Dynamic Indices of Preload

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Hypotension and shock are important issues confronting the intensivist. The question that confronts most intensive care providers on a daily basis is: will fluid increase perfusion to end organs, or will it worsen pulmonary or systemic edema? This can be especially true when treating septic patients, where volume expansion is often one of the cornerstones of early resuscitation. Volume overload can have dire consequences such as decreased gas exchange and increased myocardial dysfunction. Several studies suggest that even experienced intensivists using traditional parameters are correct only about 50% of the time when determining preload responsiveness.[1–6]

As the importance of early goal directed therapy in the successful treatment of septic shock becomes increasingly apparent, it is all the more imperative that goals be based in science and supported by evidence. Clearly, static measurements have failed as a meaningful endpoint for fluid resuscitation.

Clinically, many practitioners rely on the central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), or other static measurements to determine the volume status of a patient. Studies in recent years have confirmed that these filling pressures have little correlation with fluid responsiveness.[5–9]

In many patients, a rapid fluid bolus is a reasonable diagnostic and potentially therapeutic option, but in others (eg, acute respiratory distress syndrome [ARDS]), it has the potential to cause harm, and may delay institution of appropriate therapy. Ideally, it would be possible to determine if a patient will be preload responsive before the volume is given. The poor predictive value of static measures and clinical examination has led to investigation of the dynamic measures of fluid responsiveness. In contrast to static measures, dynamic indices rely on the changing physiology of heart lung interactions to determine whether a patient will benefit from increased preload.

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PHYSIOLOGIC RATIONALE OF DYNAMIC INDICES

Preload of the heart is defined as the wall stress at the end of diastole.[10] Direct measurement of wall stress in vivo is difficult; end diastolic volumes or pressures have been used as proxies, but both have significant limitations. Perhaps most importantly, an accurate measure of preload at a point in time does not necessarily reflect preload responsiveness.

An understanding of the Frank-Starling curve is fundamental to understanding the concept of preload responsiveness. The slope of the relationship between ventricular preload and stroke volume (SV) depends on ventricular contractility. As contractility increases, the Starling curve shifts upwards and to the left and increases its slope. Decreasing contractility has the opposite effect. Increasing preload serves to augment ventricular output predominantly on the steep portion of the curve. As seen in **Fig. 1**, augmenting preload on the flat portion of the curve produces minimal increases in SV.

As a ventricle fails, its contractility and therefore the slope of its Frank-Starling curve decreases, and a preload that would indicate volume responsiveness in the normal heart may not apply to a failing heart. Therefore even a precise measurement of left ventricular (LV) preload does not determine if that LV is fluid-responsive (ie, if it will increase cardiac output in response to increased volume). Additionally, the relationship between preload and SV is curvilinear rather than linear.

Dynamic indices apply a controlled and reversible preload variation and measure the hemodynamic response. This can be done by observing the cardiovascular response to positive pressure ventilation, or to reversible preload-increasing maneuvers, such as passive leg raising.

Cavallaro has proposed a useful classification of dynamic indices that predict volume responsiveness. Group A consists of indices based on cyclic variation in SV or SV-related hemodynamic parameters determined by mechanical ventilation-induced cyclic variation in intrathoracic pressure, and includes such metrics as pulse pressure variation (PPV), its derivatives, and aortic blood flow. Group B is made up of indices based on cyclic variations of nonstroke volume-related hemodynamic parameters determined by mechanical ventilation, and includes vena cava diameter or
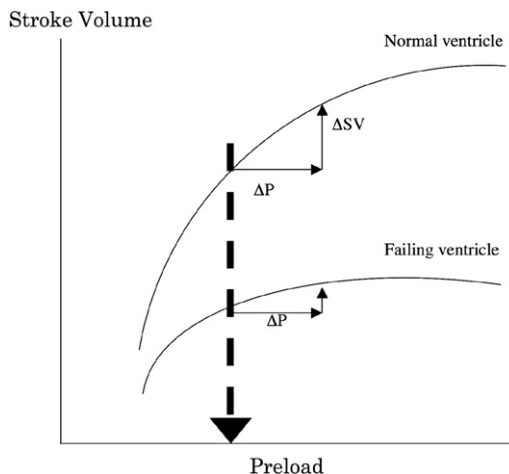
Fig. 1. Frank-Starling curves demonstrating relationship between change in preload to change in SV in a normal and failing ventricles. A given change in preload may cause variable changes in SV, depending on the slope of the curve.

ventricular pre-ejection period. Group C consists of indices based on preload redistribution maneuvers; mechanical ventilation is not required, and group C includes passive leg raising and Valsalva maneuvers.[11]

