

CONSENSUS

Open Access



Perioperative Quality Initiative (POQI) consensus statement on fundamental concepts in perioperative fluid management: fluid responsiveness and venous capacitance

Greg S. Martin¹, David A. Kaufman², Paul E. Marik³, Nathan I. Shapiro⁴, Denny Z. H. Levett^{5,17}, John Whittle⁶, David B. MacLeod⁶, Desiree Chappell^{7,18}, Jonathan Lacey⁸, Tom Woodcock⁹, Kay Mitchell¹⁰, Manu L. N. G. Malbrain¹¹ , Tom M. Woodcock¹², Daniel Martin¹³, Chris H. E. Imray¹⁴, Michael W. Manning⁶, Henry Howe⁷, Michael P. W. Grocott^{5,17}, Monty G. Mythen¹⁵, Tong J. Gan¹⁶ and Timothy E. Miller^{6*}

Abstract

Background: Optimal fluid therapy in the perioperative and critical care settings depends on understanding the underlying cardiovascular physiology and individualizing assessment of the dynamic patient state.

Methods: The Perioperative Quality Initiative (POQI-5) consensus conference brought together an international team of multidisciplinary experts to survey and evaluate the literature on the physiology of volume responsiveness and perioperative fluid management. The group used a modified Delphi method to develop consensus statements applicable to the physiologically based management of intravenous fluid therapy in the perioperative setting.

Discussion: We discussed the clinical and physiological evidence underlying fluid responsiveness and venous capacitance as relevant factors in fluid management and developed consensus statements with clinical implications for a broad group of clinicians involved in intravenous fluid therapy. Two key concepts emerged as follows: (1) The ultimate goal of fluid therapy and hemodynamic management is to support the conditions that enable normal cellular metabolic function in order to produce optimal patient outcomes, and (2) optimal fluid and hemodynamic management is dependent on an understanding of the relationship between pressure, volume, and flow in a dynamic system which is distensible with variable elastance and capacitance properties.

Keywords: Perioperative fluid management, Physiology, Fluid responsiveness, Venous capacitance, Goal-directed fluid therapy

* Correspondence: timothy.miller2@duke.edu

⁶Department of Anesthesiology, Division of General, Vascular and Transplant Anesthesia, Duke University School of Medicine, Duke University Medical Center, Durham, NC, USA

Full list of author information is available at the end of the article



© The Author(s). 2020 **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Consensus statements

Physiological principles of fluid resuscitation

1. The ultimate goal of fluid and hemodynamic management is to support normal cellular metabolic function.
2. Achieving normal cellular metabolic function requires maintenance or restoration of effective coordinated function of the macrocirculation and the microcirculation, as well as intact cellular metabolism.
3. Practically speaking, most clinical management is currently targeted at macrocirculatory variables and surrogates of cellular metabolism (e.g., lactate, base excess).
4. The therapeutic rationale of intravenous fluid administration is to optimize macrocirculatory function in order to improve or optimize microcirculatory and cellular function.
5. There is a minimal intravascular volume required to maintain cardiac output and stroke volume and normal tissue perfusion. Below this volume, cardiac output and blood pressure may be maintained at the expense of microcirculatory blood flow and cellular function.
6. The majority of intravascular volume is in the venous circulation; therefore, the venous capacitance is a critical determinant of effective macrocirculatory function.

Physiology of fluid responsiveness

1. There is no readily available method of measuring intravascular volume and it is uncertain if knowing this static value would have clinical utility.
2. Optimal intravascular volume can only be characterized through dynamic evaluation.
3. Administration of a fluid bolus as part of a fluid challenge is a means of increasing intravascular volume to evaluate the effect on stroke volume.
4. Fluid responsiveness is defined as a state of recruitable stroke volume in response to intravascular fluid administration.

Venous capacitance

1. The venous circulation is comprised of stressed and unstressed volumes.
2. Stressed volume is the (theoretically measurable) volume of blood that exerts distending pressure against the venous wall. In contrast, unstressed volume is the volume of blood up to the point of filling the veins but without exerting any pressure on the vessel walls.

3. Stressed volume determines the mean systemic filling pressure (MSFP, the pressure of venous return when cardiac activity is absent), related to the elastic recoil of the venous system. The difference between the MSFP and right atrial pressure is the major factor determining venous return to the heart. The MSFP provides driving pressure against right atrial pressure which creates a gradient promoting forward flow.

Practical implications

1. Full characterization of fluid responsiveness requires consideration of the type, amount and timing of fluid as well as the expected change in stroke volume.
2. The best method of measuring fluid responsiveness is a continuous or rapidly repeatable measure of stroke volume.
3. A common approach to test fluid responsiveness is the administration of 250-500 mL bolus in < 15 min with a positive response defined by a 10-15% increase in stroke volume.
4. The passive leg-raise maneuver replicates a transient fluid bolus and predicts fluid responsiveness without administration of intravenous (IV) fluids (positive response defined as > 10% increase in stroke volume), thereby mitigating the risks of excess IV fluid administration. This maneuver has limited utility in the intraoperative setting.
5. Alternative methods for predicting fluid responsiveness include stroke volume variation (SVV), pulse pressure variation (PPV), systolic pressure variation (SPV), and (in certain mechanically ventilated patients) end-expiratory occlusion test and respiratory systolic variation test. All have limitations (Table 1).
6. Sonographic evaluation of IVC size, distensibility, or collapsibility has limited and unproven utility at the present time.
7. The actions of vasoactive drugs are typically considered in relation to the arterial circulation but many have significant effects on the venous circulation.
8. Venoconstrictors (e.g., alpha agonists) increase venous tone and thereby reduce venous capacitance, thus increasing the stressed volume at the expense of the unstressed volume. In a hypovolemic patient, this reduction in unstressed volume may in turn reduce microcirculatory blood flow and thereby compromise cellular metabolism, due to reduced perfusion despite maintenance of normal blood pressure.

Table 1 Summary of methods predicting fluid responsiveness

Method	Threshold (%)	Main limitations
Pulse pressure/stroke volume variations (PPV/SVV) (Michard et al., 2000)	12	Cannot be used in case of spontaneous breathing, low tidal volume/lung compliance. Need regular cardiac rhythm
Inferior vena cava diameter variations (Vignon et al., 2017)	12	Cannot be used in case of spontaneous breathing, low tidal volume/lung compliance. Need regular cardiac rhythm
Superior vena cava diameter variations (Vignon et al., 2017)	36	Requires performing transesophageal Doppler. Cannot be used in case of spontaneous breathing, low tidal volume/lung compliance. Need regular cardiac rhythm
Passive leg raising (Monnet et al., 2006)	10	Requires a direct measurement of cardiac output. May be inaccurate in intra-abdominal hypertension
End-expiratory occlusion test (Monnet et al., 2009)	5	Cannot be used in non-intubated patients. Cannot be used in patients who interrupt a 15-second respiratory hold
“Mini” fluid challenge (Muller et al., 2011)	6	Requires a precise technique for measuring cardiac output
“Conventional” fluid challenge (500 mL) (Vincent & Weil, 2006)	15	Requires a direct measurement of cardiac output. Can induce fluid overload if repeated

9. Venodilators (e.g., nitroglycerin) reduce venous tone and thereby increase venous capacitance and decrease the stressed volume. This typically decreases venous return and left ventricular end-diastolic volume.
10. Intra-abdominal hypertension (e.g., pneumoperitoneum) may reduce venous return or venous capacitance.

