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Using Functional Hemodynamic Indicators to Guide Fluid Therapy

A more accurate and less invasive way to gauge responsiveness to IV volume replacement.

OVERVIEW: Hemodynamic monitoring has traditionally relied on such static pressure measurements as pulmonary artery occlusion pressure and central venous pressure to guide fluid therapy. Over the past 15 years, however, there's been a shift toward less invasive or noninvasive monitoring methods, which use "functional" hemodynamic indicators that reflect ventilator-induced changes in preload and thereby more accurately predict fluid responsiveness. The author reviews the physiologic principles underlying functional hemodynamic indicators, describes how the indicators are calculated, and discusses when and how to use them to guide fluid resuscitation in critically ill patients.

Keywords: critical care nursing, evidence-based practice, functional hemodynamic indicators, fluid responsiveness, physiologic monitoring, pulse pressure, stroke volume, systolic blood pressure

Consider the following hypothetical situation: An 80-kg man with severe sepsis has been admitted to the ICU from the medical–surgical unit. He has signs of hypoperfusion and an increased lactate level. He is sedated and receiving ventilatory support. The ventilator settings are as follows: tidal volume (Vt), 8 mL/kg; respiratory rate, 14 breaths per minute; positive end-expiratory pressure, 5 cm H_2O. The patient's heart rate is 105 beats per minute, indicating sinus tachycardia without ectopy. His mean arterial pressure (MAP) is 60 to 65 mmHg, and his central venous pressure (CVP) is 8 mmHg. An arterial catheter shows his blood pressure to be markedly variable. Before his transfer to the ICU, the patient received two liters of fluid. How do you think his ICU treatment should proceed? Is it appropriate to administer another fluid bolus, or should he be given vasopressor therapy?

In patients with signs of poor perfusion—such as hypotension, oliguria (urine output below 0.5 mL/kg per hour for more than two hours), lactate levels above 2 mmol/L, or hemodynamic instability (MAP below 60 mmHg)—and in those whose vasopressor dosage is being reduced, intravenous fluids are often administered to increase end-diastolic volume. This strategy emanates from the Frank–Starling law of the heart, which states that the greater the myocardial fiber stretch at end diastole (preload), the greater the force of cardiac contraction and, therefore, the greater the stroke volume (SV)—that is, the amount of blood the heart pumps in one contraction. In such cases, the key question is whether the patient's heart is

ABBREVIATION GLOSSARY

CI – cardiac index
CO – cardiac output
CVP – central venous pressure
MAP – mean arterial pressure
PAOP – pulmonary artery occlusion pressure
PP – pulse pressure
PPV – pulse pressure variation
SBP – systolic blood pressure
SPV – systolic pressure variation
SV – stroke volume
SVV – stroke volume variation
Vt – tidal volume

capable of increasing SV in response to the increased preload a fluid bolus provides.

Traditionally, either we've used the static indicators CVP and pulmonary artery occlusion pressure (PAOP) to predict whether patients will respond to fluid therapy, or we've administered a fluid bolus and then evaluated its effect on such outcomes as cardiac output (CO), blood pressure, and urine output. The use of the CVP and PAOP, which reflect a snapshot of the assumed relationship between pressure, volume, and ventricular function, is problematic because research has shown that these measures do not accurately predict patient responsiveness to a fluid bolus.[1,2] A systematic analysis of 29 studies involving 685 patients who had signs of hypoperfusion found that only 56% of patients responded to a fluid bolus, despite having a CVP or PAOP that suggested they would respond.[3] The practice of administering fluids and then evaluating outcomes may place patients at risk for volume overload.

Over the past 15 years, there has been a shift toward less invasive or noninvasive monitoring methods that are based on ventilator-induced changes in systolic blood pressure (SBP), pulse pressure (PP), and SV—indicators that reflect the functional ability of the heart to respond to a fluid bolus. These "functional" hemodynamic indicators are more accurate than the static measures of CVP and PAOP in predicting whether a patient will respond to a fluid bolus with a clinically significant (greater than 15%) increase in SV or CO.[2-4] This article reviews the physiologic principles underlying the functional hemodynamic indicators, describes how the indicators are calculated, and discusses when and how to use them to guide fluid resuscitation in critically ill patients.

VENTILATOR EFFECTS ON SBP, PP, AND SV

Positive pressure mechanical ventilation increases both intrathoracic and right atrial pressures, setting in motion a cascade of events that affect SBP, PP, and SV (see Figure 1). In addition, the rise in intrathoracic and right atrial pressures reduces venous return and right atrial and ventricular preload, while increasing right ventricular afterload, ultimately lowering right ventricular SV. After several beats (time for the blood to pass through the pulmonary circuit), there is a reduction in left ventricular preload and left ventricular SV. Generally, the greatest drop in left ventricular SV occurs during expiration and can be seen as a decline in SBP and PP during the expiratory phase of the ventilator cycle.[5]

The relationship between ventilator-induced changes in blood pressure, SV, and fluid responsiveness can be explained using the Frank–Starling

