Critical review

Fluid optimization strategies in critical care patients

X García*, G Gruartmoner, J Mesquida

Abstract

Introduction

Fluid optimization is an important feature in haemodynamic resuscitation. Despite recent advances, fluid management in clinical practice remains sometimes highly empirical. Well-defined endpoints of resuscitation, not only global but also focused on the microcirculatory level, as well as the correct timing for fluids administration, always according to any of the available parameters to asses fluid-responsiveness, are the essential points in order to optimize resuscitation with fluids avoiding deleterious effects. The aim of this paper is to discuss fluid optimization strategies in critical care patients.

Conclusion

Fluid management is a key feature in the haemodynamic resuscitation of critically ill patients and its optimization is important for a patient's outcome.

Introduction

In daily practice, the clinician is often confronted with situations in which an intervention is required to treat haemodynamic instability due to cardiovascular insufficiency, characterized by cellular dysoxia that, maintained over time, might progress to multi-organ failure and death. There are several approaches to haemodynamic resuscitation but since most common causes of shock have some degree of insufficient intravascular volume, expansion with fluids is recognized as one of the first steps of haemodynamic resuscitation.

Despite many advances in the last years such as new parameters and techniques to assess fluid-responsiveness or clinical studies focused in searching optimal fluid balance, clinical guidelines not always reflect these advances and fluid optimization in clinical practice remains sometimes highly empirical.

This paper aims to analyse the parameters and techniques we should use in our clinical practice to assess fluid management and the best strategies for fluid optimization in critical care patients.

Discussion

Resuscitation strategies: Trying to optimize fluid load

The goal of fluid therapy in critically ill patients is to restore tissue perfusion. The use of standardized algorithms of resuscitation, with validated global endpoints like central venous oxygen saturation (SvO_2), lactate clearance or a certain rate of oxygen delivery in surgical patients, has resulted in substantial improvements in morbidity and mortality of critically ill patients[1, 2]. Although current sepsis management guidelines have well-established tissue perfusion endpoints, dosing intravenous fluid administration remains highly empirical during the resuscitation process. The Surviving Sepsis Campaign guidelines for management of sepsis recommend the initial administration of repeated fluid challenges of >1000 ml of crystalloids or 300–500 ml of colloids[3]. According to these guidelines, the infusion of fluids should be maintained until certain predetermined values of central venous pressure (CVP) are achieved. Importantly, CVP is presented as an endpoint *per se*, not only as a tool for assessing volume responsiveness. On a physiological basis, volume expansion should be only performed when an increase in stroke volume is expected and, CVP has repeatedly failed in predicting preload-dependency[4]. Therefore, CVP seems not to be a reliable surrogate of the adequacy of intravascular volume status, and using CVP not only as a tool, but also as an endpoint in the resuscitation process might be deleterious for our patients. Importantly, a more positive fluid balance has been associated to increased mortality[5,6]. Whether fluid balance independently affects outcome or it is just a confounder, a marker of severity of illness, remains unclear, but clearly aggravating fluid balance by using the wrong tools and the wrong endpoints should not take place in the context of current knowledge.

Another important question we should take into account is whether the patient's tissue is fully resuscitated when the classical endpoints are achieved. Some interesting studies in the last years have shown that patients can still have hypoperfusion markers despite classical resuscitation endpoints are achieved. The study by Vallée *et al.*[7] found that patients with a central venous-to-arterial pCO_2 difference $[P(v-a)CO_2]$ higher than 6 mmHg had worse prognosis when compared to those with $[P(v-a)CO_2]$ lower than 6 mmHg despite central venous saturation was over 70% in both groups.

