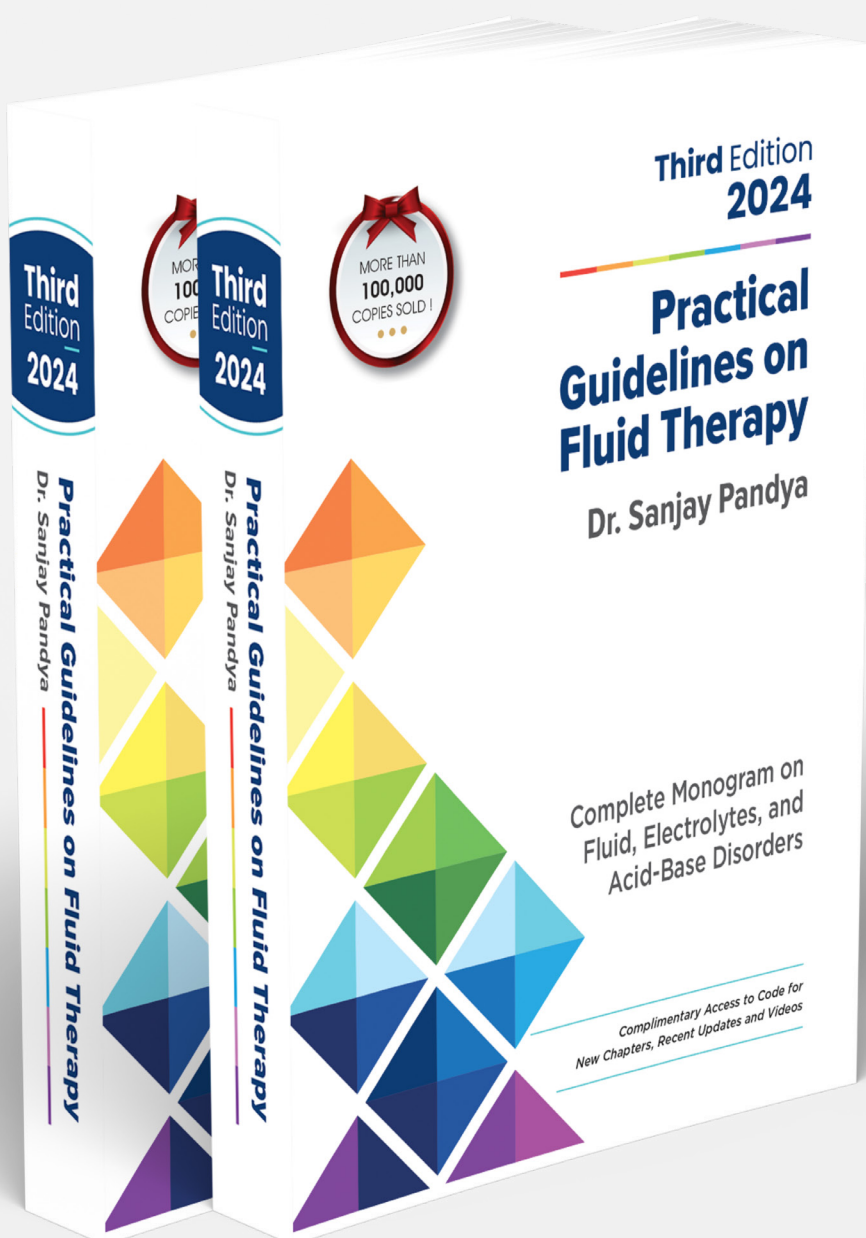


## Chapter 18:

# Fluid Responsiveness: Provocative Techniques and Dynamic Parameters



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# 18

## Fluid Responsiveness: Provocative Techniques and Dynamic Parameters

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Detection of fluid responsiveness is essential as it helps clinicians for the proper fluid management in critically ill patients. Various techniques are available to assess fluid responsiveness in hemodynamically unstable patients, including pulse pressure variation (PPV) and stroke volume variation (SVV), which are common dynamic measurements based on cardiopulmonary interaction derived from arterial waveform analysis.

Additionally, the plethysmographic variability index (PVI) is a simple, easily doable, noninvasive, and dynamic method that accurately predicts fluid responsiveness in mechanically ventilated patients by continuously and automatically estimating respiratory variations in the pulse oximeter waveform.

### PROVOCATIVE TECHNIQUES TO DETECT FLUID RESPONSIVENESS

Why is it important to differentiate between fluid responsive from fluid nonresponsive patients by hemodynamic monitoring?

In hemodynamically unstable patients, prompt and adequate fluid administration is essential to increase blood volume, which increases venous return, cardiac output (CO), and organ perfusion. Assessment of volume responsiveness is vital in such patients because with fluid boluses, only 50% of patients with shock are benefited, and excess fluid may worsen patient outcomes [1, 2].

#### In which patients fluid responsiveness should be tested?

Patients do not require a test for fluid responsiveness if hypovolemia is evident on clinical examination. Avoid fluid challenge if volume overload is obvious clinically. Fluid responsiveness should be tested in hemodynamically unstable patients if fluid losses are not apparent.

