Critical Review Form

Meta-analysis

Does Central Venous Pressure Predict Fluid Responsiveness?

Chest 2008; 134:172-178

Objective: **"Since CVP plays such a central role in the fluid management strategy of hospitalized patients, the goal of this study was to systemically review the evidence that supports this practice". (p. 173)**

Methods: **Three authors conducted an independent literature search of MEDLINE using the following search terms: central venous pressure AND blood volume OR fluid therapy OR fluid responsiveness. In addition, the authors searched EMBASE, Cochrane Database of Systematic Reviews, and individual article bibliographies. They also searched their personal literature archives and contacted experts in the field. They did not explicitly contact industry or review scientific abstracts.**

Only studies that included either a) the correlation coefficient between CVP and measured blood volume or b) the correlation coefficient or ROC between CVP or change in CVP and change in stroke index/cardiac output following a fluid challenge. Fluid responsiveness was defined by >10% increase in stroke index or cardiac index. Using standardized forms, investigators independently abstracted study design, size, setting, patient population, correlation coefficients, and area under the ROC curve, proportion of patients responding to a fluid challenge and baseline CVP measures.

Statistical heterogeneity was assessed using the Cochrane Q-statistic (significant heterogeneity if p <0.1). The meta-analysis was conducted using the random-effects model.

Guide	Question	Comments
I	***Are the results valid?***	
1.	Did the review explicitly address a sensible question?	Yes. 1) Relationship b/w CVP and blood volume? 2) Ability of CVP to predict FR (fluid responsiveness)? 3) Ability of ΔCVP to predict FR. Since 93% of intensivists use CVP to guide fluid management (Boldt 1998) and the Surviving Sepsis guidelines advocate a CVP target 8-12 mm Hg (non ventilated), what is the scientific basis for relying upon CVP?
2.	Was the search for relevant studies details and exhaustive?	No. The investigators used a limited number of search terms and did not employ the PUBMED MESH terms. Furthermore, they did not perform a hand-search of the literature or include scientific abstracts from relevant meetings. Finally, they did not contact industry (unless those individuals were among the ill-defined "experts" contacted).
3.	Were the primary studies of high methodological quality?	Unknown since methodological quality was not assessed.
4.	Were the assessments of the included studies reproducible?	Probably since standardized data abstraction forms were used. However, the authors do not report discrepancies or discrepancy resolution.
II.	***What are the results?***	

<table>
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<td>1.</td>
<td>What are the overall results of the study?

r= correlation coefficient (>0.8 strong, <0.5 weak)
AUC= 0.9-1 Ideal
0.8-0.9 Adequate
0.7-0.8 Fair
0.6-0.7 Poor
<0.6 Failure</td>
<td>

206 citation were identified in the electronic search and seven from the bibliography review with 24 studies ultimately included in the meta-analysis (5 comparing CVP to blood volume, 19 comparing CVP to fluid responsiveness).
830 subjects from medical to surgical post-op and ICU patients were included (Table 1 and Table 2, p. 174).
Except for the studies evaluating CVP and blood volume, there was no statistically significant heterogeneity noted (unfortunately, neither the Q-statistic nor the p-value were reported).
The correlation coefficient and AUC were clinically useless between both CVP/blood volume and CVP/fluid responsiveness:

<table>
<tr><th>Association</th><th>Correlation Coefficient (95% CI)</th><th>ROC AUC</th></tr>
<tr><td>CVP blood volume</td><td>0.16 (0.03-0.28, r^2=0.02)</td><td>n/a</td></tr>
<tr><td>CVP-CI/SV</td><td>0.18 (0.08 – 0.28)</td><td>0.56 (0.51 – 0.61)</td></tr>
<tr><td>ΔCVP - ΔCI/SI</td><td>0.11 (0.01 – 0.21)</td><td></td></tr>
</table>

The baseline CVP in fluid-challenge non-responders was 9.7 ± 2 mm Hg compared with 8.7 ± 2 mm Hg in fluid responders.
Overall, 56% of patients responded to a fluid challenge.

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<td>2.</td>
<td>How precise are the results?</td>
<td>See 95% CI reported above.</td>
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<td>3.</td>
<td>Were the results similar from study to study?</td>
<td>Per Cochrane’s Q-test, no significant heterogeneity was noted for CVP or ΔCVP for fluid responsiveness. However, there was heterogeneity noted for CVP vs. blood volume. (p. 174) The problem with the Cochrane’s Q-test is that it is often under-powered to detect significant heterogeneity, therefore most systematic review experts advocate reporting the I^2 statistic, too.</td>
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<td>III.</td>
<td>Will the results help me in caring for my patients?</td>
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1.	How can I best interpret the results to apply them to the care of my patients?	The authors conclude that "Neither a high CVP, a normal CVP, a low CVP, nor the response of the CVP to fluid loading should be used in the fluid management strategy of any patient". (p. 175) "The Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock recommend a target CVP of 8 to 12 mm Hg (12 – 15 mm Hg in ventilated patients)". "The results of our study suggest that these recommendations should be revisited." (p. 176)
2.	Were all patient important outcomes considered?	No patient important outcomes were included (i.e. mortality, morbidity, length of stay).
3.	Are the benefits worth the costs and potential risks?	Potentially. Although CVP monitoring is not supported by this meta-analysis, prior studies utilizing CVP as part of EGDT or other bundled sepsis therapies have shown overall mortality benefit. It remains unclear if achieving an isolated CVP goal of 8-12 (12-15 if mechanically ventilated) imparts univariate mortality benefit or if there are other confounders imparting benefit (early fluids/antibiotics/source control/PRBCs/BP support/inotropes, monitored more closely, etc.). If there becomes an increased risk of mortality by abandoning CVP monitoring as part of an EGDT protocol, then there's a piece of the puzzle that may be missing despite the premise of preload responsiveness being "misrepresented" via CVP monitoring. Both under- and over-volume resuscitation (SOAP 2006, Wheeler 2006, Brandstrup 2003, Wiedemann 2006) in critically ill patients impart increased morbidity and mortality. Therefore, a more accurate means of gauging volume responsiveness is needed.

Limitations

1) **Did not use guidelines for diagnostic meta-analysis nor did they follow all the recommendations of Quality of Reporting of Meta-analysis guidelines referenced.**
2) **No search of scientific abstracts, industry of grey literature.**

3) **No assessment for publication bias.**
4) **Limited assessment for heterogeneity (I^2).**
5) **No flow diagram or references for excluded studies. Why were studies excluded? How were discrepancies between investigators to exclude or not exclude resolved?**
6) **No quality assessment of the included literature.**

Bottom Line

Neither a high, normal, or low CVP nor the response of CVP to fluid loading should be used in the fluid management of ICU/post- or peri-operative patients. However, additional studies should assess the role of CVP measurements in conjunction with respiratory variations and it's relation to patient-oriented outcomes when monitored specifically as part of an EGDT protocol. Furthermore, as a direct measure of right ventricular function CVP may be useful in certain patient populations: heart transplant, RV infarct, cardiac tamponade or acute PE patients. These populations, therefore, should also be assessed in future CVP research.