In addition, during the last decade, overwhelming evidence has emerged indicating that, despite normalization of global surrogates of tissue perfusion, local tissue hypoperfusion might persist, and these microcirculatory alterations are associated to

* Corresponding author
Email: xgarcia@tauli.cat

Critical Care Center, Hospital de Sabadell, Corporació Sanitària Universitària Parc Taulí, Universitat Autònoma de Barcelona, Barcelona, Spain

worsen the outcome[8]. Nevertheless, microcirculatory endpoints have not been prospectively tested. Therefore, if we expect to use them, we need to consider that the response of the microvascular system might, in some situations, differ from the macrohaemodynamic behaviour. Then, macrohaemodynamic fluid-responsiveness might not be equal to microcirculatory fluid-responsiveness. Using video-microscopic imaging techniques, several authors have reported persistent microcirculatory alterations despite improvements in cardiac output after volume expansion, with dissociated response of the micro- and the macro-vascular compartments[9–11]. Therefore, one of the further steps in haemodynamic resuscitation research may be to develop parameters for assessing fluid-responsiveness targeted to microcirculatory perfusion. Nevertheless, microcirculatory monitoring probably needs to be complementary to the macrovascular approach, and further clinical investigations should explore whether this combined approach results in better patient outcomes.

Regardless of the chosen endpoint, fluid administration is crucial for any of the proposed algorithms, and fluids should be given while fluid-responsiveness is demonstrated and global tissue perfusion surrogates have not normalized.

Finally, another crucial point is timing of fluid resuscitation. Some studies have brought into light that resuscitation interventions did not result in outcome improvements when initiated too late in the time course of the disease[12], once tissue damage was established. The significance of the time factor has been also endorsed by some observations at the microcirculatory level, where the response to fluid administration has proven to differ according to the elapsed time since the onset of the disease, so that perfusion of small vessels in response to volume

expansion improves only when fluids were administered early (within 24 h) after diagnosis of septic shock, but not when administered late in the course of the disease. Importantly, this effect was again independent from those at the global haemodynamic level[10].

Summarizing, volume should be administered early in the time course of tissue hypoxia and, ideally, only when the patient has benefits from this intervention. In order to avoid unnecessary (and potentially deleterious) fluid administration, assessing fluid-responsiveness is mandatory.

Assessing volume responsiveness at the bedside

A primary resuscitation question is whether or not patients will increase their cardiac output (CO) in response to a fluid challenge. Volume responsiveness is arbitrarily defined as an increase of ≥15% in cardiac output in response to a 500 ml bolus fluid challenge[13]. Although the presence of fluid-responsiveness in a subject does not equate for the need of fluids, it does define that if fluids are

infused, CO will increase. Importantly, all static haemodynamic estimates of preload, including central venous pressure, pulmonary artery occlusion pressure, right ventricular end-diastolic volume and left ventricular end-diastolic area are poor predictors of volume responsiveness[4].

According to Frank–Starling law (Figure 1), there is a positive relationship between preload (defined as end-diastolic volume) and stroke volume, and this relation follows a curvilinear shape. Consistently, a certain increase in preload will produce a significantly greater increase in stroke volume on the steep ascending portion of the curve, defining a preload-dependent area, where volume expansion would significantly increase cardiac output. On the opposite flatter part of the curve, we can define a preload-independent area, where volume expansion produces no significant changes in stroke volume.