Background

More than 230 million major surgical procedures are undertaken worldwide each year (Weiser et al., 2008). Data from the USA and Europe suggests that approximately 18% of patients undergoing surgery will develop a major postoperative complication and 3 to 5% will die before hospital discharge (Weiser et al., 2008; Khuri et al., 2005; Ghaferi et al., 2009; Pearse et al., 2012). Those patients who develop a postoperative complication and survive to hospital discharge have diminished functional independence and reduced long-term survival up to 8 years after major surgery (Khuri et al., 2005). Interventions that reduce the risks of postoperative death and complications, particularly in high risk patients have become a priority in perioperative medicine (Jacobs, 2009). Perioperative goal-directed therapy (GDT), based on the titration of fluids and vasoactive drugs to achieve physiological, flow-related end points, is a promising approach to reduce postoperative complications and deaths (Bednarczyk et al., 2017; Pearse et al., 2014; Hamilton et al., 2011).

Optimal fluid therapy in the perioperative and critical care settings depends on understanding the underlying cardiovascular physiology and individualizing assessment of the dynamic patient (Malbrain et al., 2018). Historical approaches to fluid administration based on clinical examination (e.g., “volume status”) or static measures of cardiovascular function (e.g., central venous pressure or pulmonary artery occlusion pressure) do not adequately

determine fluid needs or to predict response to fluid administration (Van der Mullen et al., 2018). Dynamic indices, such as SVV, utilize the concepts of the Frank-Starling relationship that implicitly incorporate venous capacitance and mean systemic filling pressure to predict fluid responsiveness with good accuracy. However, in the context of optimal fluid administration, knowledge gaps remain for several key physiologic concepts and clinical scenarios. This manuscript from the 5th Perioperative Quality Initiative (POQI) group addresses fundamental concepts in fluid responsiveness and venous capacitance in order to provide an educational update and clinical guidance related to perioperative fluid management.

Methods

POQI is an international, multidisciplinary non-profit organization that organizes consensus conferences on clinical topics related to perioperative medicine (Miller et al., 2016). Each conference assembles a collaborative group of diverse international experts from multiple healthcare disciplines to develop consensus-based recommendations in perioperative medicine.

Applying a modified Delphi method, designed to use the collective expertise of a diverse group of experts to answer clinically important questions, we achieved consensus on several topics related to fluid responsiveness and fluid management.

Expert group

An international group of authorities, with specific content area expertise (based on the conduct of research and education in this area), was invited to participate. In total, 21 experts from around North America and Europe met in Durham, NC, on June 16-17, 2018, to iteratively discuss the clinical and physiological evidence of fluid responsiveness and venous capacitance as relevant factors in fluid management, in order to develop consensus statements with practical recommendations

for a broad group of clinicians involved in intravenous fluid therapy.

Process

Based on literature searches performed by POQI group members, a list of relevant questions was collectively formulated and circulated electronically prior to the meeting. In the first plenary session, these questions were presented to receive feedback and assistance in refining the questions. There were then at least two Delphi rounds to develop the statements before final agreement. This manuscript is based on these multiple rounds of feedback from all the experts present at the POQI meeting.

Results/discussion

Key physiologic and clinical terminology are shown in Tables 2 and 3. Based on the literature identified by the participants and discussions held both prior to the conference and during the iterative consensus-building process, the following key concepts and core questions were considered most relevant to perioperative fluid management with respect to fluid responsiveness and venous capacitance:

Key concepts

- I. *The ultimate goal of fluid therapy and hemodynamic management is to provide the conditions that enable normal homeostasis and cellular metabolic function in order to produce optimal patient outcomes.*
- II. *Fluid and hemodynamic management is dependent on the relationship between pressure, volume, and*

flow in a dynamic system which is distensible with variable elastance and capacitance properties.

Core questions

What are the physiologic and clinical goals of therapeutic fluid (hemodynamic) resuscitation?

The ultimate goal of fluid therapy and hemodynamic management is to provide the conditions that enable normal cellular metabolic function in order to produce optimal patient outcomes. The discrete goals of fluid therapy exist at several levels: at the level of the macrocirculation, the microcirculation, and at the cellular level (Fig. 1). It is a limitation of medical science that cellular metabolic function cannot be discretely and specifically measured in the clinical context, particularly locally for each of the wide variety of organ systems, and in continuous or repeatable series that permit clinical decision-making. Because of this limitation, for clinical care, we target intermediate variables of varying sensitivity, such as cardiac output (CO), stroke volume (SV), mean arterial pressure (MAP), central venous pressure (CVP), mixed venous saturation (SvO₂) and central venous oxygen saturation (ScvO₂), heart rate (HR), and urine output. While these parameters may indicate the presence of, or the risk for, cellular metabolic dysfunction, they are insensitive in this regard and do not differentiate cellular dysfunction due to macrocirculatory versus microcirculatory abnormalities.

Although restoration of the macrocirculation provides the basis for normal microcirculatory and cellular metabolic function, it does not guarantee them. Microcirculatory and cellular metabolic dysfunction may develop or persist despite establishing normal microcirculatory parameters, such as MAP and CO. However, because dysfunction of the macrocirculation (e.g., hypotension) often produces dysfunction at the microcirculatory and cellular levels, the first step in therapeutic fluid resuscitation is restoration of the macrocirculation. It is worth noting that restoration of the macrocirculation is not achieved by reaching the same target in every patient. Macrocirculatory parameters such as MAP and CO should be personalized both for the individual and for the patients' current condition.