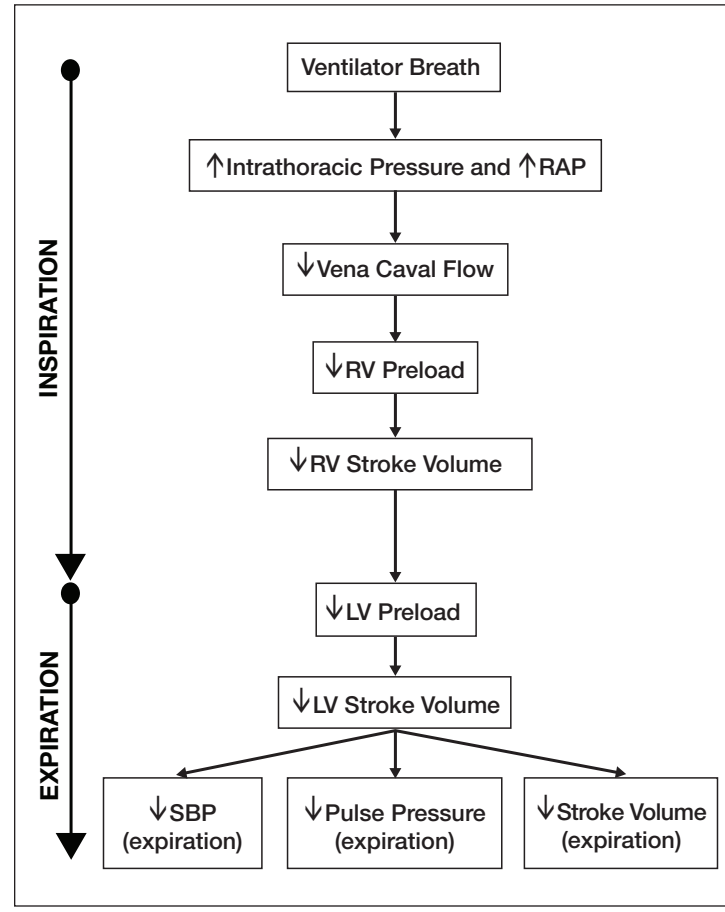

Figure 1. Primary mechanisms for ventilator-induced variation in systolic blood pressure, pulse pressure, and stroke volume observed during the expiratory phase of mechanical ventilation. LV = left ventricular; RAP = right atrial pressure; RV = right ventricular; SBP = systolic blood pressure.

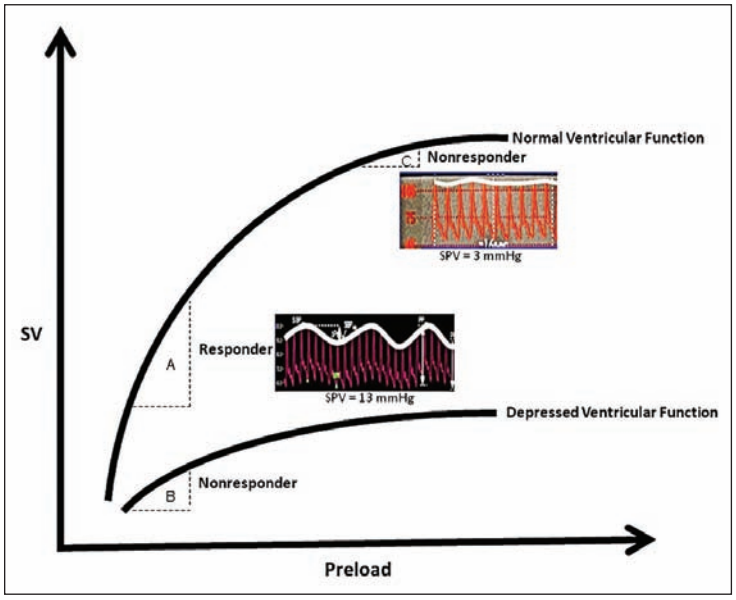

Figure 2. The Frank–Starling ventricular function curve illustrates the relationship between ventricular function and fluid responsiveness. Whether a patient responds to a fluid bolus with an increase in preload depends on the shape of the right and left ventricular function curves. If both ventricles are functioning on the steep portion of the curve (A), regardless of the absolute preload (CVP or PAOP), the patient is likely to be fluid responsive. For example, a patient with a low CVP who has normal ventricular function will respond to a fluid bolus with an increase in SV if on the steep portion of the ventricular function curve. A patient with the same CVP and a flat ventricular function curve (B), which indicates failure, will not respond to a fluid bolus with an increase in SV. Similarly, patients with normal ventricular function are not likely to respond to fluid therapy if their ventricles are functioning on the flat portion of the normal curve (C). CVP = central venous pressure; PAOP = pulmonary artery occlusion pressure; SPV = systolic pressure variation; SV = stroke volume.

ventricular function curve (Figure 2). When both ventricles are on the steep (ascending) portion of the ventricular function curve, ventilator-induced variation in preload causes greater variations in SBP, PP, and SV.[5] At that point, a fluid bolus is more likely to elicit a clinically significant rise in SV, indicating fluid responsiveness. In contrast, if either ventricle is on the flat portion of the curve (as occurs with volume overload) or the curve is flat (as occurs in ventricular failure), ventilator-induced variability is decreased. When the variability in blood pressure and SV is minimal, it suggests that a fluid bolus is *not* likely to significantly increase SV, indicating fluid nonresponsiveness. We can thus use variations in blood pressure and SV, observed in the form of functional hemodynamic indicators, to predict whether a patient will respond to a fluid bolus.