#### Which dynamic methods are used to detect fluid responsiveness?

The use of dynamic variables is preferred over static variables to predict fluid responsiveness [3]. The fluid challenge, passive leg raising, and end-expiratory occlusion test are reliable provocative,

**Table 18.1 Summary of provocative dynamic methods to detect fluid responsiveness**

Method	Fluid challenge	Passive leg raising	End-expiratory occlusion test
Nature	Non-invasive	Non-invasive	Invasive
Ventilation mode	Spontaneous	Spontaneous	Mechanical
Technique	Intravenous fluid loading	Internal volume challenge	Internal volume challenge
Effect of maneuver	Non-reversible	Reversible	Reversible
Parameters assessed	Cardiac output	Cardiac output	Cardiac output
Threshold	15% standard FC 6% mini FC	10%	5%
Methods to measure CO	Needs a very precise technique	Direct continuous measurement of CO	Direct continuous measurement of CO
	PCA, echocardiography	PCA, echocardiography, or bioreactance	PCA, echocardiography
Limitations/Exclusion criteria	Risk of volume overload	High intra-abdominal pressures, head trauma, and movement of the legs are not compatible	Non-intubated patients, 15 second respiration hold is not possible

ARDS: Acute respiratory distress syndrome; CO: Cardiac output; FC: Fluid challenge; PCA: Pulse contour analysis

dynamic methods used for the assessment of fluid status, which detects or unmask the fluid responsive state (Table 18.1). For the assessment of fluid responsiveness, parameters such as pulse pressure variation, stroke volume variation, Plethysmograph variability index, and cardiac output are measured with commercially available various devices and monitors.

## A. Fluid challenge

In the fluid challenge, a small amount of fluid is administered quickly, and the left ventricle's ability to increase stroke volume (SV) is assessed precisely [4, 5].

Fluid challenge (FC) is an effective diagnostic intervention designed to identify the "fluid responsiveness" in hemodynamic compromise patients. The fluid challenge guides clinicians to administer the optimum volume of fluid to

avoid over and under-fluid resuscitation [6]. The fluid challenge is usually performed in patients with hypotension and oliguria [7].

Balanced crystalloid solutions are usually preferred for the fluid challenge because the selection of the type of fluid does not affect the proportion of fluid responders [8]. Usually, 500 mL crystalloid is administered over 20–30 minutes (or 200–250 mL is administered over 5–10 minutes) [2, 7].

### How to assess the response to the fluid challenge?

The "fluid responsiveness" cannot be predicted by heart rate, blood pressure measurements, clinical signs, or static hemodynamic parameters such as central venous pressure (CVP) or pulmonary artery occlusion pressure (PAOP) [9, 10].

The current recommendation is to monitor dynamic over static hemodynamic

parameters after fluid challenge to predict the “fluid responsiveness” in mechanically ventilated patients [3, 10]. Even in spontaneously breathing patients, respiratory changes in dynamic parameters after fluid challenge predicts “fluid responsiveness” [11].

Cardiac output monitoring is used to assess pulse pressure variation, stroke volume, stroke volume variation, and cardiac index. Precise monitoring of these parameters is essential because the maximal effect on cardiac output occurs approximately one minute after the fluid challenge is over [12].

#### **Which criteria define fluid responsiveness in the fluid challenge?**

Usual parameters suggestive of fluid responsiveness are 10–15% increase in stroke volume [4] with a  $\geq 15\%$  increase in cardiac index [7]. Only fluid responsive patients should receive additional fluids [13].

#### **Why is large volume fluid administration avoided for the fluid challenge?**

The standard challenge with 300–500 mL of fluid is more a treatment than a test and, when repeated, carries the potential risk of volume overload. Volume overload is deleterious and probably more harmful than hypovolemia [14]. Potential harms of large volume fluid bolus are hypervolemia, pulmonary edema, bowel wall edema, endothelial glycocalyx damage, increased vascular permeability, tissue hypoxia, and organ dysfunctions [15, 16].

Positive fluid balance also increases the risk of acute kidney injury, slower recovery in acute respiratory distress syndrome, and higher mortality [17–21].

After large volume fluid bolus, clinical and physiological improvement occurs initially, but no long-term improvement, and on the contrary, causes higher mortality due to delayed cardiovascular collapse [22–24].

#### **Why hemodynamics improvement following fluid bolus is short-lived?**

Short-lived hemodynamics improvement following fluid bolus is because of rapid “Third” Spacing. In critical patients with leaky capillaries, 95% of the infused fluid shifts to interstitial space within 90 minutes, so transient benefit is lost rapidly [21, 25].

#### **What is a mini-fluid challenge?**

A mini-fluid challenge is an alternative approach that can reliably predict fluid responsiveness without a large amount of fluid infusion and the potential risk of fluid overload [26–29].

Protocols in the mini-fluid challenge includes:

- 100 ml of the crystalloid bolus is infused rapidly over one minute [26].
- A fluid bolus of 4 mL/kg of a balanced crystalloid solution is quickly infused over 5 minutes [30].

Fluid responsiveness in the mini-fluid challenge can be reliably predicted by velocity-time integral (VTI) measured by transthoracic echocardiography [29], pulse contour analysis derived from cardiac output [26], or changes in SVV [31]. As a small volume of fluid administration causes small and short-lived hemodynamic changes, response assessment should be monitored by very sensitive and precise techniques [26].