Recently, several investigators introduced the term "hemodynamic coherence" to describe the physiologic state in which improved macrocirculatory function results in improvements in the microcirculation (Ince, 2015; Morelli & Passariello, 2016). In contrast, the term "hemodynamic incoherence" describes a physiological state in which resuscitation to adequate macrocirculatory parameters does not result in an improved microcirculation. This state appears to happen frequently in patients with sepsis. Four subsets of hemodynamic incoherence are proposed. In the first, obstruction of some small blood vessels results in heterogeneous perfusion of

Table 2 Physiologic terminology

Term	Definition
Arterial elastance	The ratio of left ventricular end-systolic pressure and stroke volume
Intravascular volume	The blood volume within the vascular system (arteries, capillaries, veins)
Mean systemic filling pressure	The pressure of venous return when cardiac activity is absent
Preload	Volume defined by the distending pressure it generates. In the heart, preload is LV wall stress at end of diastole (= EDV)
Stressed volume	The (theoretically measurable) volume of blood that exerts distending pressure against the vascular wall
Total body water	The amount of sodium-free water in the whole body, commonly divided into the extracellular fluid space and the intracellular fluid space
Unstressed volume	The volume of blood just to the point of filling the blood vessels but without exerting any pressure on the vessel walls
Vascular capacitance	The change in volume divided by the change in pressure (i.e., the inverse of elastance)

Table 3 Clinical terminology

Term	Definition
Fluid bolus	The rapid administration of intravenous fluid with therapeutic intent, most often to rapidly replace intravascular volume in patients who are presumed to be fluid responsive.
Fluid challenge	The rapid administration of intravenous fluid with diagnostic intent, most often to determine whether a patient with hemodynamic compromise will benefit from further fluid administration.
Fluid overload (overhydration)	Increased total body fluid volume (intravascular, interstitial, and intracellular). Fluid overload may be defined by at least 10% increase in total body fluid volume. Sometimes referred to as “overhydration” or “hyperhydration.” Fluid overload is the opposite of dehydration.
Fluid underload (dehydration)	Decreased total body fluid volume. The percentage of fluid loss is defined by dividing the cumulative fluid balance in liters by the patient’s baseline body weight and multiplying by 100%. Dehydration is defined by a minimum value of 5% fluid loss. Dehydration is considered mild (5-7.5%), moderate (7.5-10%), while loss of over 10% is considered severe. Sometimes referred to as “fluid underload.” Dehydration is the opposite of fluid overload.
Fluid responsiveness	An increase in stroke volume in response to an increase in intravascular volume. Also referred to as “volume responsiveness.”
Hypovolemia	Reduced intravascular volume and marked by increases in stroke volume when intravenous fluid is given (i.e., the state of being fluid responsive). Clinical “hypovolemia” may exist, for example, from loss of intravascular volume (e.g., hemorrhage) or from reductions in intravascular volume due to increases in venous capacitance. Sometimes referred to as “fluid underload.”
Hypervolemia	Hypervolemia is above normal or increased intravascular volume. Hypervolemia is the opposite of hypovolemia.
Passive leg raise	A diagnostic postural maneuver raising the lower extremities up to 45 degrees from the recumbent position, to transiently increase venous return from the lower extremities in order to measure the hemodynamic effect and thus determine if a patient is fluid responsive.

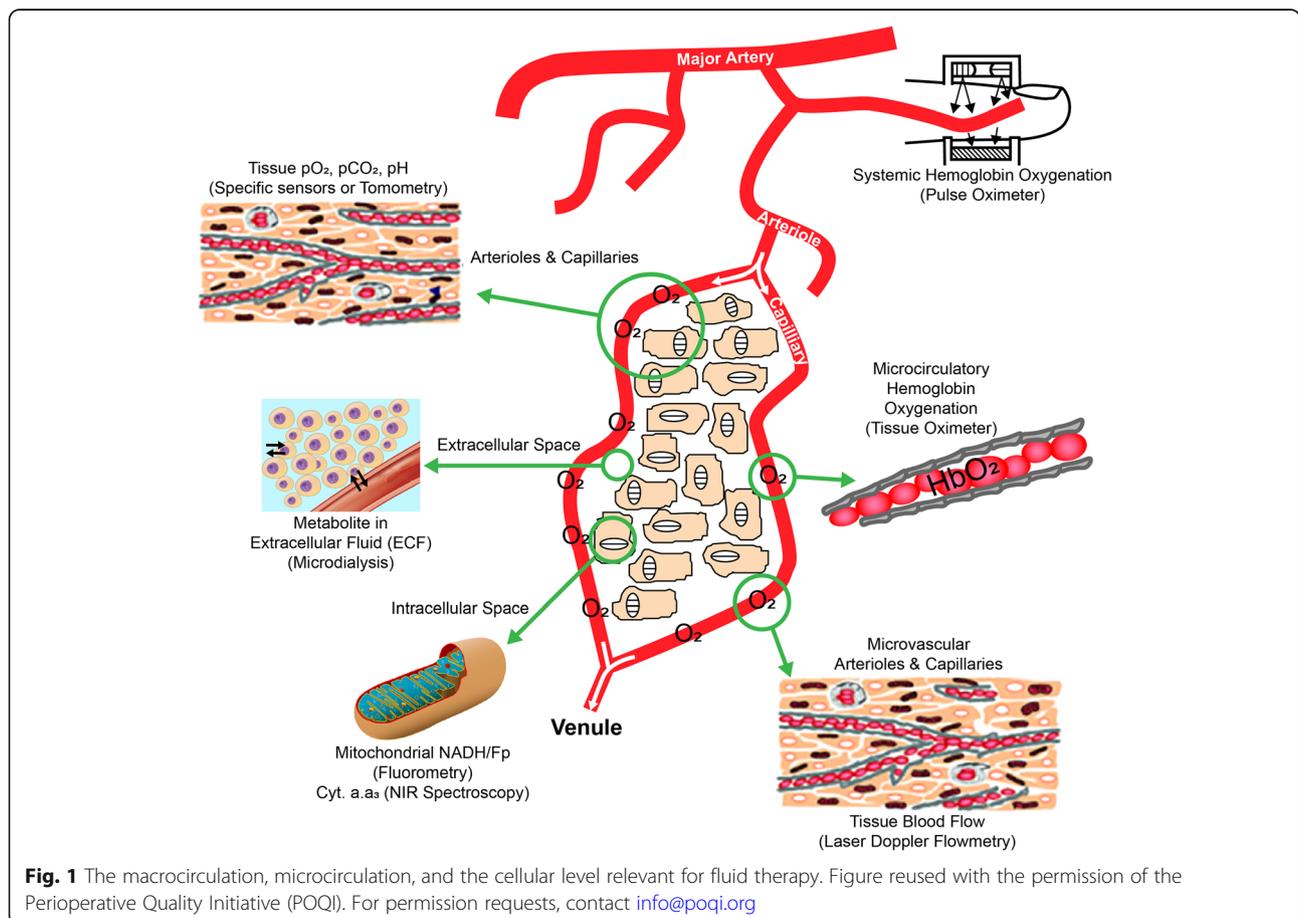


Fig. 1 The macrocirculation, microcirculation, and the cellular level relevant for fluid therapy. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org

the microcirculation. In the second, hemodilution results in perfusion of capillaries with blood that has a low oxygen carrying capacity. In the third, increased arterial resistance and increased venous pressures lead to capillary stasis due to low arterial-venous pressure gradients (see below). In the fourth, edema causes large distances between capillaries and target tissues across which oxygen and other energy substrates must diffuse to reach their targets. Notably, administration of IV fluid may lead to hemodilution, increased venous pressures, and edema formation, thus contributing to hemodynamic incoherence.

