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Development of a fluid resuscitation protocol using inferior vena cava and lung ultrasound☆,☆☆

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ABSTRACT

Appropriate fluid resuscitation has been a major focus of critical care medicine since its inception. Currently, the most accurate method to guide fluid administration decisions uses "dynamic" measures that estimate the change in cardiac output that would occur in response to a fluid bolus. Unfortunately, their use remains limited due to required technical expertise, costly equipment, or applicability in only a subset of patients. Alternatively, point-of-care ultrasound (POCUS) has become widely used as a tool to help clinicians prescribe fluid therapy. Common POCUS applications that serve as guides to fluid administration rely on assessments of the inferior vena cava to estimate preload and lung ultrasound to identify the early presence of extravascular lung water and avoid fluid overresuscitation. Although application of these POCUS measures has multiple limitations that are commonly misunderstood, current evidence suggests that they can be used in combination to sort patients among 3 fluid management categories: (1) fluid resuscitate, (2) fluid test, and (3) fluid restrict. This article reviews the pertinent literature describing the use of inferior vena cava and lung ultrasound for fluid responsiveness and presents an evidence-informed algorithm using these measures to guide fluid resuscitation decisions in the critically ill.

1. Introduction

Appropriate fluid administration is a cornerstone in the management of acutely ill patients with shock. Inadequate fluid resuscitation results in tissue hypoperfusion and worsening end-organ dysfunction [1,2], and resuscitation strategies that avoid underresuscitation have a proven mortality benefit [3,4]. Yet, overresuscitation leading to a positive fluid balance has been associated with worsened mortality [5,6]. Establishing measures of adequate fluid resuscitation in critically ill patients with shock has been a major focus of critical care since its inception, with multiple strategies and devices having been adopted and abandoned over time [3,7-10]. In the past 2 decades, a growing body of research has established the use of dynamic measures to determine fluid responsiveness (FR) when making fluid administration decisions [11-13]. A "fluid responder" has been defined as a patient whose cardiac output (CO) increases by 15% in response to a fluid bolus, whereas nonresponders either show decreased CO or minimal increases. Pulse pressure variation, stroke volume variation, and systolic pressure variation are established dynamic measures that estimate changes in CO before and after induced fluid shifts into the heart, by the cyclic changes caused by a mechanical ventilator, passive leg raises, or rapid infusions of small fluid volumes. Using dynamic measures to determine FR is now considered the optimal approach to guide fluid decisions given their superior predictive characteristics, with areas under the receiver operating characteristic curves of 0.84 to 0.94 [14]. However, the dynamic measures are almost all limited by the need for either expert echocardiographers, costly equipment, or physiologic applicability in only a small subset of patients [15]. As a result, point-of-care ultrasound (POCUS) has garnered attention as a viable tool to help clinicians prescribe fluid therapy given its rapid, repeatable, and noninvasive nature [16-21]. The use of POCUS assessments included within basic critical care echocardiography and general critical care ultrasound to improve assessment of FR is in line with current trends, where whole-body ultrasound for shock or respiratory failure is growing more common [22-25]. An example of this practice is the adoption of POCUS measured inferior vena cava (IVC) parameters within widely disseminated sepsis resuscitation protocols [26]. Others have promoted the use of lung ultrasound (LUS) to identify the presence of extravascular lung water as a method for avoiding fluid overresuscitation in shock patients [22,23,25]. These IVC and LUS assessment skills are being taught and have been integrated into practice by both nonexpert and expert POCUS practitioners [27]. In the following, we (1) explore the physiologic rationale and current literature supporting the use of IVC and LUS in helping to identify the

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boundaries of fluid underresuscitation and overresuscitation and (2) provide a decision support tool that integrates this literature to provide clinicians with an evidence-informed algorithm to qualitatively guide fluid administration decisions.

2. Fluid responsiveness and IVC parameters

Considering the complex nature of critically ill patients and the multiple variables that influence FR, insufficient evidence is available to support the use of IVC ultrasound to definitively determine FR in most clinical scenarios; however, several IVC parameters may serve as a guide to fluid administration decisions as described in the following paragraphs.