The simplest method to assess fluid-responsiveness is to give an intravenous volume bolus and evaluate the haemodynamic response.
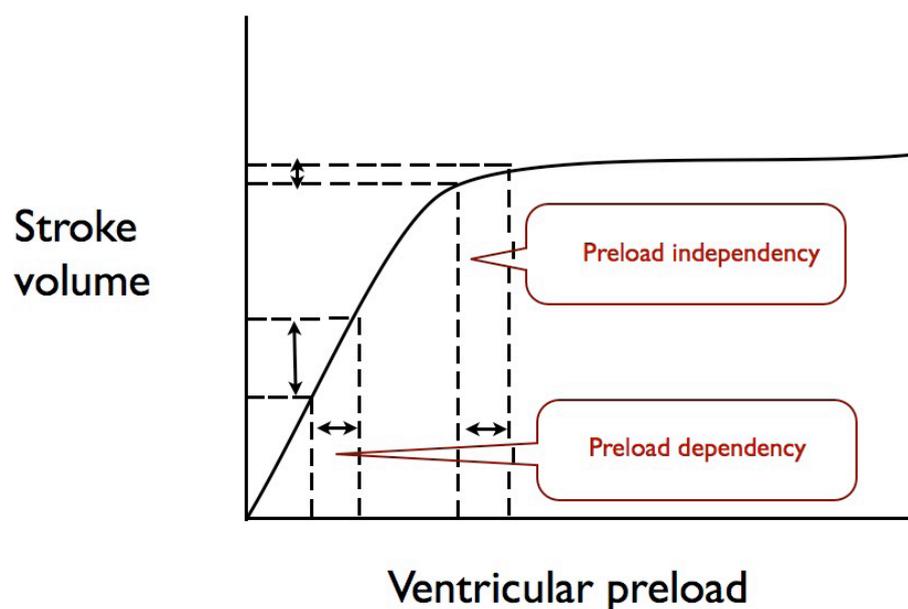
Figure 1: Frank–Starling curve. A certain increase in ventricular preload produces a greater increase in stroke volume in the steep part of the curve (preload dependency zone) than in the flat part (preload independency zone).

Critical review

Volume expansion in normal individuals almost always produces an increase in stroke volume, but in shock states the rate of response markedly falls to approximately 50%. Furthermore, fluid overload due to aggressive volume expansion may lead to deleterious effects, such as an increase in extravascular lung water or acute cor pulmonale[4]. Therefore, it seems crucial to have the possibility to discriminate those patients who will increase their CO and those who will develop injurious effects after the fluid challenge. There are different parameters and techniques we can use in our daily practice to assess volume responsiveness depending on patient characteristics.

Changes in left ventricular output during positive pressure ventilation
During the inspiratory phase of positive pressure ventilation, intrathoracic pressure increases passively, increasing right atrial pressure causing venous return to decrease, decreasing right ventricular output, and after two or three heart beats, also left ventricular output if both ventricles are volume responsive[13]. Thus, cyclic changes in left ventricular stroke volume and its coupled arterial pulse pressure are seen and the magnitude of these changes is proportional to volume responsiveness. From this physiological approach, we can obtain the following parameters to assess volume responsiveness:

- Stroke volume variation (SVV): Values of SVV > 10% have shown a high-predictive power[14] of volume responsiveness. This parameter requires a monitoring tool with the capability to measure pulse-contour analysis.
- Pulse pressure variation (PPV): Since pulse pressure is primarily determined by left ventricular stroke volume in a given respiratory cycle, the PPV in this space of time will be dependent only on stroke volume variation. PPV is easily obtained at the bedside, automatically calculated from the signal of the arterial line in most haemodynamic monitors. A value of PPV > 13% predicts fluid responsiveness with high sensibility and specificity. Similarly, a systolic pressure variation (SPV) ≥ 10 mmHg (or 5 mmHg of its Δdown component) (see Figure 2) can be used as a predictor of fluid-responsiveness, but its predictive power is slightly lower than PPV[15].
- Changes in the diameter of inferior vena cava (ΔD_{IVC}): Based in the same physiologic concept of the increase in thoracic pressure during positive pressure ventilation, flow changes in inferior vena cava reflected by measuring its diameter, also demonstrate excellent discrimination in predicting volume responsiveness. Therefore, positive-pressure inspiration associated caval collapse, quantified as a decrease in the inferior caval diameter of >12% predicts volume responsiveness[16].

The concept applies to superior caval vein too[17].

