Critical Appraisal of Evidence

Markers of fluid responsiveness in hemodynamically unstable patients

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Summary Heading	Change in cardiac output following passive leg raising is an accurate predictor of fluid responsiveness
Positive findings (likelihood ratio for a positive test, +LR)	**1. Increase in cardiac output or related parameters following passive leg raising**: +LR: 11 [95% CI, 7.6 - 17] Sensitivity: 88% Specificity: 92% **2. Respiratory variation in vena cava diameter measured by ultrasound in mechanically ventilated patients (dispensability index >15%)*:** +LR: 5.3 [95% CI, 3.5 - 8.1] Sensitivity: 85% Specificity: 84% **3. Pulse pressure variation in mechanically ventilated patients, V_t< 7.0mL/kg:** +LR: 7.9 [95% CI, 4.1 - 16] Sensitivity: 72% Specificity: 91%
Negative findings (likelihood ratio for a negative test, -LR)	**1. No increase in cardiac output with passive leg raising:** -LR: 0.13 [95% CI, 0.07-0.22] Sensitivity: 88% Specificity: 92% **2. Respiratory variation in vena cava diameter measured by ultrasound in mechanically ventilated patients (dispensability index <15%)*:** -LR: 0.27 [95% CI, 0.08 - 0.87] Sensitivity: 77% Specificity: 85%
Who was in the studies	2260 hemodynamically unstable patients admitted to intensive care units

Abbreviations: LR: likelihood ratio, CI: Confidence interval, ICU: Intensive care unit
*: Subgroup of intubated patients without spontaneous respiratory efforts

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Narrative

Hemodynamically unstable patients are often given intravenous (IV) crystalloids and colloids to increase cardiac output and improve tissue perfusion[1]. If successful, this is called fluid responsiveness. However, IV fluid therapy may cause pulmonary or peripheral edema, abdominal compartment syndrome, or impair oxygen diffusion[2]. The clinician must decide, based on static and dynamic tests, whether vasopressors or inotropes should be used instead.

Static tests measure central venous pressure, often a good approximation of right atrial pressure, and pulmonary capillary wedge pressure[3]. In contrast, dynamic measurements analyze changes in cardiac output or related parameters in response to bedside maneuvers that transiently change preload. The purpose of the systematic review summarized here is to provide summary estimates of the accuracy of the various symptoms, signs, and measurements used to predict fluid responsiveness in patients with refractory hypotension, signs of organ hypoperfusion, or both.

The systematic review discussed here, included 50 studies (n=2260) from intensive care unit settings, using a variety of invasive and noninvasive reference standards[4]. Fluid responsiveness was defined as an increase in cardiac output of at least 15% in 39 of 50 trials and at least 10% in the other 11 trials. Mean prevalence of fluid responsiveness was 50% (95% CI, 42% - 56%)[4]. In all studies indices were measured before assessment of fluid responsiveness.

In pooled estimates, an increase in cardiac output with passive leg raising had the strongest likelihood ratios for an indicator of fluid responsiveness, as did the presence of respiratory variation in vena cava diameter measured with ultrasound and pulse pressure variation in the subset of mechanically ventilated patients. Lack of change in cardiac output with passive leg raise was the strongest indicator of the absence of fluid responsiveness.

Adverse effects

No direct adverse effects were reported for the tests summarized here.

Caveats

This meta-analysis has several limitations, mainly that generalizability is uncertain. Individuals with arrhythmias, cardiogenic pulmonary edema, oxygen deficits, valvular disease, and ventricular failure were excluded[4]. Some were also excluded if it was deemed dangerous or unethical to withhold fluids, and in some cases patients had already been extensively fluid resuscitated and on vasopressors prior to enrollment. Cardiac output measurements via TTE in these studies were performed by individuals with specific echocardiography training, hence applicability to physicians without equivalent skill is low.

Definitions of fluid responsiveness varied (from 10 to 15%) and most studies did not use thermodilution via pulmonary artery catheter, the reference standard for cardiac output[5,6]. Some trials also used poorly validated methods to determine fluid responsiveness, and virtually all studies enrolled a small convenience sample[4]. The review authors deemed the overall quality of evidence to be high. However, there is tremendous variation in reference standards, shifting definitions of fluid responsiveness, and small convenience samples of often dissimilar subjects. This brings us to question the generalizability of the studies and validity of pooling data.

