Assessing hypovolaemia and predicting volume responsiveness is a difficult challenge in most critically ill patients and surgical patients. Clinicians have to deal with three different scenarios:

- Patients who present in the Emergency Department with evident acute body fluid losses. The diagnosis of hypovolaemia is almost certain and a positive haemodynamic response to volume resuscitation will occur. Patients admitted to the Emergency Department likely to be in septic shock. There is no need for sophisticated parameters to predict volume responsiveness since a positive haemodynamic response is always expected.

- Patients who have been in the ICU for several hours or patients in the operating room who experience haemodynamic instability. Fluid administration may represent a therapeutic dilemma. On one hand, one may expect a beneficial effect of fluid administration if the heart still has some preload reserve. On the other hand, because the patient has often been resuscitated already, the presence of preload reserve is not guaranteed and further fluid infusion has the potential to cause harm through development of pulmonary oedema.

A positive cumulative fluid balance has been shown to be an independent risk of death in septic patients [1]. In patients with acute lung injury, a restrictive fluid strategy has been shown to be superior to a liberal fluid strategy in terms of ventilator-free days [2].

Only half of ICU patients with haemodynamic instability are able to 'respond' to fluid loading. This is explained by the shape of the Frank-Starling curve (Figure 1). On the initial and steep limb of the curve, the stroke volume is highly dependent on preload: administering fluid will result in a significant increase in stroke volume. In contrast, if the heart is working on the terminal and flat portion of the Frank-Starling curve, it cannot utilize any preload reserve and fluid administration will not increase stroke volume significantly. Accordingly, we need predictors of volume responsiveness to distinguish between those patients who can benefit from fluid and those in whom fluid is useless and hence deleterious.

**Figure 1**

*The Frank-Starling relationship*

The shape of the relationship between stroke volume and cardiac preload depends upon the ventricular systolic function. Volume expansion by increasing cardiac preload (from A to B) can induce a significant increase of stroke volume with normal ventricular systolic function (normal preload reserve) or no effect on stroke volume with impaired ventricular systolic function (no preload reserve). This also explains why the effects of a volume expansion cannot be predicted from a static value of cardiac preload (A).
Assessment of volume responsiveness

When considering the Frank-Starling relationship (Figure 1), we know that a response to volume infusion is more likely to occur when the ventricular preload is low than when it is high. Thus, markers of ventricular preload were first proposed to predict volume responsiveness.

Static markers of cardiac preload

None of the measures of cardiac preload enables us to accurately predict fluid responsiveness: neither the central venous pressure, nor the pulmonary artery occlusion pressure, nor the left ventricular end-diastolic dimensions, nor biomarkers such as B-type natriuretic peptide can discriminate between responders and non-responders to fluid therapy [3]. Indeed, there is no one single curve, but several curves relating stroke volume to cardiac preload depending on the ventricular contractility (Figure 1). Thus, a given value of cardiac preload can be associated with the presence of preload reserve in cases of normal cardiac contractility or with the absence of preload reserve in cases of decreased contractility (Figure 1).

Dynamic markers of volume responsiveness

The alternative method for predicting volume responsiveness is simply to induce a change in cardiac preload and to observe the resulting effects on stroke volume, cardiac output or any available surrogate. In other words, perform a ‘functional assessment’ of cardiac function [3]. In fact, this is done during a fluid challenge. Nonetheless, this method can be criticized because repeated infusion of 300-500 ml of crystalloids could eventually exert adverse effects if there is no preload reserve, especially if pulmonary permeability is increased.

The respiratory variation of haemodynamic signals

Observing the respiratory variation of haemodynamic signals has emerged as an alternative for assessing volume responsiveness without administering fluid. The concept is based on the assumption that the cyclic changes in right ventricular preload induced by mechanical ventilation result in greater cyclic changes in left ventricular stroke volume when the both ventricles operate on the steep rather than on the flat portion of the Frank-Starling curve, that is, when there is biventricular preload reserve.

