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Fluid therapy recommendations for major abdominal surgery. Via RICA recommendations revisited. Part II: Goal directed hemodynamic therapy. Rationale for optimising intravascular volume

Recomendaciones de fluidoterapia perioperatoria para la cirugía abdominal mayor. Revisión de las recomendaciones de la Vía RICA. Parte II: Terapia hemodinámica guiada por objetivos. Fundamento para la optimización del volumen intravascular

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Introduction

Goal-directed hemodynamic therapy (GDHT) is one of the cornerstones of enhanced recovery after surgery (ERAS) protocols. Over the years, the initial concept has shifted further to prevent volume depletion or overload, and GDHT is now only used in moderate–high risk anaesthetic-surgical patients. The fundamental principle behind GDHT is to optimise tissue perfusion by identifying physiological parameters that are associated with an improved outcome and to maintain physiological haemostasis to achieve these goals. Although retrospective studies have repeatedly shown that GDHT is one of the factors independently associated with reduced complications, the controversy
surrounding the use of perioperative GDHT in patients within an ERAS environment persists.\textsuperscript{1,10}

Fluid deficits in surgical patients in the absence of bleeding can be caused by disturbances in capillary permeability or vasodilatation. This can lead to organ hypoperfusion which is associated with increased morbidity and mortality after major surgery, even in seemingly hemodynamically stable patients.\textsuperscript{11} Occult hypovolemia may be present despite normalisation of the heart rate and mean arterial pressure, resulting in inadequate blood flow for the increased metabolic requirements. Therefore, volume optimisation is the first and crucial step for hemodynamic optimisation of patients undergoing major surgery. Accurate correction of hypovolemia will be enough to achieve the goals of therapy in the large majority of surgical patients. The term GDHT usually refers to the optimisation of dynamic preload parameters, such as cardiac output (CO) or stroke volume (SV), as a therapeutic goal, along with the predefined pre-emptive interventions. This review aims to explain the physiological basis for individualised application of this first step of GDHT in patients undergoing major surgery, and revisits the VIA RICA recommendations recently formulated by the Spanish Ministry of Health\textsuperscript{11,12} (Table 1).

A functional definition of normovolaemia

Perioperative assessment of changes in blood volume is difficult and requires the evaluation of several clinical and physiologic events that accompany major surgery. Moreover, blood volumes vary considerably, both between individuals and within the same individual.\textsuperscript{10,11} Standard hemodynamic monitoring devices fail to detect occult hypovolaemia\textsuperscript{13}; CO monitoring must be used for this purpose.\textsuperscript{23} Truijen et al. state that “for supine healthy humans, the heart is operating on the plateau of the Frank–Starling curve, since further expansion of central blood volume does not increase SV or CO”.\textsuperscript{24} Bundgaard-Nielsen et al. showed that for awake healthy humans the expansion of central blood volume does not increase SV measured by oesophageal Doppler\textsuperscript{25}; Godfrey et al., however, investigated fluid responsiveness in the same state and reported different results: after conducting a passive leg raise test (PLRT) to increase preload, 45% of the apparently normovolaemic patients became volume responders. However, preload was not the sole cardiovascular variable that changed.\textsuperscript{26} The statistically significant increase in heart rate and CI, independent of SV, suggests that the leg raise manoeuvre may not be a suitable experimental model for an isolated increase in preload, since in the conscious patient the adrenergic pathways produce potential changes in vasomotor tone, venous capacitance and cardiac contractility, none of which were directly measured but all of which may have an effect on SV.\textsuperscript{27} This complicates the definition of normovolaemia and calls into question the functional definition proposed by Truijen and Bundgaard-Nielsen.\textsuperscript{24,25,27} Normovolaemia was defined as the total amount of blood volume able to provide the heart with optimal filling to meet metabolic demand.\textsuperscript{28}

Hypovolaemia could be defined as a decrease in blood volume resulting from sufficient loss of blood, plasma and/or plasma and water\textsuperscript{29} to trigger the sympathetic compensatory response to maintain hemodynamic stability. Thus, when those mechanisms start to fail, hypovolaemia may be characterised by a reduced cardiac preload.\textsuperscript{24}

The ability of the heart to change its force of contraction and therefore SV in response to changes in venous return is called the Frank–Starling mechanism (Fig. 2).\textsuperscript{30} In normal physiological conditions, both ventricles operate on the ascending portion of the Frank–Starling curve. This mechanism provides a functional reserve to the heart in situations of acute stress.\textsuperscript{31} The implication of individualised GDHT is that when maximal SV is established,
cardiac preload is comparable to that of supine healthy subjects. In a healthy subject, this volume of blood would be enough to maintain adequate tissue DO₂. In the absence of adequate SV, occult hypovolaemia may lead to splanchnic vasoconstriction and reduced DO₂. Mythen et al. showed that 60% of patients undergoing major surgery had gut hypoperfusion.

