2 Same relation as shown in Figure 1.1, except left ventricular (LV) stroke work is substituted for stroke volume.

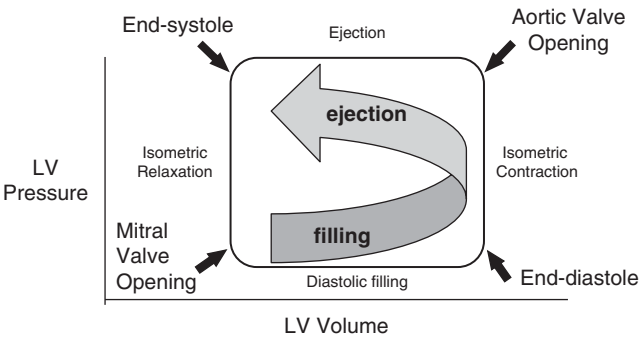

Figure 1.3 Stylized representation of the left ventricular (LV) pressure–volume relation over a complete cardiac cycle, referred to as the LV pressure–volume loop. Note that filling, contraction, emptying and relaxation proceed in a counterclockwise fashion.

The Left Ventricular Pressure–Volume Loop: When displayed as the changes in LV pressure and volume during a cardiac cycle, time is not seen (Fig. 1.3). Traditionally, LV volume is shown on the x-axis and LV pressure on the y-axis. Filling occurs during diastole when LV chamber pressure decreases to less than left atrial pressure. The slope of the passive LV distention is diastolic compliance. Right before the end of diastolic filling, the atria contract, rapidly increasing LV pressure at end-diastole. This results in a higher EDV but a lower overall filling pressure over diastole because LV end-diastolic pressure only increases rapidly at the end of diastole. Accordingly, myocardial blood flow is less impeded into the subendocardial regions during diastole than would otherwise be the case if LV filling pressure were always elevated across all diastolic pressure values. At end-diastole, defined by the electro-mechanical coupling of contraction, there exists the minimal LV pressure/volume ratio. This point is often used to assess diastolic compliance but is influenced the absolute volume restraint imposed by the pericardium, lungs and right ventricle. Thus, measures of LV end-diastolic pressure to LV EDV often vary widely without any actual changes in LV diastolic compliance. LV EDV is often used synonymously with LV preload as applied to the Frank–Starling relationship. However, LV preload by the Frank–Starling relationship is LV myocardial wall stress. If LV diastolic compliance changes from one beat to the next, as can easily occur with acute RV overload or hyperinflation, then for the same LV myocardial fiber stress LV EDV will be less. Thus, the bedside clinician is often left with the confusing situation of seeing increasing LV end-diastolic pressures without an increase in LV stroke volume and inferring that LV contractility is depressed. Although contractility may well be depressed, it is more likely in a non-cardiac patient that the decreased LV stroke volume reflects RV overload or hyperinflation. This process by which increased RV EDV or

RV end-diastolic pressures limit LV filling is referred to as ventricular interdependence and occurs commonly in both health and disease, making estimates of LV function by plotting the Frank–Starling curve using Ppao and LV stroke volume or stroke work inaccurate at best and often misleading.

With systolic contraction, LV intra-cavitary pressure rises, causing a passive closing of the mitral valve, changing the shape of the LV from an ellipsoid into a sphere as LV intra-cavitary pressure rapidly rises. The increased LV systolic intra-cavitary pressure caused by myofibril contraction results from three inter-related mechanisms. First, the myofibrils contract, shortening their individual fibers' long axis. This causes the circumference of fibrils to shorten along their myofibril orientation. Myofibrils are oriented in three ways: longitudinal, horizontal and spiral, relative to the long axis of the ventricle. Longitudinal myofibril contraction shortens the long axis from apex to base, causing the mitral annulus to migrate toward the base. Thus, mitral annual velocity measures reflect LV contraction. Horizontal myofibril contraction makes the cross-sectional circumference smaller. Finally, spiral myofiber contraction twists the chamber in a fashion analogous to the wringing of a washcloth. Second, myofibril contraction also results in thickening of the myofibrils at right angles at their longitudinal orientation. This thickening in a shortening circumference further increases the tension within the ventricle. Myofibril thickening primarily compresses the horizontal diameter of the LV chamber, whereas shortening primarily shortens the long axis and twists the heart. Third, the coordination of myofibril contraction allowing first the closure of the mitral and tricuspid values by the papillary muscles and then a generalized ventricular wall contractions requires an integrated His–Purkinjean conduction system that transfers atrio-ventricular nodal activation into myofibril activation. However, alterations in contraction synchrony caused by arrhythmias and regional contractile impairments induced by ischemia can profoundly impair LV contraction effects, rapidly leading to LV failure. All these processes combine to allow a single contraction to generate enough wall tension with a minimal amount of cellular energy requirement to cause effective LV ejection many times a minute for many years without the need for hypertrophy or the development of ischemia.