Group A and B techniques are based on the physiologic interaction of the heart and lungs within a closed thoracic cavity, and rely on the phasic changes in SV created by changing intrathoracic pressure due to positive pressure mechanical ventilation. During positive pressure inspiration, preload to the right heart is decreased because of increased intrathoracic pressure, both from compression of the vena cava (decreased venous return) and increased right atrial pressure. This decrease in right ventricular (RV) preload leads to a decrease in RV output, which subsequently leads to a decrease in pulmonary artery blood flow, LV filling, and LV output.[12] Other mechanisms postulated to increase LV SV variation with PPV include the following changes during inspiration, caused by increased transpulmonary pressure

Increased RV afterload
Increased LV preload
Decreased LV afterload.[12]

The end result of these pressure changes is that LV SV increases, while RV SV decreases during positive pressure inspiration. The delay of pulmonary blood transit time results in decreased RV SV translating to a decreased LV SV a few heartbeats later (ie, usually during expiration).[8]

These phasic differences are exaggerated in the setting of hypovolemia for several reasons:

The underfilled vena cava is more collapsible
The underfilled right atrium is more susceptible to increased intrathoracic pressure
More of the lung demonstrates the physiology of West Zones 1 and 2 (in West Zone 1 the alveolar pressure is greater then the arteriolar pressure, which is greater than venous pressure; in West Zone 2 the arteriolar pressure is greater than alveolar pressure, which is greater than venous pressure), which effectively increases RV afterload
Larger changes are seen when operating on the steeper portion of the Frank-Starling curve.[12]

This increased variation in pressures between the inspiratory phase and the expiratory phase can be used to identify hypovolemia and volume responsiveness, and is the basis for Cavallaro's group A and B indices, including stroke volume variation (SVV) and pulse pressure variation.

SVV

SVV examines the difference between the SV during the inspiratory and expiratory phases of ventilation, and requires a means to directly or indirectly assess SV. This eliminates arterial compliance as a variable, but until recently, has required invasive monitoring such as aortic flow probes. Now, the PiCCO (Pulsion Medical Systems, Munich, Germany), LiDCO (LiDCO Group PLC, London, England) and FloTrac sensor (Edwards Lifesciences, Irvine, CA, USA) monitors uses pulse contour analysis through a proprietary formula to measure cardiac output and SVV. Because arterial compliance is not a factor in this index, it should most closely represent the change in cardiac output during the respiratory cycle, and also be the most predictive of volume responsiveness. Indeed, some studies do suggest that SVV, as measured by pulse contour

technique, can be helpful as a fluid responsiveness predictor.[13] This has not been consistently reproducible, however, and other studies find poor predictive value.[14,15]

Systolic Pressure Variation

Systolic pressure variation (SPV) is the difference between the maximum and the minimum systolic pressure over a single respiratory cycle and can be expressed in millimeters of mercury (SPmax − SPmin) or as a percent (SPV(%) = $100 \times (SP_{max} - SP_{min})/[(SP_{max} + SP_{min})/2]$). Increased SPV was the first of these indices to be recognized to correlate with hypovolemia and was later shown to have a sensitivity of 82%, specificity of 86%, and area under the receiver operator characteristic (ROC) curve (AUC) of 0.92, using a threshold of 8.5 mm Hg.[16,17]

SPV can be broken down into delta up (dUp) and delta down (dDown). These two components are calculated using a reference systolic pressure measured during an end–expiratory pause according to the following equations:

dUp = SPmax − SPref
dDown = SPref − SPmin

where SPmax is the maximum systolic pressure in a single respiratory cycle; SPref is the reference systolic pressure at end–expiration, and SPmin is the minimum systolic pressure measured in a single respiratory cycle.

dUp reflects the inspiratory increase in systolic pressure, resulting from an increase in extramural aortic pressure (increase in diastolic pressure) and an increase in LV SV. As the extramural aortic pressure component seems more significant in many patients,[18] increased dUp is not a reliable indicator of fluid responsiveness. Indeed, in animal models, dUp is increased in congestive heart failure[19] and with increasing volume resuscitation in the presence of cardiac ischemic dysfunction.[20]

dDown reflects the expiratory decrease in LV SV related to the inspiratory decrease in RV SV.[12]

PPV

Arterial pulse pressure is the difference between arterial systolic and diastolic pressure. This difference is influenced by SV and the arterial compliance. Comparison of the pulse pressure during inspiration with pulse pressure during expiration demonstrates the degree to which the pulse pressure is preload-limited. As comparison is being made during a single respiratory cycle, change in arterial compliance theoretically should be minimal. Analysis of the PPV thus can be used to predict volume responsiveness, and is expressed as a percentage: PPV(%) = $100 \times (PPmax - PPmin)/[(PPmax + PPmin)/2]$.