There are three arterial-based functional hemodynamic indicators in current use: systolic pressure variation (SPV), pulse pressure variation (PPV), and stroke volume variation (SVV). SPV may be expressed as a measurement of either pressure change or percentage change, whereas PPV and SVV are expressed as measurements of percentage change. Both SPV and PPV can be calculated from data taken directly from the bedside monitor, using simple equations that incorporate change in SBP and PP occurring over one ventilator cycle (from inspiration to expiration) (see Figure 3[3, 6-8]). To minimize the slight variability in change between ventilator cycles, measurements should be repeated over three to five ventilator cycles and then averaged. Alternatively, all three measurements can be obtained continuously using proprietary equipment.

PREDICTING FLUID RESPONSIVENESS

Similar to the way reference values are used in laboratory tests to enable diagnosis of particular conditions, thresholds for SPV, PPV, and SVV have been established above which patients are more likely to be fluid responsive. For example, patients with an SPV greater than 10 mmHg are likely to be responsive to fluid therapy. By contrast, patients with little ventilator-induced change in SBP (that is, with an SPV less than 10 mmHg) are less likely to respond to a fluid bolus. It's important to note that these thresholds are not perfect predictors of fluid response. Although the threshold for PPV is generally considered to be above 12.5%,[3] one study found a "gray zone" between 9% and 13% in which fluid response is not as accurately predicted.[9]

These indicators can also be used to determine when to stop administering fluids. A fluid bolus increases preload, causing the patient to "move up" the ventricular function curve.[10] This tends to decrease functional hemodynamic indicator values. For example, a fluid bolus might reduce PPV from 15% to 13%. With additional boluses, the PPV may fall below the 12.5% threshold. When a functional indicator is below its threshold, further administration of fluids will not increase the SV. In such cases, if the patient still has signs of hypoperfusion, another therapy (for example, a vasopressor) may be needed.

Although functional hemodynamic indicators may not perfectly predict fluid responsiveness, a growing number of research studies demonstrate their accuracy in doing so for a variety of ICU patient populations, including cardiac patients in the postsurgical period and patients with circulatory failure, severe sepsis, or septic shock.[4, 6-8, 11-15] Among the three indicators, PPV is considered to be the most accurate (as indicated by area under the curve [AUC]), sensitive, and specific.[3, 4, 11, 12, 14] (For definitions of these and other terms, see *Statistics Primer for Use with Functional Hemodynamic Indicators*.[4, 6, 11-14, 16, 17])

While providing adequate fluid resuscitation is critical to achieving positive outcomes, administering fluids to patients who are not fluid responsive increases their risk of complications and poor outcomes

associated with volume overload. Functional hemodynamic indicators are useful in deciding whether to administer or discontinue fluid therapy and when to consider diuresis or dialysis.[18] When interpreting functional hemodynamic indicators, bear in mind that fluid responsiveness does not necessarily suggest the need for a fluid bolus. Fluid therapy should be administered only in response to signs of hypoperfusion, and the potential benefit must be weighed against the risk of volume overload. Functional hemodynamic indicators may be integrated into a simple fluid resuscitation protocol, based on expert opinion derived from a review of pertinent literature (for an example, see Table 1[19]).

FACTORS THAT LIMIT USE OF FUNCTIONAL HEMODYNAMICS

Functional hemodynamic indicators can be obtained only from patients who are intubated and mechanically ventilated. Four major factors, identified by the acronym SOS, affect the use and interpretation of these indicators: **s**mall tidal volume or **s**pontaneous ventilation, **o**pen chest, and **s**ustained arrhythmias.[20] In a study of 29 consecutive patients undergoing cardiac surgery, the ability to predict fluid responsiveness was highest in patients with a Vt above 7 mL/kg and no arrhythmias, with the values calculated breath by breath (AUC: PPV, 0.95; SPV, 0.93; SVV, 0.90).[21] In this study, the lowest predictive values were seen when the Vt was below 7 mL/kg and measurements were obtained over 30 seconds, including periods in which arrhythmias occurred (AUC: PPV, 0.51; SPV, 0.63; SVV, 0.51).

Small tidal volume. In a majority of the studies conducted to establish threshold values for functional hemodynamic indicators, the Vt was over 8 to 12 mL/kg.[4, 6-8, 11-14, 17] As Vt rises, so does ventilator-induced variability in SBP, PP, and SV.[22-24] In a study of 20 patients who had undergone elective aortocoronary bypass grafting, SVV increased with Vt as follows (mean ± SD): Vt = 5 mL/kg, SVV = 7 ± 0.7%; Vt = 10 mL/kg, SVV = 15 ± 2.1%.[24]

When a functional indicator is below its threshold, further administration of fluids will not increase the SV.

The accuracy of functional hemodynamic indicators in predicting fluid responsiveness is reduced in patients receiving low Vt (below 8 mL/kg), such as those with acute respiratory distress syndrome receiving lung protective ventilation.[21, 25-27] In such cases, although the patient may be fluid responsive, the change in intrathoracic pressure is so small that the variation in blood pressure and SV does not raise PPV beyond its 12.5% threshold. For this reason, best practice is to use functional hemodynamic indicators to predict fluid responsiveness only in mechanically ventilated patients with Vt above 8 mL/kg.