The first goal of therapeutic fluid and hemodynamic resuscitation is targeted at macrocirculatory parameters (usually MAP) because they are measurable and they represent the most apparent clinical markers of organ or tissue perfusion, particularly in combination with other clinical and laboratory assessments. When the MAP falls below an organ's autoregulatory range, there is an almost linear decrease in organ blood flow (Ackland et al., 2019). The fall in blood flow is likely to occur at a higher MAP in patients with long-standing hypertension due to a shift in the autoregulatory range. Furthermore, different vascular beds will lose autoregulation at different MAPs. For example, the mammalian kidney loses autoregulation at a MAP of about 70 mmHg, the brain between 60-70 mm Hg, while the coronary circulation loses autoregulation at a MAP of about 50-55 mmHg (Drummond, 1997; Drummond, 2019; Paulson et al., 1990; Bellomo & Di Giandomasso, 2001; Meng, 2019). Therefore, the first hemodynamic goal is to achieve a MAP > 65-70 mmHg to preserve organ perfusion (Sessler et al., 2019).

The second and third goals of fluid and hemodynamic resuscitation are targeted at the microcirculation and the cellular levels. As noted above, dysfunction at these levels may develop or persist despite the appearance of normal macrocirculatory parameters, and devices to characterize the microcirculation and cellular function are not routinely available for clinical use. The microcirculation may be assessed directly using tools such as intravital microscopy or laser Doppler flowmetry, or indirectly using tissue oximetry and near infrared spectroscopy (Tafner et al., 2017). Clinical examination (e.g., examination of capillary refill time or assessing for skin mottling) may also give important clues about the adequacy of perfusion in the microcirculation (Hernandez et al., 2019). Efforts to realize the potential for microcirculatory monitoring for point-of-care diagnosis in real-time at the bedside are currently underway (Naumann et al., 2016).

In the clinical setting, the only reason to give any patient a fluid bolus is to increase the SV. In the absence of an increase in SV, giving a fluid challenge serves no useful purpose and is likely to be harmful. An increase in SV will only occur if two conditions are met: (1) that

the fluid bolus increases the stressed blood volume causing an increase in MSFP, thereby increasing venous return, and (2) that both ventricles are functioning on the ascending limb of the Frank-Starling curve.

Organ blood flow is driven by the difference in the pressure between the arterial and venous circulation. For example, the MAP minus the CVP is the driving force for organ blood flow while the difference between post-arteriolar and venular pressure determines microcirculatory flow. In circumstances of increased venous pressure, such as high right atrial pressure, the backwards transmission of pressure may impede microcirculatory flow in the tissues and organs.

What is the role of venous capacitance in fluid and hemodynamic therapy?

Fluid optimization must consider each of the fluid compartments in the body: total body water divided into the intracellular and extracellular spaces, and more discretely the plasma volume and blood volume, the interstitial fluid volume, and the tissue-bound water volume (Fig. 2).

The left ventricle can only pump into the arterial circulation; the volume of blood that it receives from venous return (Funk et al., 2013). Because approximately two-thirds of the total blood volume is in the venous system, the roles of the venous system in general and venous capacitance specifically are important for fluid therapy and hemodynamic management. Through their capacitance function, veins and venules regulate both regional and central blood volume and therefore cardiac preload: changes in venous tone directly influence SV and CO via the Frank-Starling mechanism. It is important for anesthesia providers to understand venous return, venous capacitance, and their role in determining CO.

With two-thirds of the blood volume within the venous system, changes in venous blood volume play a major role in determining venous return and CO (Fig. 3). The venous system can be divided into two theoretical compartments, the unstressed and the stressed volume (Gelman, 2008). The intravascular volume that fills the venous system to the point just before intravascular pressure starts to rise is called unstressed volume, whereas the volume that stretches the veins and causes intravascular pressure to rise is called the stressed volume (Figs. 4, 5). Another way to think of stressed volume is the (theoretically measurable) portion of blood that exerts distending pressure against the vein wall. Differentiating between these two volumes is important because stressed volume determines the MSFP, which is the pressure of venous return when cardiac activity is absent, representing the elastic recoil of the venous system. Through MSFP, the stressed blood volume is a major contributor of venous pressure and therefore venous return.

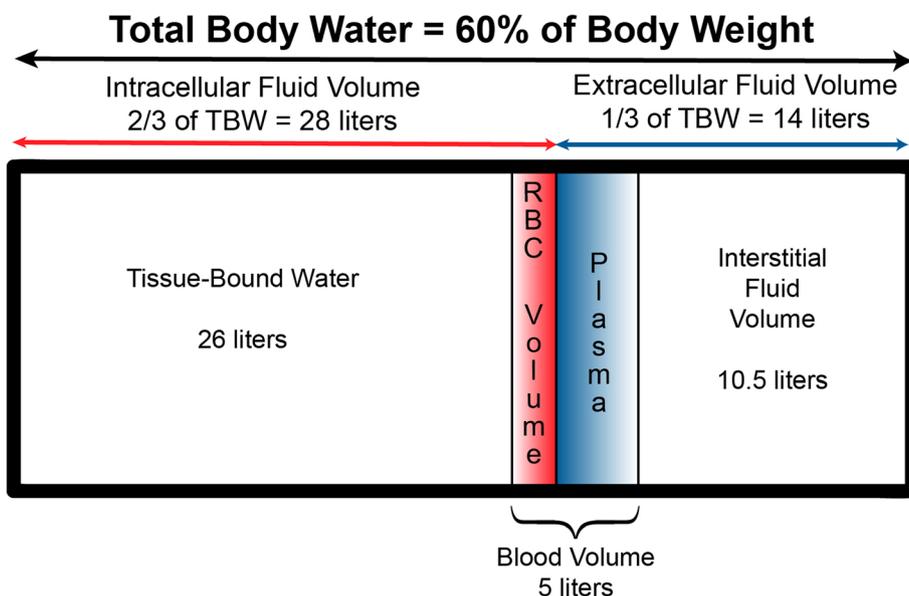


Fig. 2 Fluid compartments in adult humans. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org