2.1. Inferior vena cava distensibility

Although many studies have been conducted, conclusive evidence supporting IVC ultrasound as a predictor of FR exists only for the small subset of patients who are perfectly synchronous with a mechanical ventilator [16,17]. Intubated and fully ventilated patients do not actively participate in their ventilation and, therefore, have near-identical respirophasic loading conditions, allowing dynamic changes in the IVC to be measured in a reliable manner. Two studies, both published in 2004, looked at this group of patients and defined IVC distensibility measurements that were associated with volume responsiveness [16,17]. Barbier et al [16] defined a “distensibility index of the IVC” as dIVC, calculated as the difference between IVC diameter at end-inspiration (D_{max}) and IVC diameter at end-expiration (D_{min}), expressed as a percentage of D_{min}, that is, $[(D_{max} - D_{min})/D_{min}] \times 100\%$. A threshold value of 18% for dIVC was reported to discriminate with 90% sensitivity and specificity for volume responsiveness. Similarly, Feissel et al [17] defined “respiratory variation in IVC diameter” as $\Delta D_{IVC} = (D_{max} - D_{min})/[(D_{max} + D_{min})/2]$ and found that a ΔD_{IVC} value of 12% discriminated between responders and nonresponders with a positive predictive value of 93% and a negative predictive value of 92%.

2.2. Inferior vena cava diameter

Although the above studies revealed excellent test characteristics in the ability of IVC distensibility to predict FR, this measure is severely limited by a lack of generalizability given the small subset of patients that meet inclusion criteria [15].

In patients not meeting the above inclusion criteria, maximal diameter of the IVC can be helpful in identifying hypovolemic patients. Although maximal IVC size in healthy patients has a wide range from 9 to 27 mm, there appears to be discriminatory power in identifying small IVC sizes; Yanagawa et al [28] found an average diameter of 6 mm in early trauma patients with shock, Brennan et al [29] found that 92% of patients with low blood pressure on hemodialysis had an IVC size less than 8 mm, and a meta-analysis of studies measuring IVC size in shock patients found all had an IVC size less than 15 mm with an average of 11 mm [21]. Lastly, in the study above by Feissel et al [17], 29 of 30 nonresponders had IVC sizes more than 15 mm. Based on these data, we submit that a maximal IVC diameter less than 1.5 cm will provide sufficient sensitivity and specificity in identifying FR. Thus, for critically ill patients with an IVC diameter less than 1.5 cm or in intubated and passively ventilated patients with a ΔD_{IVC} value of 12% or more, crystalloid volume expansion should be administered as this subgroup of patients is likely volume responsive.

Conversely, a large absolute IVC diameter, which we have defined as greater than 2.5 cm, can be consistent with a volume-loaded state unlikely to respond to further fluid resuscitation. A study by Feissel et al on IVC distensibility [11] found only 2 of the 16 fluid responders had a max IVC diameter greater than 2.5 cm. Similarly, in a recent abstract, Jordan et al showed that only 1 of 15 fluid responders as defined by bioreactance had a maximum IVC diameter more than 2.5 cm [30]. It must be remembered that large, nonvarying IVC diameters are not specific for volume-loaded states, and this distinction can only be made in the correct clinical context. Thorough consideration of the multiple etiologies that can produce a distended IVC such as tamponade or pulmonary hypertension must be completed. Valuable information regarding the etiology of a distended IVC can be added with complimentary echocardiographic views for those users versed in their acquisition. Depending on the clinical scenario, volume administration may still be reasonable. If, however, IVC distension is considered secondary to fluid status, further volume expansion is contraindicated due to risk of contributing to patient morbidity.

2.3. Inferior vena cava collapsibility

As opposed to the IVC distension that occurs in passively ventilated patients, the evidence for respiratory collapse in IVC diameter among spontaneously breathing patients is less robust, although it may provide further guidance. Muller et al [31] defined respiratory variation of the IVC (cIVC) as $[(D_{max} - D_{min})/D_{min}] \times 100\%$ and found that a cIVC greater than 40% is usually associated with volume responsiveness, whereas another small study of 14 patients reported a cIVC value of 15% or less had a negative predictive value of 100% for volume responsiveness [32]. In a population of hypotensive emergency department patients with shock, Weekes et al [33] showed that the cIVC decreased from an initial value of 45% to 22% after fluid loading. This suggests that, at large or small values of cIVC, some utility exists in further estimating the likelihood of FR in spontaneously breathing patients.

3. Lung ultrasound–guided fluid resuscitation

Given that the information available from respirophasic and static IVC measurements in many patients will not always be predictive, supplementary data should be acquired to further guide management. A number of studies have shown a correlation between extravascular lung water and mortality in the critically ill [34,35]. As such, LUS has been suggested as an additional tool that can rapidly and accurately identify the early pulmonary edema that develops when patients are overresuscitated, thus providing a signal in the risk-benefit consideration of further volume expansion.

