Declaration of interest

None declared.

Funding

Neither M.B. nor P.G.B. has received funding for the preparation of this manuscript.

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British Journal of Anaesthesia **112** (4): 617–20 (2014)
Advance Access publication 16 February 2014 · doi:10.1093/bja/aet590

EDITORIAL II

Fluid responsiveness: an evolution of our understanding

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Decisions regarding fluid therapy, whether this be in the operating theatre (OT), intensive care unit (ICU), emergency department (ED), or general ward, are among the most challenging and important tasks that clinicians face on a daily basis. Specifically, almost all clinicians would agree that both hypovolaemia and volume overload increase the morbidity and mortality of patients. What is not widely appreciated is that when a fluid challenge is given on 'clinical grounds', only 50% of haemodynamically unstable patients (in the OT, ICU, or ED) are volume responders [i.e. they will increase their stroke volume (SV) by >10–15%].[1] This emphasizes that clinicians have great difficulty in estimating the preload condition of their patients.

Fundamentally, the only reason to give any patient a fluid challenge is to increase their SV; if this does not happen, the fluid administration serves no useful purpose and is likely to be harmful.[2] Furthermore, the increase in SV (and thus cardiac output) must be judged to be beneficial. Fluid loading *per se* is not always the correct therapy for hypotension or a reduced urine production. Fluid therapy acts by increasing

the stressed venous volume, thereby increasing venous return to the heart. As the venous system has a much greater capacity for blood compared with the arterial system, it is a normal physiologic condition to be a fluid responder. However, being a fluid responder is not equal to being hypovolaemic. This suggests that not all patients who are fluid responders necessarily require volume expansion. Our homeostatic mechanisms have evolved (over thousands of years) to deal with hypovolaemia (tachycardia, vasoconstriction, and blood flow redistribution), whereas volume overload is a more recent, largely iatrogenic phenomenon (last 40 yr or so) for which the body is ill equipped to manage. An analysis of the overlapping Frank–Starling and extra-vascular lung water (EVLW) curves demonstrate that as patients become less fluid responsive, EVLW (and tissue oedema) increases markedly (see Fig. 1) because of the increased cardiac filling pressures and transmitted hydrostatic pressures.[3] This process is accentuated in patients with endothelial damage (sepsis, ARDS, pancreatitis, burns).[4] Increased cardiac filling pressures trigger the release of natriuretic peptides, presumably to assist in fluid removal. What is most troubling about this sequence of events is that natriuretic peptides cleave membrane-bound proteoglycans and glycoproteins (most notably syndecan-1 and hyaluronic acid) off the endothelial glycocalyx.[5 6] The endothelial glycocalyx plays a major role in regulating endothelial permeability.[7] Therefore, excessive volume expansion increases the release of natriuretic peptides, which in turn damages the endothelial glycocalyx, and this is followed by a rapid shift of intravascular fluid into the interstitial space, leading to a marked increase in EVLW and tissue oedema.[5 6] Increased EVLW has been demonstrated to be a very strong predictor of death.[8 9] Indeed in a cohort of patients with sepsis, Zhang and colleagues[10] demonstrated a strong correlation between the net fluid balance, the increase in brain natriuretic peptide, and the risk of death. This suggests that it may be beneficial to allow patients to be somewhat fluid responsive instead of fluid loading until they have reached the top of the Frank–Starling curve.

Only patients who are likely to show a significant increase in SV with a fluid challenge and in whom the increased SV is considered to be beneficial should be given a fluid challenge. Furthermore, all attempts should be made to limit the volume of fluid administered. This begets the question of how to predict fluid responsiveness. After Hughes and Magovern[11] described the technique of central venous pressure (CVP) monitoring in 1959, this method became a standard tool for guiding fluid therapy. It has now been clearly established that there is a poor relationship between the CVP and the intravascular volume status, and no relationship between the CVP and fluid responsiveness.[1] In 1970, the flow-directed pulmonary artery catheter was developed by Swan and Ganz, allowing measurement of the pulmonary artery occlusion pressure (PAOP). However, the PAOP suffers from the same limitation as the CVP, and multiple studies have demonstrated that, like the CVP, the PAOP is unable to predict fluid responsiveness.[12 13]