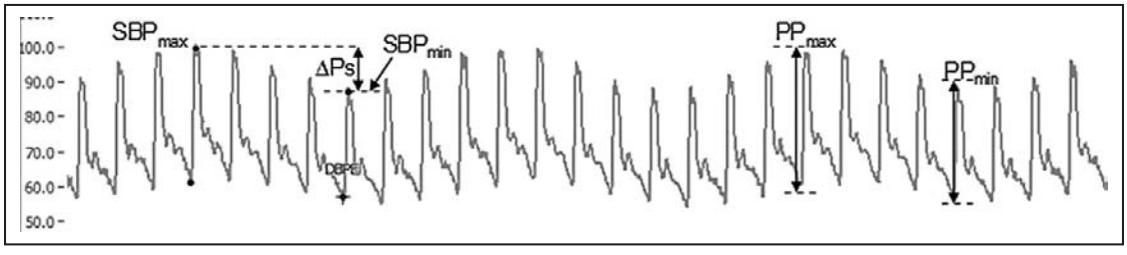

Figure 3. Arterial pressure data from a bedside monitor during one respiratory cycle. Measurements can be used to calculate systolic pressure variation, pulse pressure variation, and stroke volume variation using the following equations:

Variable	Equation	Threshold[a]
SPV mmHg	$SBP_{max} - SBP_{min}$	> 10 mmHg[6]
SPV%	$[(SBP_{max} - SBP_{min})/(SBP_{max} + SBP_{min}/2)] \times 100$	> 10%[6]
PPV	$[(PP_{max} - PP_{min})/(PP_{max} + PP_{min}/2)] \times 100$	> 12.5%[3]
SVV	$[(SV_{max} - SV_{min})/(SV_{max} + SV_{min}/2)] \times 100$	≥ 12%[7, 8]

max = maximum; min = minimum; ΔPs = respiratory change in systolic pressure; PP = pulse pressure; PPV = pulse pressure variation; SBP = systolic blood pressure; SPV = systolic pressure variation; SV = stroke volume; SVV = stroke volume variation; Vt = tidal volume.
[a]Threshold values are based on a Vt ≥ 8 mL/kg.

Table 1. Simplified Treatment Algorithm for Using Pulse Pressure Variation to Guide Fluid Resuscitation[19]

- Assess patient for indications of end-organ hypoperfusion or hemodynamic instability.
- Measure PPV.
- If PPV is above threshold, give 500 mL bolus over 15 minutes and reassess.
- Repeat boluses every 15 minutes until PPV is below threshold—then stop.
- If MAP remains above 60 mmHg after initial fluid bolus, initiate vasopressor therapy.
- If MAP is below 60 mmHg, response to vasopressor therapy may be inadequate; evaluate cardiac function.
- If contractility is impaired, consider inotropic therapy.
- If hemodynamic instability persists, consider pulmonary artery catheter or further echocardiographic assessment.

MAP = mean arterial pressure; PPV = pulse pressure variation.

Spontaneous ventilation. SPV and PPV do not accurately indicate fluid responsiveness in spontaneously breathing patients, including those who are breathing spontaneously while receiving mechanical ventilation or pressure support ventilation.[28, 29] With spontaneous breathing, Vt may be too low (below 8 mL/kg) to affect intrathoracic pressure and ventricular preload. In addition, the variations in Vt that occur with spontaneous breathing may trigger changes in blood pressure or SV that are unrelated to fluid responsiveness.

Open chest conditions. No studies have established thresholds for functional hemodynamic indicators that can be used to predict fluid responsiveness in patients with an open chest. Following cardiac surgery, however, functional indicators are accurate predictors of fluid responsiveness in patients with a closed chest.[15, 17, 30]

Sustained arrhythmias. Functional hemodynamic indicators cannot be measured accurately in the presence of sustained arrhythmias, because under such conditions it's impossible to determine whether observed variability in SBP and PP reflects fluid responsiveness or arrhythmia-induced changes in SV. Fluid responsiveness is most accurately predicted when SPV and PPV are measured manually over three to five ventilator cycles, excluding any cycles where an ectopic beat occurs.[21] The accuracy of functional hemodynamic indicators in patients undergoing pacing has not been established.

Other factors that may affect threshold values of functional hemodynamic indicators or limit their use include the following[29, 31-50]:

- intraabdominal hypertension
- ventilator mode
- positive end-expiratory pressure
- respiratory rate
- vasoactive medications
- ventricular function
- right ventricular dysfunction or cor pulmonale
- head of bed elevation
- lateral position
- prone position

EFFECTS ON OUTCOMES

Most research into whether outcomes are improved by using functional hemodynamic indicators to guide fluid resuscitation has been performed on surgical patients.[51-55] One such study, however, focused on nonsurgical patients treated in the ICU for cardiogenic shock following out-of-hospital cardiac arrest.[56]

Functional hemodynamic indicators cannot be measured accurately in the presence of sustained arrhythmias.

High-risk surgery. Improved outcomes have been reported in studies using PPV or SVV to guide fluid therapy in patients undergoing high-risk surgery. One such study included 33 patients, 17 of whom were assigned to an intervention group in which PPV was monitored continuously throughout surgery and boluses containing hydroxyethylstarch 6% were administered to minimize PPV, maintaining a value below 10%.[54] The remaining 16 patients were assigned to a control group that received intraoperative fluid at the discretion of the anesthetist. Significantly fewer patients in the intervention group than in the control group, seven (41%) versus 13 (75%), developed complications ($P < 0.05$). In addition, both the median duration of mechanical ventilation and the number of per-patient complications were lower in the intervention group compared with the control group—one versus five days of mechanical ventilation ($P < 0.05$), and 1.4 ± 2.1 versus 3.9 ± 2.8 per-patient complications ($P = 0.015$).