Although powerful tools, these parameters are highly dependent on the cyclic changes in intrathoracic pressure being regular and great enough to alter central venous pressure. Thus, tidal volumes of ≤7 ml/kg or the imposition of variable spontaneous respiratory efforts often result in PPV and SVV values invalid as fluid-responsiveness predictors. Similarly, all these techniques assume a fixed heart rate. Thus, in the setting of atrial fibrillation or frequent premature ventricular contractions, these measures become inaccurate[15] as well as in patients with right heart failure[18].

Assessing fluid-responsiveness during spontaneous breathing
- Right atrial pressure changes during inspiration:
During spontaneous inspiration, intrathoracic pressure decreases and it allows an increase in venous return. Therefore, if right ventricular function is preserved and transfers this increased blood through the pulmonary circulation then right atrial pressure will decrease with inspiration. An inspiratory decrease in right atrial pressure of more than 1 mmHg when intrathoracic pressure decreases more than 2 mmHg may predict preload responsiveness. Though measuring such small changes in right atrial pressure is often difficult, greater negative changes in right atrial pressure are usually easier to identify and may be useful to predict fluid-responsiveness in spontaneously breathing patients[19].
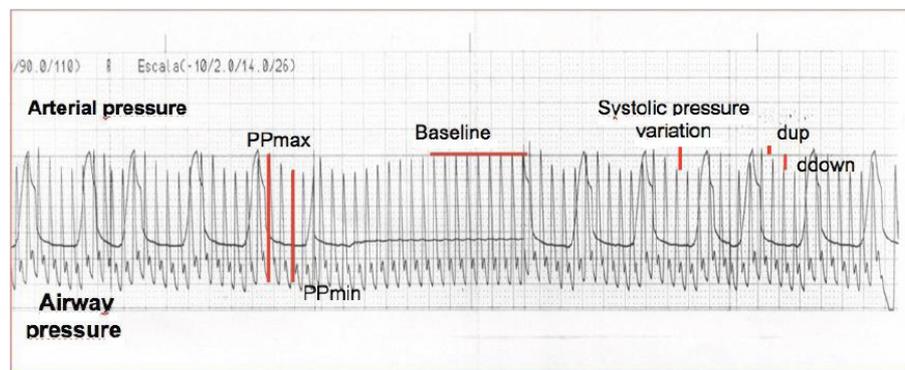
$$\text{PPV: PPmax-PPmin / [(PPmax + PPmin)] /2 x 100}$$

Figure 2: How to calculate systolic pressure variation and pulse pressure variation.

OA Critical Care
Open Access

Critical review

- Passive leg raising manoeuvre:
Passive leg raising (PLR) to 45° for 3 min while keeping the head at 0° (Figure 3) transiently increases venous return to the heart. In fluid responders, we should expect a transient increase of CO[20]. The advantage of the PLR manoeuvre is that it can be done without special equipment, is easy and quickly reversible and can be repeated safely over time. It can be performed in patients breathing spontaneously and also in absence of sinus rhythm, thus makes it the election test to assess volume responsiveness in elective patients. Its primary limitation is that in profoundly hypovolemic patients the transfer of blood may be insufficient to cause a CO response, and it could not be done in some patients with abdominal or lower limb trauma due to inability to perform the manoeuvre. This parameter can also be used in patients under mechanical ventilation.
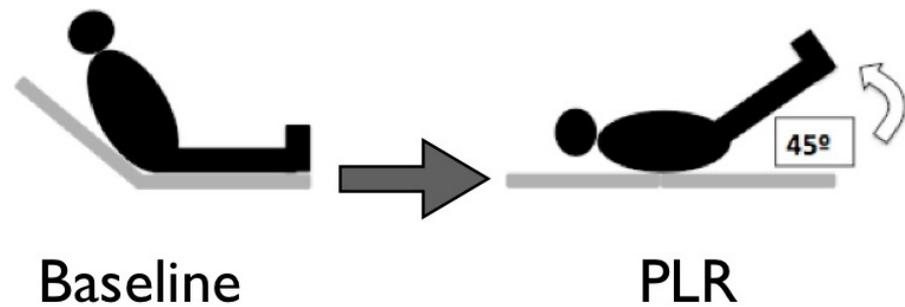
- Arterial pressure changes during Valsalva manoeuvre:
Pulse pressure changes and systolic pressure changes during a Valsalva manoeuvre (a forced expiration against a closed glottis) may be a feasible tool for assessing fluid-responsiveness (Figure 4) in patients without mechanical ventilation. In a single study, a pulse pressure change of 52% or a systolic pressure change of 30% during the Valsalva manoeuvre showed a good predictive power for volume responsiveness[21]. However, the technique requires previous patient training and only this study supports these data.