Several studies have demonstrated the utility of increased PPV as a predictor of fluid responsiveness. Michard and colleagues found that in mechanically ventilated patients with septic shock, a PPV of 13% identified patients who had a greater than or equal to 15% increase in cardiac output in response to volume expansion with 500 mL of 6% hydroxyethylstarch, with a sensitivity of 94% and specificity of 96%. Additionally, this group found that using ROC analysis, PPV was a more accurate predictor of volume responsiveness than SPV.[21] Auler and colleagues[22] had similar findings in a population of patients mechanically ventilated after cardiac surgery.

dDown and PPV since have been demonstrated to be more sensitive and specific predictors of volume responsiveness than SPV. At a threshold of 5 mm Hg, dDown has a sensitivity and specificity of 86% in patients undergoing cardiac surgery, and an AUC of 0.92%.[19] In another study, Tavernier and colleagues[23] found that in successive volume loading steps in 15 septic and mechanically ventilated patients, a dDown

of 5 mm Hg had a 95% positive predictive value and 93% negative predictive value, with an area under the ROC of 0.97 (95% confidence interval [CI] 0.9 to 1.0). PPV was not evaluated in this study, but SPV was found to have an area under the ROC of 0.91 (95% CI of 0.76 to 0.98).

Kubitz and colleagues compared SPV and PPV with aortic flow probe-derived SVV in pigs undergoing pharmaceutical alteration of blood pressure with phenylephrine and adenosine. At decreased pressures, SPV decreased compared with baseline, while PPV stayed the same across the range of decreased and increased pressures. Both SPV and PPV showed good correlation with SVV at baseline and decreased pressures, and slightly less correlation at increased pressures, although both maintained significance. Bland-Altman analysis found a mean bias of SPV and SVV of 5.35% (standard error [SE] 0.42, limits of agreement 8.31% and 2.40%). Similar analysis of PPV and SVV revealed a mean bias of 1.41% (SE 0.58, limits of agreement 5.46% and −2.63%). From this, the authors concluded that PPV is a more reliable value than SPV when blood pressure is being augmented by vasoconstrictors. This study did not include a volume expansion component to the experiment.[24]

Plethmysography

Examining amplitude variation between inspiration and expiration phases has been extended to the plethysmographic waveform. Although this technique has several similarities to arterial pulse pressure variation, there are several important differences. The plethysmographic waveform obtained from a standard pulse oximeter probe is based on transmission and reflection of infrared wavelengths of light by tissue. The pulsatility is a function of changing tissue volume between systole and diastole, producing the familiar wave tracing.[25]

The pulse oximeter as a gauge of volume status first was suggested by Partridge[26] in 1987. Variation in the plethysmographic waveform has been referred to by many names: change in pulse oximetry plethysmography (dPOP), ventilation-induced plethysmographic variation (VPV), and DP$_{PLET}$. For the sake of this article, the authors will refer to VPV (VPV(%) = 100 × ([Max amplitude − Min amplitude]/[(Max amplitude − Min amplitude)/2])). Cannesson and colleagues[27] reported the strong correlation (r^2 = .82, P<.001) of VPV with PPV in 22 mechanically ventilated patients. It should be noted that the precision of this correlation appears to decrease as variation increases. The Cannesson study did not demonstrate volume responsiveness, but only that VPV of greater than or equal to 15% was predictive of having PPV greater than or equal to 13%, the threshold value for volume responsiveness sited in many studies. Wyffels and colleagues[28] reported that in 32 postoperative cardiac surgery patients, PPV and VPV reliably predicted at least a 15% increase in cardiac index in response to administration of 500 mL 6% hydroxyethylstarch with an AUC (95% CI) of 0.937 (0.792 to 0.991) and 0.892 (0.731 to 0.972), respectively. Feissel and colleagues[29] demonstrated in 23 septic patients that a VPV of 14% allowed discrimination of volume responders and nonresponders with a sensitivity of 84% and specificity of 80%.

Several concerns have been raised regarding the use of VPV in clinical care. Landsverk and colleagues showed large inter- and intra-individual variation in VPV in 14 mechanically ventilated intensive care unit (ICU) patients. In addition, Bland-Altman analysis demonstrated poor agreement between VPV and PPV.[30] There is also acknowledgment by several authors that proprietary signal processing by different manufacturers may alter the raw data such that it interferes with the use of the waveform for purposes other than oxygen saturation monitoring. For example, the auto–gain function on most pulse oximeters will conceal amplitude changes.[25]

Some monitors allow this function to be turned off, while others do not. As there is no accepted standard of signal processing between manufacturers, this may prevent the reproduction of results between institutions using different monitors, as well as reliable clinical use of this technique.