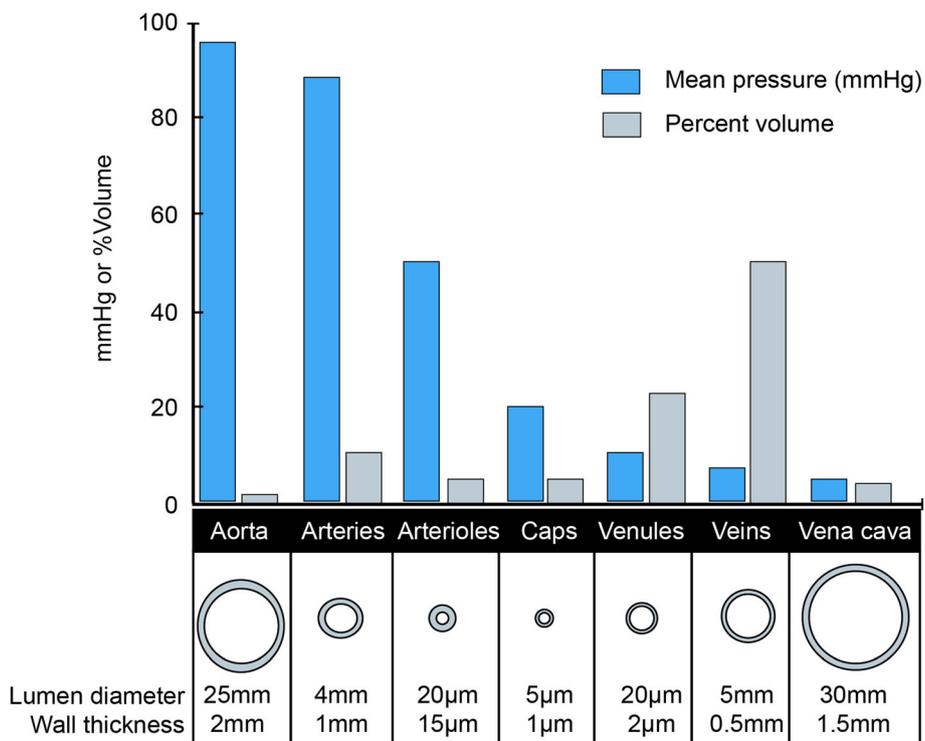


Fig. 3 Pressure and volume in the venous system. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org

Stressed & Unstressed Volume

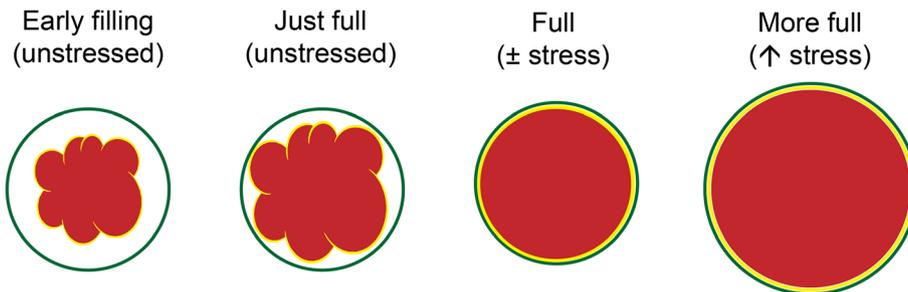


Fig. 4 Depiction that differentiates stressed and unstressed volumes in the venous circulation. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org

The unstressed volume normally accounts for about 75% of the venous blood volume, thus the venous system acts as a reservoir that can rapidly recruit blood from the unstressed blood volume to maintain venous return to the right heart (Gelman, 2008; Peters et al., 2001). Splanchnic and cutaneous veins are highly compliant and represent the largest blood volume reservoirs. Alterations in venous tone can change the relative proportions of the unstressed and stressed volumes. For example, alpha adrenergic receptor agonists may increase venous tone and thus increase the stressed volume (and simultaneously lower the unstressed volume), increasing venous return to the heart, raising SV and CO. (Kalmar et al., 2018; Hamzaoui et al., 2010)

What is fluid responsiveness? How do we define it, is there variation in proposed definitions, and is there variation from those in clinical practice?

Assessing fluid responsiveness is the safest and most effective method to guide fluid therapy. Conceptually, fluid responsiveness is defined as a state of recruitable SV in response to fluid administration (see Table 3).

Intravascular volume and other measures of volume status have limited utility and must always be considered in the context of fluid responsiveness. Intravascular volume is distinct from total body fluid volume and must be interpreted in the context of the individual patient. For example, patients with excess total body fluid volume may have normal or low intravascular volume and favorably respond to intravenous fluid administration. Common clinical terminology is shown in Table 3, and core concepts regarding volume status and fluid responsiveness include the following:

- All hypovolemic patients are fluid responsive but not all fluid responsive patients are hypovolemic.
- Euvolemic and hypervolemic patients may be fluid responsive (i.e., have preload recruitable SV).

Therefore, fluid non-responsiveness does not indicate hypervolemia.

- The term fluid overload is confusing and is not the appropriate term to indicate intravascular hypervolemia (Vincent & Pinsky, 2018).

Clinically, fluid responsiveness is defined as an increase in SV in response to an increase in intravascular volume. Fluid responsiveness is one component of preload responsiveness, which indicates a state of recruitable SV and is defined as a state in which increases in end-diastolic volume (EDV) produce an increase in SV (Pinsky, 2015). At the bedside, there are varying definitions of fluid responsiveness based upon the setting and the monitoring available for the patient, with the most common definition being an increase of SV of 15% after the patient receives 500 mL of crystalloid administered over 10-15 min (Marik et al., 2009; Marik & Cavallazzi, 2013). Full characterization of fluid responsiveness requires consideration of the type, amount and timing of fluid, and the expected change in SV. It is noteworthy that even among hemodynamically unstable patients, only approximately half of patients are fluid responsive, which means that fluid loading in the approximately 50% of non-responsive patients will likely cause more harm than benefit.

The only method of directly measuring fluid responsiveness is continuous or rapidly repeatable measures of SV in response to a fluid challenge, a passive leg raise (PLR) maneuver, or controlled changes in intra-thoracic pressure. Passive leg raising is a postural maneuver raising the lower extremities up to 45 degrees from the recumbent position, which results in a transient increase in the venous return from the lower extremities in order to measure the hemodynamic effect and thus determine if a patient is responsive to fluid therapy (Fig. 6). Because PLR replicates a transient fluid bolus and predicts fluid responsiveness without administration of IV fluids, it