The use of 2 LUS signatures, A-line and B-line predominance, are used as a framework to assess likelihood of interstitial edema and guide fluid administration in the Fluid Administration Limited by Lung Sonography protocol [25]. This protocol is predicated on the fact that A-line predominance indicates dry interlobular septa and low or normal left atrial pressure [23], whereas B-line predominance is associated with the alveolar-interstitial syndrome, an often preradiographic and preclinical sign consistent with pulmonary edema [25,36]. Thus, for intubated and nonintubated spontaneously breathing patients with a normal-sized IVC, observed A-line predominance suggests that fluid administration is safe in reference to lung function, that is, that further fluid administration will not immediately cause or worsen hydrostatic pulmonary edema. Although fluid administration in patients with A-line predominance is likely permissible, it may not necessarily be required and should be considered in the entire clinical context. B-line predominance suggests that interstitial edema may be present, and fluid administration may incur patient morbidity. A suggested practical approach is to use 2 standardized BLUE protocol scanning points in each hemithorax (Fig. 1) to obtain the lung signature and direct fluid administration based on the concept of fluid tolerance for triggering or spontaneously breathing patients with an otherwise normal IVC diameter [22]. Although additional techniques such as passive leg raise [37,38] or mini-fluid challenge [39] have shown some promise, the additional time, ultrasound proficiency, or cost required to use these techniques properly limits their generalizability and serves as further evidence that a protocol relying on more widely practiced POCUS skills is needed.

Although the most common cause of symmetric anterior-lateral chest wall B-line predominance is hydrostatic pulmonary edema, this pattern can also be observed in other clinical scenarios, for example, infections, malignancy, interstitial disease, and, therefore, is not specific to hydrostatic pulmonary edema. In patients with normal-sized IVCs observed to have B-line predominance, thorough consideration of the clinical context is required to direct fluid administration correctly. B-lines produced from interstitial processes other than hydrostatic edema may yet necessitate fluid administration. However, if hydrostatic pulmonary edema is considered to be the likely etiology of B-lines, a "volume-loaded" state is recognized, and different agents should be considered to support shock rather than further volume expansion. For users comfortable with bedside echocardiography, this juncture also affords the opportunity for further assessment of right and left ventricular function, which may help to characterize and better assign likelihoods for B-line origins as well as direct adjunctive therapy (ie, inotropes). However, if permeability edema or interstitial disease is already present, risks of lung water from further resuscitation are notably higher in this group with marginalized lung parenchyma [40].

4. Fluid resuscitation guide

Although the ideal methods to identify FR in critically ill patients with shock are to rely upon dynamic measures, such options are often either not available or applicable in a majority of clinical situations and environments [15]. Even when appropriate, busy clinical teams within emergency departments and intensive care units are not always able to perform repeated dynamic testing in a timely fashion during resuscitation of patients. Thus, use of more widely practiced and readily acquired POCUS assessments of the lungs and IVCs of patients as a method for guiding fluid administration is desirable and can serve to narrow down the number of patients who would most benefit from a passive leg raise or other dynamic test of FR. Given that IVC and LUS measures alone are unable to discriminate patients precisely into the binary categories of FR or non-FR, we propose to instead separate patients among 3 broad, qualitative fluid resuscitation categories by using a combination of LUS and IVC findings, based on the existing literature above for these POCUS assessments: (1) fluid resuscitate, (2) fluid test, or (3) fluid restrict (Fig. 2). The fluid resuscitation guide begins with an IVC diameter that initially sorts patients into underfilled, normal, and distended categories. Within the subset of patients with a normal-sized IVC, those with spontaneous respirations are further investigated with LUS to determine A-line or B-line predominance. Each category subsequently supports an approach to fluid resuscitation or further appropriate investigation, always in consideration of the clinical context of an individual patient. Because of the rapid and noninvasive nature of ultrasound assessments, repeated use of the guide to assess response to therapy and clinical trajectory is thus encouraged.

