REVIEW ARTICLE

Paul G. Barash, MD
Giovanni Liandoni, MD
Section Editors

Fluid Status Assessment and Management During the Perioperative Phase in Adult Cardiac Surgery Patients

Stefano Romagnoli, MD,* Alessandra Rizza, MD,† and Zaccaria Ricci, MD†

PERIOPERATIVE FLUID MANAGEMENT has been studied extensively, especially in noncardiac surgery populations, and hypovolemia and hypervolemia clearly have been identified as major contributors of morbidity and mortality.[1] It has been demonstrated that both hypovolemia, eventually leading to inadequate oxygen delivery (DO_2), and hypervolemia, which causes tissue edema, organ dysfunction, and coagulation system alterations, are associated with increased perioperative morbidity risk that has been well-described as a "parabolic-U-shape" relationship.[2] Nonetheless, to date, the optimal regimen of fluids administration still is a matter of debate, and great concerns remain about the type (colloids *v* crystalloids), the ideal composition, and the amount of fluids that should be administered.[3] Whereas in low-risk patients undergoing minor surgery, "liberal" fluid administration (or "nonrestrictive") seems to improve outcome, reducing complications and length of stay,[4,5] but in high-risk and pediatric surgeries, the issue is much more complex and individualized fluid administration (goal-directed therapy [GDT]) seems to be reasonable.[6,7] In cardiac surgery patients, the distribution of fluids in the intravascular or extravascular spaces depends on a number of intraoperative and postoperative factors that highly influence the pathophysiology of body fluid kinetics, including the patients' body surface area; cardiopulmonary bypass (CPB) (starting, conducting, and weaning); CPB priming solution (volume and composition); cardioplegic solutions (volume, composition, and temperature); CPB circuits and artificial lungs; thermal management; and vasoactive and inotropic drugs. Patient age is another key factor determining different fluid kinetics during cardiac surgery. This review is the first of 2 concerning fluid management during and after adult and pediatric cardiac surgery, and it addresses evidence on perioperative fluid administration and goal-directed fluid therapies in adult patients.

CRYSTALLOIDS VERSUS COLLOIDS: THE IMPORTANCE OF THE ENDOTHELIAL GLYCOCALYX

Fluid overload has been demonstrated to be detrimental[8] as fluids cross the vascular barrier, moving from the intravascular to the extravascular space.[9] Classically, colloid solutions would be expected to produce a larger volume effect than crystalloids do, and according to a classic prediction, a 1:3 ratio for colloid-to-crystalloid volume expansion is expected.[9] Nonetheless, endothelial glycocalyx (EG) dysfunction, caused by systemic inflammation secondary to surgical trauma and extracorporeal circulation, may lead to protein and fluid spillover toward the extravascular space, producing interstitial edema at various levels and complicating fluid regulation during the perioperative period.[10] The role of the EG, a tight and negatively charged endothelial surface layer, is central in explaining the colloids-to-crystalloids ratio behavior for volume expansion. The crucial role of the EG, an "active interface between blood and capillary wall" that tightly regulates fluid kinetics, has been described effectively by Woodcock et al in a revisiting of Starling's principle.[11] Healthy EG is semi-permeable with respect to anionic macromolecules (eg, albumin and other plasma proteins), whose size and structure appear to determine their ability to cross the layer. However, the EG is compromised in many diseases, surgery, and sepsis.[11] It has been demonstrated in large clinical trials performed in patients experiencing sepsis that the "classic view" of a 1:3 ratio may be modified profoundly to 1:1.2 or 1:1.4 (30%-40% greater efficacy rather than 300%).[10,12,13] Loss of constituents of the EG due to ischemia-reperfusion injury,[14] oxidative stress, systemic inflammatory responses,[15] and hypervolemia,[16] eventually leads to capillary leak, tissue swelling, amplification of inflammation, platelet hyperaggregation, hypercoagulation, and loss of vascular responsiveness to local mediators.[17] It has been demonstrated that the transcapillary escape rate of albumin from the circulation significantly increases within 3 hours of cardiac surgery.[18] In light of this, the relative effect of crystalloids and colloids on volume expansion has to be related to EG dysfunction. The recent warnings raised after the publication of randomized controlled trials performed in patients with sepsis have led to restrictions in the use of hydroxyethyl starches in patients with renal failure or at risk of kidney injury.[19] These still-debated aspects on hydroxyethyl

*From the *Department of Health Science, University of Florence, Department of Anesthesia and Intensive Care, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy; and †Department of Cardiology and Cardiac Surgery, Pediatric Cardiac Intensive Care Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy.*

Address reprint requests to Zaccaria Ricci, MD, Department of Cardiology, and Cardiac Surgery, Pediatric Cardiac Intensive Care Unit, Bambino Gesù Children's Hospital, IRCCS, Piazza S.Onofrio 4, 00165, Rome, Italy. E-mail: zaccaria.ricci@gmail.com

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starches have added further complexity by limiting fluid administration to crystalloids use only, especially in centers that do not use albumin as a potential plasma expander.

