Intensive Care Med (2016) 42:1461–1463
DOI 10.1007/s00134-015-4172-8

EDITORIAL

Jukka Takala

Volume responsive, but does the patient need volume?

Received: 26 November 2015
Accepted: 29 November 2015
Published online: 29 January 2016

J. Takala (✉)
Department of Intensive Care Medicine, University Hospital Bern (Inselspital), 3010 Bern, Switzerland
e-mail: jukka.takala@insel.ch
Tel.: +41-31-632 4144

Rapid administration of intravenous fluid or a "fluid challenge" is one of the most common interventions in the intensive care patient with manifest or perceived hemodynamic problems. The concept of fluid administration to evaluate cardiovascular function in shock was probably first introduced by Max Harry Weil more than 50 years ago [1] and has been referred to as fluid challenge in textbooks and papers since the mid-1970s [2]. The fluid challenge was described as a concept to evaluate the ability of the heart to handle the fluid load in the presence of clinical signs and symptoms of insufficient circulation. A fundamental principle of fluid challenge was defined by Weil in 1965: "The effect of fluid replacement on the clinical status of the patient in shock is gauged by objective changes in circulation, such as blood pressure, mental alertness, urine flow, peripheral venous filling, and appearance and texture of the skin" [1]. Impaired tissue perfusion was already then recognized as a key defect in acute circulatory failure. Subsequently, administration of large volumes of fluids became popular in the management of the widest spectrum of disorders in intensive care patients. Much of this evolution can be traced back to misinterpretations and oversimplification of basic physiology and pathophysiology—often accompanied by invasive hemodynamic monitoring with the pulmonary artery catheter.

Criticism against the apparently excessive and unnecessary volume loading started to evolve early: lung edema (including ARDS), edema in burns, surgical wounds, and gut were associated with excessive fluid loading [3–6], and positive fluid balance appeared as an independent predictor of mortality in various categories of critically ill patients [7].

The concept of predicting fluid responsiveness, an increase in cardiac output or its surrogates in response to fluid bolus, was introduced in clinical practice in the 1990s. Dynamic variations in systolic arterial pressure, arterial pulse pressure, or stroke volume induced by positive pressure ventilation have been used in attempts to guide volume administration. These approaches have several limitations, including highly variable predictive cutoff values, need for controlled mechanical ventilation without inspiratory efforts, and misleading results in the presence of right heart dysfunction. In order to avoid these problems, alternative approaches to predict fluid responsiveness have been developed. Perhaps the best documented is passive leg raising (PLR). The concept is simple: raising the patient's legs should enhance venous return by increasing the stressed volume. If this results in increased cardiac output, then the heart can handle a volume expansion. The advantage is that no volume needs to be given and the change in stressed volume should be reversible. The prerequisite for PLR is rapidly responsive, reproducible measurement of cardiac output or stroke volume.

In a recent article in *Intensive Care Medicine*, Monnet, Marik, and Teboul present a systematic review and meta-analysis of literature on the use of PLR to predict volume responsiveness [8]. They analyzed 21 studies including 991 patients and found in the pooled data that a PLR-induced increase of at least 10 % in cardiac output

predicted an increase in cardiac output that was considered relevant in the original studies with a good pooled sensitivity and specificity. The increases in cardiac output considered relevant in the original studies ranged from more than 7 % to more than 15 %. Using surrogate markers resulted in poor sensitivity but good specificity.

The research group of Teboul et al. has had a leading role in testing and applying in clinical research the concept of predicting fluid responsiveness, with the laudable goal of avoiding unnecessary volume loading. It is not surprising that the bulk of the reviewed papers comes from their own work. Although evaluation of one's own work for quality and bias is itself susceptible to bias, publication bias of less well predictive results cannot be excluded, and the statistical approach can always be discussed, the physiologic and clinical message seems very clear: if cardiac output increases following PLR, it is also likely to do so following a fluid bolus. As pointed out by the authors, a standardized procedure including starting from a semirecumbent rather than horizontal supine position may augment the test effect.