Another study, which included 60 high-risk patients scheduled for major abdominal surgery, assigned 30 patients to a control group that received standard monitoring (of electrocardiographic, arterial blood pressure, CVP, pulse oximetry, temperature, and inspiratory and expiratory gas concentration data) and 30 to an intervention group that received standard monitoring supplemented with enhanced hemodynamic monitoring, including SVV, to determine whether patients required fluids or treatment with vasopressor or inotropic agents. Additional therapy was guided by measurements of SV index or cardiac index (CI), that is, by SV or CO adjusted for body surface area.[55] There were fewer complications in the intervention group than in the control group—17 versus 49 ($P = 0.001$). Additionally, fewer patients in the intervention group developed complications—six (20%) versus 15 (50%) ($P = 0.03$)—and median hospital length of stay was significantly shorter for the intervention group: 15 (12 to 17.75) versus 19 (14 to 235) days ($P = 0.006$).

A third study compared the outcomes of 105 patients undergoing intraabdominal surgery who were assigned either to a control group receiving normal intraoperative care (crystalloid or colloid fluids or vasoactive therapy to maintain MAP above 65 mmHg, heart rate below 100 beats per minute, CVP between 8 and 15 mmHg, and urine output greater than 0.5 mL/kg per hour) or to a goal-directed therapy group treated according to an algorithm that integrated SVV, CVP, and CI (see Figure 4[51]).[51]

Patients in the goal-directed group received colloid fluid boluses (3 mL/kg over five minutes) if they had a sustained increase (of at least 10% after the five-minute infusion) in SVV or if their CI increased more than 10% after a fluid bolus. Fluid boluses were repeated if the patient remained fluid responsive (that is, if in response to the bolus, SVV remained at or above 10% or CI increased more than 10%) and the increase in CVP was no more than 3 mmHg. CVP was used as a safety measure to ensure that the patient was not at risk for volume overload; fluids

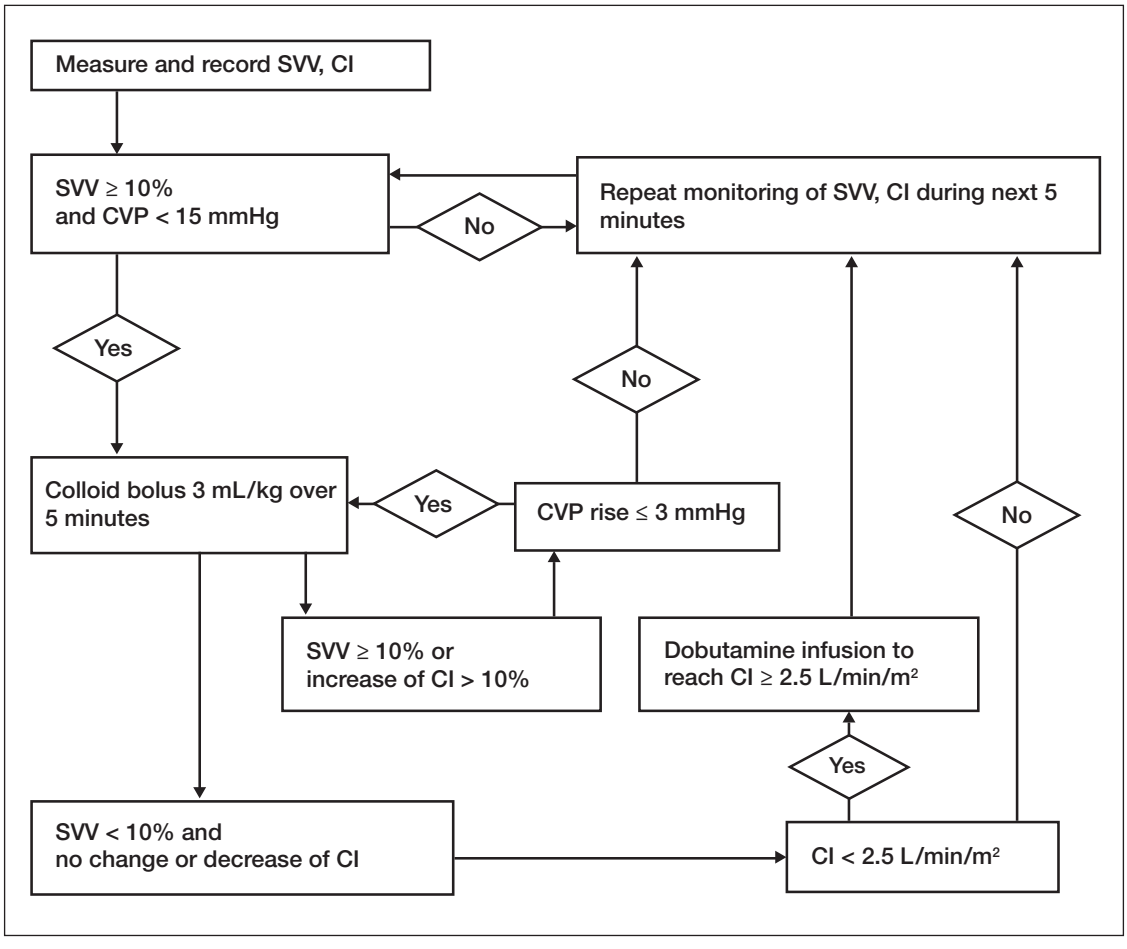

Figure 4. This algorithm uses functional hemodynamic indicators to direct fluid management in patients undergoing intraabdominal surgery. CI = cardiac index; CVP = central venous pressure; SVV = stroke volume variation. Adapted from Benes J, et al. *Crit Care* 2010;14(3):R118.[51]

Statistics Primer for Use with Functional Hemodynamic Indicators

Threshold values are established for each functional indicator to identify patients who are responsive to fluid therapy. Threshold values function much like reference values in diagnostic laboratory tests.