## **B. Passive leg raising test**

The passive leg raising (PLR) test is a simple, safe, reliable non-invasive, and reproducible bedside test to evaluate fluid responsiveness in patients with spontaneous breathing, on a ventilator, low lung compliance, and even in the presence of cardiac arrhythmias [32–36]. Three meta-analyses have confirmed the role of the PLR test in the assessment of fluid responsiveness [33, 37, 38].

In the PLR test, about 300 mL of blood from the lower extremities' veins is transferred into the thorax, which increases cardiac output [39]. The temporary gravitational shift of venous blood into the central circulation mimics a fluid challenge. Prediction of fluid responsiveness without administering a single drop of fluid avoids the risks of fluid overload. Rapidly reversible hemodynamic effects and no need for mechanical ventilation or sedation are the advantages of this test.

### **How to perform the passive leg raising test?**

The basic method to perform the PLR test is [40]:

- Start the test by placing the patient 45 degrees head-up semi-recumbent (and not supine position) for 3 minutes and obtain the baseline hemodynamic values.
- The next step is to lower the patient's upper body and head to the horizontal position and passively raise legs at 45 degrees by changing the bed position (i.e., not manually) and holding in this position for one minute. Immediately assess the effects of PLR by obtaining the hemodynamic values again.
- As hemodynamic effects of the PLR test are short-term and transient, obtain the subsequent hemodynamic values fast within the first 90 seconds following leg elevation.

### **Assessment of the effect of the PLR test and its clinical utility**

- To assess the hemodynamic effect of the PLR test, techniques which directly measure cardiac output should be used rather than methods that measure arterial pressure or pulse pressure [40]. Direct measurement of cardiac output is the more reliable

hemodynamic parameter to assess the effects of the PLR test [37].

- Positive PLR test is defined as a 10% or more increase in cardiac output/stroke volume or pulse pressure, and it predicts fluid responsiveness [38, 41]. If, in response to the PLR test, an increase in cardiac output is less, it predicts a poor response to fluid administration.
- The most frequently used measurement/monitoring techniques for the direct measurement of cardiac output in the PLR test are arterial pulse contour analysis, transthoracic echocardiography, esophageal doppler, bioreactance, and contour analysis of the volume clamp-derived arterial pressure. In the PLR test, simple measurement and monitoring of systolic blood pressure by the oscillometric non-invasive method is not a sensitive or specific predictor of fluid responsiveness [42].
- During renal replacement therapy, a positive PLR test predicts subsequent hypotension even before fluid removal [43].
- As a positive PLR test predicts fluid responsiveness, a negative PLR test provides an important clinical clue to discontinue or stop fluid administration [40]. The negative PLR test helps the clinician to avoid fluid overload and guides them to select other measures like vasopressors rather than fluid administration in hemodynamically unstable patients.
- PLR test is not useful in patients with raised intra-abdominal pressure (may cause false-negative result), not feasible intraoperatively during anesthesia or in agitated patients, avoided in neurotrauma patients (may increase intracranial pressure), and in those requiring immobilization (traumatic hip or lower limb fractures)



or using compression stocking [32, 44–46].

### **C. End-expiratory occlusion test**

The end-expiratory occlusion (EEO) test is a simple test in patients undergoing mechanical ventilation, which predicts fluid responsiveness reliably in the operating room and ICU [27, 47, 48].

In this preload responsiveness test, a ventilator is interrupted for 15 seconds at the end of expiration, and cardiac output is measured. A more than 5% increase in cardiac output predicts fluid responsiveness with a high degree of accuracy [9, 49]. The standard method used to measure cardiac output in this test is pulse contour analysis, but recent evidence supports the use of even echocardiography [48, 50, 51].

Physiological basis [52, 53]:

- In patients on positive pressure ventilation, during inspiration, intrathoracic pressure increases, which pushes blood back from the right atrium and reduces the systemic venous return.
- In patients on a ventilator, during the expiratory phase, intrathoracic pressure reduces, which allows the return of systemic venous blood. When a ventilator is stopped for 15 seconds at the end-expiration, the reduced intrathoracic pressure will persist for additional 15 seconds, permit venous return for a more extended period, and allow a larger volume of venous blood return.
- The effect of increased venous return will be like a mini self-volume fluid challenge, a transient increase in the venous blood return with a resultant increase in the left ventricular stroke volume and cardiac output.
- With the EEO test, cardiac output will increase in fluid responsive patients while no significant increase in cardiac

output in non-volume responders.

- When a 15-second end-inspiratory hold is added to hold in the end-expiratory phase, the combined effect induces more substantial cardiac output changes in fluid responders, increasing the diagnostic threshold of this test to 13% and the assessment possible by echocardiography examination [50].

Reliability, even in patients with cardiac arrhythmias, acute respiratory distress syndrome, low lung compliance, and low tidal volume, are the advantages of this easy-to-use test [9, 53–55]. But this test can be performed only in patients on a ventilator who can hold respiration for 15 seconds without interruption by a spontaneous breath.

EEO test is a preferred technique to measure CO in surgical patients in the operating theatre. It can be conveniently and safely performed in sedated patients on a ventilator and with the benefit of the assessment without fluid administration (i.e., risk of volume overload). In addition, it has no technical constraints like a passive leg raising test [27, 56].