The main issue concerning all attempts to predict fluid responsiveness is what to do with the results. Although the authors briefly discuss the crucial point that fluid responsiveness is not equal to need for fluid, this issue appears to have broad implications in clinical practice. As the recent European Society of Intensive Care Medicine supported FENICE survey shows, fluid challenges are repeated equally frequently regardless of whether the response to initial challenge was positive, uncertain, or negative [9]. Although the survey does not address specific techniques to evaluate the response to fluids, clinicians appear to be predisposed to give fluids even in patients considered to be non-responders according to the response criteria of their choice. The mere expression "fluid responsive" with its positive tone may predispose clinicians to give more fluids independent of whether the patient needs fluids. Indeed, being fluid responsive is normal, whereas giving fluids until the patient is no longer fluid responsive equals creating a new pathologic state—a new iatrogenic problem.

Studies on fluid responsiveness indicate that around 50 % of the fluid challenges studied do not increase cardiac output, i.e., half of the patients are non-responders at the time of the fluid challenge—a surprisingly high proportion. Two very different mechanisms can explain the non-responsiveness. One is limitation of cardiac function; in this case giving more fluids is counterintuitive and may cause harm. The other one is failure to increase stressed volume; this may be due to too small a fluid bolus or slow infusion rate or, more importantly, ongoing vasodilation. Vasoconstriction is very common in hemodynamically unstable patients as a result of hypovolemia and administration of vasoconstricting drugs, and a relevant cause of tissue hypoperfusion. Vasodilatation is needed to restore the perfusion and more fluids will be necessary to maintain the stressed volume and avoid reduction of cardiac output. Importantly, cardiac function limitation and vasoconstriction do coexist; failure to provide fluids to enhance vasodilatation and restoration of tissue perfusion as a result of lack of concomitant increase in cardiac output is misguided. I therefore do disagree with the opening statement by Monnet et al.: "Fundamentally, the only reason to give a patient a fluid challenge is to increase cardiac output"; in my view, the only reason to give a patient a fluid challenge is to restore tissue perfusion. Giving volume to fluid responders as long as they respond should not become the iatrogenic syndrome of the decade; the same is true for failure to give volume to fluid non-responders, who need fluids to maintain their stressed volume while restoring perfusion of vasoconstricted vascular beds.

Compliance with ethical standards

Conflicts of interest None.

References

1. Weil MH, Shubin H, Rosoff L (1965) Fluid repletion in circulatory shock: central venous pressure and other practical guides. JAMA 192:668–674
2. Weil MH, Henning RJ (1979) New concepts in the diagnosis and fluid treatment of circulatory shock. Thirteenth annual Becton, Dickinson and Company Oscar Schwidetsky Memorial Lecture. Anesth Analg 58:124–132
3. Eisenberg PR, Hansbrough JR, Anderson D, Schuster DP (1987) A prospective study of lung water measurements during patient management in an intensive care unit. Am Rev Respir Dis 136:662–868
4. Roth E, Lax LC, Maloney JV Jr (1969) Ringer's lactate solution and extracellular fluid volume in the surgical patient: a critical analysis. Ann Surg 169:149–164
5. Cope O, Moore FD (1947) The redistribution of body water and the fluid therapy of the burned patient. Ann Surg 136:1010–1045
6. Weinstein PD, Doerfler ME (1992) Systemic complications of fluid resuscitation. Crit Care Clin 8:439–448

7. Vincent J-L, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, Moreno R, Carlet J, Le Gall J-R, Payen D, on behalf of the Sepsis Occurrence in Acutely Ill Patients Investigators (2006) Sepsis in European intensive care units: results of the SOAP study. Crit Care Med 34:344–353

8. Monnet X, Marik P, Teboul J-L (2015) Passive leg raising for predicting fluid responsiveness: a systematic review and meta-analysis. Intensive Care Med. doi: 10.1007/s00134-015-4134-1

9. Cecconi M, Hofer C, Teboul J-L, Pettila V, Wilkman E, Molnar Z, Della Rocca G, Aldecoa C, Artigas A, Sameer J, Sander M, Spies C, Lefrant J-Y, De Backer D, on behalf of the FENICE Investigators and the ESICM Trial Group (2015) Fluid challenges in intensive care: the FENICE study. A global inception cohort study. Intensive Care Med 41:1529–1537