Evaluation of fluid responsiveness in circulatory shock

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Abstract
Shock is a frequent syndrome in critical care medicine, and fluids represent the first therapeutic approach. Nevertheless, fluids overload could have harmful side effects for the patients, leading to a higher mortality rate and length of stay on intensive care unit. Therefore, in the last decade, several methods have been developed and validated in order to correctly assess the fluid responsiveness, defined as a rise in cardiac output or stroke volume greater than 10-15%. These techniques are represented by stroke volume variation, pulse pressure variation, the variation of the diameter of the inferior vena cava, the test of the Passive Leg Raising, and the mini-fluid challenge test.

Abbreviations: \(O_2\): oxygen, \(D_0_2\): delivery of oxygen, CO: cardiac output, ICU: intensive care unit, SV: stroke volume, SVV: stroke volume variation; PPV: pulse pressure variation, IVC: inferior vena cava, PLR: passive leg raising

Introduction
Shock is universally defined as a state of generalized hypoperfusion in which the contribution of mitochondrial oxygen \((O_2)\) is inadequate to meet the metabolic needs of the patient. The steps for the treatment are targeted to the optimization of the delivery of \(O_2\) \((D_0_2)\), through the supplement of \(O_2\) and the correction of the cardiac output \((CO)\). Additionally, the second aim is represented by the identification, and consequently the treatment of the specific cause of shock. In order to properly support the organ perfusion, the first therapeutic choice is represented by fluids, through which the pre-load and the circulating volume could be optimized. Fluid therapy is clear how fluid overload could have extremely harmful effects in shocked patients. In fact, it has been shown that fluid overload prolongs the average length of stay on intensive care unit \((ICU)\), it slows down weaning from mechanical ventilation and increases the mortality rate in cases of septic shock, acute respiratory distress syndrome, and acute kidney injury [1,2]. Therefore, the advantages obtained from the volemic expansion in terms of an increase in \(D_0_2\) and \(CO\), should be balanced with the risk of causing or aggravate a condition of pulmonary or tissutal edema [3].

The clinical response to fluid administration is directly related to the patient’s pre-load. Indeed, depending on the length of cardiac muscle fibers, fluids could lead to a significant increase in \(CO\). It is properly defined “fluid responsiveness” an increase of \(CO\) or stroke volume \((SV)\) greater than 10-15% following the administration of a fluid challenge \((3\text{ ml} / \text{kg of crystalloid in 5-10 minutes})\) [4,5].

As only 50% of patients in shock benefit from the fluid challenge, over the last decades, numerous efforts have been made to find a tool that could predict the responsiveness to fluid therapy. In fact, historically in the clinical practice, the measurements of central venous pressure and pulmonary wedge pressure have been proposed. Despite recent evidences deny that these values are predictive of fluid responsiveness, still a large number of anesthesiologists use this parameters to guide the fluid therapy [6,7].

The ideal fluid responsiveness assessment tool should be easily obtainable, non-invasive, low cost and standardized for each patient. Unfortunately, nowadays there is no such method that includes all of these advantages. Currently, the validated methods to evaluate the fluid responsiveness are represented by Stroke Volume Variation (SVV), Pulse Pressure Variation (PPV), the variation of the diameter of the inferior vena cava (IVC), the test of the Passive Leg Raising (PLR) and the mini-fluid challenge test (Table 1).

Fluid responsiveness evaluation
SVV is the first developed method of hemodynamic parameters evaluation. It could be measured only in mechanically ventilated patients. During the inspiration, the preload decreases, due to the reduction of venous return to the right atrium, and the afterload enhances, due to the increase in the ventricular transmural pressure. These changes hesitate in a reduction in the right ventricle SV, which after a few beats it is also reflected in the left chambers. Therefore, the variation of SV higher than 12% during respiratory cycles is an index of low preload, while small variations between the inspiratory and the expiratory phases are an indirect sign of greater length of cardiac muscle fibers [3]. PPV represents the variation between inspiration and expiration of pulsatory pressure, defined as the difference between systolic and diastolic blood pressure. In fact, as SV, this parameter has variations during the respiratory cycle. Therefore, a variation greater than 13% of PPV, is an index of low preload, and consequently a possibly positive responsiveness to fluid therapy. However, these methods present some limits, as they can not be adopted in patients with non-invasive mechanical ventilation, or with low tidal volume, or with poor pulmonary compliance, or with cardiac arrhythmias [8]. Mechanical ventilation induces oscillations of intra-thoracic pressure, which is reflected in variations of the diameter of the IVC.

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Key words: cardiac output, fluid challenge, fluid responsiveness, haemodynamic monitoring, passive leg raising, stroke volume

Received: May 30, 2017; Accepted: June 23, 2017; Published: June 26, 2017

Trauma Emerg Care, 2017 doi: 10.15761/TEC.1000143

Volume 2(5): 1-2
Therefore, it has been shown that the measurement of this difference obtained through bedside transthoracic ultrasound is related to a low preload value. Also the diameter variations of the superior cava vein is considered a parameter to guide fluid therapy, but it could be evaluated only with transesophageal ultrasound, that is a more invasive technique. However, there is still no agreement on the threshold value of collapsibility, which is currently considered between 12 and 40% [9]. Unfortunately, this parameter did not demonstrate reliability in patients in spontaneous breathing [10].

Also the PLR test is considered a good index of fluid responsiveness. In fact, lifting the lower limbs for 30 - 90 seconds induces a mobilization of blood from the venous compartment to the heart of about 300 ml. This test has the advantage of being able to be repeated over time, without causing fluids overload for the patient, and being completely non-invasive. Furthermore, the PLR test can be used in the presence of cardiac arrhythmias, in patients in spontaneous breathing. The effect of PLR on the CO is visible only for a few minutes and therefore the patient needs a monitoring system capable of identify sudden and short-term variations [11].

The fluid challenge test is the most direct way to evaluate responsiveness to fluid therapy. However, this method, unlike the PLR test, inevitably leads to the administration of a volume of fluid not negligible, especially in those patients in which the test should be repeated. As a result, it is has been validated the mini-fluid challenge test, in which a quantity of low fluids (100 ml of colloid) is administered. Also in this case, hemodynamic benefit is evidenced for a short period of time, and therefore the patient needs an extremely accurate monitoring system [12].

Conclusions

Nowadays, all the validated method to assess fluid responsiveness in patients with shock present some limitations. On the other hand, fluid administration without a certain guide could lead to detrimental consequences for the patient. In fact, fluids should be considered as drugs, and the dosage should be evaluated depending on the need of each specific case. However, these methods are very well applied to the operating theatre and the ICU, but the challenge for the future should be to find a non-invasive and low-cost method to assess the responsiveness to fluids, and therefore applicable also in setting of care as the emergency department or the pre-hospital medicine, where currently the tools for assessing fluid therapy are still limited.

Table 1. Methods predicting fluid responsiveness.

| Test                  | Limitations                                                                 |
|-----------------------|-----------------------------------------------------------------------------|
| SVV / PPV             | Spontaneous breathing, cardiac arrhythmias, right ventricle failure, low tidal volume. |
| Diameter variations of IVC | Spontaneous breathing, low lung compliance, operator-dependent technique. |
| PLR Test              | Requires accurate and constant monitoring of the CO, intra-abdominal hypertension. |
| Mini-fluid challenge test | Requires accurate and constant monitoring of the CO, risk of fluid overload if repeated several times. |

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