As previously shown, there are many techniques and parameters to assess fluid-responsiveness but each of them has its own limitations that makes it useless in certain situations. If none of the predictors can be used, we can always perform a fluid challenge giving a bolus of intravenous
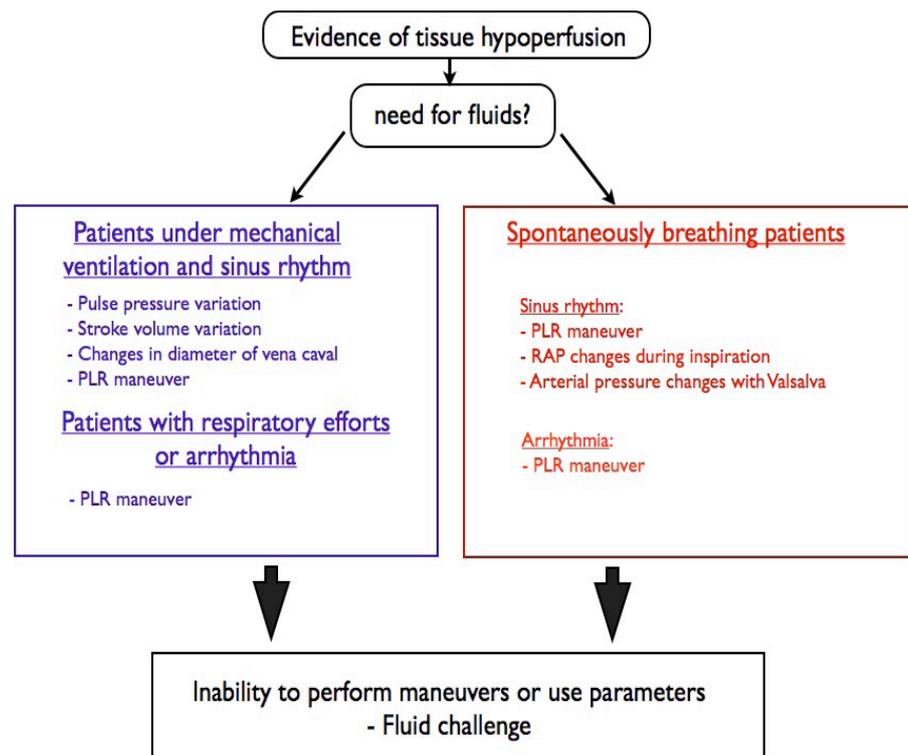

Figure 3: PLR manoeuvre

Figure 4: Available parameters for assessing fluid-responsiveness.

fluid and assessing the cardiovascular response measuring the variation of cardiac output after it.

Conclusion
Fluid management is a key feature in the haemodynamic resuscitation of critically ill patients and its optimization is important for a patient´s outcome. Resuscitation with fluids should be done according to parameters capable to assess patient's volume responsiveness, if possible, must be started quickly after shock diagnosis, if indicated, and referred

to reach concrete endpoints. The relationship between resuscitation (also with fluids) and microcirculation targets seems to have a high importance but needs to be further explored.

References
1. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001 Nov;345(19):1368–77.
2. Pearse R, Dawson D, Fawcet J, Rhodes A, Grounds RM, Bennett D. Early

goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial. Crit Care. 2005 Nov;9(6):R687–93.