Although the obvious and tantalizing advantage to the use of the pulse oximeter to determine fluid responsiveness is the complete noninvasiveness of the technique, at this time, evidence does not support reliance on this method.

Respiratory variability of the superior and inferior vena cava

The inferior and superior venae cavae are distensible blood vessels whose diameters and flow vary with respiration.[31] These variations are reflected by changes in aortic flow within a few beats of the heart.[32] The IVC enters the right atrium almost immediately after crossing the diaphragm. Therefore its extramural pressure is equivalent to abdominal pressure, and its intramural pressure is close to right atrial pressure. The transmural pressure versus volume relationship of the venae cavae is nonlinear, with a steep slope at low distention and a plateau at full volume.[33,34] In PPV, the increase in pleural pressure is transmitted fully to the right atrium, and partially transmitted to the abdomen via depression of the diaphragm, causing an overall increase in transmural pressure of the IVC. Because the IVC is distensible, this increase in pressure causes an increase in diameter of the IVC. In hypovolemic patients (ie, those on the steep part of the pressure volume curve), these diameter changes should be larger than if the IVC is full (ie, on the flat part of the pressure volume curve).[31–33,35,36]

Unlike the IVC, the course of the SVC is mainly intrathoracic. Positive pressure ventilation then should cause a decrease in transmural pressure, and subsequent decrease in the diameter of the SVC, especially in hypovolemic patients.[33]

Using different indices as reference standards, three groups tested the hypothesis that changes in the diameter of the IVC and the SVC with PPV are predictive of fluid responsiveness, and independently concluded that respiratory variations in IVC and SVC diameter during mechanical ventilation could be used to determine preload responsiveness in sedated, mechanically ventilated patients.

Barbier and colleagues determined that the distensibility index of the IVC (dIVC), defined as (Dmax − Dmin)/Dmin and expressed as a percentage, was predictive of fluid responsiveness with a sensitivity of 90% and a specificity of 90%. Twenty-three septic patients were evaluated with subcostal images of the IVC and cardiac index measured by esophageal Doppler. They concluded that a dIVC above 18% was predictive of an increase in cardiac index of at least 15% with fluid loading.

Feissel and colleagues used a slightly different index to reach similar conclusions. Using subcostal imaging of the IVC, they measured the maximum and minimum IVC diameters over a single respiratory cycle in fully sedated, mechanically ventilated patients without arrhythmias. They calculated DD_{IVC} as maximal IVC diameter – minimum IVC diameter divided by the mean of the two values and expressed as a percentage. Cardiac output was measured by volume time integral (VTI) of aortic blood flow via transthoracic echocardiography. Defining responders as those whose cardiac output increased by at least 15%, they found that DD_{IVC} of 12% predicted fluid responsiveness with a positive predictive value of 93% and negative predictive value of 92%.[32]

Viellard-Baron studied the effect of PPV on the SVC and the ability to predict volume responsiveness. They studied 66 mechanically ventilated patients in septic shock with acute lung injury. An SVC collapsibility index (maximum diameter on expiration – minimum diameter on inspiration/maximum diameter on expiration) threshold of 36% allowed discrimination between nonresponders and responders with sensitivity of 90% and specificity of 100%.[36]

The dIVC and DD$_{IVC}$ are appealing, because both techniques are noninvasive and relatively easy to learn. The SVC collapsibility index requires esophageal Doppler placement, which is not routine in many ICUs. In all of these studies, the patients were sedated and fully ventilated in volume control mode with an average tidal volume close to 8 mL/kg. It is unclear how smaller or larger tidal volumes would affect the results. Patients with arrhythmias were excluded. Only 7 out of 123 patients in the three studies were excluded, because the examiners were unable to obtain adequate imaging. Certainly in some ICU patient populations (postlaparotomy, morbidly obese), one would anticipate more difficulty obtaining images.[31] It is also unclear how elevated intra-abdominal pressures would affect the validity of dIVC and DD$_{IVC}$.

Using respiratory variation in IVC and SVC diameter has potential for predicting pre-load responsiveness in septic patients. Phasic variation of SVC diameter may be more accurate, as it is not influenced by intra-abdominal pressure. However, it necessitates a transesophageal, rather than transthoracic, approach. Further validation of these concepts in large, multicenter trials is warranted.

Cautions Regarding Cavallaro Group A and B Indices

There are several important caveats to keep in mind when using these dynamic indices to predict fluid responsiveness:

Positive pressure, controlled ventilation is required to obtain meaningful values for any of the Cavallaro group A or B indices. Spontaneous respiratory efforts, even when supported by the ventilator, alter the mechanics such that these numbers lose their reliability.

