What is a fluid challenge?

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Purpose of review

The fluid challenge is used in the fluid management of many sick patients. The principle behind the fluid challenge technique is that by giving a small amount of fluid in a short period of time, the clinician can assess whether the patient has a preload reserve that can be used to increase the stroke volume with further fluids. The key components of a fluid challenge are described.

Recent findings

Dynamic predictors of fluid responsiveness are increasingly used in preference to the central venous and pulmonary artery occlusion pressure. The gold standard to monitor the response to a fluid challenge is using a continuous cardiac output monitoring. Fluid therapy guided by flow monitoring has been shown to reduce hospital stay and postoperative complications.

Summary

A fluid challenge identifies and simultaneously treats volume depletion, whilst avoiding deleterious consequences of fluid overload through its small volume and targeted administration.

Keywords

cardiac function, colloid, crystalloid, preload response, stroke volume

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Introduction

The fluid challenge is a test that allows the clinician to give fluids and at the same time to test the preload reserve of the patient. The judicious administration of intravenous fluid is an essential part of the management of many sick patients. An inadequate cardiac output (*CO*) and systemic arterial pressure reduces the delivery of oxygen to a level below the necessary requirements, leading to a cascade of cellular changes that ultimately can result in organ dysfunction and failure.

Cardiovascular dysfunction may result from a number of causes that can be simply described as being secondary to either hypovolaemia, pump dysfunction, altered vascular tone or more rarely because of an obstructive pathology. Hypovolaemia may be actual secondary to haemorrhage, or dehydration or relative due to an increased venous capacitance. Irrespective of the cause, it has long been recognized that prolonged hypovolaemia is grave, requiring urgent intervention to improve haemodynamics. We believe that this is best done with a 'fluid challenge' [1].

A fluid challenge is a method of identifying those patients likely to benefit from an increase in intravenous volume in order to guide further volume resuscitation. It is a dynamic test of the circulation. The use of a 'test' that uses a small amount of fluid to assess the volume responsiveness may reduce the risk of a too liberal fluid strategy and the possible consequences of fluid overload. In 2006, in a multicentric study design, positive fluid balance in ICU was associated with a worse outcome [2]. It is important to stress that a patient who responds to fluid may not, however, need fluid, with preload dependence likely to be the normal cardiovascular state. Healthy volunteers demonstrate significant increases in stroke volume (SV) in response to head-down tilt (a 'virtual' fluid challenge equivalent to around 500 ml volume) [3].

In health, the peripheral circulation is the primary controller of *CO*, the heart automatically pumping all the blood returned to it as described by the Frank–Starling mechanism. Increased stretch of heart muscle causes increased contractile strength, and an increased volume ejected. This property exists in all striated muscle, and is consequent to the degree of overlap of actin and myosin filaments, and in cardiac muscle also to increased sensitivity of troponin C to calcium [4]. Right atrial stretch also leads to increased heart rate secondary to sinus node automaticity and sympathetic stimulation.

The term preload refers to the myocardial sarcomere length just prior to contraction. SV is determined by preload, afterload, contractility and heart rate. Venous return is the most important determinant of *CO* and is defined by three parameters: the mean systemic filling pressure, the right atrial pressure and the venous resistance. The mean systemic filling pressure is generated by the volume in the systemic circulation, driving blood to the heart. Right atrial pressure opposes blood flow into the right atrium, decreasing if contractility increases, whereas the resistance to venous return is the intrinsic resistance to flow within the venous compartment. These parameters can be described by a venous return curve, which when combined with the cardiac function curve is useful to explain the response to a fluid challenge (Fig. 1).

The main point to remember with a fluid challenge is the fact that the given fluid must be of sufficient volume to stretch the right heart [increasing the right ventricular end-diastolic volume (RVEDV)]. Only then, can the Starling's law be implicated to suggest that right ventricular (and left ventricular) SV will increase. Different hearts in different positions of the curve will respond in different ways, but if the RVEDV has not increased sufficiently, then there is no way that SV will be able to increase with the risk of a false negative test.