5. Limitations

The included ultrasonographic assessments serve as evidence-based tools to guide fluid management decisions, yet some limitations exist in using such categorical discriminators. The predictive power of some categories will vary depending on the pathophysiologic cause of shock, a limitation most relevant in the "underfilled IVC" category. Inferior vena cava measurements in patients with conditions resulting in absolute hypovolemic states, for example, trauma, diarrhea, gastrointestinal bleeding, predict the need for fluids with high accuracy [28,29], whereas underfilled IVCs in patients with vasodilatory shock, such as in sepsis, are less predictive of FR. Thus, in vasodilatory conditions such as sepsis, earlier consideration for performing dynamic FR testing is warranted. Moreover, thorough knowledge of other clinical situations where IVC parameters may be inaccurate in judging fluid needs is necessary to

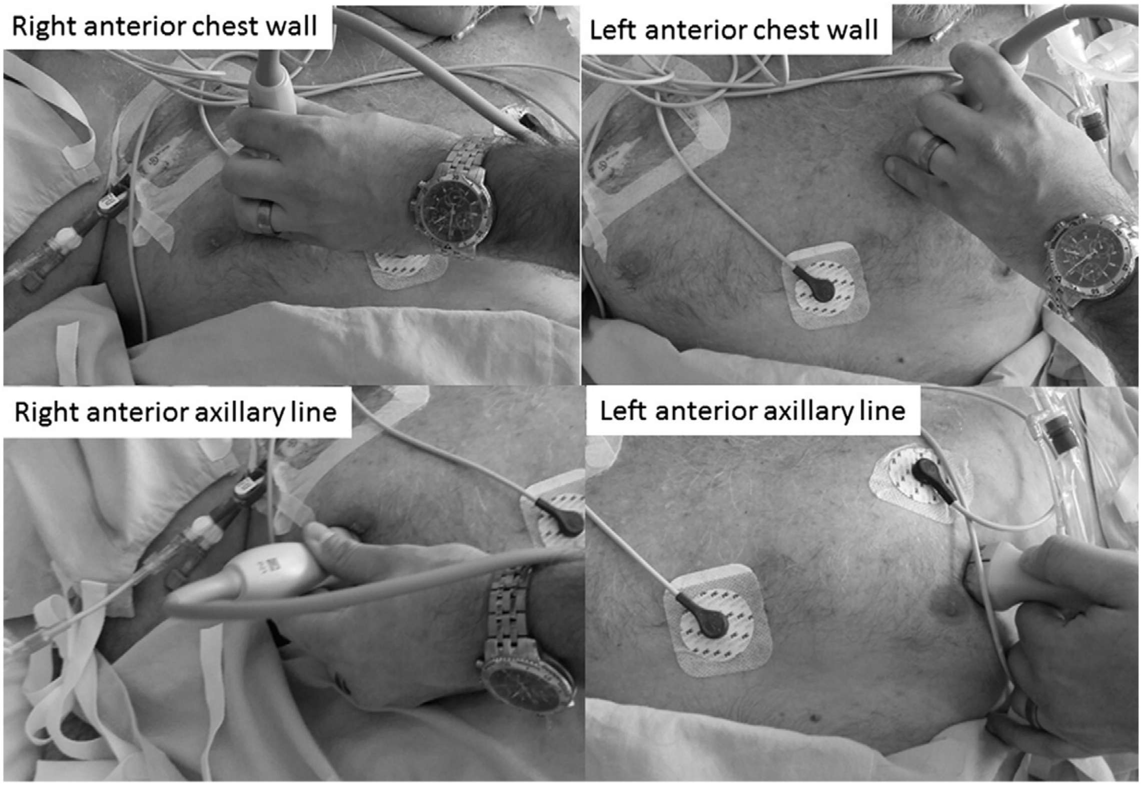
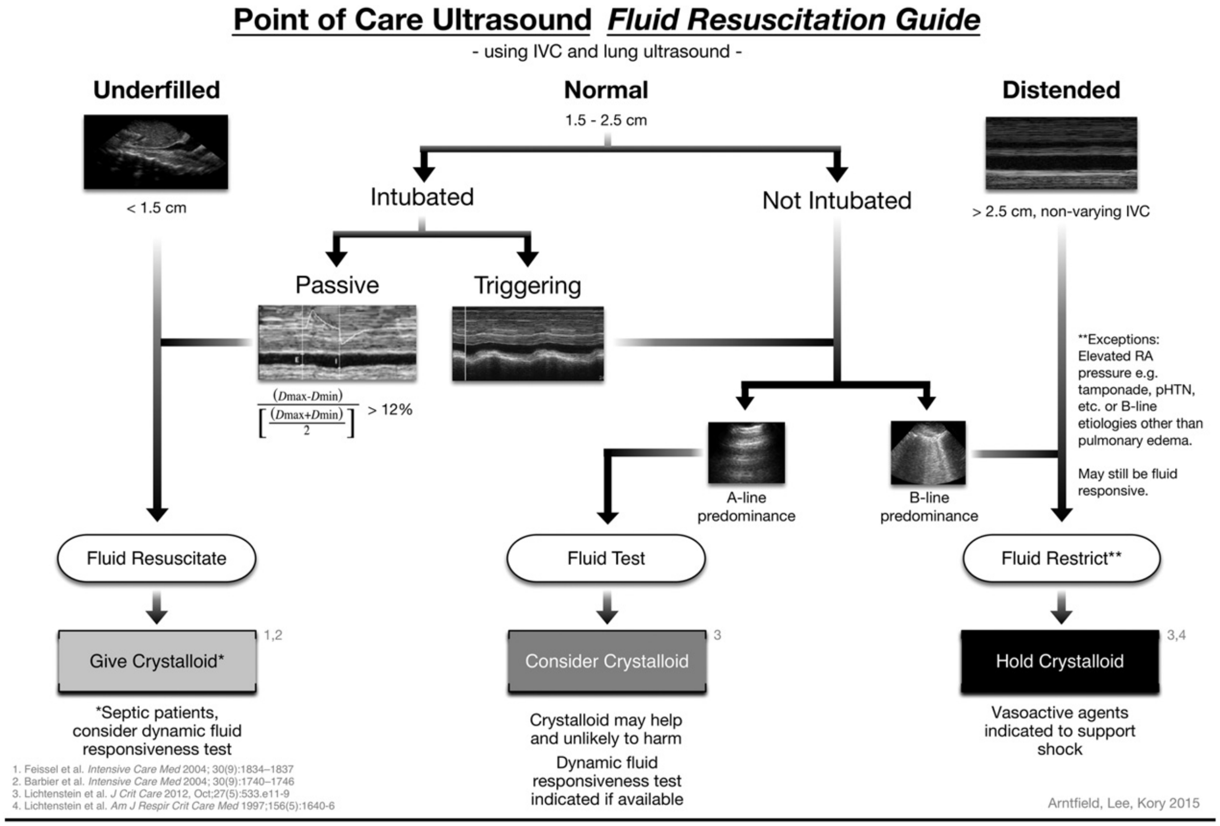