Sinus rhythm is required. Arrhythmia or frequent extra systoles result in altered SV and invalidate these tools to predict volume responsiveness.

Many of these techniques require invasive arterial blood pressure monitoring with a catheter, and as such, they are prone to the same errors in measurement associated with invasive blood pressure monitoring: air bubbles in the catheter tubing, excessive tubing length, kinks in the tubing, excessively compliant tubing, and other errors.

A single value never should replace clinical judgment. A high PPV value in a normo-tensive patient with evidence of normal tissue perfusion does not mean that person requires volume expansion.

Further investigation of these techniques in the setting of vasoactive medications is needed. Animal data suggest that group A dynamic indicators are useful even in the setting of high doses of vasoconstricting agents. In a swine model, PPV appears to maintain more fidelity to SVV measured by aortic flow probe than SPV when blood pressure is modified pharmacologically using phenylephrine and adenosine.[24] Nouira and colleagues[37] observed a decrease in SPV and PPV with norepinephrine infusion after hemorrhage in anesthetized dogs. Further investigation is needed in people.

How extremes of ventilation (ie, low tidal volume, high respiratory rate, high positive end-expiratory pressure [PEEP]) affect group A and B indices is not yet clear. Most of the early data came from patients ventilated with at least 10 mL/kg tidal volumes. Huang and colleagues[38] found that PPV remains a valuable indicator of volume responsiveness in patients with ARDS and ventilated with a lung protective strategy, although the area under the ROC curve, at 0.768, was small-er than in the studies using 8 to 12 mL/kg tidal volumes. Mean tidal volume in the Huang study was 6.4 mL/kg with a standard deviation of 0.7. Interestingly, in another trial by De Backer and colleagues[39] involving 17 hypovolemic patients

ventilated with low (14 to 16 breaths per minute) and high (30 to 40 breaths per minute) respiratory rates, the authors concluded that respiratory variation in SV and its derivates is affected by respiratory rate, and caution against using these indices as predictors of volume responsiveness at high respiratory rates. Mean tidal volumes in this study were 8.5 mL/kg (8.2 to 9.2) ideal body weight.

Further investigation of these indicators in the setting of the open abdomen or open thorax is needed before their use should be relied upon in these populations.

Passive Leg Raising

Passive leg raising (PLR) is a form of reversible volume challenge that can be used to evaluate which patients will benefit from intravenous fluid and increased preload. Elevating a patient's legs allows a passive transfer of blood from the lower part of the body toward the central circulation. The amount of blood transferred from the legs is variable and has been estimated to be between 150 to 750 mL depending on technique and study.[1,40–42] If the heart is preload-responsive, the shift of fluid from the lower part of the body to the thorax should result in increased cardiac output. This requires that both the right and left ventricles be preload-dependent. If the right ventricle cannot increase cardiac output with increased preload, the left ventricle will not see the increased preload, and cardiac output will not improve.[43]

Several studies have determined that PLR is effective in determining which patients are preload-responsive.[1–4,43,44] Importantly, PLR can be used in spontaneously breathing patients and in patients not in sinus rhythm.[1] The increase in preload from the maneuver is reversed completely when the legs are returned to horizontal,[1,43,44] meaning it is safe even in cases in which increasing blood volume may be harmful, such as ARDS. International consensus guidelines now recommend PLR to evaluate fluid responsiveness in patients with shock.[45]

Boulain and colleagues[44] was the first to demonstrate the utility of PLR clinically. He demonstrated that in sedated, mechanically ventilated patients in sinus rhythm, PLR induced changes in radial arterial pulse pressure correlated with subsequent volume-induced changes in SV. This study, however, gave no threshold value to distinguish between those who responded to an intravenous fluid bolus and those who did not.

In 2002, Monnet and colleagues[1] evaluated PLR to assess fluid responsiveness in spontaneously breathing patients and those with arrhythmias. Using esophageal Doppler measurements of aortic blood flow as a surrogate of cardiac output, Monnet found that an increase in aortic blood flow of at least 10% with PLR predicted volume responsiveness with a sensitivity of 97% and specificity of 94%. Changes in aortic blood flow were rapid (within 30 seconds of PLR) and transient. The authors found that the PLR-induced changes in aortic blood flow and arterial pulse pressure variation were predictive of volume responsiveness, but the former was more accurate than the latter. Of note, this is the first study in which the starting position of the patients before PLR was semirecumbent, rather than supine.