A meta-analysis published in 2016 found similar numbers to this review for the passive leg raise test, noting that mode of ventilation, type of fluid, starting position for the test, and measurement technique did not affect diagnostic performance[7]. Conversely, a more recent, more rigorous review of dynamic tests found fewer acceptable studies, and weaker estimates of accuracy, particularly for passive leg raise. The authors also found pooling of data to be inappropriate based on high heterogeneity, low study quality, and different reference standards[8]. Finally, a recent review of respiratory variation in vena cava diameter also found this test's utility to be limited, especially when used in spontaneously ventilated patients, and negative results could not be used to rule out fluid responsiveness[9].

Notably, no patient-centered outcomes were examined or reported in this systematic review. The tests assessed were designed to predict fluid responsiveness, a characteristic never rigorously evaluated as a guide for improving resuscitation, despite widespread use. Ultimately, therefore, the tests are physician-centered, and while we have reason to hope they are patient-centered as well, they may or may not lead to improved patient outcomes even if accurate.

In conclusion, we find serious flaws in the evidence base. It is promising that results across these studies—the best data presently available—were generally consistent, but more rigorous, larger investigations are badly needed, both to determine the accuracy of these tests and, of greater importance, to determine the utility of fluid responsiveness as a resuscitation guide. In terms of findings, change in cardiac output following passive leg raising was the most accurate predictor of fluid responsiveness in critically ill subjects who had already undergone initial resuscitation. The accuracy of change in IVC diameter with respiration to predict fluid responsiveness was modest in mechanically ventilated patients, and no test summarized here could rule out fluid responsiveness with certainty.

Author contributions

Li JJ summarized the evidence and drafted the manuscript. Hassel J and Gernsheimer J reviewed the contents, cross-checked the accuracy of the presented data, and edited the manuscript.

Competing interests

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

References

1. Finfer S, Liu B, Taylor C, Bellomo R, Billot L, Cook D et al. Resuscitation fluid use in critically ill adults: an international cross-sectional study in 391 intensive care units. Crit Care. 2010;14(5):R185. doi: 10.1186/cc9293

2. Arikan AA, Zappitelli M, Goldstein SL, Naipaul A, Jefferson LS, Loftis LL. Fluid overload is associated with impaired oxygenation and morbidity in critically ill children. Pediatr Crit Care Med. 2012;13(3):253-8. doi: 10.1097/PCC.0b013e31822882a3

3. Swan HJ, Ganz W, Forrester J, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med. 1970;283(9): 447-451. doi: 10.1056/NEJM197008272830902

4. Bentzer P, Griesdale DE, Boyd J, MacLean K, Sirounis D, Ayas NT. Will This Hemodynamically Unstable Patient Respond to a Bolus of Intravenous Fluids? JAMA. 2016;316(12):1298-1309. doi: 10.1001/jama.2016.12310

5. Sakka SG, Reinhart K, Meier-Hellmann A. Comparison of pulmonary artery and arterial thermodilution cardiac output in critically ill patients. Intensive Care Med. 1999;25(8):843-846. doi: 10.1007/s001340050962

6. Sakka SG, Kozieras J, Thuemer O, vanHout N. Measurement of cardiac output: a comparison between transpulmonary thermodilution and uncalibrated pulse contour analysis. Br J Anaesth. 2007;99(3):337-42. doi: 10.1093/bja/aem177

7. Cherpanath TG, Hirsch A, Geerts BF, Lagrand WK, Leeflang MM, Schultz MJ et al. Predicting Fluid Responsiveness by Passive Leg Raising: A Systematic Review and Meta-Analysis of 23 Clinical Trials. Critical Care Medicine. 2016;44(5):981-91. doi: 10.1097/CCM.0000000000001556

8. Seccombe A, McCluskey L, Moorey H, Lasserson D, Sapey E. Assessing Fluid Resuscitation in Adults with Sepsis Who Are Not Mechanically Ventilated: A Systematic Review of Diagnostic Test Accuracy Studies. Journal of General Internal Medicine. 2019;34(9):1874-1883. doi: 10.1007/s11606-019-05073-9

9. Long E, Oakley E, Duke T, Babl FE. Does Respiratory Variation in Inferior Vena Cava Diameter Predict Fluid Responsiveness: A Systematic Review and Meta-Analysis. Shock. 2017;47(5):550-559. doi: 10.1097/SHK.0000000000000801