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Ultrasound Assessment of the Inferior Vena Cava for Fluid Responsiveness: Making the Case for Skepticism

Scott J. Millington, MD[1] and Seth Koenig, MD[2]

Abstract

Determining whether a patient in shock is in a state of fluid responsiveness (FR) has long been the Holy Grail for clinicians who care for acutely ill patients. While various tools have been put forth as solutions to this important problem, ultrasound assessment of the inferior vena cava has received particular attention of late. Dozens of studies have examined its ability to determine whether a patient should receive volume expansion, and general enthusiasm has been strengthened by the fact that it is easy to perform and non-invasive, unlike many competing FR tests. A deeper examination of the technique, however, reveals important concerns regarding inaccuracies in measurement and a high prevalence of confounding factors. Furthermore, a detailed review of the evidence (small individual studies, multiple meta-analyses, and a single large trial) reveals that the tool performs poorly in general and is unlikely to be helpful at the bedside in circumstances where genuine clinical uncertainty exists.

Keywords

ultrasound, intensive care, shock, fluid therapy

Introduction

Determining whether a patient in shock is in a state of fluid responsiveness (FR) has long been the Holy Grail for clinicians who care for acutely ill patients. Defined as the physiologic state where the administration of an intravenous (IV) fluid bolus will cause an increase in stroke volume (SV),[1] it reflects the hope that oxygen delivery will be improved and the state of shock subsequently ameliorated. This problem is important, given that critically ill patients consistently have a near 50% probability of being in a FR state,[2,3] indicating that we are typically operating in a zone of perfect uncertainty. Additionally, while the potential benefits of IV fluids are intuitive, overzealous fluid administration has been associated with various adverse outcomes including longer hospital stays,[4] longer duration of mechanical ventilation,[4] and increased morbidity & mortality.[5-7] Intravenous fluids, like any other drug, should be administered in exactly the right dose.

Despite a lengthy and enthusiastic search, we presently do not have any tools which are both practical to perform and accurate in determining FR. Straightforward techniques such as physical examination and central venous pressure measurement have no meaningful relationship to FR. Tools which seem to work reasonably well in some circumstances are either cumbersome to deploy (passive leg raise, end-expiratory occlusion test), unavailable in many centers (PiCCO), invasive (Swan-Ganz catheterization), of controversial precision (bioreactance), or applicable to only a small subset of patients (arterial pulse pressure variation).

Dynamic change in the diameter of the inferior vena cava (IVC), measured with ultrasound, is a technique that has received tremendous recent attention for its potential ability to aid in determining FR. Numerous small studies, dating as far back as 15 years, attest to its utility. However, interpreting the physiology of IVC respiratory variation is fraught with potential danger for 2 principle reasons. First, there is a prevailing misunderstanding as to the technical limitations of measuring IVC diameter accurately, as well as the common physiologic states which confound its relationship to FR. Secondly, there is a strong bias toward the application of an oversimplified binary approach which fails to consider the actual performance characteristics of the tool in the real-world clinical environment.

[1] Intensive Care Unit, University of Ottawa/The Ottawa Hospital, Ottawa, Ontario, Canada
[2] Kent Hospital, Warwick, RI, USA

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Corresponding Author:
Scott J. Millington, Intensive Care Unit, Ottawa Hospital, General Campus, Box 207, 501 Smyth Road, Ottawa, Ontario, Canada K1H 8L6.
Email: smillington@toh.ca

