TAKE-HOME MESSAGE
Existing evidence suggests that central venous pressure poorly predicts fluid responsiveness in acute and critically ill patients.

Utility of Central Venous Pressure as a Predictor of Fluid Responsiveness

EBEM Commentators
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Results

Comparison of low, intermediate, and high central venous pressure subgroups.

<table>
<thead>
<tr>
<th>CVP Subgroup (mm Hg)</th>
<th>Number of Patients (%)</th>
<th>Positive Likelihood Ratio (95% CI)</th>
<th>Negative Likelihood Ratio (95% CI)</th>
<th>AUC-ROC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (&lt; 8)</td>
<td>537 (47)</td>
<td>1.40 (1.24–1.59)</td>
<td>0.74 (0.66–0.83)</td>
<td>0.57 (0.52–0.62)</td>
</tr>
<tr>
<td>Intermediate (8–12)</td>
<td>348 (30)</td>
<td>0.78 (0.65–0.94)</td>
<td>1.11 (1.03–1.20)</td>
<td>0.54 (0.48–0.60)</td>
</tr>
<tr>
<td>High (&gt;12)</td>
<td>263 (23)</td>
<td>0.69 (0.55–0.85)</td>
<td>1.12 (1.05–1.19)</td>
<td>0.56 (0.48–0.63)</td>
</tr>
</tbody>
</table>

CVP, Central venous pressure; CI, confidence interval.

METHODS

DATA SOURCES
Two authors independently searched PubMed and EMBASE through April 2015, without language restrictions. Bibliographies of included studies were also reviewed. Authors of all identified studies were contacted and asked for patient-level data.

STUDY SELECTION
Included trials evaluated hospitalized adult patients, reported baseline central venous pressure values, performed at least 1 fluid loading, and evaluated fluid responsiveness. Data on central venous pressure had to be presented in a way to discriminate fluid responders from nonresponders.

DATA EXTRACTION AND SYNTHESIS
Two authors independently extracted study data, using standardized forms. Patient population and size, definition of and technique for evaluating fluid responsiveness, fluid type and volume used in loading, and key results were extracted. The authors contacted individual trial authors to request individual patient baseline central venous pressure data grouped by fluid responders and nonresponders. Studies and individual patient data were subgrouped according to baseline central venous pressure values (<8, 8 to 12, and >12 mm Hg).

The search strategy identified 4,767 potential studies. After review, 51 total studies were selected and the authors were contacted for raw patient data. No formal assessment of study quality was performed. Twenty-two studies were performed in operative or postoperative patients, and the remainder evaluated ICU patients. Patients received mechanical ventilation in most trials. Only 4 studies assessed mixed populations of patients receiving both mechanical ventilation and no ventilation and 1 study assessed exclusively patients with no ventilation. Colloids and starches were used for fluid challenges in the majority of trials, with crystalloids allowed in only 7 studies. Most studies used a bolus of fluid of either 500 mL or 7 to 10 mL/kg, with values ranging from 100 to 1,000 mL. Thermodilution was the most common method for determining fluid responsiveness, typically defined as an increase in stroke volume or cardiac output. Two thirds of studies used stroke volume index or cardiac index in place of stroke volume or cardiac output. Stroke volume index and cardiac index are calculated by dividing a patient’s stroke volume or cardiac output by his or her total body surface area, potentially providing a more accurate measure of fluid responsiveness. Twenty-two studies, comprising 1,148 total patient data sets, submitted raw data, which was included in the final analysis.

The median central venous pressure was 9 mm Hg (interquartile
range 6 to 12 mm Hg). The accompanying Table demonstrates the positive likelihood ratios, negative likelihood ratios, and AUC-ROC for each of the central venous pressure groups. Subgroup analyses comparing patients who received only mechanical ventilation, studies performed only in the ICU setting, and studies using only thermodilution or lithium dilution or transesophageal echocardiography for assessment of fluid responsiveness demonstrated no significant difference in results. The authors found a maximum positive likelihood ratio of 2.04 (95% confidence interval 1.27 to 3.26) at a central venous pressure of 2 to 3 mm Hg and a minimum negative likelihood ratio of 0.56 (95% confidence interval 0.77 to 10.41) at a central venous pressure of 14 to 15 mm Hg.

Commentary

Fluid therapy has been demonstrated to be a key intervention among critically ill patients.1 The Surviving Sepsis Campaign has listed this as one of the core interventions necessary in the early treatment of critically ill patients.2 However, previous studies have suggested that only 50% of patients respond to fluid administration with an increase in stroke volume or cardiac output, referred to as fluid responsiveness.3 It is important to identify which patients will respond to fluid therapy because fluid overload may be associated with increased morbidity and mortality.4 Previous meta-analyses have suggested that central venous pressure has no value in predicting fluid responsiveness.5 This review analyzed more trials than did previous reviews and was the first to assess patient-level data, thus allowing better assessment at the extremes of central venous pressure values.

The AUC-ROC was poor for all 3 subgroups of central venous pressure values. For the lowest central venous pressure subgroup, it was minimally above 0.5, whereas the other 2 subgroups included 0.5 in the 95% confidence interval, wherein 0.5 suggests no predictive value to the test. Additionally, the positive and negative likelihood ratios at all individual cutoffs were minimally different from 1, suggesting very poor predictive utility, even at extreme values. This meta-analysis adds to the existing evidence that central venous pressure is not useful as a predictor of fluid responsiveness. Poor utility of central venous pressure could be due to a variety of factors that have been shown to affect central venous pressure values, including inadequate zeroing of the transducer, poor baseline cardiac function, pericardial effusion, increased intrathoracic pressure, and increased intrabdominal pressure.6 Additionally, relying on preload to assess volume responsiveness neglects the importance of cardiac function. A given preload value may be associated with either preload responsiveness (in the case of normal ventricular contractility) or preload unresponsiveness (in the case of poor ventricular contractility) and therefore cannot reliably predict how cardiac output will respond in isolation. Finally, obtaining central venous pressure requires the placement of a central venous catheter, which is invasive and unnecessary in many patients, prompting some authors to suggest different measures of fluid response in critically ill patients.7,8

This patient-level meta-analysis adds to the existing knowledge of central venous pressure and fluid responsiveness. One potential limitation is that none of the included trials appear to have been performed in an emergency department setting, and few used crystalloid for fluid challenges. Besides limited applicability, other limitations include the potential for unidentified cases. In fact, of the 51 identified studies, only 22 study authors provided patient-level data (45% of total potential patient-level data). No quality appraisal of the existing trials was undertaken. Moreover, although there was a wide range of central venous pressure values, there were fewer patients in the high central venous pressure group (>12 mm Hg) compared with the intermediate and low groups. Finally, the included studies assessed only static measurements of central venous pressure. It is possible that dynamic changes in central venous pressure better predict fluid responsiveness than static measurements, but current evidence for dynamic central venous pressure.
pressure measurements is very limited.

Although existing data are limited, they suggest that there is no role for the use of central venous pressure to predict fluid responsiveness in acute and critically ill patients.

Editor’s Note: This is a clinical synopsis, a regular feature of the Annals’ Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: Eskesen TG, Weterslev M, Perner A. Systematic review including re-analyses of 1148 individual data sets of central venous pressure as a predictor of fluid responsiveness. Intensive Care Med. http://dx.doi.org/20.1007/s00134-015-4168-4.


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