Difference between fluid challenge and fluid loading

It is important to remember that the fluid challenge technique is first of all a test of the cardiocirculatory system. It allows the clinician to test whether the patient has a preload reserve that can be used to increase the SV with further fluids. These further fluids can be given after a positive response to a fluid challenge or they can be given in a controlled way by repeating the fluid challenge as long as there is a positive response. This controlled approach is also called SV maximization and is the base of most goal-directed therapy protocols [5–7]. This is very different from fluid loading in which fluids are given without monitoring the response in real time. The only 'excess' fluid that may be given with the fluid challenge technique is the amount of fluid used when the patient fails to respond. This is usually equal to 200 ml or 3 ml/kg.

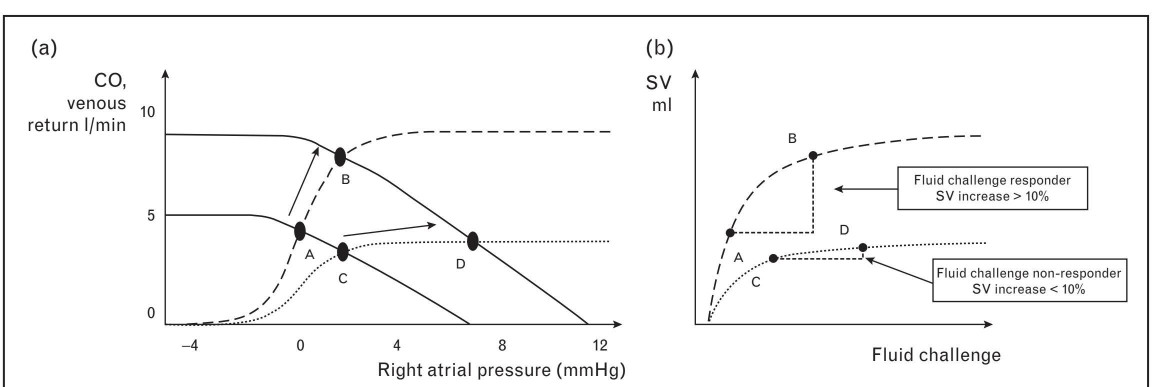
Key points

- A fluid challenge identifies and simultaneously corrects volume depletion in order to optimize tissue perfusion.
- Administration of fluid using a fluid challenge protocol avoids unnecessary fluid administration and may improve outcome in critically ill and elective surgical patients.
- Dynamic noninvasive predictors of volume responsiveness such as SV, PLR and $\Delta ScVO_2$ should be used in preference to the CVP and PAOP for guiding fluid therapy.
- Continuous *CO* monitors are the best option to monitor the response to a fluid challenge.
- The physiological properties of the fluid and the clinical picture should be considered when choosing which fluid to use.

When and how to give a fluid challenge?

The primary indication for a fluid challenge is the intention by the clinician to increase SV and *CO*. This is usually the case when there is evidence of hypoperfusion [8], but there may be clinical situations in which a SV increase is sought preemptively, as in goal-directed therapy in high-risk surgical patients [9].

Figure 1 Relationships between cardiac output and venous return and stroke volume and fluid challenge for different levels of contractility



(a) In a heart with normal contractility (dashed line), the equilibrium point is point A, cardiac output (CO) equals venous return and right atrial pressure is 0 mmHg. In a heart with impaired contractility (dotted line), the equilibrium point is C. A fluid challenge increases the mean systemic filling pressure. The venous return curve shifts upward and right, which now intersects the cardiac function curve at point B for the heart with normal contractility, where we can see a significant rise in CO and right atrial pressure. In the failing heart, the increase in pressure is much higher than the effect on CO (from C to D). (b) The correspondent stroke volume (SV)/fluid challenge relations for the two hearts. If SV is measured, the response to the same fluid challenge will be very different depending on the contractility (normal or failing) and on which part of the curve the starting point is.

