Clinical Question
What methods are most effective at determining if a patient will be fluid responsive?

The most recent Common Sense Resident Journal Review article looked at the utility of ultrasound to accurately assess fluid responsiveness in the Emergency Department (ED). In this article, we attempt to look at other modalities that ED physicians may use to quickly determine how patients with various etiologies of hypotension and shock respond to fluid. Initial intervention often involves a fluid bolus of varying amounts to determine if increasing preload can improve the patient’s hemodynamic status along the Frank-Starling curve. Other factors affect the patient’s hemodynamics, however, including systemic vascular resistance and the contractility of the myocardium. Vital signs and the rest of the physical exam are inadequate in determining response to fluid and persistent hypotension may represent alterations in these other factors. Invasive measurements of a patient’s hemodynamic status can be performed with insertion of a Swan-Ganz catheter but its lack of proven benefit in the ED and associated potential complications has led to a decline in its use. As such, patients often receive varying amounts of fluid by ED providers, which is often a large amount of the initial resuscitation volume. As it has also been established that a positive fluid balance is associated with a variety of negative effects and worsened patient outcomes, identifying means to help avoid unnecessary fluid administration is crucial.


The passive leg raise (PLR) has been proposed as an alternative to the traditional fluid challenge with a bolus of IV fluids. It involves straightening and lifting the lower limbs to an angle of 45 degrees, causing an increase in venous return with effects that last about one minute. Cherpanath et al. sought to evaluate the predictive value of PLR in various settings and patients to validate its use. They designed a meta-analysis to compare PLR to fluid challenge using variable outcome measures and measurement techniques, intending to evaluate not only PLR’s utility as a surrogate fluid challenge, but also its use in different clinical settings and across different patient groups.

In compliance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, they reviewed the literature and identified 23 articles to include, totaling 1,034 fluid challenges. The variable practice settings included one obstetrics/anesthesia unit, one ED, and 21 intensive care units. The fluids used in the fluid challenge were mostly normal saline with some colloid and one gelatin. Regardless of fluid composition, the “gold standard” bolus to which PLR was compared was always 500 mL over 10 to 30 minutes.

The outcome measures were divided into “flow” variables (cardiac index, cardiac output, stroke volume, and aortic blood flow) and “pressure” variables (pulse pressure). These measures could be evaluated using four different methods: transthoracic echocardiography, esophageal Doppler, pulse contour analysis, or bioimpedance. Of note, most of these methods are not available in the ED. Many studies used multiple methods and/or outcome variables.

Fluid responsiveness was defined as an increase of 10-15% in cardiac output or its direct derivatives depending on the study. PLR was found to have a pooled sensitivity of 86% (95% CI, 79–92) and a pooled specificity 92% (95% CI, 88–96) when compared to a fluid challenge. The pooling refers to using data from all four measurement methods. They also quote sensitivities and specificities for each individual method and cite no significant difference between the individual methods or the pooled numbers. They performed subgroup comparisons without finding any significant difference between the following groups: studies in France vs. not in France, old studies vs. recent studies, spontaneously breathing vs. mechanically ventilated patients, saline vs. other fluid types, and supine vs. semi-recumbent patients. In terms of the outcome measures, the “pressure” variable of pulse pressure was found to be inferior to all of the “flow” variables, all of which were found to be equivalent.

The authors conclude that PLR, when interpreted using a “flow” outcome measure, is an acceptable surrogate fluid challenge. Their goal was to demonstrate this in various settings and patient populations. They do demonstrate it, but the variety of settings was not sufficient. The study authors mention specific situations in which the response to PLR may be confounded such as in patients on norepinephrine, on propofol, or with intra-abdominal hypertension, and emphasize the importance of avoiding pain during the PLR, as it can cause a sympathetic surge that would affect the interpretation. Overall, this paper supports the use of PLR as a surrogate fluid challenge, however its conclusion is strongest in the ICU population and may require further validation in other clinical settings.