Jabot and colleagues confirmed that maximal fluid shifts, and therefore better predictive value, are obtained when patients are shifted from the semirecumbent (chair) position to supine with legs elevated 45°. Elevating the legs of a horizontal supine patient may still be helpful, but sensitivity is decreased.[42]

In follow-up to Monnet's study, Maizel and colleagues[4] examined the predictive value of PLR in spontaneously breathing patients using transthoracic echocardiographic measures of SV and cardiac output. Patients with arrhythmias were excluded. He found that in increase of cardiac output or SV of greater than 12% with PLR

predicted volume responsiveness. There was no change in heart rate with PLR, indicating lack of catecholamine response to any stimulus the PLR maneuver may have created in these awake patients. This confirms earlier findings of Gaffney and colleagues[41] in healthy volunteers.

In the largest study to date, Thiel and colleagues measured SV changes with PLR in 89 medical ICU patients determined to need volume expansion by their attending clinician. Using a transthoracic Doppler device (USCOM Limited, Sydney, Australia), they determined that a greater than or equal to 15% increase in SV with PLR predicted volume responsiveness with sensitivity and specificity of 81% and 93%, respectively. Less than 50% of the patients given fluid boluses were volume-responsive, once again confirming the poor ability to determine preload responsiveness clinically.[3]

Because the hemodynamic response to PLR is rapid and transient,[5,41,46] real-time assessment of cardiac output is needed, which generally means some form of invasive monitoring. It is not clear how much blood is autotransfused, how much this varies between patients and patient populations, and if the variation is significant. Importantly, the characterization of responders versus nonresponders has not been defined clearly. Vasoconstrictors, increased intra-abdominal pressures, and elastic compression stockings all may have an impact on validity of PLR; further studies are needed to clarify these issues. It would be prudent to avoid PLR in patients with increased intracranial pressure.

Respiratory Systolic Variation Test

The respiratory systolic pressure variation (RSVT) is a technique whereby three or four consecutive pressure-controlled breaths of increasing peak inspiratory pressures are administered over a brief period of time to intubated, sedated patients. The minimum systolic blood pressure (SBP) value following each of these breaths is recorded, and the results plotted against their respective airway pressures. A steeper slope (ie, larger decrease in SBP with increasing tidal volume) implies that the patient will be fluid-responsive, whereas less of a slope implies the patient's ventricles are on the flat part of the Frank-Starling curve, and the patient will not increase cardiac output with fluid loading.[19,47]

Two studies have demonstrated the potential utility of the RSVT to predict fluid responsiveness. Preisman and colleagues[20] compared several different dynamic preload indicators, including RSVT, before and after fluid loading. Eighteen patients undergoing elective coronary artery bypass graft (CABG) were evaluated preoperatively after induction of anesthesia, and again postoperatively before transfer to the ICU. Operators used transesophageal echocardiography to measure LV end–diastolic area index (LVEDAI) and fractional area change (FAC), and a PiCCO femoral arterial catheter to measure intrathoracic blood volume index (ITBVI), LV stroke volume index (LVSVI), systolic pressure variation (SPV), dDown, PPV, and SVV along with the RSVT (**Fig. 2**). Area under ROC curve was used to evaluate the ability of the tested hemodynamic parameters to predict fluid responsiveness. Patients were considered volume-responsive if the LVSVI increased by at least 15%. Forty-six percent of study patients were responders. SVV, PPV, SPV, dDown, and RSVT were all very good predictors of fluid responsiveness. RSVT had similar predictive value as PPV, with area under ROC curve of 0.96 and 0.95 respectively. The predictive value of CVP was little better than chance.

Perel and colleagues[47] studied 14 patients after abdominal aortic surgery. They also found that steeper RSVT slopes were associated with a greater than or equal to 15% increase in cardiac index after fluid administration with a sensitivity of 87.5% and a specificity of 83%.