## **DYNAMIC PARAMETERS TO PREDICT FLUID RESPONSIVENESS**

Pulse pressure variation, stroke volume variation, and plethysmographic variability index are common dynamic measurements based on cardiopulmonary interaction derived from the arterial waveform analysis, which is used to predict fluid responsiveness.

### **Pulse pressure variation (PPV) and stroke volume variation (SVV)**

Arterial waveform derived dynamic parameters such as pulse pressure

variation and stroke volume variation are accurate and excellent predictors of fluid responsiveness in mechanically ventilated patients [57–60]. Dynamic parameters PPV and SVV are superior to traditionally used static indices to predict fluid responsiveness, such as central venous pressure and pulmonary artery occlusion pressure [57, 61–64].

PPV, SVV, and cardiac output can be easily recorded and automatically calculated by many modern commercially available bedside monitors.

## A. Pulse pressure variation

Pulse pressure is the difference between systolic and diastolic blood pressure, which varies with respiration. Pulse pressure variation is calculated from the maximum pulse pressure (PPmax), minimum PP (PPmin), and mean PP (PPmean) during a respiratory cycle. These values can be obtained accurately by arterial catheters, and for the calculation, the values from three or more breaths are measured and averaged.

$$\text{Pulse Pressure Variation} = 100 \times \frac{\text{PPmax} - \text{PPmin}}{\text{PPmean}}$$

Interpretation of PPV for fluid administration:

1. PPV >13% is strongly associated with volume responsiveness [57, 58].
2. If PPV is low (<9), it suggests fluid unresponsiveness, and administration of fluids should be avoided [60].
3. PPV 9–13% is a grey zone value, and a definite strategy to administer intravenous (IV) fluid cannot be made on its basis [65, 66].

PPV has a higher predictive value for fluid responsiveness compared to SVV [67, 68]. Values of PPV are reliable, provided the patient is intubated and is on a volume cycled ventilator making

no spontaneous respiratory efforts, tidal value >8 mL/kg body weight, and no arrhythmias [69, 70]. However, the accuracy of PPV in patients with increased intra-abdominal pressure is questionable as there is evidence supporting [71, 72] and against [73] its reliability.

Role of PPV to guide and monitor fluid administration in clinical practice [60]:

1. Surgical patients: Its applicability is higher during major surgery because PPV improves postoperative outcomes, and in patients on mechanical ventilator accuracy of PPV is greater.
2. ICU patients: Use of PPV is lesser in ICU because in the presence of commonly encountered conditions in ICU such as cardiac arrhythmias, spontaneous breathing, ventilatory support with low tidal volume, low lung compliance (e.g., acute respiratory distress syndrome), etc., the predictive value of PPV is unreliable.
3. Interpretation in low tidal volume ventilation: In patients on low tidal volume ventilation, PPV value can be misleading as it can be low even in fluid responsiveness patients. The 'tidal volume challenge' is a simple bedside test that helps to overcome the difficulty in interpretation in such patients. In this technique, tidal volume is increased from 6 to 8 mL/kg for 1 minute, and the resultant absolute changes in PPV are measured [69, 74]. If an increase in the absolute value of PPV is 3.5% or more, it predicts fluid responsiveness with excellent accuracy [74].
4. Interpretation in grey zone values of PPV: In patients with PPV 9% and 13% and tidal volume ≥8 mL/kg, PPV is inconclusive in predicting fluid responsiveness [65]. In such patients, augmented PPV (i.e., transient increase in tidal volume from



8 mL/kg to 12 mL/kg, known as a tidal volume challenge technique) can offer excellent predictability of fluid responsiveness [75].

## **B. Stroke volume variation**

Left ventricular stroke volume variation, like PPV, is a dynamic parameter useful in diagnosing volume deficit and is a reliable predictor of fluid responsiveness in mechanically ventilated patients. Stroke volume variation is the percentage change between the maximal and minimal stroke volumes (SV) averaged over several respiratory cycles.

$$\text{Stroke Volume Variation} = \frac{\text{SV}_{\text{max}} - \text{SV}_{\text{min}}}{\text{SV}_{\text{mean}}}$$

SVV greater than 10% is associated with fluid responsiveness [76, 77]. The SVV is commonly measured by an arterial catheter but can also be measured by other methods such as esophageal doppler, bioimpedance, and bioreactance.

PPV and SVV are unreliable in patients with spontaneous breathing, on a mechanical ventilator with low tidal volume (<8 mL/kg), cardiac arrhythmias, right ventricular dysfunction, and low lung compliance [78–80].

## **C. Plethysmographic variability index**

The plethysmographic variability index (PVI, Pleth variability index) is a simple, completely noninvasive, and dynamic method that accurately predicts fluid responsiveness in mechanically ventilated patients [81–83].

In this easy-to-use method, the pulse oximeter measures the light transmitted through the vascular bed of a finger and detects the dynamic change in the perfusion index during a complete respiratory cycle [84].

Continuous measurement derived from the plethysmographic waveform signals of the pulse oximetry is automatically calculated and displayed on the monitor's screen [85].