Once LV intra-cavitary pressure exceeds aortic pressure, the aortic valve passively opens, and ejection begins with continued LV contraction but now decreasing LV volume with no measurable resistance created by the aortic value. In normal subjects, the point where ejection occurs represents the maximal LV wall stress. By the law of Laplace, wall stress is the product of radius of curvature and developed pressure. Thus, diastolic arterial pressure being the pressure at which the aortic value opens during ejection is a major determinant of LV wall stress. LV wall stress is LV afterload and is often referred to inaccurately as LV ejection pressure. This concept is important because any therapy that selectively decreases diastolic arterial pressure will reduce LV afterload more than therapies that selectively decrease systolic arterial pressure. Similarly, if a vasodilator therapy, for example, induced both vasodilation and increased LV stroke volume, then diastolic arterial pressure will decrease, but systolic arterial pressure may either remain constant or increase. If the clinician were specifically targeting systolic arterial pressure as LV afterload, then they would incorrectly presume that the vasodilator therapy paradoxically increased afterload. This presumption potentially could lead to an incorrect decision to either increase vasodilator therapy further, which may induce coronary ischemia by further decreasing coronary perfusion pressure, or stop vasodilator therapy altogether despite the fact that such

patients who increase their arterial pulse pressure in response to vasodilator therapy are actually showing a positive response to this treatment.

Importantly, for the LV pressure–volume loop, we see that LV ejection occurs as LV volume decreases and both LV pressure and aortic pressure rise. As LV ejection continues transferring blood into the thoracic aorta, the aorta distends. becoming stiffer. Thus, arterial pressure rises more toward the end of ejection even though the actual amount and rate of volume being ejected at the end is much less than in the beginning. Accordingly, most of the increase in arterial pressure occurs when the LV volume is already small. Interestingly, LV afterload is approximated by the product of the LV radius of curvature and the LV pressure; although LV pressure rises during ejection, the radius of curvature decreases. Thus, in otherwise normal subjects the product of LV radius of curvature and ejection pressure decreases during ejection. For example, assuming an ejection fraction of 60% and a normal LV EDV, then the LV radius of curvature should decrease by >300% from end-diastole to end-systole, while LV ejection pressure only increases by 20–40% from the opening of the aortic value (diastolic arterial pressure to systolic arterial pressure). Thus, LV wall stress should decrease by more than half from the start to the end of ejection. That the left ventricle unloads itself during ejection has important clinical implications. First, systolic hypertension is reasonably well tolerated on a short-term basis without much increase in myocardial O_2 demand (MVO_2). Diastolic hypertension, however, immediately increases MVO_2 and stimulates the development of LV hypertrophy. If the left ventricle is dilated and at end-ejection still has a large volume, then systolic pressure will be a major contributor to both LV wall stress and MVO_2. Under dilated cardiomyopathy conditions, a reduction of LV afterload only occurs if the LV cavity gets much smaller during ejection. So in dilated heart failure states, ejection only minimally decreases LV volumes, and systolic arterial pressure becomes the determinant of LV afterlaod. Accordingly, such patients are very sensitive to changes in systolic arterial pressure and specific decreases in systolic arterial pressure should decrease LV end-systolic volume and MVO_2.

Interestingly, LV end-ejection occurs at a pressure–volume ratio that appears to be only minimally altered by ejection history but highly influenced by end-ejection pressure and intrinsic contractility. If arterial resistance is high, then LV end-systolic pressure and end-systolic volume (ESV) increase, whereas if arterial resistance is low, both decrease. However, both end-systolic pressure and volume do so along an end-systolic elastance line, called the end-systolic pressure–volume relationship (ESPVR) that is independent of the actual pressure or volume. Importantly, the ESPVR slope varies in proportion to changes in contractility: increasing with increased contractility and decreasing with decreased contractility.[3] Thus, one can say that LV ESV then is a function of both afterload and contractility. As such increases in afterload will increase ESV whereas decreases in afterload will decrease ESV, the slope of the ESPVR, however, remains unchanged.