Figure 1  Optimal fluid volume, defined as normalised convective flow with an optimal density of perfused capillaries. Modified from Can Ince et al. with permission.

Optimising intravascular volume

Given that hypovolemia is a frequent cause of hemodynamic deterioration in high-risk surgical patients, adequate intravascular volume is essential for hemodynamic management. The basis of most GDHT protocols was "maximisation" of the SV using a sequence of fluid challenges until the plateau of the Frank Starling curve is achieved. This "maximisation" of SV may not be always necessary to achieve adequate DO₂ or tissue perfusion because if volumetric expansion does not result in significant hemodynamic improvement, it inherently leads to haemodilution, increased cardiac filling pressures, and ultimately fluid overload. This is one of the reasons why this concept is widely contested. GDHT protocols need to be tailored to the individual patient, particularly in patients with limited cardiac function. This can be done by using hemodynamic endpoints, such as the oxygen delivery index (DO₂I), which is associated with improved mortality. SV, stroke volume variation (SVV) or pulse pressure variation (PPV) in combination with assessment of fluid responsiveness, such as passive leg raising test (PLRT) or central venous oxygen saturation (SCvO₂), instead of more static parameters, such as mean arterial pressure (MAP) or central venous pressure (CVP). GDHT should not lead to complacency towards aggressive and potentially detrimental fluid overload.

The fluid challenge

Fluid responsiveness is defined as an increase in CO or SV in response to an increase in intravascular volume (Fig. 3). This is not a pathological condition; quite the contrary,
result in major miscalculation of SV; 2) the Doppler scan line must be parallel to the jet of the ascending aorta for correct measurements; 3) as in any ultrasound technique, this measurement needs a good window of visualisation from the anterior side of the chest, which is not always possible in postoperative patients, particularly those still under mechanical ventilation. In addition, as Aya et al. showed, the time point at which response is assessed seems to be crucial, as the hemodynamic effect of a fluid challenge dissipates rapidly. They found that the effect of a fluid challenge performed with 250 mL of crystalloid does not seem to last more than 10 min, and the predicted maximal effect on CO was observed at 1.2 min in responders. More recently, the same research group found that a bolus of 4 mL/kg over 5 min was the smallest volume for an effective fluid challenge. Interestingly, when an effective fluid challenge was performed, mean arterial pressure and CO increased, while CVP increased in both responders and non-responders.

Risks associated with inadequate administration of fluids led to the development of a variety of strategies to assess “fluid responsiveness” prior to volume expansion. These tests are used to determine the degree of curvilinearity of the individual Frank–Starling curve when the clinician plans to administer a therapy, and thus determine whether the patient is likely to be fluid responsive or not. Stroke volume variation (SVV) is the change in SV during one respiratory cycle. SVV can be assessed continuously by a beat-to-beat CO monitor. Many studies have shown this to be a reliable predictor of fluid responsiveness. The use of respiratory variation of SV or surrogates to predict fluid responsiveness has some limitations, such as the presence of spontaneous breathing activity, cardiac arrhythmias, or increased abdominal pressure; furthermore, in the case of low tidal volume ventilation, the variations of intrathoracic pressure might be too small and thus insufficient to cause any significant changes in preload, even in the case of preload responsiveness.

Overall, the limitations of dynamic indices are much more frequently encountered in the intensive care setting than in the operating room. This might be particularly suited to the respiratory variation of SV or surrogates in anesthetised patients, except when low tidal volumes are used for mechanical ventilation or laparoscopic surgery is performed, which is increasingly common within ERAS programmes. This greatly limits the use of hemodynamic algorithms based on SVV. In order to impact survival, hemodynamic monitoring must be able to provide early warnings to allow care providers to immediately act to rectify the problem, because inadequate DO2 is certain to cause damage, and fluids and drugs must be administered at the right time.

**Venous return**

The circulatory effects of fluid administration are determined by the interaction of venous return (VR) and cardiac function, which was originally described by Guyton et al. in 1955. Nevertheless, for many years, venous physiology has not been as appreciated as the arterial component. The two functions of the venous system are to return the blood from the periphery to the right atrium (RA) and to store large

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**Figure 3** Relationship between cardiac output and venous return. In a heart with normal contractility, cardiac output (CO) equals venous return (VR) at the point of equilibrium, and right atrial pressure (RAP) is 0 mmHg. Since VR and CO should be equal in a closed circuit, as both the right ventricle CO function curve and the VR curve use RAP pressure as an independent variable, the 2 curves can be superimposed. The intersection of the curves defines the behaviour of VR and CO in different situations. A horizontal line from this intersection defines the value of VR and CO.
Figure 4  Effects of a fluid challenge on venous return. Fluid challenge increases mean systemic filling pressure. The venous return curve shifts upward and right, and then intersects the cardiac function curve at point B in a heart with normal contractility, where we can see a significant rise in cardiac output and right atrial pressure.