The accuracy with which many of the dynamic preload indicators predict fluid responsiveness can be affected by variations in tidal volume.[47,48] The main advantage
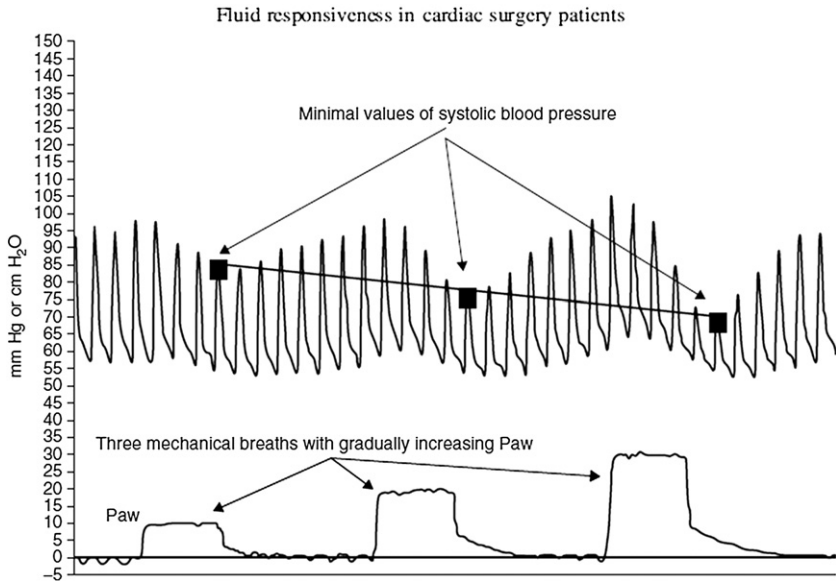
Fig. 2. Response of the arterial blood pressure (BP) to the RSVT. Three consecutive mechanical pressure-controlled breaths are delivered with inspiratory pressures of 10, 20, and 30 cm H_2O. Minimal values of SBP in response to each breath are recorded, and then the slope of the relationship between the decrease in BP and inspiratory pressure is calculated. (*From* Preisman S, Kogan S, Berkenstadt H, et al. Predicting fluid responsiveness in patients undergoing surgery: functional haemodynamic parameters including the Respiratory Systollic Variation Test and static preload indicators. Br J Anaesth 2005;95:746–55; with permission.)

of RSVT is that it is independent of set tidal volume. A complex respiratory maneuver is required, combined with complicated off-line measurements and calculations, making it unsuitable for routine clinical practice. Newer ventilators that are able to perform the RSVT while integrating with hemodynamic monitors may make this feasible in the near future.[19]

End–Expiratory Occlusion Pressure

Recently, Monnet and colleagues proposed a promising new dynamic indicator of fluid responsiveness. Positive pressure ventilation increases intrathoracic pressure and impedes venous return, which in turn reduces cardiac preload. Monnet hypothesized that an end–expiratory occlusion (EEO) may abolish the inspiratory increase in intra-thoracic pressure, prevent the cyclic drop in cardiac preload, and allow an increase in venous return, thus acting like a fluid challenge.[49] They tested whether this could serve as a functional test for fluid responsiveness in patients with circulatory failure.

Thirty-four mechanically ventilated patients with shock in whom volume expansion was planned by their clinician were studied. Blood pressure and cardiac index (pulse contour-derived via PiCCO) were measured at baseline, during PLR, during the last 5 seconds of EEO, and after 500 mL normal saline. Hemodynamic measurements obtained during the 15-second EEO were compared with those obtained during PLR. All patients were ventilated in volume-assist controlled mode with tidal volumes of 6.8 ± 1.1 mL/kg. Thirty two percent had arrhythmias. The remainder had some spontaneous breathing effort, but mild enough that it did not interrupt the 15-second EEO. Ten patients were

excluded, because they triggered the ventilator during occlusion. Responders to volume expansion were defined as those with an increase in cardiac index of at least 15%. Twenty-three patients were responders. An increase in arterial pulse pressure or cardiac index of at least 5% during EEO was both sensitive and specific for volume responsiveness, as was an increase in cardiac index of at least 10% with PLR.

Because the duration of the EEO in this experiment encompassed several cardiac cycles, determination of fluid responsiveness would perhaps be independent from cardiac arrhythmias. Patients with spontaneous breathing were included, as long as they did not trigger the ventilator during the test.

This appears to be a new and novel test for volume responsiveness with several advantages. It is simple to perform, and can be used in patients with arrhythmias and those with some spontaneous respiratory effort. As yet, it only has been demonstrated in one small study, and needs further validation, but it does offer promise as a useful clinical tool.
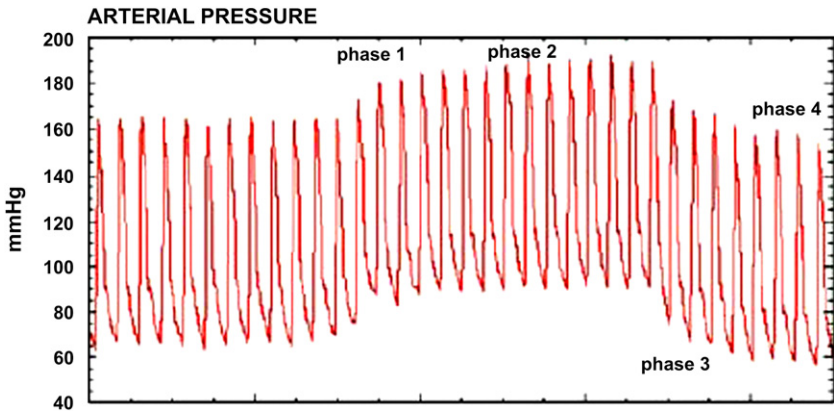
Valsalva Maneuver

The physiologic response to the Valsalva maneuver is complex, but its main hemodynamic effect is to impair venous return to the right ventricle by rapidly increasing intrathoracic pressure. If both ventricles are preload-dependent (ie, on the steep part of the Frank-Starling curve), LV SV, and hence cardiac output, should decrease. In this way, the Valsalva maneuver theoretically could be used, like PLR, as a reversible gauge of preload dependency.