Once end-ejection has occurred, the left ventricle actively relaxes. Diastolic relaxation, or lusitropy, is the energy-dependent part of the cardiac cycle, causes LV intra-cavitary pressure to decrease faster than would be predicted by passive relaxation alone (i.e., sucking action occurs) and is impaired by myocardial ischemia. Thus, impaired active diastolic relaxation is the earliest manifestation of myocardial ischemia. Once LV intra-cavitary pressure decreases below aortic pressure, the aortic valve passively closes, allowing LV pressure to continue to decrease as aortic pressure remains elevated, creating a coronary artery pressure gradient needed to support LV coronary flow during diastole. Since coronary artery blood flow occurs primarily in diastole, when LV wall stress is low whereas

perfusion pressure is high, any process that impairs diastolic relaxation will decrease coronary blood flow.

Expanding the ESPVR to Encompass All of Systole: Time-Varying Elastance: The entire LV contractile process can be understood better from the perspective not of a single pressure–volume loop, but from the pressure–volume domain of contraction across many potential LV pressure–volume loops that might be created for the same level of contractility but by varying preload and afterload. Within this analysis, one may describe increasing LV stiffness as an increasing slope of a theoretical LV pressure–volume domain as one point in time post-initiation of LV contraction, identical to the LV ESPVR but at earlier points during systole. Thus, as time progresses from the start of contraction to end-ejection the left ventricle becomes progressively stiffer, such that the slope of the unique LV elastance curves for each time post the start of contraction will become progressively greater until they merge with the ESPVR curve. Since stiffness is also referred to an elastance, this time-dependent increase in stiffness is referred to as time-varying elastance (Et). In essence, time-varying elastance describes the progressive stiffening of the left ventricle through systole and then its relaxation in diastole within the pressure–volume domain.[3] Time-varying elastance can be calculated as a plot of the slopes of the isochronic (similar point in time relative to the start of contraction) LV pressure–volume relations during ejection as the end-diastolic volume is rapidly varied (Fig. 1.4). The slopes of these sequential pressure–volume lines reflect the obligatory LV pressure–volume domain that must be followed during systole. Importantly, Et defines the LV systolic function. The slope of the ESPVR can then be defined as end-systolic elastance (E_{es}) and is usually calculated from the regression line of the ESPVR data pairs of repetitive LV pressure–volume loops.

Although this discussion may seem esoteric, it has important direct clinical applications and explains many of the previously unexplained physiological determinants of LV systolic function. Recall that the Frank–Starling relationship maintains that as LV EDV increases, LV stroke work also increases. Indeed, any ejection phase index, like stroke volume, velocity of circumferential fiber shortening, ejection fraction and LV pressure change (dP) over a period of time (dt), dP/dt, will all show an increase with increasing LV EDV. But why? Time varying elastance explains all these phenotypic outputs as epi-phenomena of time varying elastance. Note that as systole progresses, Et also increases. Since E_{es} is greater than end-diastolic elastance, any increase in LV EDV will create a lesser increase in ESV, if LV ejection pressure does not also increase significantly. Since the Et is always increasing up to

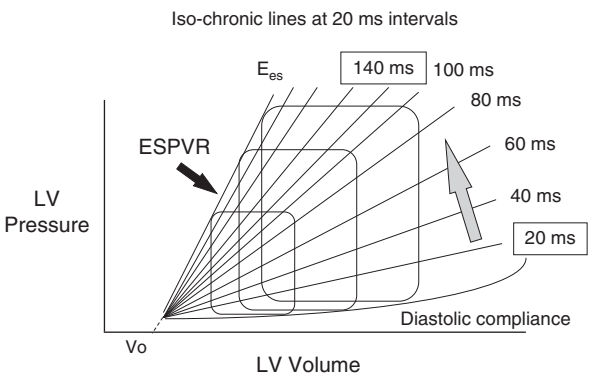

Figure 1.4 Stylized representation of three left ventricular (LV) pressure–volume loops at differing volumes showing how diastolic compliance, end-systolic elastance and the isochronic (same point in time following the start of systole) time-varying elastance are calculated. The estimated zero LV pressure residual volume of the heart is called V_o. E_{es}, end-systolic elastance; ESPVR, end-systolic pressure–volume relationship.

E_{es}, the resultant stroke volume, stroke work, LV d*P*/d*t* and velocity of circumferential fiber shortening must also increase for a given diastolic compliance and E_{es}. When does this not happen? When does increasing LV EDV not increase stroke volume or other ejection phase indices? This occurs when LV contractile function is depressed or LV diastolic compliance reduced so much that the slopes of the diastolic compliance and ESPVR become equal.