The PVI is calculated from the perfusion index (PI) variation between inspiration and expiration phases, as follows:

$$\text{PVI} = \frac{\text{PI}_{\text{Maximum}} - \text{PI}_{\text{Minimum}}}{\text{PI}_{\text{Maximum}}} \times 100\%$$

Generally, a PVI value >14% predicts preload dependence and is suggestive of fluid responsiveness [81, 86, 87].

PVI is a reasonably reliable predictor of fluid responsiveness in perioperative and critically ill patients with mechanical ventilation [88–92]. PVI guided goal-directed fluid management has been shown to improve outcomes in major surgery [93, 94]. However, in a recent meta-analysis, the reliability of PVI to predict fluid responsiveness was found to be limited, but it can play a role as a continuous bedside monitor in ICU [95].

Results of PVI are less reliable in pediatric patients with spontaneously breathing, with cardiac arrhythmias [88], probe malposition, patient motion, and in patients receiving norepinephrine (due to vasopressor induced dampened plethysmographic signals) [96, 97].

## **REFERENCES**

1. Mackenzie DC, Noble VE. Assessing volume status and fluid responsiveness in the emergency department. *Clin Exp Emerg Med*. 2014;1(2):67–77.
2. Cecconi M, Hofer C, Teboul JL, et al. Fluid challenges in intensive care: the FENICE study: A global inception cohort study. *Intensive Care Med*. 2015;41(9):1529–37.
3. Cecconi M, De Backer D, Antonelli M, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. *Intensive Care Med*. 2014;40(12):1795–1815.
4. Cecconi M, Parsons M, Rhodes A. What is a fluid challenge? *Department of Intensive Care Medicine, St*

- George's Healthcare NHS Trust, London, UK Current Opinion In Critical Care 2011;17(3):290–295.
5. Hasanin A. Fluid responsiveness in acute circulatory failure. *J Intensive Care*. 2015;3:50.
6. Vincent JL, Weil MH. Fluid challenge revisited. *Crit Care Med* 2006;34(5):1333–7.
7. Messina A, Longhini F, Coppo C, et al. Use of the fluid challenge in critically ill adult patients: A systematic review. *Anesthesia and analgesia*. 2017;125(5):1532–1543.
8. Toscani L, Aya HD, Antonakaki D, et al. What is the impact of the fluid challenge technique on diagnosis of fluid responsiveness? A systematic review and meta-analysis. *Crit Care*. 2017;21(1):207.
9. Marik PE, Monnet X, Teboul JL. Hemodynamic parameters to guide fluid therapy. *Ann Intensive Care*. 2011;1(1):1.
10. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Crit Care Med*. 2017;45(3):486–552.
11. Lanspa MJ, Grissom CK, Hirshberg EL, et al. Applying dynamic parameters to predict hemodynamic response to volume expansion in spontaneously breathing patients with septic shock. *Shock*. 2013;39(2):155–160.
12. Aya HD, Ster IC, Fletcher N, et al. Pharmacodynamic analysis of a fluid challenge. *Crit Care Med* 2016;44(5):880–91.
13. Anand Swaminathan, “Fluid responsiveness and the six guiding principles of fluid resuscitation”, REBEL EM blog, February 27, 2017. Available at: <https://rebelem.com/fluid-responsiveness-and-the-six-guiding-principles-of-fluid-resuscitation/>.
14. Farkas J. *PulmCrit: Myth-busting the fluid bolus*. June 3, 2019 Available at: <https://emcrit.org/pulmcrit/bolus/>.
15. Becker BF, Chappell D, Jacob M. Endothelial glycocalyx and coronary vascular permeability: The fringe benefit. *Basic Res. Cardiol*. 2010;105(6):687–701.
16. Malbrain MLNG, Van Regenmortel N, Saugel B, et al. Principles of fluid management and stewardship in septic shock: it is time to consider the four D's and the four phases of fluid therapy. *Ann Intensive Care*. 2018;8(1):66.