Sensitivity is the ability of an indicator to identify patients as fluid responsive based on an established threshold value. For example, in one study,[4] pulse pressure variation (PPV) with a threshold set at 13% discriminated between fluid responsiveness and nonresponsiveness with a sensitivity of 94%. This means that 94% of fluid responsive patients could be identified; only 6% would be missed.

Specificity is the ability of an indicator to identify patients who are not responsive to fluid therapy. For example, in the study mentioned above,[4] PPV with a threshold set at 13% discriminated between fluid responsiveness and nonresponsiveness with a specificity of 96%. This means that 96% of patients not responsive to fluid could be identified; only 4% would be missed.

Area under the curve (AUC) is a measure of an indicator's accuracy in discriminating between two conditions (responsiveness and nonresponsiveness to fluid therapy, for example). An indicator with an AUC of 1 would be perfectly accurate; an indicator with an AUC of 0.5 would be useless—no better at discriminating between two conditions than a coin flip. The closer the AUC is to 1, the better the test. As a general rule, for diagnostic tests, an AUC above 0.9 is considered excellent, an AUC above 0.8 is considered good, and an AUC below 0.7 is considered poor. The AUC for the functional hemodynamic indicators systolic pressure variation, PPV, and stroke volume variation are above 0.9 in many studies,[6, 11-14, 16] suggesting that they are very good or excellent tools for predicting fluid responsiveness. In contrast, central venous pressure and pulmonary artery occlusion pressure have an AUC near 0.5 in many studies,[4, 17] indicating that they are no better than chance in predicting fluid responsiveness.

95% confidence interval is a reflection of the confidence we have that the true value of a parameter lies within a specified range. For example, if an indicator's AUC is 0.91, with a 95% confidence interval of 0.76-0.98, there's a 95% probability that the true AUC lies between 0.76 and 0.98.

were not administered if CVP was greater than 15 mmHg or increased more than 3 mmHg after a fluid bolus. Following a fluid bolus, if SVV was less than 10% or CI did not increase more than 10% (indicating fluid nonresponsiveness) and CI was below 2.5 L/min/m^2, dobutamine was administered to maintain CI between 2.5 L/min/m^2 and 4 L/min/m^2. A vasopressor was added to the fluid bolus if SBP was below 90 mmHg or MAP was below 65 mmHg.

Compared with the control group, the goal-directed group had fewer intraoperative hypotensive events (2 versus 3.5; $P < 0.05$) and lower lactate levels at the end of surgery (1.8 mmol/L versus 2.2 mmol/L, $P < 0.05$); lactate levels remained elevated in the control group at four and eight hours after surgery. The goal-directed group also had fewer postoperative complications (30% versus 58%, $P < 0.05$), including severe complications (12% versus 35%, $P < 0.05$). There were no differences between groups in mortality or in ICU or hospital length of stay.

Elective surgery. By contrast, a study of 80 healthy patients undergoing elective abdominal surgery, which randomly assigned 40 patients to receive fluid resuscitation guided by SPV and 40 to receive standard resuscitation, found no difference between the two groups in terms of ventilator days, ICU length of stay, or mortality.[52] The researchers suggest that the difference between their outcomes and those of previous studies may be explained by the relative good health of the subjects at the start of the surgery. Alternatively, the results may reflect that both groups were nonresponsive to fluid (with an SPV below 10%) before the start of surgery.

Cardiogenic shock. A retrospective study of 51 patients treated in an ICU for cardiogenic shock following out-of-hospital cardiac arrest analyzed the relationship between guided fluid therapy and the development of acute kidney injury.[56] All patients received inotropic agents and vasopressor therapy to achieve a MAP greater than 65 mmHg and were treated with mild therapeutic hypothermia. Initially, fluids had been guided by standard monitoring (of CVP, urine output, and any clinical indications of volume overload) as well as physician preference. Beginning in 2009, however, additional monitoring with a pulse indicator continuous cardiac output system was introduced, permitting CI, global end-diastolic volume index (a measure of preload), and extravascular lung water index (an indication of pulmonary edema) to be measured less invasively than with a pulmonary artery catheter. Fluids were

administered with the aim of keeping PPV and SVV below 10% while avoiding pulmonary edema. Researchers compared outcomes for the 28 patients monitored prior to the change (the conventional monitoring group) and for the 23 patients monitored under the new system (the enhanced monitoring group).

The potential benefit of fluid therapy must be weighed against the risk of volume overload.

Over the first 24 hours of care, the enhanced monitoring group received more fluids than the conventional monitoring group, but there was no indication of pulmonary edema in either group. Although urine output did not differ between groups, patients in the conventional monitoring group were significantly more likely to develop acute kidney injury than those in the enhanced monitoring group (odds ratio: 14.1, 95% confidence interval, 3.3-60.0, $P < 0.001$). This study demonstrates the potential benefit and safety of volume resuscitation guided by functional hemodynamic indicators in high-risk cardiac patients.