Applying Cardiac Physiology at the Bedside: The preload-dependent nature of LV performance is a primary characteristic of normal ventricular function. Demonstrating that LV EDV is above some minimal value, despite cardiac output and stroke work both being depressed, and with increases in LV EDV further, neither cardiac output nor LV stroke work increase is a fundamental attribute of the phenotype of systolic heart failure. Regrettably, the opposite is not true. Documenting that LV EDV is reduced in the setting of hemodynamic instability does not identify hypovolemia because reduced LV EDV is also seen commonly in conditions associated with diastolic dysfunction, such as tamponade, cor pulmonale, hyperinflation and pulmonary hypertension. These conditions are common in the critically ill, making finding a reduced LV EDV not synonymous with volume responsiveness. These points are addressed further in the chapter on functional hemodynamic monitoring.

Right Ventricular Function: The *Forgotten Ventricle:* Traditionally, cardiovascular chapters would now switch to discussing the peripheral circulation, which is appropriate if the major aspects of ventricular pump function had already been covered. Regrettably, they have not. The right ventricle behaves in a very different manner when presented with increased volume (preload) or ejection pressure (afterload).

Under normal conditions, it is extremely difficult to document that RV filling pressure changes during RV filling. When RV filling pressure, defined as Pra minus pericardial pressure, was directly measured in patients undergoing open chest operations as RV volume was varied by acute volume loading, RV filling pressure is insignificantly altered.[5] Although Pra increases with volume loading, pericardial pressure also increases, such that RV filling pressure, defined as right atrial pressure minus pericardial pressure, remains unchanged. Similar data are seen when RV volumes are reduced by the application of positive end-expiratory pressure (PEEP) in post-operative cardiac patients.[6] Thus, under normal conditions, RV diastolic compliance is very high and most of the increase in Pra seen during volume loading reflects pericardial compliance and cardiac fossa stiffness. If RV wall stress is not increased during filling, then RV myofibril length remains constant. Presumably, conformational changes in the RV more than wall stretch are responsible for RV enlargement.[7] Accordingly, changes in Pra do not follow changes in RV end-diastolic volume, as has recently been validated to define why measures of right atrial pressure, or central venous pressure, cannot predict either intravascular volume status or RV preload.[8] When cardiac contractility is reduced and intravascular volume is expanded, RV filling pressure does increase as a result of either decreased RV diastolic compliance, increased pericardial compliance, increased end-diastolic volume or a combination of all three. RV over-distention has important clinical consequences. As RV EDV increases, the absolute volume remaining in the cardiac fossa decreases, making LV diastolic compliance less, by a process referred to as ventricular interdependence.[7] Lung expansion if causing hyperinflation compresses the heart within the cardiac fossa in a fashion analogous to pericardial tamponade, but in this setting, it is the expanding lungs that increase intrathoracic pressure (ITP), and not pericardial restraint, limiting ventricular filling.[6]

As will be described further below, venous return, the primary determinant of cardiac output,[9] is maintained near maximal levels at rest [10] because RV filling occurs with minimal changes in filling pressure. This is because Pra is the back pressure to venous return. Accordingly, the closer Pra remains to zero relative to atmospheric pressure, the maximal is the pressure gradient for systemic venous blood flow.[11] For this mechanism to operate efficiently, RV output must equal venous return, otherwise sustained increases in venous blood flow would overdistend the RV, increasing Pra. Fortunately, under normal conditions of spontaneous ventilation this is not a problem because most of the increase in venous return is in phase with inspiration, when ITP decreases, such that Pra when measured relative to atmosphere also decreases. Likewise, the pulmonary arterial inflow circuit is highly compliant and can accept large increases in RV stroke volume without changing pressure. Thus, any transient increase in venous return within limits is proportionally delivered to the pulmonary circuit without forcing the RV to increase its force of contraction or myocardial oxygen demand.

This normal adaptive system will rapidly become dysfunctional if RV diastolic compliance decreases or if Pra increases independent of changes in RV EDV. Clinical examples of states where this usually occurs include acute RV dilation or cor pulmonale (pulmonary embolism, hyperinflation and RV infarction), which induce profound decreases in cardiac output not responsive to fluid resuscitation. Dissociation between Pra and RV EDV also occurs during either cardiac tamponade or positive-pressure ventilation. Thus, positive-pressure ventilation impairs circulatory adaptive processes normally occurring during spontaneous ventilation. Since the primary effect of ventilation on cardiovascular function in normal subjects is to alter RV preload via altering venous blood flow, the detrimental effect of positive pressure ventilation on cardiac output can be minimized by either fluid resuscitation to increase venous return or by keeping PEEP and tidal volumes as small as possible. Finally, over-resuscitation causes transient acute right heart failure, and though often underappreciated, it probably occurs more often than not with aggressive resuscitation scenarios not targeted as limited resuscitation to only preload responsive subjects. Excessive fluid resuscitation either by too much infused or too rapid an infusion rate will cause Pra to rise. Thus, a rising Pra of >2 mmHg during a fluid bolus maneuver is a stopping rule to limit fluid infusion. Such patients need to be reassessed as to the status of their right ventricle and their level of fluid responsiveness. Fluid responsiveness will be discussed below.