When the decision of increasing the *CO* is made, optimization of preload is usually the first step taken. It goes without saying, therefore, that the primary target of a fluid challenge is an increase in SV or *CO*. An increase of at least 10–15% is considered a positive response [10]. Traditionally, the measurement of SV and *CO* was possible only with an invasive device such as the pulmonary artery catheter (PAC) [11]. The availability of new less invasive *CO* monitors has made possible the real-time assessment of SV changes during a fluid challenge in a less invasive fashion [12–14].

If the primary target of a fluid challenge is an increase in SV, the primary safety limit is failure of SV to increase. When fluid loading does not produce any improvement in haemodynamics, it can increase the risk of fluid overload. Data suggest that only 50% of critically ill patients respond to a fluid challenge [10]. For this reasons investigators have been looking for indices of fluid responsiveness that can be used to predict the response to a fluid challenge [15,16].

With continuous *CO* monitors, both the target (SV increase) and the safety limit (failure of SV to increase) can be measured in real time. If *CO* monitors are not used, clinicians may use different variables in order to identify surrogate targets that correlate with an increase in SV and surrogate safety limits that correlate with failure of SV to increase. On the basis of these assumptions, different strategies to perform a fluid challenge have been proposed.

Clinicians report using multiple tools as indicators for fluid administration [17] which may also act as predictors, targets and safety limits. (Table 1). The choice of target and safety limit depends also on the clinical situation and availability of monitors. In ICU and operating rooms, sophisticated *CO* monitors allow the clinician to focus accurately on SV. In other circumstances, the mean arterial pressure (MAP) can be chosen as a target and the central venous pressure (CVP) as a safety limit [17]. A rise in MAP can indicate a positive response (the SV has increased and produced a rise in MAP); the CVP can be used as a safety limit [if the MAP does not increase substantially and the CVP rise is very marked, it will suggest that the patient is not likely to respond to an increased intravascular volume and indeed harm (such as increased peripheral oedema) may be the result].

Fluid challenge and CVP

CVP has been used to guide fluid challenges for over 40 years [18], and is considered an indicator for fluid challenge by the Surviving Sepsis Campaign [19]. This comes from one study only where a CVP of 8–12 cm H_2O was considered a target and a CVP less than 8 cm H_2O an indicator. Although that study was successful in improving outcome, it is unlikely based on the most up to date evidence that a CVP less than 8 cm H_2O can be recommended as an indicator [20].

The CVP, which is equivalent to right atrial pressure, does not predict RVEDV, but indicates the relationship between blood volume and cardiac function. The transmural right atrial pressure gradient, as opposed to the ‘intracavity’ CVP, and ventricular compliance are more influential to ventricular filling. Myocardial ischaemia reduces contractility and can increase CVP; improving cardiac function will decrease CVP. Any cause of decreased right ventricular compliance, such as pulmonary hypertension or raised pleural pressure, will further

Table 1 Parameters used to guide fluid administration

Parameter	Indicator	Predictor	Target	Safety limit
Clinical judgement	Yes	Yes	Yes	Yes
Thirst/diminished skin turgor/dry mouth/cool extremities	Yes	No	No	No
Perioperative therapy (fasting/maintenance/insensible/evaporative/haemorrhagic losses)	Yes	No	No	No
Hypernatraemia	Yes	No	Yes	No
Use of vasopressors	Yes	No	Yes	No
HR >100	Yes	No	Yes	No
Oliguria <0.5 ml/kg/h	Yes	No	Yes	No
Systolic BP <90 mmHg	Yes	No	Yes	No
Cardiac index <2.5 l/min/m^2	Yes	No	Yes	No
Central venous pressure ≤ 15 mmHg	Yes	No	Yes	Yes
ΔCVP with spontaneous respiration	Yes	Yes	Yes	Yes
PAOP <18 mmHg	Yes	No	Yes	Yes
Serum lactate >2 mmol/l	Yes	No	Yes	No
$ScVO_2$ $<70\%$	Yes	Yes (Δ)	Yes	No
DO_2i <600 ml/min/m^2 (41)	Yes	No	Yes	No
Corrected flow time (FTc) <400 ms	Yes	No	No	Yes
Stroke volume variability $\geq 10\%$	Yes	Yes	Yes	Yes
Systolic pressure variability $>10\%$	Yes	Yes	Yes	Yes
Pulse pressure variability $\geq 13\%$	Yes	Yes	Yes	Yes
Response to straight leg raising	Yes	Yes	No	No

