Editorial

Fluid responsiveness raises many questions—echocardiography may be the answer

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Vignon *et al*. (1) are to be commented for their well-designed and written manuscript on the diagnostic accuracy of echocardiographic parameters for fluid responsiveness in ventilated patients with various types of shock.

Fluid responsiveness is a common challenge for an intensivist in everyday clinical practice but so far no technique has been recognized as the most sensitive for its assessment and for the evaluation of the complex interactions of multiple organ dysfunctions and the dynamic effects of therapeutic interventions, especially in unstable hemodynamic conditions. Echocardiography has been investigated as a potential tool for fluid responsiveness since it is feasible even at bedside, useful for monitoring and able to provide real time information on heart-lung interaction, volume status and the effect of mechanical ventilation. Unfortunately available evidence on the ability of echocardiography for the assessment of fluid responsiveness is so heterogeneous for methodology (transthoracic *vs.* transesophageal), clinical conditions (stable/unstable, ventilated/spontaneous breathing) and etiology of disease (sepsis/other types of shock) that echocardiographic parameters may be used in the wrong context/patient with unpredictable consequences on management.

On a conceptual basis, when assessing fluid responsiveness in a single patient, it should be considered that if cardiopulmonary function cannot compensate for the increase in preload, fluid loading (even small volumes) may compromise microvascular perfusion and oxygen delivery and cause or aggravate peripheral and pulmonary edema (2-5). Thus, the first question for a front line intensivist managing a critical care patient is: in my patient can fluid responsiveness be assessed or may it be deleterious? For instance, the presence of right ventricular (RV) dilatation and RV dysfunction stands against fluid challenge which can itself worsen RV dysfunction and thus aggravate hemodynamic instability. In other terms, fluid responsiveness assessment needs a preliminary echocardiographic exam, including the evaluation of biventricular function, systolic pulmonary arterial pressure, the presence or absence of valvular disease and diastolic function.

If volume expansion is not contraindicated, which echocardiographic parameter should be used in our patient? It is conceivable that each parameter should be chosen on the basis of available evidence, type of echocardiography (transthoracic *vs.* transesophageal) and, if possible, etiology of disease in which this parameter has been tested (6). The methodology used for fluid responsiveness is also influenced by the patient's clinical conditions (i.e., passive leg rising should not be performed in post abdominal surgery).

Table 1 summarizes the main investigations assessing fluid responsiveness in ventilated critically ill patients according to the type of echocardiography (transthoracic, transesophageal or both). Investigations performed in cardiac surgery and in the operating room have not been included. The contribution of each investigation on a clinical ground stems from the critical interpretation of

Table 1 Main studies investigating fluid responsiveness by means of echocardiography in adult ventilated patients

Investigations	Population	Methods	Results
Transthoracic echocardiography			
Machare-Delgado *et al.* [2011] (7)	Eighteen mechanical ventilated patients on vasopressor support and with worsening organ function	Volume expansion (500 mL of saline); IVC variations	IVC variation proved to be a useful technique to predict fluid responsiveness
Muller *et al.* [2012] (8)	Thirty nine ventilated critically ill patients with acute circulatory failure	100 mL hydroxyethyl starch infusion (1 minute), and an additional infusion of 400 mL hydroxyethyl starch (14 minutes); subaortic velocity-time integral (VTI)	ΔVTI 100 accurately predicted fluid responsiveness
Wu *et al.* [2014] (9)	Fifty five ventilated patients	50 mL infusion of crystalloid solution over 10 seconds	CO and VTI after the administration of 50 mL crystalloid solution can accurately predict fluid responsiveness
de Oliveira *et al.* [2016] (10)	Twenty post-operative ventilated patients	500 mL of crystalloids over 15 minutes	PPV showed superior discriminative abilities than ΔIVC
Both transthoracic and transesophageal echocardiography			
Charbonneau *et al.* [2014] (11)	Forty four ventilated septic shock patients	7 mL/kg volume expansion with plasma expander	ΔSVC was superior to ΔIVC in predicting fluid responsiveness
Transesophageal echocardiography			
Feissel *et al.* [2001] (12)	Nineteen ventilated septic shock patients with preserved LVEF	Volume expansion	Analysis of respiratory changes in aortic blood velocity is an accurate method for predicting the hemodynamic effects of volume expansion (threshold value 12%)
Wilkman *et al.* [2014] (13)	Twenty ventilated septic shock patients	Temporary elevation of PEEP from 10 to 20 cmH_2O during an end-expiratory pause; fluid responsiveness defined as an increase in cardiac output of 15% following fluid challenge	Decrease in MAP related to elevation of PEEP predicted fluid responsiveness