Arterial Pressure and Blood Flow Distribution

Arterial pressure is a primary determinant of organ perfusion. The other factor determining organ blood flow is intra-organ vascular resistance. Importantly, organ perfusion is independent of cardiac output. Cardiac output is only important within this context to maintain an adequate organ perfusion pressure, allowing autoregulation of organ blood flow by the organs themselves. Thus, hypotension blunts autoregulation of blood flow and directly reduces organ blood flow. Systemic hypotension is synonymous with cardiovascular instability. Since a fundamental goal of hemodynamic monitoring is to identify cardiovascular instability,[12] documenting systemic hypotension is essential in defining profound circulatory shock. Operationally, mean arterial pressure (MAP) is presumed to be the input pressure to the organs. However, LV perfusion occurs primarily during diastole and brain and intra-abdominal organs also see intra-cranial and intra-abdominal pressures as their

back pressures to flow, respectively. Thus, actual organ perfusion pressure may be quite different amongst vital organs for the same MAP.

If MAP is the primary pressure defining organ perfusion, can a patient be in circulatory shock and not be hypotensive? The answer is yes. Normal homeostatic mechanisms functioning via carotid body baroreceptors vary arterial peripheral vascular tone through sympathetic nerves to maintain MAP relatively constant despite varying cardiac output. This profoundly conserved cardiovascular sympathetic reflex process is done to maintain cerebral and coronary blood flow at the expense of the remainder of the body. In an otherwise healthy subject, this reflex response can totally mask global hypoperfusion. For example, in the postoperative period, if occult hemorrhage causes progressive hypovolemia, then the initial findings are usually hypertension and tachycardia, not hypotension, as the increased sympathetic drive caused marked peripheral vasoconstriction. Clearly, baroreceptor response can only work effectively in the long term if the low cardiac output is not sustained; otherwise, marked end-organ hypoperfusion will manifest as decreased urine output, ileus and cold cyanotic extremities. Thus, MAP is a remarkably stable measure and relatively insensitive as a marker of cardiovascular instability or organ blood flow. Indirect measures of sympathetic tone, such as heart rate, respiratory rate and peripheral capillary filling and peripheral cyanosis, reflect better estimates of cardiovascular status than does MAP. Still, hypotension is a medical emergency because its presence defines that tissue hypoperfusion must exist and that normal homeostatic defense processes are inadequate.

MAP monitoring is still essential in the assessment and management of hemodynamically unstable subjects for several reasons. Measures that specifically increase MAP should also increase organ perfusion pressure if critical closing pressure does not also increase equally. In healthy subjects, vasopressors increase tone at all levels so organ blood flow usually remains constant despite increasing MAP. Vasoconstrictor therapies may increase vasomotor tone more in non-vital peripheral organs but almost always will maintain flow to the cerebral and coronary beds because their arteries have little or no alpha-adrenergic receptors, whereas the gut, kidneys, muscles and skin demonstrate a marked reduction in blood flow in response to marked sympathetic stimulation. Accordingly, short-term survival of the host is closely linked to MAP through the maintenance of cerebral and coronary blood flows. If profound hypotension persists for even a brief period of time, irreversible cerebral and cardiac damage can occur. Thus, the initial priority in resuscitation of a hypotensive patient is to restore MAP above a level that will ensure coronary and cerebral perfusion, usually >65 mmHg, and then to restore cardiac output once MAP is stabilized to restore vital organ blood flow.

The primary method of increasing vascular tone is to infuse vasopressor agents, like norepinephrine. Regrettably, vasopressor support in the absence of fluid resuscitation may improve transiently both global blood flow and MAP but worsen local non-vital blood flow and hasten tissue ischemia. Thus, initial resuscitative efforts should always include a volume expansion component and fluid challenge to identify preload-responsive shock states, prior to relying solely on vasopressors to support the unstable patient.

Arterial pressure is created by the ejection of LV stroke volume into the aorta, causing it to distend. Since LV ejection is rapid, absolute arterial blood volume increases with each systole and then decreases slowly during diastole as the arterial blood runoff into the organs continues. Since neither arterial pressure nor blood flow is ever constant during life, it is fundamentally difficult to assess arterial vasomotor tone from mean values of arterial pressure and cardiac output. Simplistically, one can estimate MAP and plot the relation