Numerous studies have consistently demonstrated that the magnitude of respiratory variation of surrogates of stroke volume such as pulse pressure variation allows accurate prediction of fluid responsiveness [3]. Other surrogates of the stroke volume can be used at the bedside to assess the response to cyclic changes in preload during mechanical ventilation: the sub-aortic flow, the descending aortic blood flow, and the pulse contour-derived stroke volume have all been used, as has the amplitude of the pulse oximetry plethysmography signal [4]. Other heart-lung interaction indices such as respiratory variation of inferior or superior vena cava diameter detected by echocardiography have been also validated as accurate predictors of volume responsiveness [3].

However, some limitations of heart-lung interaction to detect volume responsiveness must be remembered. Firstly, the predictive value of pulse pressure variation is lower during low ( < 7 ml/kg) as opposed to normal (> 7 ml/kg) tidal volume ventilation [5]. However, in patients with severe acute respiratory distress syndrome with reduced chest and lung compliances, low tidal volume ventilation is often associated with sufficiently high changes in intrathoracic pressure for heart-lung interaction indices being still able to predict volume responsiveness. Secondly, and more importantly, in cases of spontaneous breathing activity or cardiac arrhythmias, the beat-to-beat variations in haemodynamic signals are clearly not related to biventricular preload reserve [6].
The ‘passive leg raising’ test

Most critically ill patients experience spontaneous breathing activity during mechanical ventilation since less sedative drugs are used than in the past. In such cases, the passive leg raising (PLR) test has been proposed as an alternative [7]. Lifting the legs from the horizontal position induces a gravitational transfer of blood from the lower limbs toward the intrathoracic compartment. It significantly increases the right and left sided cardiac preload, and the volume of blood transferred to the heart during PLR is sufficient for challenging the Frank-Starling curve.

The ability of PLR to serve as a test of preload responsiveness was demonstrated in patients with acute circulatory failure [6, 8, 9]. A 10-12 % increase in cardiac output (measured by oesophageal Doppler, echocardiography, or pulse contour method) during PLR enabled prediction of fluid responsiveness, even patients with cardiac arrhythmias or spontaneous ventilator triggering.

The best way to perform the PLR test is to elevate the lower limbs at 45° (automatic bed motion) from the 45° semi-recumbent position rather than from the supine position [10]. This has the advantage of mobilizing not only the blood in the legs, but also the blood in the splanchnic reservoir, significantly improving the sensitivity of the test [10].

The end-expiratory occlusion test

This is another alternative for testing fluid responsiveness. During mechanical ventilation each insufflation interrupts the venous return. In a recent study, we hypothesized that stopping the respiratory cycle during an end-expiratory occlusion could increase the venous return by interrupting the cyclic impediment in venous return and that this could serve for predicting fluid responsiveness [9]. In patients with cardiac arrhythmias or spontaneous triggering of the ventilator, an increase by more than 5% in arterial pulse pressure or in pulse contour-derived cardiac index (PICCO device) during a 15 s end-expiratory occlusion enabled us to predict fluid responsiveness with good accuracy. This test’s main advantage is its ease of application, although it cannot be used in patients in whom the spontaneous triggering of the ventilator is sufficient for interrupting the end-expiratory occlusion and, obviously, it cannot be used in non-ventilated patients.

Conclusion

In patients with haemodynamic instability who have been in ICU for several days, predicting volume responsiveness is an important issue since the haemodynamic response to volume resuscitation is uncertain and fluid overload carries risks of pulmonary oedema formation. In patients receiving full mechanical ventilation, the assessment of the respiratory variation of surrogates of stroke volume is the best option to predict volume responsiveness at the bedside, unless the tidal volume is too low. In patients with spontaneous breathing activity, examining the real-time response of surrogates of stroke volume to a PLR test or to an end-expiratory occlusion test is emerging as a valuable approach.

Key learning points

- Only half of ICU patients are able to ‘respond’ to fluid loading
- Static markers of cardiac preload cannot discriminate between responders and non-responders to fluid therapy
- The respiratory variation of surrogates of stroke volume helps to predict fluid responsiveness in mechanically ventilated patients
- The ‘passive leg raising’ test is helpful to predict fluid responsiveness in cases of spontaneous breathing activity, arrhythmias, and low tidal volume ventilation, where heart-lung interaction indices are no longer reliable
References