Garcia and colleagues tested this hypothesis on 30 spontaneously breathing, nonintubated patients in a mixed ICU. Patients with arrhythmias were excluded, as were those who could not achieve at least 20 cm H_2O of airway pressure. Cardiac outputs and SVs were measured via FloTrac (Edwards LifeSciences) sensor attached to an arterial line.[50] PPV and SPV were measured during a 10-second Valsalva maneuver, and after a 500 mL colloid bolus. Responders were classified as those with an increase in SV index of at least 15% after the fluid bolus. A threshold PPV during Valsalva of 52% predicted fluid responsiveness with a sensitivity and specificity of 91% and 95% respectively. For a cutoff SPV of 30%, sensitivity was 73% and specificity
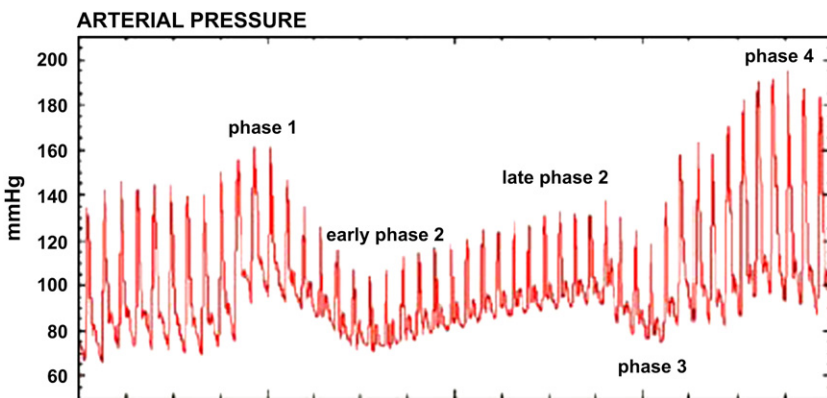
Fig. 3. Normal arterial pressure response during the Valsalva maneuver is characterized by a sinusoidal pattern due to a fall in arterial pressure during phase 2 and overshot during phase 4. (*From* Garcia S, Cano A, Monrove J. Arterial pressure changes during the Valsalva maneuver to predict fluid responsiveness in spontaneously breathing patients. Intensive Care Med 2009;35:77–84; with permission.)

Fig. 4. Abnormal arterial response is characterized by absence of decreased pulse pressure during phase 2, producing the typical square wave pattern. (*From* Garcia M, Cano A, Monrove J. Arterial pressure changes during the Valsalva maneuver to predict fluid responsiveness in spontaneously breathing patients. Intensive Care Med 2009;35:77–84; with permission.)

79%. The authors conclude that the arterial pressure response to a 10-second Valsava maneuver could be a useful clinical tool to measure preload responsiveness in spontaneously ventilating patients.

There are limitations to this study. Study patients were deemed to need fluid based on hypotension, tachycardia, or oliguria. No data were presented on urine output, but the average SBP before Valsalva or fluid was nearly 130, mean arterial pressure 90, and heart rate 83 beats per minute. These data would not trigger fluid administration in most ICUs. Although there were statistically significant differences between responders and nonresponders with respect to SPV with Valsalva, there remained considerable overlap between the two groups. Proper interpretation of the measurements required measuring PPV during early phase 2 of the Valsalva response (**Figs. 3** and **4**). Although the Valsalva maneuver is relatively simple and noninvasive, and may easily be performed at the bedside,[51] it requires active cooperation of the patient. Ultimately, the ability to accurately assess preload responsiveness in nonintubated patients would be of great use, and the concept deserves further exploration.

SUMMARY

Dynamic indices repeatedly have been shown to be superior to static measures for determining preload responsiveness in critically ill patients. The number of options for assessing fluid responsiveness available to the clinician is increasing; however, few have been evaluated in large, multicenter trials. Currently there are no data on whether managing patients using dynamic indices affects outcomes. It is important to remember that preload responsiveness does not equate to needing more preload. Healthy individuals are preload-responsive, and will increase their cardiac output in response to a fluid challenge, but they do not require increased blood volume. Therefore even with accurate measures of preload responsiveness, clinical judgment remains essential.

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