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EDITORIAL

Perioperative fluid therapy: more questions than definitive answers

"Everything in excess is opposed to nature" — Hippocrates.

Fluid administration is a powerful instrument for anesthesiologists and intensivists to treat disturbances in total body water compartments, hemodynamic changes related to vascular smooth muscle tone, and disorders of cardiovascular function, all commonly encountered in critical care and perioperative settings. However, very few subjects are as controversial as fluid management in perioperative medicine literature. Accordingly, there is a wide variability of practice, both between individuals and institutions, and even within individuals and institutions, which means that the same practitioner can significantly vary in his/hers fluid strategy during different cases in the same settings.[1] While fluids can be a crucial tool for anesthesiologists to prevent or treat hemodynamic instability due to acute hypovolemia or changes in the loading conditions, inadequate fluid administration might also be harmful, leading to edema and impairment of the microcirculation oxygenation. As a consequence, considering numerous disrupted cellular transduction mechanisms related to surgical trauma and underlying diseases, it is unsurprising that perioperative morbidity is linked to the quantity of intravenous fluid administered during this period, whether in insufficient amounts or, more commonly, in excess. Both situations are potentially harmful and may be associated with poorer postoperative outcomes.[2] Moreover, adding one more layer of complexity to the topic, another question needs to be addressed: how much is too little or too much fluid?[3]

This issue of the *Brazilian Journal of Anesthesiology* highlights several controversial topics related to perioperative fluid therapy, including the volume of fluids infused during the perioperative period and its effects on postoperative outcomes. In a prospective, multicenter, observational cohort study that was set at two high-complexity teaching hospitals in Brazil, Palomba et al evaluated the relationship between restrictive versus liberal intraoperative fluid regimes with the incidence of cardiac-surgery-associated acute kidney injury (CSA-AKI) in patients that underwent on-pump coronary artery bypass grafting (CABG). Furthermore, their study also addressed the influence of intraoperative strategies on in-hospital mortality, cardiovascular complications, and length of stay in the ICU and hospital.[4] Although the authors found no significant association between CSA-AKI and intraoperative fluid delivery, their results suggested a higher relative risk of in-hospital mortality and cardiovascular complications among patients under a liberal fluid regime compared with those in the restrictive matched group. These results may offer a window for future observations, seeking to analyze what kind of additional mechanisms related to the myocardial cell and overall cardiac function can represent the "point of no return" in terms of degeneration.

The ideal perioperative fluid therapy strategy has been debated for decades due to its crucial role in the oxygen supply and demand balance, fluid and electrolyte homeostasis, and adequacy of tissue perfusion.[5] However, the most effective perioperative fluid management is still unclear. Paracelsus (1493—1541), a Swiss physician, alchemist, and lay theologist from the German Renaissance, mentioned that "Poison is in everything, and no thing is without poison. The dosage makes it either a poison or a remedy". Data from studies in patients undergoing non-major cardiac surgery comply with the Paracelsus philosophy, suggesting that the regime of intraoperative fluid therapy — i.e., liberal and restrictive strategies — affects patient outcomes.[2] In 2018, a paper published in the *New England Journal* evidenced poorer postoperative outcomes (a higher rate of AKI) in non-cardiac surgical patients treated with a restrictive fluid strategy and shook the scientific community.[6] Later, a systematic review with meta-analysis that excluded cardiac surgical patients from their data analysis confirmed those results, showing lower overall renal major events when liberal fluid therapy was compared to the restrictive approach.[2] Interestingly, the trial by Myles et al[5] enrolled more patients than 17 RCTs combined in the previous 15 years. For this reason, the weight of this trial significantly

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impacted the results of Messina et al's systematic review on postoperative major renal events.[2]

The literature analysis in this field is rather complex due to the number of variables potentially affecting the outcomes, which includes the overall complexity and the intrinsic risks of each specific type of surgery. The definition of liberal and restrictive strategies concerning perioperative fluid management is inconsistent among published papers on this matter, with different interpretations on how to define it and overlapping cut-off points referring to the volume of fluids given per day.[2] Although many comparative studies on the use of fluids in non-cardiac surgery have been published, there is a significant knowledge gap in the cardiac surgery setting. The great differences in the pathophysiology of patients' diseases and the higher burden of comorbidities in cardiac patients hinder a straightforward translation of existing knowledge from one field to another.

Systemic microcirculatory dysfunction is the primary pathophysiologic phenomenon of cardiac surgery, particularly with on-pump CABG, in the operating room and during the immediate postoperative phase. This may be caused by several common features of cardiac surgery such as cardiopulmonary bypass, inflammatory response, hypothermia, anemia, ischemia and reperfusion injury, and coagulation disturbances.[7] Specifically, cardiopulmonary bypass inflammatory response plays a vital role in the pathophysiology of hemodynamic alteration after cardiac surgery because it derives, among others, from the endothelial shear stress, which leads to a disruption in the endothelial membrane physiology including the glycocalyx surface, an intrinsic mechanism of the resultant Frank-Starling's flow forces. Not surprisingly, postoperative major adverse events frequently occur in this scenario, particularly considering the increasing number of older and clinically complex patients presenting for cardiac surgical care.[8]

Several clinical factors should be carefully judged and weighted to plan fluid administration in cardiac surgical patients. The patient's overall cardiac function and hemodynamic status should be considered to define the need for cardiovascular support, including fluid therapy, vasoactive drugs, and inotropes. Nonetheless, deciding when and how much fluid to infuse during surgery is notoriously tricky. For better guidance, many current protocols in perioperative fluid therapy are based on fluid responsiveness. Although fluid responsiveness may also apply to cardiac surgery patients, one must realize that, due to the swift changes in the patient's hemodynamic status, using this concept is not always feasible. Moreover, the fluid challenge technique tests the cardiovascular system function, allowing clinicians to assess whether a patient will benefit from additional fluid administration to increase stroke volume. Fluid therapy should be considered after a positive response to a fluid challenge. Nonetheless, fluids should not always be given when hemodynamic assessment suggests potential fluid responsiveness. An overzealous fluid optimization may not ultimately be beneficial, and a positive fluid balance has been repeatedly associated with worse outcomes in different settings.[9]

Currently, it is impossible to recommend the best evidence-based strategy for fluid therapy in cardiac surgery since existing trials are small, discordant, and inconclusive. For this reason, the contribution of Palomba et al's paper[4] is relevant, opportune, and valuable to cast some evidence on this controversial field.

Conflicts of interest

The authors declare no conflicts of interest.

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