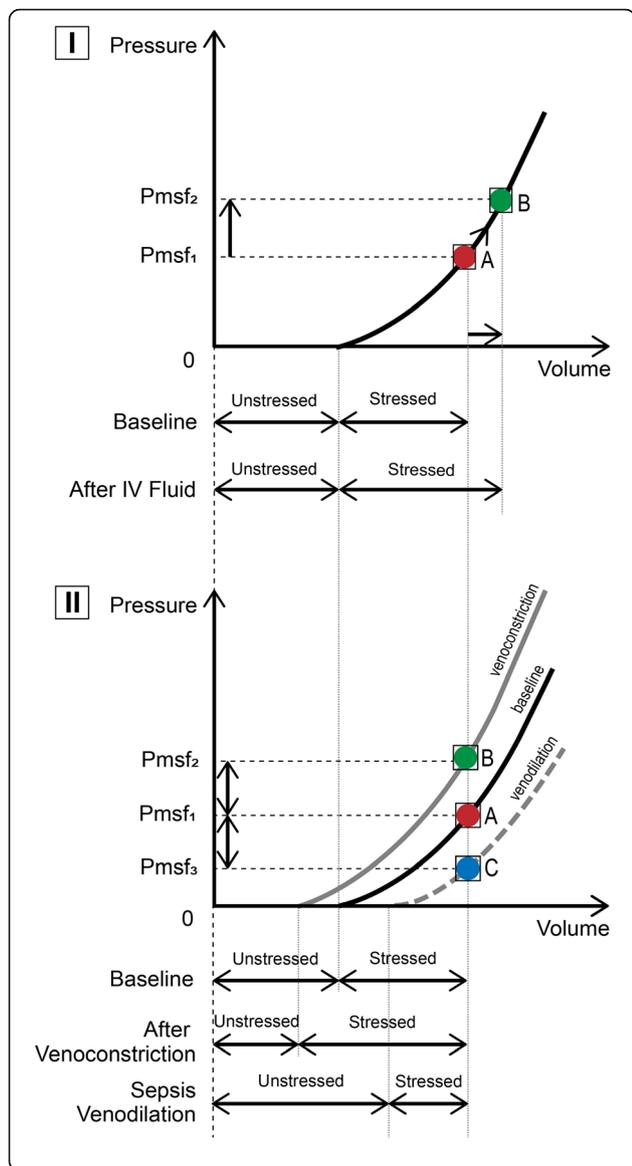


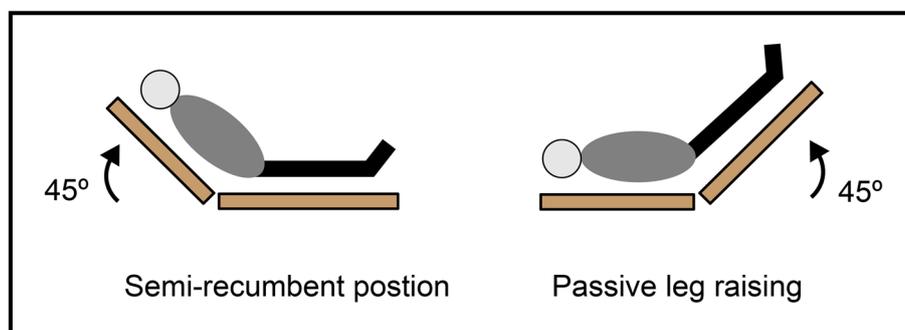
Fig. 5 Effects of fluid and vasoactive agents on cardiovascular performance and the venous system. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org. **I** Effect of volume loading on mean systemic filling pressure (Pmsf) and (un)stressed volume. Administration of a fluid bolus increases Pmsf (from Pmsf1 to Pmsf2, indicated respectively by position A (red dot) to B (green dot) on the pressure/volume curve). Unstressed volume remains constant while stressed volume increases. Total volume = unstressed + stressed increases, carrying a risk for fluid overload. See text for explanation. **II** Effect of venoconstriction and venodilation on mean systemic filling pressure (Pmsf) and (un)stressed volume. Venoconstriction increases Pmsf (from Pmsf1 to Pmsf2, indicated respectively by position A (red dot) to B (green dot) on the pressure/volume curve). Unstressed volume decreases while stressed volume increases. Total volume = unstressed + stressed remains constant, resulting in an auto-transfusion effect. Venodilation as seen in sepsis (vasoplegia) decreases Pmsf (from Pmsf1 to Pmsf3, indicated respectively by position A (red dot) to C (blue dot) on the pressure/volume curve). Unstressed volume increases while stressed volume decreases. Total volume = unstressed + stressed remains constant, resulting in an intravascular underfilling effect

mitigates the risk of excessive IV fluids that may be particularly deleterious in patients at greater risk for or poor tolerance of hypervolemia (e.g., heart failure, chronic kidney disease, chronic lung disease). Alternative methods for predicting fluid responsiveness include SVV, PPV, SPV, and (in certain mechanically ventilated patients) the end-expiratory occlusion test and respiratory systolic variation test (see Table 1).

A common approach to test fluid responsiveness is the administration of a 500 mL fluid challenge over < 15 min with a positive response defined by a ≥ 15% increase in SV, or a 250 mL fluid challenge over < 15 min with a positive response defined by a ≥ 10% increase in SV. However:

- Investigations into fluid responsiveness vary in fluid type, volume, infusion time, and consequent change in SV.
- Patients at risk for adverse effects from fluid administration, such as CHF and ESRD, may receive lower volume fluid challenges (e.g., 100 mL), although the accuracy of the test to predict fluid responsiveness is reduced (i.e., greater risk of false negative test).
- The volume of fluid challenge depends on the type of fluid given: crystalloid, colloid, or blood.

Recognizing that SV cannot be measured in all settings, MAP or HR may be used as crude surrogate indicators, recognizing they have limited predictive value. Although the existing literature has examined the effect of a fluid challenge on SV, a fluid challenge or PLR could be useful in detecting whether inadequate preload is contributing to hypotension. If the fluid challenge/



The passive leg-raising test consists of measuring the hemodynamic effects of a leg elevation up to 45°. A simple way to perform the postural maneuver is to transfer the patient from the semi-recumbent posture to the passive leg-raising position by using the automatic motion of the bed.

Fig. 6 Stylized depiction of the passive leg raise (PLR) maneuver. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org

PLR does not correct hypotension, additional monitoring may be appropriate and further management should focus on vascular tone and chronotropy/inotropy (McEvoy et al., 2019).

Under what situations can fluid responsiveness be used clinically to decide when to give, and when to stop giving fluid?

In the perioperative period, when fluid losses may be substantial, fluid responsiveness is generally an indication for fluid administration but should be interpreted in the clinical context of the patient. In patients who are predicted to be non-responsive to fluid administration, fluids should not be given unless other clinical indicators suggest net benefit (e.g., need for water). The same assessments apply to the decision to stop giving intravenous fluids, which may be based upon the parameters judging fluid responsiveness and the clinical context of the patient for a global assessment or benefit and risk.

A key clinical question to ask when assessing a patient's fluid responsiveness is whether increasing the SV and CO is beneficial. For example, a patient might have an adequate or high SV index and cardiac index and still show evidence of fluid responsiveness. Giving fluid might not be indicated since achieving a still higher SV index and cardiac index might not yield important clinical benefits.

All tests for fluid responsiveness have limitations (Table 1). For example, SVV testing requires a regular cardiac rhythm, the lack of patient inspiratory efforts, and consistent changes in intrathoracic pressure produced by mechanical ventilation with tidal volumes of at least 8 mL/kg predicted body weight. PLR testing requires measurement of SV or CO and may produce false negative results in the setting of intra-abdominal hypertension.

While ultrasonographic evaluation of vena cava diameter, distensibility, and collapsibility are increasingly used in emergency medicine and critical care, its use has numerous confounders (right heart dysfunction, obstructive cardiac physiology, transpulmonary and intraabdominal pressure, mode of ventilatory support) and is not currently supported by evidence in the perioperative setting (Millington, 2019; Via et al., 2016). Finally, it is important to note that fluid bolus therapy rapidly impacts the macrocirculation but does not necessarily alter the microcirculation or cellular function, especially during the short time frame used to assess fluid responsiveness. Further, the effects of crystalloid boluses on SV and CO are often short-lived, as the crystalloid fluid redistributes into the extravascular extracellular space (Nunes et al., 2014; Aya et al., 2016).