17. Vincent JL, Sakr Y, Sprung CL, et al. Sepsis in European intensive care units: results of the SOAP study. *Crit Care Med*. 2006;34(2):344–353.
18. Payen D, de Pont AC, Sakr Y, et al. Sepsis Occurrence in Acutely Ill Patients (SOAP) Investigators. A positive fluid balance is associated with a worse outcome in patients with acute renal failure. *Crit Care*. 2008;12(3):R74.
19. Prowle JR, Echeverri JE, Ligabo EV, et al. Fluid balance and acute kidney injury. *Net Rev Nephrol*. 2010;6(2):107–115.
20. Wiedemann HP, Wheeler AP, Bernard GR, et al. Comparison of two fluid-management strategies in acute lung injury. *The New England Journal of Medicine*. 2006;354(24):2564–75.
21. Malbrain ML, Marik PE, Witters I, et al. Fluid overload, de-resuscitation, and outcomes in critically ill or injured patients: a systematic review with suggestions for clinical practice. *Anaesthesiol Intensive Ther*. 2014;46(5):361–80.
22. Maitland K, Kiguli S, Opoka R, et al. Mortality after fluid bolus in African children with severe infection. *N Engl J Med*. 2011;364(26):2483–2495.
23. Andrews B, Semler M, Muchemwa L, et al. Effect of an early resuscitation protocol on in-hospital mortality among adults with sepsis and hypotension: a randomized clinical trial. *JAMA*. 2017;318(13):1233–1240.
24. Hjortrup PB, Haase N, Bundgaard H, et al. Restricting volumes of resuscitation fluid in adults with septic shock after initial management: the CLASSIC randomised, parallel-group, multicentre feasibility trial. *Intensive Care Med*. 2016;42(11):1695–1705.
25. Nunes TS, Ladeira RT, Bafi AT, et al. Duration of hemodynamic effects of crystalloids in patients with circulatory shock after initial resuscitation. *Ann Intensive Care*. 2014;4:25.
26. Biais M, de Courson H, Lanchon R, et al. Mini-fluid challenge of 100 ml of crystalloid predicts fluid responsiveness in the operating room. *Anesthesiology* 2017;127(3):450–456.
27. Messina A, Dell'Anna A, Baggiani M, et al. Functional hemodynamic tests: a systematic review and a metanalysis on the reliability of the end-expiratory occlusion test and of the mini-fluid challenge in predicting fluid responsiveness. *Crit Care* 2019;23(1):264.
28. Marik PE. Fluid therapy in 2015 and beyond: the mini-fluid challenge and mini-fluid bolus approach. *Br J Anaesth*. 2015;115(3):347–9.
29. Muller L, Toumi M, Bousquet PJ, et al. An increase in aortic blood flow after an infusion of 100 ml colloid over 1 minute can predict fluid responsiveness: the mini-fluid challenge study. *Anesthesiology* 2011;115(3):541–7.
30. Aya HD, Rhodes A, Ster IC, et al. Hemodynamic effect of different doses of fluids for a fluid challenge: a quasi-randomised controlled study. *Crit Care Med*. 2017;45(2):e161–e168.
31. Mallat J, Meddour M, Durville E, et al. Decrease in pulse pressure and stroke volume variations after mini-fluid challenge accurately predicts fluid responsiveness. *Br J Anaesth*. 2015;115(3):449–56.
32. Monnet X, Teboul JL. Passive leg raising. *Intensive Care Med* 2008;34(4):659–63.
33. Cavallaro F, Sandroni C, Marano C, et al. Diagnostic accuracy of passive leg raising for prediction of fluid responsiveness in adults: systematic review and meta-analysis of clinical studies. *Intensive Care Med* 2010;36(9):1475–83.
34. Duus N, Shogilev DJ, Skibsted S, et al. The reliability and validity of passive leg raise and fluid bolus to assess fluid responsiveness in spontaneously breathing emergency department patients. *J Crit Care* 2015;30(1):217.e1–5.