3. Dellinger R, Levy M, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013 Feb;41(2):580–637.

4. Michard F, Teboul JL. Predicting fluid responsiveness in ICU patients: a critical analysis of the evidence. Chest. 2002 Jun;121(6):2000–8.

5. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, et al. Sepsis in European intensive care units: results of the SOAP study. Crit Care Med. 2006 Feb;34(2):344–53.

6. Boyd JH, Forbes J, Nakada TA, Walley KR, Rusell JA. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. Crit Care Med. 2011 Feb;39(2):259–65.

7. Vallée F, Vallet B, Mathe O Parraguette J, Mari A, Silva S, et al. Central venous-to-arterial carbon dioxide difference: an additional target for goal-directed therapy in septic shock? Intensive Care Med. 2008 Dec;34(12):2218–25.

8. de Backer D, Creteur J, Preiser JC, Dubois MJ, Vincent JL. Microvascular blood flow is altered in patients with sepsis. Am J Respir Crit Care Med. 2002 Jun;166(1):98–104.

9. Trzeciak S, Dellinger RP, Parrillo JE, Guglielmi M, Bajaj J, Abate NL, et al. Early microcirculatory perfusion derangements in patients with severe sepsis and septic shock: relationship to hemodynamics, oxygen transport, and survival. Ann Emerg Med. 2007 Jan;49(1):88–98.

10. Ospina-Tascon G, Neves AP, Occhipinti G, Donadello K, Büchele G, Simion D, et al. Effects of fluids on microvascular perfusion in patients with severe sepsis. Intensive Care Med. 2010 Jun;36(6):949–55.

11. Monnet X, Julien F, Ait-Hamou N, Lequoy M, Gosset C, Jozwiak M, et al. Lactate and veno-arterial carbon dioxide difference/arterial-venous oxygen difference ratio, but not central venous oxygen saturation, predict increase in oxygen consumption in fluid responders. Crit Care Med. 2013 Feb.

12. Kern JW, Shoemaker WC. Meta-analysis of hemodynamic optimization in high-risk patients. Crit Care Med. 2002 Aug;30(8):1686–92.

13. Michard F, Boussat S, Chemla D, Anguel N, Mercat A, Lecarpentier Y, et al. Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. Am J Respir Crit Care Med. 2000 Jul;162(1):134–8.

14. Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. Crit Care Med. 2009 Sep;37(9):2642–7.

15. Berkenstadt H, Margalit N, Hadani M, Friedman Z, Segal E, Villa Y, et al. Stroke volume variation as a predictor of fluid responsiveness in patients undergoing brain surgery. Anesth Analg. 2001 Apr;92(4):984–9.

16. Feissel M, Richard F, Faller JP, Teboul JL. The respiratory variation in inferior vena cava diameter as a guide to fluid therapy. Intensive Care Med. 2004 Sep;30(9):1834–7.

17. Vieillard-Baron A, Chergui K, Rabiller A. Superior vena cava collapsibility as a gauge of volume status in ventilated septic patients. Intensive Care Med. 2004 Dec;30(12):1734–9.

18. Vieillard-Baron A, Charron C. Preload responsiveness or right ventricular dysfunction? Crit Care Med. 2009 Sep; 37(9):2662–3.

19. Magder SA, Georgiadis G, Tuc C. Respiratory variations in right atrial pressure predict response to fluid challenge. J Crit Care. 1992;7:76–85.

20. Monnet X, Teboul JL. Passive leg raising. Intensive Care Med. 2008 Apr; 34(4):659–63.

21. Monge García MI, Gil Cano A, Díaz Monrové JC. Arterial pressure changes during the Valsalvamaneuver to predict fluid responsiveness in spontaneously breathing patients. Intensive Care Med. 2009 Jan;35(1):77–84.