CO, cardiac output; VTI, aortic velocity time index; ΔSVC, respiratory variation of superior vena cava; PPV, pulse pressure variation; ΔIVC, respiratory variations of inferior vena cava; LVEF, left ventricular ejection fraction; PEEP, peak end expiratory pressure.

reliability and accuracy of the single parameter investigated, taking into account not only the number of patients enrolled but also methodology used to assess fluid responsiveness (i.e., volume expansion *vs.* passive leg raising). To make things worse, thresholds may vary from one study to another. The major task for a clinician is probably to "adapt" methodology and parameters to the single patient, in other term to choose them accordingly to the clinical conditions of the patients and/or to the availability and/or expertise in the echocardiographic technique.

Fluid responsiveness was investigated by means of transesophageal echocardiography in septic shock in three studies published in 2001 and in 2014, respectively, all assessing different parameters. Wilkman *et al.* (13) observed that decreased in mean arterial pressure (MAP) due to an increased in peak end-expiratory pressure (PEEP) predicted fluid responsiveness (cut off value of ΔMAP for clinical use –8%) while Feissel *et al.* (12), in a small subgroup of 19 patients with septic shock and preserved LV systolic function, observed that analysis of respiratory changes in aortic blood velocity was an accurate method for predicting the hemodynamic effects of volume expansion. Different parameters were assessed by Charbonneau *et al.* (11) who observed that variations in superior vena cava diameters (ΔSVC) was significantly more accurate than changes in inferior vena cava width (ΔIVC) in predicting

fluid responsiveness in 44 mechanical ventilated septic shock. The design of the latter study was more complex since they used both transthoracic and transesophageal echocardiography. However, in all these investigations, fluid responsiveness was defined as the volume expansion-induced increase in cardiac index was > or =15%.

In the last years, an increasing number of papers have been published on fluid responsiveness assessed by means of transthoracic echocardiography. Two are the parameters mainly investigated: subaortic velocity-time integral (VTI) and variation in inferior vena cava (IVC) diameters. Variations in VTI proved to predict fluid. responsiveness in ventilated septic shock even after 100 mL of hydroxyethyl starch infusion (1 minute) (8), and this finding was confirmed in ventilated patients also with the infusion of smaller amounts of crystalloid solution (50 mL over 15 seconds) (9).

Assessment of IVC size and its change in diameters has been investigated as a tool for fluid responsiveness (14,15), thanks to easy of acquisition and reproducibility of measurements, even if with conflicting results (8,11). However, IVC size and variations may not indicate volume status and therefore predict fluid responsiveness such as mechanical ventilation with high PEEP which itself increase IVC pressure thus increasing or leaving unaltered IVC diameter (16). Similarly, in patients with critical intra-abdominal hypertension and abdominal compartment syndrome it is conceivable to suppose that IVC variations are determined by its transmural pressure, (the pressure gradient between abdominal and intrathoracic compartments) regardless volume status. IVC width and changes are influenced by several cardiac conditions.

A cardiac condition, frequently encountered in the ICU setting, is represented by right ventricle dysfunction (independently of its etiology, ischemic or not) which leads to increase in right side filling pressure and systemic venous congestion and therefore to IVC dilatation. Obviously, in this clinical condition, fluid responsiveness cannot be assessed by IVC variations. Also cardiac tamponade is associated with an IVC fixed and dilated (due to venous congestion). This finding does not mean the absence of fluid responsiveness and should not obviously preclude volume expansion.

According to this growing body of evidence, echocardiography appears as a feasible tool for the assessment of fluid responsiveness in intensive care, since it offers multiple capabilities represented by different parameters and techniques. In this constellation of technical opportunities, the front line intensivist should orientate the decision making process using two principles. Firstly, clinical judgement guides techniques. In other words, a clinical adaptation of methodology and echocardiographic parameters should be made on the single patient, based on a preliminary echocardiographic examination, the underlying disease (i.e., sepsis *vs.* primary cardiac conditions), the actual clinical conditions (i.e., mechanical ventilation, abdominal surgery, atrial fibrillation) and finally the technique (transthoracic *vs.* transesophageal echocardiography) the physician is more skilled and expert. All these factors deeply affect the usefulness of the fluid responsiveness test in the single patient. Secondly, the results of the echocardiographic assessment of fluid responsiveness (that is responder or not responder) should be integrated with other findings, such as indexes of hypoperfusion. A strict echocardiographic monitoring of the patient should then follow since the condition of "fluid responder" may be time-limited and the identification of the switch to "non-responder" is crucial for avoiding fluid overload.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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