BP, blood pressure; CVP, central venous pressure; HR, heart rate; PAOP, pulmonary artery occlusion pressure; ScVO2, central venous oxygen saturation.

elevate the CVP. Myocardial hypertrophy or dilation can also alter the volume/pressure relationship. A recent systematic review has demonstrated no association between CVP and blood volume, with patients with high or low CVPs equally likely to be volume responsive [20]. During spontaneous respiration, however, a decrease in CVP during inspiration indicates that the right ventricle has preload reserve, and is therefore on the ascending part of the cardiac function curve. A fall of 1 mmHg or less during spontaneous breathing strongly predicts a subsequent response to a fluid challenge [21].

A CVP of 8–12 or 12–15 cm H_2O, if mechanically ventilated, is recommended by the Surviving Sepsis Campaign [19]. It is important to remember, though, that significant increases in *CO* with fluid can occur in patients with CVPs greater than 15 mmHg and many patients with a low CVP fail to respond to a fluid challenge [22]. Indeed, neither CVP nor ΔCVP can be used as good targets (i.e. preload indicators) of volume responsiveness.

ΔCVP as a marker of adequacy of a fluid challenge?

Recently, Lakhal *et al.* [23] have demonstrated that ΔCVP can be tested to identify in which patients a passive leg raising (PLR) has been successful in adequately increasing the preload of the ventricles. It may be that in some patients a fluid challenge does not produce a response in SV because insufficient volume has been given to stretch a ventricle that otherwise may still have a preload reserve. In this sense, ΔCVP could be used to identify an adequate fluid challenge: for example, a change in ΔCVP of 2 cmH_2O being the evidence of appropriate stretch in the right ventricle or increases in the RVEDV. This approach was described initially by Weil and Henning [1] and more recently by Vincent and Weil [17]. To our knowledge, only one study [24] has successfully used ΔCVP in this way. It remains to be proven if this approach can be used coupled with a *CO* monitor.

Fluid challenge and pulmonary artery occlusion pressure

Analogous to CVP, the pulmonary artery occlusion pressure (PAOP) purports to estimate left ventricular end-diastolic volume (LVEDV), and is subject to the same caveats. PAOP assists in diagnosing the cause of pulmonary oedema and pulmonary hypertension, but does not predict fluid responsiveness better than chance [25,26].

Fluid challenge and central venous oxygen saturation

Central venous oxygen saturation ($ScVO_2$) represents the relationship between tissue oxygen supply and demand. An $ScVO_2$ of less than 70% is defined as an indicator and target for early resuscitation in sepsis, reducing in-hospital mortality [27]. A recent RCT of intraoperative fluid challenges to achieve an $ScVO_2$ of 75% did not show a reduction in postoperative complications [28]. Interestingly, the $ScVO_2$ group received less fluids than the control group. ΔScVO2 may be a more useful predictor and target – a change in $ScVO_2$ of 4% has been shown to correlate with response to fluid challenge [29].

Prediction of fluid responsiveness before giving a fluid challenge

There are a number of tests that have been studied to predict whether a fluid challenge will lead to an increase in SV (fluid responsiveness).