INCORPORATING FUNCTIONAL HEMODYNAMICS INTO PRACTICE

In the hypothetical case presented earlier, the patient had signs of hypoperfusion (an elevated lactate level and low urine output). CVP is not useful in determining whether to administer additional fluid or a vasopressor to such a patient, but it may be used as a safety check to ensure that the patient is not at risk for volume overload; if CVP rises above 3 mmHg after a fluid bolus or exceeds 15 mmHg, fluid resuscitation should stop.[5,6] This patient is sedated, mechanically ventilated, and has an arterial line. Since he is not breathing spontaneously, has no arrhythmias, and has a Vt of 8 mL/kg, there is no major factor limiting the use of functional hemodynamics to guide fluid resuscitation.

You can calculate his PPV using PP values on the bedside monitor. A PPV greater than 12.5% would suggest fluid responsiveness.[3] If his PPV is above that threshold and he has signs of hypoperfusion, the next step would be to administer an additional bolus and reassess him. If his PPV dropped below the 12.5% threshold following the bolus, he would no longer be considered fluid responsive. If he continued to show signs of hypoperfusion, additional assessment would be required to determine whether vasopressor or inotropic therapy would be the most appropriate intervention. ▼

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REFERENCES

1. Durairaj L, Schmidt GA. Fluid therapy in resuscitated sepsis: less is more. *Chest* 2008;133(1):252-63.
2. Marik PE, et al. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest* 2008;134(1):172-8.
3. Marik PE, et al. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med* 2009;37(9):2642-7.
4. Michard F, et al. Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. *Am J Respir Crit Care Med* 2000;162(1):134-8.
5. Michard F, Teboul JL. Using heart-lung interactions to assess fluid responsiveness during mechanical ventilation. *Crit Care* 2000;4(5):282-9.
6. Tavernier B, et al. Systolic pressure variation as a guide to fluid therapy in patients with sepsis-induced hypotension. *Anesthesiology* 1998;89(6):1313-21.
7. Biais M, et al. Evaluation of stroke volume variations obtained with the pressure recording analytic method. *Crit Care Med* 2012;40(4):1186-91.
8. Broch O, et al. Variation of left ventricular outflow tract velocity and global end-diastolic volume index reliably predict fluid responsiveness in cardiac surgery patients. *J Crit Care* 2012;27(3):325:e7-e13.
9. Cannesson M, et al. Assessing the diagnostic accuracy of pulse pressure variations for the prediction of fluid responsiveness: a "gray zone" approach. *Anesthesiology* 2011;115(2):231-41.
10. Cecconi M, et al. What is a fluid challenge? *Curr Opin Crit Care* 2011;17(3):290-5.
11. Feissel M, et al. Pre-ejection period variations predict the fluid responsiveness of septic ventilated patients. *Crit Care Med* 2005;33(11):2534-9.
12. Feissel M, et al. Plethysmographic dynamic indices predict fluid responsiveness in septic ventilated patients. *Intensive Care Med* 2007;33(6):993-9.
13. Khwannimit B, Bhurayanontachai R. Prediction of fluid responsiveness in septic shock patients: comparing stroke volume variation by FloTrac/Vigileo and automated pulse pressure variation. *Eur J Anaesthesiol* 2012;29(2):64-9.
14. Loupec T, et al. Pleth variability index predicts fluid responsiveness in critically ill patients. *Crit Care Med* 2011;39(2):294-9.
15. Reuter DA, et al. Optimizing fluid therapy in mechanically ventilated patients after cardiac surgery by on-line monitoring of left ventricular stroke volume variations. Comparison with aortic systolic pressure variations. *Br J Anaesth* 2002;88(1):124-6.