Fig. 1. BLUE protocol LUS scanning points.



**Exceptions: Elevated RA pressure e.g. tamponade, pHTN, etc. or B-line etiologies other than pulmonary edema.

May still be fluid responsive.

*Septic patients, consider dynamic fluid responsiveness test

Crystalloid may help and unlikely to harm

Dynamic fluid responsiveness test indicated if available

Vasoactive agents indicated to support shock

1. Feissel et al. *Intensive Care Med* 2004; 30(9):1834–1837
2. Barbier et al. *Intensive Care Med* 2004; 30(9):1740–1746
3. Lichtenstein et al. *J Crit Care* 2012, Oct;27(5):533.e11-9
4. Lichtenstein et al. *Am J Respir Crit Care Med* 1997;156(5):1640-6

Fig. 2. Point-of-care ultrasound fluid resuscitation guide.

use this tool effectively. Some examples of such situations include increased abdominal pressure, high levels of positive end-expiratory pressure, or less conventional modes of ventilation (ie, oscillation, bilevel).

Finally, the lack of a mandated direct examination of the heart chambers and their function in the fluid resuscitation guide may also limit the accuracy of fluid prescriptions. Although cardiac chamber assessments are recommended and should be performed if possible, their inclusion was not mandated for 2 reasons: (1) the levels and changes in right and left ventricular function in regard to fluid administration are believed to be well reflected in IVC and lung water parameters and (2) a reliance on more widely held sonographic image acquisition skills allows for wider application of the guide at the bedside.

6. Conclusions

Fluid resuscitation in the critically ill can be categorized in 3 broad management categories when using IVC and LUS measures: fluid resuscitate, fluid test, and fluid restrict. Combining both lung and IVC POCUS is easy to accomplish and provides valuable information for determination of FR. Although not capable of matching the predictive power of more sophisticated dynamic tests of FR, this manuscript and accompanied fluid administration guide present an interim synthesis of existing literature and expert opinion on the ability of transthoracic ultrasound to predict FR. Use of this qualitative fluid administration guide, in addition to careful consideration of the clinical context, can provide an evidence-informed, safe, and practical framework for decisions on fluid administration in the critically ill. Prospective validation of this fluid administration guide is desirable and should rely on a comparison with results obtained from dynamic measures to further understand its strengths and limitations.

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