Technical Problems and Confounding Factors

A detailed technical explanation of how to perform the specific ultrasound skill of IVC analysis is beyond the scope of this paper and has been covered in detail elsewhere.[8] Similarly, the potential technical issues associated with IVC measurements have been well described in other reviews[9] and will be discussed here only briefly. While there is a natural human tendency to assume that personally performed measurements are accurate, as an operator-dependent skill that relies heavily on patient anatomy and body habitus this is not likely to be true for IVC assessment for several reasons. The specific point along the length of the IVC where its diameter should be measured is not standardized, leading to measurement variability.[10] The IVC may not be measured perfectly perpendicular to the long axis, resulting in an overestimations of vessel diameter (here new technologies such as automated IVC wall tracing may help, but remain unproven). Diaphragmatic and IVC translation with respiration often results in foreshortening of the vessel, which is erroneously interpreted as collapse.[11] The IVC itself does not collapse (or distend) in a perfectly sagittal plane, which tends to underestimate changes with respiration.[11] Many busy clinicians prefer rough “eyeball” estimates to quantitative measurements, to the detriment of accuracy.[12] Operators might mistake the abdominal aorta for the IVC on occasion. There is significant documented inter-rater variability in IVC measurements, raising the possibility that 2 clinicians assessing the same patient at the same time could come to opposite conclusions with respect to FR.[13,14]

Even if we were to assume perfect accuracy in measurements, several common clinical scenarios will confound the relationship between IVC variability and FR. Changes in intrathoracic pressure, the force responsible for the change in IVC size with respiration, are unpredictable in spontaneously breathing patients. Severely dyspneic patients with wide variations in intrathoracic pressures may be able to collapse a “full” IVC, or an obtunded patient taking shallow breaths may fail to collapse an “empty” one. In mechanically ventilated patients changes in intrathoracic pressure are heavily dependent on the set tidal volume and most ICU patients have abnormal lung compliance, blunting the effect of positive pressure on IVC size to some unpredictable degree.

Cardiac factors, most importantly right ventricular dysfunction, can also confound the results; such patients typically have a chronically dilated IVC which renders interpretation difficult. A chronically dilated IVC can also be seen in elite athletes and with certain anatomical variants such as the presence of a Eustachian valve. Finally, there is the important and often overlooked effect of increased intra-abdominal pressure (IAP): once IAP exceeds the (modest) level of 12 mmHg, any relationship between the IVC and FR is lost.[15]

Supporting Literature

Setting aside technical concerns and potential confounding factors, there is an extensive literature to examine. Unfortunately, most studies are small and difficult to interpret due to high heterogeneity: Are the patients breathing spontaneously or are they mechanically ventilated? If mechanically ventilated, are they actively making respiratory efforts or are they passive on the ventilator? What tool is being used to assess FR? How sick are the patients?

One large, high-quality study by Vignon and colleagues[3] studied 540 critically ill patients, all mechanically ventilated (with an average tidal volume of 7.7 mL/kg) and passive on the ventilator, under ideal circumstances (such as we presently understand them) for analyzing IVC variability. Of the 4 methods tested for determining FR (respiratory variation of superior vena cava diameter, respiratory variation of IVC diameter, variability of the maximal Doppler velocity at the left ventricular outflow tract, and pulse pressure variation), IVC variability performed worst of all, with an area under the receiver operator curve (AUROC) of just 0.635.

Looking at this data from a Bayesian perspective highlights how the analysis of IVC variability is unlikely to be useful at the bedside. Beginning with a pre-test probability for FR of 50% (a very reasonable proposition for most critically ill patients[2]), a positive result on the test (ΔIVC >8% in the Vignon study) would only increase the post-test probability of a FR state to 65% (specificity 70%, positive likelihood ratio 1.83). A negative result (ΔIVC <8% in the Vignon study) would decrease the post-test probability of a FR state to 39% (sensitivity 55%, negative likelihood ratio 0.64). This clinician is therefore left in a position of great uncertainty: After examining the IVC there is either a 65% chance of a FR state (with a positive test) or a 41% chance (with a negative test). In either scenario, confident action regarding the giving or withholding of a fluid challenge is impossible.

While this analysis is based on data from a single study, it is the largest study to date and should therefore be given special emphasis. Even if we treat this result as a hypothesis to be confirmed by further study, it certainly suggests that IVC assessment generally performs poorly.