Fluid therapy recommendations for major abdominal surgery

Amounts of unneeded blood as an adjustable reservoir. About 70% of the blood is stored in the veins, whereas the arterial system contains only 13%–18% of blood, and capillaries contain 7%. Due to the greater compliance of the veins in comparison with other parts of the cardiovascular system the venous system is able to alter its blood volume without producing any significant changes in venous pressure.

Approximately three quarters of all venous blood is contained in small veins and venules, at a pressure of around 8–10 mmHg (assuming an RA pressure of close to 0 mmHg), especially in the systemic venous circulation. Since the splanchnic region has the highest compliance, holding about 30% of the total blood volume, and is richly innervated by the sympathetic nervous system, it is the most important blood reservoir within the venous system. The rate of VR to the right heart through the venous system is equal to CO at steady hemodynamic conditions (Fig. 4).

Venous return, and consequently CO, are directly proportional to the pressure gradient of venous return (dVR), which is the difference between mean systemic filling pressure (Pmsf) and right atrial pressure (RAP) and inversely related to the resistance of venous return. The mean systemic filling pressure (Pmsf), the pressure in the cardiovascular system when there is no blood flow, is determined by the volume that distends all elastic structures in the

Figure 5  Infographics article summary. MAP: mean arterial pressure; HR: heart rate; GDHT: goal directed hemodynamic therapy; CO: cardiac output; SV: stroke volume; VR: venous return; PPV: pulse pressure variation; SVV: stroke volume variation; Pmsf: mean systemic filling pressure; RAP: right atrial pressure; RVR: resistance to venous return.
circulation (stressed volume) and the mean vascular capacitance. It was originally described by Starling and Byliss, who pointed out that there must be a point in the vascular system where the pressure does not change when the heart stops, and is therefore independent of blood flow. Some studies have observed that Pmsf measured in patients after cardiac surgery in the intensive care unit is approximately 18 mmHg.

Only about 30% of total blood volume actually distends vessel walls and creates Pmsf. The pivotal point of the circulation, where the pressure is independent of blood flow, occurs between the venous capillaries and small venules. The pressure at this point is the same as Pmsf and is considered the main driving force (the upstream pressure) of VR according to the "guytanian" model of circulation. The volume that expands the vessels but does not produce pressure is called the unstressed volume. This volume represents a wide reservoir of blood that can be recruited to increase VR in accordance with the tissues metabolic demands.

In other words, unstressed volume can become stressed volume, acting as a blood volume reserve. Experimentally, near-maximal venoconstriction with norepinephrine can shift nearly 15–20 mL/kg of unstressed blood volume (nearly 1.5 l in adults) to stressed volume. This allows venous pressure to be maintained at near normal levels despite significant blood loss.

Venous return can be represented mathematically in the following equation:

\[
VR = \frac{(Pmsf - RAP)}{RVR}
\]

RVR: resistance to venous return.

Therefore, the cardiac function can only affect VR indirectly by changing right arterial pressure (downstream pressure), and consequently altering the driving pressure gradient. When RAP is 0 mmHg, the gradient between the upstream and downstream pressures is the greatest and VR reaches a peak value.

An effective fluid challenge should be able to increase systolic volume and with it, Pmsf. If the ventricle is able to handle the increase in volume, the VR gradient will increase, and with it, VR (assuming steady vascular resistances) (Fig. 5). Thereby, RAP should not be considered a parameter of intravascular filling, as it is the result of VR and cardiac performance. Cecconi et al. found similar increases in Pmsa (Pmsf analogue) in responders and non-responders, while dVR increased only in responders, since in non-responders the increase in CVP neutralised the changes in Pmsa.

Despite the technical difficulty in measuring Pmsf at the bedside, it is useful to understand what is expected when a fluid challenge is administered. The effects of volume administration are determined by the interaction of Pmsf and cardiac function. An effective fluid challenge should increase Pmsf; if it does not, the volume given may not have increased the stressed volume enough to challenge the ventricular function. All the above-mentioned parameters can now be used to describe the determinants for VR and control of CO in patient populations with different pathophysiological conditions, and also to describe different treatment options (volume expansion, vasoactive medication). Further studies are needed to clarify their practical application.

Conclusions

Perioperative fluid management influences patient outcome. All clinicians need to follow basic physiologic end points in order to perform rational, consistent, and standardised fluid administration, and to avoid the complications derived from an unreasonable administration of fluids in terms of quantity, time, and type.

Conflict of interest

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