Heart–lung interaction

The consistent fluctuation of SV, systolic pressure and pulse pressure with the mechanically ventilated breath have consistently been shown to be sensitive and specific predictors of volume responsiveness, providing a number of caveats are followed. These caveats include a tidal volume of over 8 ml/kg and the absence of either spontaneous respiratory activity or arrythmogenic activity [30].

Passive leg raising

Elevation of the lower limbs induces an auto-transfusion haemodynamically equivalent to an exogenous fluid challenge. *CO* and pulse pressure changes in response to PLR are predictive of fluid responsiveness and independent of mode of ventilation [31].

Corrected flow time

The corrected flow time (FTc), derived from oesophageal Doppler monitoring, has been described as indicating fluid challenge and predicting response in surgical patients [32]. The FTc should not be considered an accurate marker of left ventricular preload [33], being inversely proportional to systemic vascular resistance, and therefore describing left ventricular afterload.

What fluid?

Fluid challenges may be performed with crystalloid (isotonic or hypertonic) or colloids. The ability of colloids to maintain or increase *CO* should reduce fluid extravasation into the lung, but increased capillary permeability may negate this advantage. Crystalloid distributes rapidly through the extracellular compartment, reducing its haemodynamic effect. Colloid will stay in the intravascular compartment for longer, and hyperoncotic fluid will draw fluid out of the interstitial space, increasing plasma volume beyond the administered volume. Whether this has clinical relevance for the fluid challenge is unclear. A Cochrane review demonstrated no mortality difference between crystalloid and colloid for resuscitation of critically ill patients [34]. The choice of fluid for a challenge may, therefore, be colloid, crystalloid or blood, as guided by clinical need.

Rate of administration

Rate of administration is probably more important than the amount of fluid and the type of fluid. The best evidence in terms of outcome comes from studies where the fluid challenge technique has been used in goal-directed therapy [5–7,9,24]. In these studies, small boluses of fluid (250 ml, or 3 ml/kg of usually colloids) were given in a short period of time (5–10 min). A response in terms of SV with a *CO* monitor was considered positive if the SV increased by 10–15%. An algorithm mandates the clinician to repeat this process until the SV fails to increase above the chosen threshold. This process is called SV maximization.

In practice, how to give a fluid challenge?

Although many of the variables described above have been used to predict and to guide the administration of a fluid challenge, the advent of new less invasive technologies has now allowed us to look directly at SV. Probably, the most important characteristic of a *CO* monitor in order to be used to give a fluid challenge is the ability to measure small changes in SV over real time. Indeed, the quantity of fluid given in a fluid challenge is small and the rate of administration has to be fast enough to stretch the ventricle and to produce an increase in SV. After the initial increase in SV, the redistribution of fluid in a fluid responder may cause the SV to decrease again in subsequent minutes. A 'slow' monitor would not be able to detect these changes. For instance, the thermodilution of the PAC (intermittent and semicontinuous) may not always be fast enough to detect these changes unless they are very significant. The feature of monitors to detect changes in a fast way is called responsiveness [35]. Most of the new devices, from Doppler techniques to pulse pressure analysis techniques and bioreactance, have an adequate responsiveness to monitor changes in SV during a fluid challenge.

Conclusion

In summary, the fluid challenge is a controlled way of administering fluids that is at the same time a test of the cardiovascular system. If the response to the test is positive, then fluid administration may be repeated depending on the response and on the clinical effect that is sought. It is, therefore, logical that the smallest feasible volume should be used. If the volume given is too small to distend the ventricular wall then the cardiac function curve has not been 'challenged', and the test is inadequate. A volume of 200 ml or 3 ml/kg is considered standard, given in about 5 min. A reasonable way of identifying the adequate volume of fluids is a small rise in the CVP that can be used as a surrogate of an increase in EDV. Different targets and safety limits can be used (Table 1). A response in SV monitored in real-time with a *CO* monitor is the best way to assess the response to a fluid challenge.

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