Despite these limitations the assessment of fluid responsiveness probably leads to improved patient outcomes among patients who undergo high-risk and complex surgery (Bednarczyk et al., 2017).

What is the research agenda?

Our increasing understanding of the physiological and clinical consequences of intravenous fluid therapy has led to new and important questions that must be answered in order to further refine our clinical use of intravenous fluids. Future research should focus on the following key areas:

- As the fundamental therapeutic goal of intravenous fluid administration into the macrocirculation is to optimize microcirculatory and cellular function, we need better tools to assess both of those critical features at the bedside.

- We need to identify or create methods with everyday clinical utility to measure intravascular volume, and for monitoring the benefits/harm of fluid therapy.
- We need to better define exactly how to perform a fluid challenge and a fluid responsive patient.
- Emerging evidence suggests that fluid management should always be individualized based on each patient's unique hemodynamics and cardiac function, underlying disease process and co-morbidities. We must recognize the dynamic nature of patient trajectories throughout the perioperative period to better define optimal fluid administration and removal strategies.

Further research in these key areas will lay the foundation for moving from group-targeted fluid therapy to truly individualized fluid therapy.

Conclusions

In the POQI-5 consensus conference, we discussed the clinical and physiological evidence of fluid responsiveness and venous capacitance as relevant factors in fluid management and developed consensus statements with clinical implications for a broad group of clinicians involved in intravenous fluid therapy. Two key concepts emerged: (1) The ultimate goal of fluid therapy and hemodynamic management is to provide the conditions that enable normal cellular metabolic function in order to produce optimal patient outcomes, and (2) fluid and hemodynamic management is dependent on the relationship between pressure, volume, and flow in a dynamic system which is distensible and has variable elastance and capacitance.

Abbreviations

CVP: Central venous pressure; CO: Cardiac output; EDV: End-diastolic volume; GDT: Goal-directed therapy; HR: Heart rate; IV: Intravenous; MAP: Mean arterial pressure; MSFP: Mean systemic filling pressure; PLR: Passive leg raise; POQI: Perioperative Quality Initiative; PPV: Pulse pressure variation; SPV: Systolic pressure variation; ScvO₂: Mixed central venous oxygen saturation; SvO₂: Mixed venous oxygen saturation; SV: Stroke volume; SVV: Stroke volume variation

Acknowledgements

Not applicable

Authors' contributions

All authors contributed to the development of the manuscript, agree to its contents, and approved its final version.

Funding

The Perioperative Quality Initiative-5 consensus conference was supported by an unrestricted educational grant from the Perioperative Quality Initiative, which has received grants from Baxter, Bev MD, Cadence, Cheetah Medical, Edwards, Heron Pharmaceutical, Mallinckrodt, Masimo, Medtronic, Merck, Trevena, and Pacira.

Availability of data and materials

Not applicable

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

GSM - none; DAK - grant funding and travel reimbursement for Cheetah Medical, Advisory Board and speaker honoraria for Pulsion Medical Systems; PEM - advisory board and research funding from Baxter; NS - none; DL - none; JW - none; DBM - none; DC - Speakers Bureau for Edwards Lifesciences, Medtronic; JL - none; TW - none; KM - none; MLNGM - xxx; TMW - none; DM - consultant for Edwards Lifesciences and Siemens Healthineers; CHEI - none; MWM - none; HH - none; MPWG - research funding from Sphere Medical Ltd (UK) and Pharmacosmos Ltd (UK), advisory board of Sphere Medical Ltd; MGM - University Chair Sponsor at UCL by Smiths Medical, Director Evidence Based Perioperative Medicine (EBPOM) Community Interest Company (CiC), Director Medinspire Ltd (Patent holder "QUENCH"), Paid consultant for Edwards Lifesciences and Baxter; TJG - Consultant for Acacia, Edwards Lifesciences, Mallinckrodt, Medtronic and Merck; TEM - research funding and consultant for Edwards Lifesciences.

Author details

¹Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Emory Critical Care Center, Emory University School of Medicine, Grady Health System, Atlanta, GA, USA. ²Division of Pulmonary, Critical Care, and Sleep Medicine, NYU School of Medicine, New York, NY, USA. ³Division of Pulmonary and Critical Care Medicine, Eastern Virginia Medical School, Norfolk, VA, USA. ⁴Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA. ⁵Critical Care Research Group, NIHR Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust/University of Southampton, Southampton, UK. ⁶Department of Anesthesiology, Division of General, Vascular and Transplant Anesthesia, Duke University School of Medicine, Duke University Medical Center, Durham, NC, USA. ⁷TopMedTalk, London, UK. ⁸Institute of Sport Exercise & Health, University College London, London, UK. ⁹University Hospitals Southampton, Southampton, UK. ¹⁰Respiratory Biomedical Research Unit, University of Southampton, Southampton, England. ¹¹Department of Intensive Care, University Hospital Brussels, Jette, Belgium and Faculty of Medicine and Pharmacy, Vrije Universiteit Brussels, Brussels, Belgium. ¹²Elsevier R&D Solutions, 1600 JFK Blvd, Philadelphia, PA 19103, USA. ¹³Intensive Care Unit and Division of Surgery and Interventional Science, Royal Free Hospital, London, UK. ¹⁴Vascular and Renal Transplant Surgeon, National Institute of Health Research Clinical Research Facility, Coventry, UK. ¹⁵UCL/UCLH National Institute of Health Research Biomedical Research Centre, London, UK. ¹⁶Department of Anesthesiology, Stony Brook University, Stony Brook, NY, USA. ¹⁷Department of Anesthesiology and Critical Care, Stony Brook University, Stony Brook, New York, USA. ¹⁸Private address: Louisville, Kentucky, USA.

Received: 30 September 2019 Accepted: 18 March 2020

Published online: 21 April 2020

References

- Ackland GL, Brudney CS, Cecconi M, et al. Perioperative Quality Initiative consensus statement on the physiology of arterial blood pressure control in perioperative medicine. *Br J Anaesth*. 2019;122:542–51.
- Aya HD, Ster IC, Fletcher N, Grounds RM, Rhodes A, Cecconi M. Pharmacodynamic analysis of a fluid challenge. *Crit Care Med*. 2016;44:880–91.
- Bednarczyk JM, Fridfinnson JA, Kumar A, et al. Incorporating dynamic assessment of fluid responsiveness into goal-directed therapy: a systematic review and meta-analysis. *Crit Care Med*. 2017;45:1538–45.
- Bellomo R, Di Giandomasso D. Noradrenaline and the kidney: friends or foes? *Crit Care*. 2001;5:294–8.
- Drummond JC. The lower limit of autoregulation: time to revise our thinking? *Anesthesiol*. 1997;86:1411–33.
- Drummond JC. Blood pressure and the brain: how low can you go? *Anesth Analg*. 2019;128:759–71.
- Funk DJ, Jacobsohn E, Kumar A. Role of the venous return in critical illness and shock: part II-shock and mechanical ventilation. *Crit Care Med*. 2013;41:573–9.

