Assessment of adequacy of volume resuscitation

John H. Boyd[a,b,c] *and Demetrios Sirounis*[a,b]

Purpose of review
It has recently become evident that administration of intravenous fluids following initial resuscitation has a greater probability of producing tissue edema and hypoxemia than of increasing oxygen delivery. Therefore, it is essential to have a rational approach to assess the adequacy of volume resuscitation. Here we review passive leg raising (PLR) and respiratory variation in hemodynamics to assess fluid responsiveness.

Recent findings
The use of ultrasound enhances the clinician's ability to detect and predict fluid responsiveness, whereas enthusiasm for this modality must be tempered by recent evidence that it is only reliable in apneic patients.

Summary
The best predictor of fluid response for hypotensive patients not on vasopressors is a properly conducted passive leg raise maneuver. For more severely ill patients who are apneic, mechanically ventilated and on vasopressors, point of care echocardiography is the best choice. Increases in vena caval diameter induced by controlled positive pressure breaths are insensitive to arrhythmias and can be performed with relatively brief training. Most challenging are patients who are awake and on vasopressors; we suggest that the best method to discriminate fluid responders is PLR measuring changes in cardiac output.

Keywords
fluids therapy, shock, ultrasound

INTRODUCTION

At normal or low circulating volumes, there exists a well described relationship between stroke volume (SV) and ventricular end-diastolic volume [1], and SV increases rapidly with administration of intravenous fluids [2–5]. This basic physiology has been applied in practice through initiatives such as the surviving sepsis guidelines, and patients presenting with signs of shock routinely receive intravenous volume expansion of 20 ml/kg, while undergoing diagnostic evaluation [6]. This protocol-driven care results in standard and effective initial volume therapy; however, the clinical challenge lies with patients who exhibit ongoing shock. Fully 50% of patients with nonhemorrhagic shock remain in shock following initial volume expansion and needing vasopressors to achieve a minimally acceptable blood pressure (BP) [7]. Nearly 90% of patients with shock refractory to initial fluid resuscitation will require mechanical ventilation [8,9]. In these patients, mean airway pressures of nearly 18 mmHg [10] combine with recent fluid expansion of the circulation to reestablish the postresuscitation equilibrium of venous return and SV.

The patient with shock despite volume resuscitation

Upon presentation for nonhemorrhagic shock (prior to fluid administration), central venous pressure (CVP) lies between 0 and 5 mmHg [1–5,11]. Following guideline-driven intravenous fluid therapy CVP will rise to 9–15 mmHg [12,13]. With this change in CVP comes a predictable but profound effect upon inferior vena caval size when assessed by means of transthoracic echocardiography. Although subjects with a normal circulating volume have an inferior vena cava (IVC) diameter of 17 mm that collapses more than 50% during regular

[a]Critical Care Research Laboratories, Centre for Heart Lung Innovation at St. Paul's Hospital, [b]Department of Critical Care Medicine and [c]Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

Correspondence to John H. Boyd, MD, Critical Care Research Laboratories, Centre for Heart Lung Innovation at St. Paul's Hospital, University of British Columbia, 1081 Burrard Street, Vancouver, BC, Canada V6Z 1Y6. Tel: +1 604 682 2344; fax: +1 604 806 8346; e-mail: John.Boyd@hli.ubc.ca

Curr Opin Crit Care 2016, 22:000–000
DOI:10.1097/MCC.0000000000000344

KEY POINTS

- Two-thirds of patients are not fluid responsive following 30 ml/kg fluids.
- PLR is the best method to assess fluid responsiveness in hypotensive patients not on vasopressors.
- IVC variability may only be used for apneic patients.

inspiration [14–16], following initial volume resuscitation the IVC diameter increased to 23 mm, with no significant respiratory variation in 2/3 of the patients [17].

Is the patient fluid responsive?

Will an individual benefit from additional intravenous fluid therapy or is the prescription of additional fluids toxic? The decision to administer supplemental intravenous fluids to the patient at risk of progressive organ failure rests upon the belief that additional volume expansion will increase cardiac output (*CO*) and thereby increase tissue oxygen delivery. However, when SV can no longer be increased, additional administration of intravenous fluids results in tissue edema, hypoxia and is associated with higher mortality [12,18–23]. Therefore, the ability to judge where the patient lies on the Starling curve is of more than academic interest, it is clinically essential. For the purpose of this review a 'fluid responsive' patient will mean measurable increase of at least 15% in SV. Tests of fluid responsiveness began with direct measurement of right atrial pressure, commonly referred to as CVP. Exhaustively reviewed elsewhere [24], in patients who are critically ill, CVP in isolation cannot discriminate those who will respond to fluids. Experts now agree that maneuvers capable of rapidly changing preload (defining two points on the Starling curve) offer far better abilities to divine fluid responsiveness. Passive leg raising (PLR) and 'opportunistic' observation of respiratory variation in thoracic pressure may be used to rapidly alter preload.

Passive leg raising to reversibly alter preload

A period of 30–60 s following bilateral PLR, preload is increased following recruitment of blood from the legs [25]. It has been estimated that approximately 300 ml of blood is transferred from the legs to the central circulation using this method [26▪▪]. The ideal PLR begins with the patient's head elevated to at least 45° above the horizontal and consists of rapidly moving the bed to simultaneously elevate the lower limbs to 30–45° above the horizontal, whereas lowering the head of the bed to 0°. This positioning offers a greater central shift in blood compared with a patient who is supine at the onset of the maneuver [27]. PLR can be performed with good results in both mechanically ventilated and in spontaneously breathing patients [25,26▪▪,28,29]. Assessing the hemodynamic effect of the PLR-induced central blood shift is not uniform but rather must be tailored to the patient. In hypotensive individuals not on vasopressors, an increase in BP suggests that the patient will respond to a fluid bolus. The ease of measurement (invasive or noninvasive BP monitoring) of the result of the maneuver suggests that PLR is best suited to patients who are not yet on vasopressors. In patients already on vasoactive medications, there is no detectable change in BP, and so the measure of interest is change in *CO*. *CO* changes can be detected after 1–2 min after PLR by using echocardiography or alternative measures of output [29]. The increased complexity and wider confidence intervals around repeat *CO* measures makes this technique less rigorous for patients already on vasopressors.