Bentzer et al. conducted a systematic literature review of all English language studies from 1966 to June 15, 2016 on MEDLINE and EMBASE and extracted data to calculate summary measures of the diagnostic accuracy of multiple methods to predict fluid responsiveness in ED or
ICU patients with refractory hypotension: physical exam findings, central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and dynamic measurements of changes in cardiac output in response to bedside maneuvers that transiently increase preload, such as PLR or positive pressure breaths.

Initially, 651 studies were identified and screened. Only studies with over 20 patients were included. Each study was graded for quality as per the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool. Studies graded as level 1 to 3 were included, level 4 and 5 studies were excluded. The authors also excluded studies where the majority of patients had irreversible loss of brain function or major thoracic or cardiac surgery. Ultimately 50 studies, consisting of 2260 hemodynamically unstable patients, were included in the meta-analysis. The investigators extracted data directly from the articles and built a bivariate mixed-effects regression model to pool sensitivities and specificities, also addressing publication bias using the Deek's test when diagnostic tests had 10 or more studies.

Among the studies included, fluid responsiveness was defined as an increase in cardiac output of at least 10-15%. Cardiac output was measured by multiple means, primarily thermodilution using a Swan-Ganz catheter or by transthoracic echocardiography. The summary prevalence of fluid responsiveness was 50% (95% CI, 41-56%). There were two studies that assessed the accuracy of physical exam findings (e.g. dry mucous membranes, decreased skin turgor, increased capillary refill time, tachycardia, jugular venous pressure, pulmonary auscultation, presence or absence of leg edema, ascites, pleural effusion) in predicting fluid responsiveness. Neither study showed these findings increased or decreased the likelihood of fluid responsiveness.

The only static measure included was CVP as a measure of preload. In patients with a lower estimated preload as measured by CVP below the set threshold, there was a moderate likelihood of fluid responsiveness, while patients with CVP at or above the threshold had about half the likelihood of being fluid responsive. The dynamic measurements assessed included pulse pressure variation, stroke volume variation, and inferior vena cava distensibility with breaths as well as in response to passive leg raise.

The authors’ summary findings suggest that physical exam findings do not help differentiate between patients who will or will not respond to fluids, CVP measurement is both invasive and inadequate, variable pulse pressure and IVC diameter can be moderately useful in ventilated patients, and that a change in cardiac output in response to passive leg raise is the most accurate predictor of fluid responsiveness in critically ill patients who have already received initial resuscitation. None of the measures, however, were helpful in ruling out fluid responsiveness.

There were many limitations to this study especially relating to its overall generalizability. A majority of the patients included in the studies had already received fluid prior to enrollment (at least 43 of 50 studies included) and many studies excluded patients with arrhythmias, pulmonary edema, significant valvular disease, right or left ventricular failure, and...
impaired oxygenation. Also, while a change in cardiac output in response to passive leg raise was the most accurate in predicting fluid responsiveness, many studies used methods other than the standard thermodilution via pulmonary artery catheter to define the response. While the authors tried to include higher quality studies by only including studies of level 1 to 3 by the QUADAS tool and excluding studies with sample sizes 20 or less, many of the studies were still quite small (mean sample size of 45 patients) and there were wide ranges of summary measures overall.

Conclusion
While these studies demonstrate that progress has been made in the understanding of determining fluid responsiveness, they also underscore the lack of rigorous, well-validated research. The passive leg raise maneuver represents an alternative to a direct fluid challenge, but it has been less studied in the emergency department setting and it has been shown in the literature that many practitioners perform the maneuver incorrectly. The question then arises as to which method of determining a response to passive leg raise or direct fluid bolus is most accurate and effective. Direct measurement with thermodilution methods with a Swan-Ganz catheter represents a gold standard, while non-invasive methods such as transthoracic echocardiography, stroke volume variation, and pulse pressure variation do show promise but can vary with patient characteristics and different disease states. Bioimpedance monitors or other methods of performing the latter two measures are typically not performed in the ED.

Answer
Direct fluid bolus or a passive leg raise with echocardiographic measurements of a change in cardiac output are the best literature-supported noninvasive means of determining general fluid responsiveness. The incorporation of additional methods (e.g. pulse pressure variation, stroke volume variation, carotid doppler, or cardiac output measurement with a Swan-Ganz catheter) may be utilized for more confident decision-making.

References: