

Chapter 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 methodsto 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 unmasks 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 responsiveness 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 minifluid 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 shortlived 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 metanalyses 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)

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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.

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

Interpretation of PPV for fluid administration:

- 1. PPV >13% is strongly associated with volume responsiveness [57, 58].
- If PPV is low (<9), it suggests fluid unresponsiveness, and administration of fluids should be avoided [60].
- 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.
- 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].
- Interpretation in grey zone values of PPV: In patients with PPV 9% and 13% and tidal volume ≥8 mL/ kg, PVV 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.

 $\frac{\text{Stroke Volume}}{\text{Variation}} = \frac{\text{SVmax} - \text{SVmin}}{\text{SVmean}}$

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:

 $PVI = \frac{PI \ Maximum - PI \ Minimumn}{PI \ Maximum} \times 100\%$

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 goaldirected 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].

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