After the 'widespread' recognition that the CVP/PAOP had no utility in guiding fluid resuscitation,[12] the idea that heart–lung interactions during mechanical ventilation could be used to predict fluid responsiveness was championed by Michard, Pinsky, Teboul, and others in the early 2000s.[14 15] The principles underling this technique are based on simple physiology.[2 3] Intermittent positive-pressure ventilation induces cyclic changes in the loading conditions of the left ventricle (LV) and right ventricle (RV). Mechanical insufflation decreases preload and increases afterload of the RV. The reduction in RV preload and the increase in RV afterload both lead to a decrease in RV SV, which is at a minimum at the end of the inspiratory period. The inspiratory reduction in RV ejection leads to a decrease in left ventricular filling after a phase lag of two or

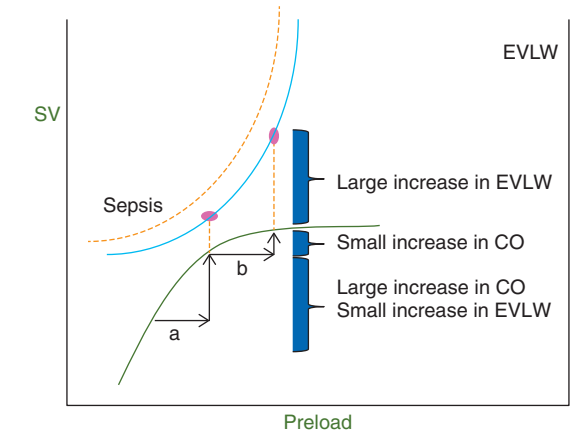

Fig 1 Superimposition of the Frank–Starling and Marik-Phillips curves demonstrating the effects of increasing preload on SV and lung water in a patient who is preload responsive (a) and non-responsive (b). With sepsis, the EVLW curve is shifted to the left. EVLW, extra-vascular lung water; CO, cardiac output; SV, stroke volume.

Table 1 Techniques for assessing fluid responsiveness. ROC, area under receiver operator characteristic curve; IVC, inferior vena cava; SVC, superior vena cava

Static pressure and volume parameters (ROC ~0.5–0.6)
CVP
PAOP
IVC/SVC diameter
Flow corrected time
Right ventricular end-diastolic volume
Left ventricular end-diastolic volume
SVC/IVC variation during mechanical ventilation
Dynamic techniques based on heart–lung interactions during mechanical ventilation (ROC ~0.7–0.8)
PPV
SVV
Pleth variability index
Aortic blood flow (Doppler or echocardiography)
Techniques based on real or virtual fluid challenge (ROC~0.9)
PLR
Rapid fluid challenge (100–250 cc)

three heartbeats. The cyclic changes in RV and LV SV are greater when the ventricles operate on the steep rather than the flat portion of the Frank–Starling curve.[2 3] A pulse pressure variation (PPV) or stroke volume variation (SVV) of >13% was shown to be predictive of fluid responsiveness.[14 15] In a meta-analysis published in 2009, it was demonstrated that the PPV was highly predictive of fluid responsiveness (ROC of 0.94).[16] Because of its sound physiological basis, good predictive ability, and apparent simplicity, this technique was met with great enthusiasm, and algorithms based on this principle were developed for use in the OT and ICU.[17 18] However, what was not fully appreciated when the meta-analysis was published was that almost all the studies were performed in a highly controlled environment (usually the OT) in a highly select group of patients.[16] It soon became apparent that a large number of clinical factors interacted to limit the accuracy of the PPV/SVV in predicting fluid responsiveness.[19 20] In a cohort of cardiac surgical patients Lansdorp and colleagues[21] demonstrated that PPV/SVV did not predict volume responsiveness in routine clinical practice. Multiple studies have now confirmed these findings.[22 23] In the largest study to date, Cannesson and colleagues[24] demonstrated that despite a strong predictive value, the PPV was inconclusive in predicting fluid responsiveness in 25% of patients during general anaesthesia. The utility of the PPV/SVV in the ICU appears significantly worse.[22 23] In a multicentre, point prevalence study published in this issue of the Journal, Mahjoub and colleagues[25] demonstrate that only 2% of ICU patients met the validity criteria for using the PPV to assess fluid responsiveness. Furthermore, only 3% of patients with an arterial line in place satisfied all the validly criteria. These data suggest that because of the frequency of confounding factors, the PPV/SVV should not be used as the primary technique for directing fluid management in the OT and ICU. Nevertheless, intravascular volume depletion should be suspected in patients who demonstrate marked PPV evident on either an arterial pressure waveform or a pulse oximetric waveform. However, in these situations, other tests should be performed to confirm fluid responsiveness.