16. Michard F, et al. Clinical use of respiratory changes in arterial pulse pressure to monitor the hemodynamic effects of PEEP. *Am J Respir Crit Care Med* 1999;159(3):935-9.
17. Yazigi A, et al. Pulse pressure variation predicts fluid responsiveness in elderly patients after coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth* 2012;26(3):387-90.
18. Mailloux PT, et al. Establishing goals of volume management in critically ill patients with renal failure. *J Nephrol* 2012:25(6):962-8.
19. Pinsky MR. Functional hemodynamic monitoring: applied physiology at the bedside. In: Vincent JL, editor. *Yearbook of emergency and intensive care medicine*. Berlin: Springer-Verlag; 2002. p. 537-52.
20. Michard F. Stroke volume variation: from applied physiology to improved outcomes. *Crit Care Med* 2011;39(2): 402-3.
21. Lansdorp B, et al. Dynamic indices do not predict volume responsiveness in routine clinical practice. *Br J Anaesth* 2012;108(3):395-401.
22. Charron C, et al. The influence of tidal volume on the dynamic variables of fluid responsiveness in critically ill patients. *Anesth Analg* 2006;102(5):1511-7.
23. Michard F, et al. Influence of tidal volume on stroke volume variation. Does it really matter? *Intensive Care Med* 2003;29(9):1613.
24. Reuter DA, et al. Influence of tidal volume on left ventricular stroke volume variation measured by pulse contour analysis in mechanically ventilated patients. *Intensive Care Med* 2003;29(3):476-80.
25. De Backer D, et al. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. *Intensive Care Med* 2005;31(4):517-23.
26. Murphy CV, et al. The importance of fluid management in acute lung injury secondary to septic shock. *Chest* 2009;136(1): 102-9.
27. Vallee F, et al. Pulse pressure variations adjusted by alveolar driving pressure to assess fluid responsiveness. *Intensive Care Med* 2009;35(6):1004-10.
28. Monnet X, et al. Passive leg raising predicts fluid responsiveness in the critically ill. *Crit Care Med* 2006;34(5):1402-7.
29. Perner A, Faber T. Stroke volume variation does not predict fluid responsiveness in patients with septic shock on pressure support ventilation. *Acta Anaesthesiol Scand* 2006;50(9): 1068-73.
30. de Waal EE, et al. Dynamic preload indicators fail to predict fluid responsiveness in open-chest conditions. *Crit Care Med* 2009;37(2):510-5.
31. Biais M, et al. Abilities of pulse pressure variations and stroke volume variations to predict fluid responsiveness in prone position during scoliosis surgery. *Br J Anaesth* 2010; 104(4):407-13.
32. Daihua Y, et al. The effect of body position changes on stroke volume variation in 66 mechanically ventilated patients with sepsis. *J Crit Care* 2012;27(4):416.e7-416. e12.
33. De Backer D, et al. Influence of respiratory rate on stroke volume variation in mechanically ventilated patients. *Anesthesiology* 2009;110(5):1092-7.
34. Gruenewald M, et al. Dynamic and volumetric variables of fluid responsiveness fail during immediate postresuscitation period. *Crit Care Med* 2011;39(8):1953-9.
35. Hadian M, et al. The effects of vasoactive drugs on pulse pressure and stroke volume variation in postoperative ventilated patients. *J Crit Care* 2011;26(3):328.e1-328.e8.
36. Heenen S, et al. How can the response to volume expansion in patients with spontaneous respiratory movements be predicted? *Crit Care* 2006;10(4):R102.
37. Jacques D, et al. Pulse pressure variation and stroke volume variation during increased intra-abdominal pressure: an experimental study. *Crit Care* 2011;15(1):R33.
38. Jardin F. Cyclic changes in arterial pressure during mechanical ventilation. *Intensive Care Med* 2004;30(6):1047-50.
39. Lee JY, et al. Comparative study of pressure- and volume-controlled ventilation on stroke volume variation as a predictor of fluid responsiveness in patients undergoing major abdominal surgery. *J Crit Care* 2012;27(5): 531.e9-531.e14.
40. Mahjoub Y, et al. Assessing fluid responsiveness in critically ill patients: false-positive pulse pressure variation is detected by Doppler echocardiographic evaluation of the right ventricle. *Crit Care Med* 2009;37(9):2570-5.
41. Malbrain ML, de Laet I. Functional hemodynamics and increased intra-abdominal pressure: same thresholds for different conditions . . . ? *Crit Care Med* 2009;37(2):781-3.
42. Marks R, et al. Does the systolic pressure variation change in the prone position? *J Clin Monit Comput* 2009;23(5): 279-82.
43. Renner J, et al. Influence of increased intra-abdominal pressure on fluid responsiveness predicted by pulse pressure variation and stroke volume variation in a porcine model. *Crit Care Med* 2009;37(2):650-8.
44. Renner J, et al. Effects of norepinephrine on dynamic variables of fluid responsiveness during hemorrhage and after resuscitation in a pediatric porcine model. *Paediatr Anaesth* 2009;19(7):688-94.
45. Reuter DA, et al. Usefulness of left ventricular stroke volume variation to assess fluid responsiveness in patients with reduced cardiac function. *Crit Care Med* 2003;31(5): 1399-404.
46. Sakka SG, et al. Effects of changes in blood pressure and airway pressures on parameters of fluid responsiveness. *Eur J Anaesthesiol* 2009;26(4):322-7.
47. Tavernier B, Robin E. Assessment of fluid responsiveness during increased intra-abdominal pressure: keep the indices, but change the thresholds. *Crit Care* 2011;15(2):134.
48. Vallet B, et al. How to titrate vasopressors against fluid loading in septic shock. *Advances in Sepsis* 2007;6(2): 34-40.
49. Wu CY, et al. Does targeted pre-load optimisation by stroke volume variation attenuate a reduction in cardiac output in the prone position. *Anaesthesia* 2012;67(7):760-4.
50. Wyler von Ballmoos M, et al. Pulse-pressure variation and hemodynamic response in patients with elevated pulmonary artery pressure: a clinical study. *Crit Care* 2010;14(3): R111.
51. Benes J, et al. Intraoperative fluid optimization using stroke volume variation in high risk surgical patients: results of prospective randomized study. *Crit Care* 2010;14(3):R118.
52. Buettner M, et al. Influence of systolic-pressure-variation-guided intraoperative fluid management on organ function and oxygen transport. *Br J Anaesth* 2008;101(2): 194-9.
53. Cannesson M. Arterial pressure variation and goal-directed fluid therapy. *J Cardiothorac Vasc Anesth* 2010;24(3): 487-97.
54. Lopes MR, et al. Goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. *Crit Care* 2007; 11(5):R100.
55. Mayer J, et al. Goal-directed intraoperative therapy based on autocalibrated arterial pressure waveform analysis reduces hospital stay in high-risk surgical patients: a randomized, controlled trial. *Crit Care* 2010;14(1):R18.
56. Adler C, et al. Fluid therapy and acute kidney injury in cardiogenic shock after cardiac arrest. *Resuscitation* 2013;84(2): 194-9.