35. Monnet X, Marik PE, Teboul J. Prediction of fluid responsiveness: an update. *Ann Intensive Care* 2016;6(1):111.
36. Monnet X, Teboul JL. Assessment of fluid responsiveness: recent advances. *Curr Opin Crit Care*. 2018;24(3):190–195.
37. Cherpanath TG, Hirsch A, Geerts BF, et al. Predicting fluid responsiveness by passive leg raising: a systematic review and meta-analysis of 23 clinical trials. *Crit Care Med*. 2016;44(5):981–91.
38. Monnet X, Marik P, Teboul JL. Passive leg raising for predicting fluid responsiveness: a systematic review and meta-analysis. *Intensive Care Med*. 2016;42(12):1935–1947.
39. Jabot J, Teboul JL, Richard C, et al. Passive leg raising for predicting fluid responsiveness: importance of the postural change. *Intensive Care Med*. 2009;35(1):85–90.
40. Monnet X, Teboul JL. Passive leg raising: five rules, not a drop of fluid. *Crit Care*. 2015;19(1):18.
41. Monnet X, Rienzo M, Osman D, et al. Passive leg raising predicts fluid responsiveness in the critically ill. *Crit Care Med* 2006;34(5):1402–7.
42. Pickett JD, Bridges E, Kritek PA, et al. Noninvasive blood pressure monitoring and prediction of fluid responsiveness to passive leg raising. *Am J Crit Care*. 2018;27(3):228–237.
43. Monnet X, Flora CF, Laurent CL, et al. The passive leg raising test to guide fluid removal in critically ill patients. *Ann. Intensive Care* 2016;6(1):46.
44. Malbrain ML, Reuter DA. Assessing fluid responsiveness with the passive leg raising maneuver in patients with increased intra-abdominal pressure: be aware that not all blood returns. *Crit Care Med*. 2010;38(9):1912–1915.
45. Beurton A, Teboul JL, Giroto V, et al. Intra-Abdominal hypertension is responsible for false negatives to the passive leg raising test. *Crit Care Med* 2019;47(8):e639–e647.
46. Chacko CJ, Wise MP, Frost PJ. Passive leg raising and compression stockings: A note of caution. *Crit. Care*. 2015;19:237.
47. Monnet X, Osman D, Ridet C, et al. Predicting volume responsiveness by using the end-expiratory occlusion in mechanically ventilated intensive care unit patients. *Crit Care Med*. 2009;37(3):951–6.
48. Georges D, de Courson H, Lanchon R, et al. End-expiratory occlusion maneuver to predict fluid responsiveness in the intensive care unit: an echocardiographic study. *Crit Care*. 2018;22(1):32.
49. Monnet X, Teboul JL. End-expiratory occlusion test: please use the appropriate tools. *Br J Anaesth*. 2015;114(1):166–7.
50. Jozwiak M, Dépret F, Teboul JL, et al. Predicting fluid responsiveness in critically ill patients by using combined end-expiratory and end-inspiratory occlusions with echocardiography. *Crit Care Med*. 2017;45(11):e1131–e1138.
51. Dépret F, Jozwiak M, Teboul JL, et al. Esophageal Doppler can predict fluid responsiveness through end-expiratory and end-inspiratory occlusion tests. *Crit Care Med*. 2019;47(2):e96–e102.
52. Biaisi M, Larghi M, Henriot J, et al. End-expiratory occlusion test predicts fluid responsiveness in patients with protective ventilation in the operating room. *Anesth Analg* 2017;125(6):1889–95.
53. Gavelli F, Teboul J, Monnet X. The end-expiratory occlusion test: please, let me hold your breath. *Crit Care* 2019;23:274.
54. Monnet X, Bleibtreu A, Ferré A, et al. Passive leg-raising and end-expiratory occlusion tests perform better than pulse pressure variation in patients with low respiratory system compliance. *Crit Care Med* 2012;40(1):152–157.
55. Shiva S, Jozwiak M, Teboul JL, et al. End-expiratory occlusion test predicts preload responsiveness independently of positive end-expiratory pressure during acute respiratory distress syndrome. *Crit Care Med* 2013;41(7):1692–701.
56. Xu LY, Tu GW, Cang J, et al. End-expiratory occlusion test predicts fluid responsiveness in cardiac surgical patients in the operating theatre. *Ann Transl Med*. 2019;7(14):315.
57. Marik PE, Cavallazzi R, Vasu T, 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.
58. Yang X, Du B. Does pulse pressure variation predict fluid responsiveness in critically ill patients? A systematic review and meta-analysis. *Crit Care*. 2014;18(6):650.
59. Hong JQ, He HF, Chen ZY, et al. Comparison of stroke volume variation with pulse pressure variation as a diagnostic indicator of fluid responsiveness in mechanically ventilated critically ill patients. *Saudi Med J*. 2014;35(3):261–8.
60. Teboul JL, Monnet X, Chemla D, et al. Arterial pulse pressure variation with mechanical ventilation. *Am J Respir Crit Care Med*. 2019;199(1):22–31.
61. Michard F, Teboul JL. Predicting fluid responsiveness in ICU patients: a critical analysis of the evidence. *Chest* 2002;121(6):2000–8.
62. Osman D, Ridet C, Ray P, et al. Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge. *Crit Care Med* 2007;35(1):64–68.
63. Marik PE, Baram M, Vahid B. 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.
64. Perel A, Pizov R, Cotev S. Respiratory variations in the arterial pressure during mechanical ventilation reflect volume status and fluid responsiveness. *Intensive care med* 2014;40(6):798–807.
65. Cannesson M, Le Manach Y, Hofer CK, et al. Assessing the diagnostic accuracy of pulse pressure variations for the prediction of fluid responsiveness: a “gray zone” approach. *Anesthesiology* 2011;115(2):231–241.
66. Biaisi M, Ehrmann S, Mari A, et al. Clinical relevance of pulse pressure variations for predicting fluid