- Gelman S. Venous function and central venous pressure: a physiologic story. *Anesthesiology*. 2008;108:735–48.
- Ghaferi AA, Birkmeyer JD, Dimick JB. Variation in hospital mortality associated with inpatient surgery. *N Engl J Med*. 2009;361:1368–75.
- Hamilton MA, Cecconi M, Rhodes A. A systematic review and meta-analysis on the use of preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. *Anesth Analg*. 2011;112:1392–402.
- Hamzaoui O, Georger JF, Monnet X, et al. Early administration of norepinephrine increases cardiac preload and cardiac output in septic patients with life-threatening hypotension. *Crit Care*. 2010;14:R142.
- Hernandez G, Ospina-Tascon GA, Damiani LP, et al. Effect of a resuscitation strategy targeting peripheral perfusion status vs serum lactate levels on 28-day mortality among patients with septic shock: the ANDROMEDA-SHOCK randomized clinical trial. *JAMA*. 2019;321:654–64.
- Ince C. Hemodynamic coherence and the rationale for monitoring the microcirculation. *Crit Care*. 2015;19 Suppl 3:S8.
- Jacobs DO. Variation in hospital mortality associated with inpatient surgery—an O.S. *N Engl J Med*. 2009;361:1398–400.
- Kalmar AF, Allaert S, Pletinckx P, et al. Phenylephrine increases cardiac output by raising cardiac preload in patients with anesthesia induced hypotension. *J Clin Monit Comput*. 2018;32:969–76.
- Khuri SF, Henderson WG, DePalma RG, et al. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. *Ann Surg*. 2005;242:326–41.
- Malbrain M, Van Regenmortel N, Saugel B, et al. Principles of fluid management and stewardship in septic shock: it is time to consider the four D's and the four phases of fluid therapy. *Ann Intensive Care*. 2018;8:66.
- Marik PE, Cavallazzi R. Does the central venous pressure predict fluid responsiveness? An updated meta-analysis and a plea for some common sense. *Crit Care Med*. 2013;41:1774–81.
- Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med*. 2009;37:2642–7.
- McEvoy MD, Gupta R, Koepke EJ, et al. Perioperative Quality Initiative consensus statement on postoperative blood pressure, risk and outcomes for elective surgery. *Br J Anaesth*. 2019;122:575–86.
- Meng L. Heterogeneity and variability in pressure autoregulation of organ blood flow: lessons learned over 100+ years. *Crit Care Med*. 2019;47:436–48.
- Michard F, Boussat S, Chemla D, et al. Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. *Am J Respir Crit Care Med*. 2000;162:134–8.
- Miller TE, Shaw AD, Mythen MG, Gan TJ. Perioperative Quality Initiative IW. Evidence-based perioperative medicine comes of age: the Perioperative Quality Initiative (POQI): the 1st consensus conference of the Perioperative Quality Initiative (POQI). *Perioper Med (Lond)*. 2016;5:26.
- Millington SJ. Ultrasound assessment of the inferior vena cava for fluid responsiveness: easy, fun, but unlikely to be helpful. *Can J Anaesth*. 2019;66:633–8.
- Monnet X, Osman D, Ridet C, Lamia B, Richard C, Teboul JL. Predicting volume responsiveness by using the end-expiratory occlusion in mechanically ventilated intensive care unit patients. *Crit Care Med*. 2009;37:951–6.
- Monnet X, Rienzo M, Osman D, et al. Passive leg raising predicts fluid responsiveness in the critically ill. *Crit Care Med*. 2006;34:1402–7.
- Morelli A, Passariello M. Hemodynamic coherence in sepsis. *Best Pract Res Clin Anaesthesiol*. 2016;30:453–63.
- Muller L, Toumi M, Bousquet PJ, et al. An increase in aortic blood flow after an infusion of 100 ml colloid over 1 minute can predict fluid responsiveness: the mini-fluid challenge study. *Anesthesiology*. 2011;115:541–7.
- Naumann DN, Mellis C, Husheer SL, et al. Real-time point of care microcirculatory assessment of shock: design, rationale and application of the point of care microcirculation (POEM) tool. *Crit Care*. 2016;20:310.
- Nunes TS, Ladeira RT, Bafi AT, de Azevedo LC, Machado FR, Freitas FG. Duration of hemodynamic effects of crystalloids in patients with circulatory shock after initial resuscitation. *Ann Intensive Care*. 2014;4:25.
- Paulson OB, Strandgaard S, Edvinsson L. Cerebral autoregulation. *Cerebrovasc Brain Metab Rev*. 1990;2:161–92.
- Pearse RM, Harrison DA, MacDonald N, et al. Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. *JAMA*. 2014;311:2181–90.
- Pearse RM, Moreno RP, Bauer P, et al. Mortality after surgery in Europe: a 7 day cohort study. *Lancet*. 2012;380:1059–65.
- Peters J, Mack GW, Lister G. The importance of the peripheral circulation in critical illnesses. *Intensive Care Med*. 2001;27:1446–58.
- Pinsky MR. Defining the boundaries of preload responsiveness at the bedside. *Pediatr Crit Care Med*. 2015;16:82–3.
- Sessler DI, Bloomstone JA, Aronson S, et al. Perioperative Quality Initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery. *Br J Anaesth*. 2019;122:563–74.
- Tafner P, Chen FK, Rabello RF, Correa TD, Chaves RCF, Serpa AN. Recent advances in bedside microcirculation assessment in critically ill patients. *Rev Bras Ter Intensiva*. 2017;29:238–47.
- Van der Mullen J, Wise R, Vermeulen G, Moonen PJ, Malbrain M. Assessment of hypovolaemia in the critically ill. *Anaesthesiol Intensive Ther*. 2018;50:141–9.
- Via G, Tavazzi G, Price S. Ten situations where inferior vena cava ultrasound may fail to accurately predict fluid responsiveness: a physiologically based point of view. *Intensive Care Med*. 2016;42:1164–7.
- Vignon P, Repesse X, Begot E, et al. Comparison of echocardiographic indices used to predict fluid responsiveness in ventilated patients. *Am J Respir Crit Care Med*. 2017;195:1022–32.
- Vincent JL, Pinsky MR. We should avoid the term “fluid overload”. *Crit Care*. 2018;22:214.
- Vincent JL, Weil MH. Fluid challenge revisited. *Crit Care Med*. 2006;34:1333–7.
- Weiser TG, Regenbogen SE, Thompson KD, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. *Lancet*. 2008;372:139–44.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