Ultimately, only two techniques are currently available that can be used to determine fluid responsiveness with a high degree of accuracy, namely the passive leg raising (PLR) manoeuvre and the fluid challenge.[2 3 26 27] These techniques are best coupled with minimally invasive cardiac output monitors that can track changes in SV and cardiac output dynamically and in real time.[2 3] For obvious technical reasons, the fluid challenge technique is preferred during anaesthesia, while the PLR is preferred in the ICU and postoperatively.

In conclusion, the methods for assessing fluid responsiveness have evolved from static pressure and volume parameters, which are unable to predict fluid responsiveness, to dynamic indices based on heart–lung interactions during mechanical ventilation, which have a modest degree of accuracy, to those techniques based on either a virtual or a real fluid challenge, which have a high degree of accuracy in predicting fluid responsiveness (see Table 1). As our understanding of this complex topic evolves, it is likely that new and improved methods of assessing fluid responsiveness and more physiological targets of fluid therapy will emerge.

Authors' contributions

Both authors were responsible for writing this editorial, reviewing the final version, and approving it for publication.

Declaration of interest

P.E.M.: in the last 5 years, P.E.M. has received an honorarium from Pulsion Medical, manufacturer of the PiCCO haemodynamic device, for a lecture delivered at an international Critical Care Symposium (~1000 GBP) and an honorarium from Cheetah Medical, manufacturer of the NiCOM haemodynamic device, for a lecture delivered at medical grand rounds (~1500 GBP). J.L.: none declared.

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British Journal of Anaesthesia **112** (4): 620–2 (2014)
Advance Access publication 20 February 2014 · doi:10.1093/bja/aeu005

EDITORIAL III

Is it safe to use supraglottic airway in children with difficult airways?

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The supraglottic airway has a potential role in patients with difficult airways. There have been numerous reports of successful use of the supraglottic airway in patients in whom both tracheal intubation and facemask ventilation were difficult, and the device is now regarded as a 'rescue' device in cases of 'cannot intubate, cannot ventilate' scenario.[1 2] The supraglottic airway can also function as an aid to tracheal intubation, and studies have confirmed that this usage is highly effective in patients with difficult airways.[3 4] In addition, in adult patients with difficult airways, the supraglottic airways (without tracheal intubation) usually can provide clear airways during anaesthesia. In contrast, little is known about its efficacy in children with difficult airways. In this issue, Jagannathan and colleagues[5] report a retrospective analysis of the efficacy of sole of a supraglottic airway in children with difficult airways.

Jagannathan and colleagues[5] searched for children who had been predicted to have difficult airways caused by anatomical deformities (such as Treacher-Collins syndrome, subglottic stenosis, and pharyngeal masses), and those with history of difficult tracheal intubation and difficult facemask ventilation. Among 77 272 children who underwent general anaesthesia during a 4-yr period, the authors identified 459 children (0.6%) with difficult airways. In 109 of the 459 children, a supraglottic airway was used as a primary airway during anaesthesia, and it provided clear airways in 105 of the 109 children. In the remaining four children, reinsertion of a supraglottic airway (two patients) and tracheal intubation (two patients) became necessary.

Indications and contraindications

So, can we regard the supraglottic airway as being able to reliably provide a clear airway in a child with difficult airway? The answer would be 'yes', as the study by Janannathan and