- responsiveness in mechanically ventilated intensive care unit patients: the grey zone approach. *Crit Care* 2014;18(6):587.
67. Preisman S, Kogan S, Berkenstadt H, et al. Predicting fluid responsiveness in patients undergoing cardiac surgery: functional haemodynamic parameters including the Respiratory Systolic Variation Test and static preload indicators. *British Journal of Anaesthesia*. 2005;95(6):746–755.
  68. Rathore A, Singh S, Lamsal R, et al. Validity of pulse pressure variation (PPV) compared with stroke volume variation (SVV) in predicting fluid responsiveness. *Turk J Anaesthesiol Reanim* 2017;45(4):210–217.
  69. Myatra SN, Monnet X, Teboul JL. Use of ‘tidal volume challenge’ to improve the reliability of pulse pressure variation. *Crit Care*. 2017;21(1):60.
  70. De Backer D, Heenen S, Piagnerelli M, et al. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. *Intensive Care Med*. 2005;31(4):517–523.
  71. Renner J, Gruenewald M, Quaden R, 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.
  72. Jacques D, Bendjelid K, Duperret S, et al. Pulse pressure variation and stroke volume variation during increased intra-abdominal pressure: an experimental study. *Crit Care* 2011;15(1):R33.
  73. Diaz F, Erranz B, Donoso A, et al. Influence of tidal volume on pulse pressure variation and stroke volume variation during experimental intra-abdominal hypertension. *BMC Anesthesiol*. 2015;15:127.
  74. Myatra SN, Prabu NR, Divatia JV, et al. The changes in pulse pressure variation or stroke volume variation after a “tidal volume challenge” reliably predict fluid responsiveness during low tidal volume ventilation. *Crit Care Med* 2017;45(3):415–421.
  75. Min JJ, Gil NS, Lee JH, et al. Predictor of fluid responsiveness in the ‘grey zone’: augmented pulse pressure variation through a temporary increase in tidal volume. *Br J Anaesth*. 2017;119(1):50–56.
  76. Biais M, Nouette-Gaulain K, Cottenceau V, et al. Uncalibrated pulse contour-derived stroke volume variation predicts fluid responsiveness in mechanically ventilated patients undergoing liver transplantation. *Br J Anaesth* 2008;101(6):761–8.
  77. Hofer CK, Müller SM, Furrer L, et al. Stroke volume and pulse pressure variation for prediction of fluid responsiveness in patients undergoing off-pump coronary artery bypass grafting. *Chest* 2005;128(2):848–54.
  78. Lefrant JY, De Backer D. Can we use pulse pressure variations to predict fluid responsiveness in patients with ARDS? *Intensive Care Med*. 2009;35(6):966–8.
  79. Lakhal K, Ehrmann S, Benzekri-Lefevre D, et al. Respiratory pulse pressure variation fails to predict fluid responsiveness in acute respiratory distress syndrome. *Crit Care*. 2011;15(2):R85.
  80. Oliveira-Costa CD, Friedman G, Vieira SR, et al. Pulse pressure variation and prediction of fluid responsiveness in patients ventilated with low tidal volumes. *Clinics (Sao Paulo)*. 2012;67(7):773–8.
  81. Cannesson M, Attof Y, Rosamel P, et al. Respiratory variations in pulse oximetry plethysmographic waveform amplitude to predict fluid responsiveness in the operating room. *Anesthesiology*. 2007;106(6):1105–1111.
  82. Cannesson M, Desebbe O, Rosamel P, et al. Pleth variability index to monitor the respiratory variations in the pulse oximeter plethysmographic waveform amplitude and predict fluid responsiveness in the operating theatre. *Br J Anaesth* 2008;101(2):200–6.
  83. Desebbe O, Cannesson M. Using ventilation induced plethysmographic variations to optimize patient fluid status. *Curr Opin Anaesthesiol* 2008;21(6):772–8.
  84. Keller G, Cassar E, Desebbe O, et al. Ability of pleth variability index to detect hemodynamic changes induced by passive leg raising in spontaneously breathing volunteers. *Crit Care* 2008;12(2):R37.
  85. Cannesson M, Sliker J, Desebbe O, et al. The ability of a novel algorithm for automatic estimation of the respiratory variations in arterial pulse pressure to monitor fluid responsiveness in the operating room. *Anesth Analg*. 2008;106(4):1195–200.
  86. Lu W, Dong J, Xu Z, et al. The pleth variability index as an indicator of the central extracellular fluid volume in mechanically ventilated patients after anesthesia induction: comparison with initial distribution volume of glucose. *Med Sci Monit*. 2014;20:386–392.
  87. Feissel M, Teboul JL, Merlani P, et al. Plethysmographic dynamic indices predict fluid responsiveness in septic ventilated patients. *Intensive Care Med* 2007;33(6):993–9.
  88. Yin JY, Ho KM. Use of plethysmographic variability index derived from the Massimo(R) pulse oximeter to predict fluid or preload responsiveness: a systematic review and meta-analysis. *Anaesthesia*. 2012;67(7):777–783.
  89. Chu H, Wang Y, Sun Y, et al. Accuracy of pleth variability index to predict fluid responsiveness in mechanically ventilated patients: a systematic review and meta-analysis. *J Clin Monit Comput*. 2015;30(3):265–74.
  90. Bahlmann H, Hahn RG, Nilsson L. Pleth variability index or stroke volume optimization during open abdominal surgery: a randomized controlled trial *BMC Anesthesiology* 2018;18(1):115.
  91. Kim DH, Shin S, Kim JY, et al. Pulse pressure variation and pleth variability index as predictors of fluid responsiveness in patients undergoing spinal surgery in the prone position. *Therapeutics and Clinical Risk Management* 2018;14:1175–1183.
  92. Sandroni C, Cavallaro F, Marano C, et al. Accuracy of plethysmographic indices as predictors of fluid responsiveness in mechanically ventilated adults: a systematic review and meta-analysis. *Intensive Care Med*. 2012;38(9):1429–37.
  93. Coeckelenbergh S, Delaporte A, Ghoundiwal D, et al. Pleth variability index versus pulse pressure variation for intraoperative goal-directed fluid

- therapy in patients undergoing low to-moderate risk abdominal surgery: a randomized controlled trial. *BMC Anesthesiol.* 2019;19(1):34.
94. Cesur S, Çardaközü T, Kuş A, et al. Comparison of conventional fluid management with PVI-based goal-directed fluid management in elective colorectal surgery. *J Clin Monit Comput.* 2019;33(2):249–57.
95. Liu T, Xu C, Wang M, et al. Reliability of pleth variability index in predicting preload responsiveness of mechanically ventilated patients under various conditions: a systematic review and meta-analysis. *BMC Anesthesiol.* 2019;19(1):67.
96. Biais M, Cottenceau V, Petit L, et al. Impact of norepinephrine on the relationship between pleth variability index and pulse pressure variations in ICU adult patients. *Crit Care.* 2011;15(4):R168.
97. Monnet X, Guerin L, Jozwiak M, et al. Pleth variability index is a weak predictor of fluid responsiveness in patients receiving norepinephrine. *Br J Anaesth.* 2013;110(2):207–13.



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