Unlike measures that compare beat-to-beat variation in *CO*, PLR performs well in arrhythmia and in those with high work of breathing as BP and *CO* are measured over a 30-s interval, smoothing distortion because of arrhythmia and respiratory efforts [26▪▪]. Of note is that PLR is not predictive of fluid response in patients with intra-abdominal hypertension [30].

Respiratory variation

Cyclical changes in intra-thoracic pressure as a result of respiration have been widely recognized to vary cardiac preload under usual circumstances. The most predictable hemodynamic effect of respiratory variation occurs in mechanically ventilated patients with no autonomous respiratory effort; the apnea generally the result of prescribed sedative-hypnotics. During a mechanical breath, a surge in intra-thoracic pressure shifts blood from the pulmonary circulation to the left heart, rapidly increasing SV. Observing BP, this is seen as a rapid increase in pulse pressure (PP) [31]. During prolonged high intra-thoracic pressure such as a 30–45-s recruitment maneuver or open lung ventilation strategies, the right heart preload is impacted with a decrease in venous return. This will be detected as a decline in PP. Concerns have been raised whether changes in PP can reliably act as a surrogate for SV, particularly those with noncompliant small arteries. In the hands of experienced operators, aortic blood flow measured with an apical five-chamber view offers more direct estimation of SV variation (SVV) [32]

with a respiratory variation of more than 12% highly predictive of a positive fluid response [33]. Whether using PP or more direct measures of SV as the indicator, because beat-to-beat variability provides the estimate of fluid responsiveness irregular arrhythmias preclude the use of SVV or pulse pressure variation (PPV). Similarly, severe pulmonary hypertension will render the (now) relatively far smaller changes in intra-thoracic pressures incapable of changing left heart preload [34]. The characteristics of mechanical ventilation are also important, and open lung ventilation strategies with tidal volumes in the 4–6 ml/kg range for those with severely impaired pulmonary compliance do not provide adequate changes in preload to assess SVV or PPV [35,36].

Focused ultrasound exam in patients without respiratory efforts

Ultrasound has emerged as an essential clinical tool in critically ill patients. A rapid hemodynamic assessment using two-dimensional ultrasound of patients in shock can screen for massive pulmonary embolus, pericardial and pleural disease. Because of the popularity of ultrasound, quantitative measures of fluid responsiveness have been widely incorporated into the focused (non-Doppler) examination. Respiratory changes transmitted to the right and left heart as detailed above also result in variation in loading of the inferior and superior vena cavae. As in all vessels, compliance is reduced when the wall tension is higher (distended). At the extreme, a static dilated IVC suggests that the patient will not respond to fluids. IVC diameter is best measured 1–2 cm from the right atrial junction using transthoracic ultrasound [14–16,37–39], and this technique has been widely adopted over the more invasive transesophageal examination of the superior vena cava. Positive intra-thoracic pressure generally increases the size of the IVC during controlled ventilation; however, neither the maximum nor minimum IVC diameter could predict fluid response [40–43]. If one calculates the relative change in IVC diameter according to [maximum – minimum IVC diameter/(maximum + minimum)/2], 12% variation predicts fluid response [42], whereas a smaller denominator calculated by (maximum – minimum IVC diameter/minimum IVC diameter) raises the threshold to 18% [40].

Focused ultrasound exam in patients making respiratory efforts

In patients who make respiratory efforts the negative inspiratory pressures transmitted to the IVC vary mainly according to the extent of patient effort [44▪▪] and pressure (if any) applied through mechanical ventilation. A challenge in the rapidly evolving mechanically ventilated patient is to accurately assess whether they have begun assisting the ventilator; however, a clinical examination including analysis of ventilator waveforms is essential because the evidence to date suggests that in spontaneously breathing patients the usual change in IVC cannot be used to predict fluid response [45▪▪].

CONCLUSION

Two-thirds of patients will not increase *CO* in response to further fluids following an initial volume resuscitation of 30 ml/kg. The single predictor of fluid response for hypotensive patients not on vasopressors is the increase in BP in response to a properly conducted passive leg raise maneuver. This reflects the ease of performing both the maneuver and assessing a positive response (BP). For more severely ill patients who are both mechanically ventilated and on vasopressors, point of care echocardiography is the best choice. Increases in vena caval diameter induced by controlled positive pressure breaths are insensitive to arrhythmias and can be performed with relatively brief training. Most challenging are patients who are awake (either spontaneously breathing or in a noncontrolled mode of mechanical ventilation) and on vasopressors; we suggest that the best method to discriminate fluid responders is PLR measuring changes in *CO* (for instance using an esophageal probe to measure descending aortic blood flow).

Acknowledgements

We would like to thank the staff of St Paul's Critical Care Unit for their assistance with this work.

Financial support and sponsorship

The work was supported by the Canadian Institutes of Health Research.

Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
- ▪▪ of outstanding interest

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This work is very important: it clearly shows that PLR is an excellent predictor of fluid responsiveness.

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