Meta-Analyses

Before we jump into a fraught analysis of individual studies, we should pause to examine the many meta-analyses which have been performed on this subject to date. To summarize succinctly, the most recent and largest meta-analysis (of 20 individual studies) concluded that: *“ultrasound evaluation of the diameter of the IVC and its respiratory variations does not seem to be a reliable method to predict fluid responsiveness.”*[16]

This analysis, as well as the 3 others published in 2018,[17-19] are all dominated by the very large Vignon paper that was discussed in detail above. If we go back to 2017, we can find the largest and most recent meta-analysis which does not include the Vignon paper and involves 17 individual studies. The authors of this paper concluded that: *“respiratory variation in IVC diameter has limited ability to predict fluid responsiveness.”*[20]

While there is ample room to debate the nuances associated with these analyses, it seems safe to conclude that they do not lend much support to the idea that IVC analysis is useful at the bedside. Working again from the perspective of hypothesis generation, our previous supposition that IVC analysis is a tool that performs poorly has certainly not been weakened.

Individual Studies in Spontaneously Breathing Patients

IVC analysis in patients who are breathing spontaneously has generally been felt to be less reliable due to the unpredictability of changes in intra-thoracic pressure with respiration, as described in the introduction. Sorting through individual studies is difficult work, primarily due to the significant heterogeneity in methodology and inclusion criteria.

There have been a total of 11 studies (note 1) in spontaneously breathing patients, all relatively small single-center efforts. Of these, six[21-26] are best described as negative endeavors (note 2), with 5 others positive.[27-31] The 5 positive papers form an interesting hypothesis which should motivate the undertaking of larger confirmatory studies, but the preponderance of small-study evidence does not clearly support the widespread use of this tool.

It is worth mentioning a subtle twist on the standard technique of IVC analysis in spontaneously breathing patients: the use of a standardized deep inspiration. Of the 5 positive studies listed above, 2 used a protocol which involved having the patients take a deep breath in while monitoring the amount of negative pressure generated.[27,29] This effort, an effort to quantify the traditional "sniff" test, seemed to work well in 2 small studies. It may have a role in the management of stable patients in the emergency department but will not be of help when managing patients who are severely ill, mechanically ventilated, dyspneic, or neurologically altered.

Individual Studies in Mechanically Ventilated Patients

While IVC analysis in mechanically ventilated patients is generally felt to be more reliable, it is burdened by most of the same technical factors and confounding issues. There have been a total of 12 individual studies here, all with relatively small sample sizes. Seven of these studies could best be described as positive[32-38] and 5 negative.[39-43] again leaving us in a position of uncertainty. Contrary to popular belief, therefore, it does not seem at all certain that IVC analysis performs better in this patient population. While there may be less effort-based variability in intrathoracic pressure changes, this effect may be outweighed by confounding factors introduced by the effects of positive pressure ventilation, worsening lung compliance, or variably set tidal volumes.

Conclusion

Analysis of the IVC with ultrasound to inform decisions related to fluid administration has become popular because it is easy to perform and due to the urgent need for a practical tool to help in understanding whether a patient is likely to be fluid responsive. While it may provide some important confirmatory value in more extreme cases, and may have a role to play in answering other clinical questions relating to pericardial tamponade and venous congestion, its overall performance characteristics related to fluid responsiveness do not appear favorable and seem unlikely to be useful where genuine clinical uncertainty exists. Given the fact that evidence from small studies is mixed and the largest study to date was not supportive, this tool should be used with caution in most cases until further data becomes available.

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ORCID iD

Scott J. Millington, MD https://orcid.org/0000-0002-2962-5771

Notes

1. Including studies in adult patients where some assessment of FR was made.
2. Concluding that a study was positive or negative is somewhat subjective, but the decision to label a study negative was based primarily on an AUROC <0.7 or a negative concluding statement by the author.

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