Ischemia-reperfusion injury has been demonstrated to cause EG disruption in patients undergoing aortic surgery.[20] The EG function also was evaluated in patients who underwent coronary artery bypass grafting with and without CPB by dosing the plasma levels of heparan sulfate and syndecan-1 (main constituents of the glycocalyx layer and biomarkers of its integrity).[21] The study demonstrated that anesthesia and initiation of surgery did not significantly modify the biomarker concentration, whereas syndecan-1 and heparan sulfate increased 2- and 4-fold, respectively, after heart-lung reperfusion. Moreover, it also was observed that syndecan-1 increased 4-fold and heparan sulfate 2-fold during off-pump myocardial revascularization. Although these studies were based on indirect indicators of EG integrity/alteration, there is a large consensus that in cardiac surgery patients, many coexisting factors may alter EG integrity, eventually leading to an increased endothelial permeability barrier, inflammation, and tissue edema also without CPB. Thus, the integrity of the EG always is hampered in cardiac surgery patients and the dynamics of colloids and crystalloids may change profoundly, influencing fluid status and fluid responsiveness. In the past, many drugs potentially protecting and preserving the EG layer by increasing its synthesis, replacing lost substance, or preventing its enzymatic degradation have been tested without positive results.[17,22–25] Capillary leakage, tissue swelling, edema, insensible perspiration, and fasting are all terms associated with the terminology of "third space," still used by many. The concept of "third space" dates to more than 50 years ago and defined a not well-identified space that sequesters the body in the perioperative phases of major surgery.[26] Because it was considered an "actively consuming" compartment, it was not uncommon that perioperative fluid regimens were based on an overzealous replacement with consequent positive fluid balance and weight gain after major surgery and increased risk of morbidity and mortality. Because it has been demonstrated definitively that the "third space" is only a fictional construct, it should be excluded from practitioners' vocabulary.[4]

PRACTICE PATTERNS IN FLUID MANAGEMENT IN CARDIAC SURGERY

During and after cardiac surgery, intravenous fluids frequently are administered to optimize DO_2 and perfusion pressure.[27] The type and amount of administered fluids and their association with vasopressors and inotropes are common subjects of debate: crystalloids, colloids, and blood products frequently are administered in combination without dedicated algorithms or protocols.[28] On the other hand, fluid overload and tissue edema secondary to capillary spillover have negative effects on cellular oxygenation, and many studies performed on cardiac and noncardiac patients have demonstrated a better outcome when restricted fluid regimens are used and negative effects in patients with significant weight gain after surgery.[29,30] During and after surgery, fluid management is complicated by several clinical (myocardial dysfunction), technical (CPB, cardioplegia), and surgical (coronary, valve, combined surgery) factors that strongly affect hemodynamics.[31,32] Fluid boluses commonly are administered to treat frequent episodes of arterial hypotension in these patients, contributing to positive fluid balance, weight gain, and tissue edema.[33] Around this issue, a multicenter Australian observational survey was performed with the aim of establishing current practice of fluid administration after cardiac surgery.[34] The study showed that in 235 patients, 1,226 fluid boluses (mean volume 504 mL each) were administered during the first 24 hours after intensive care unit (ICU) admission. The vast majority of the patients received at least 1 bolus, and the median amount of fluid given per patient was 2,250 mL. Interestingly, the decision to administer a fluid bolus was made in 40% of cases by nursing staff, in 45% by an ICU resident, and only in 12% by an ICU specialist. The main cause of volume expansion was arterial hypotension (64.7%), and in 64.4% of the cases, crystalloids were used. Although highly questioned as a marker of circulating volume, low values of central venous pressure (CVP) after hypotension were indicated as secondary reason that induced practitioners to administer a fluid bolus. Even in patients with cardiac output (CO) monitoring in situ, arterial hypotension still was cited as the primary reason for fluid administration, with low CO only being cited in 12.5% of cases. In a retrospective analysis performed by Pradeep et al, 1,358 cardiac surgery patients were divided into the following 2 groups: Those who received intravenous fluids above the median volume of 3.9 L and those who received a lesser amount.[35] Logistic regression and Cox proportional models demonstrated an increased 90-day mortality (hazard ratio, 2.8; 95% CI, 1.16-7.01) in the group that received more fluids. In addition, the results demonstrated a significant decrease in survival after 4 L of fluid administration, which drastically changed above 9 L. The authors considered the CPB-related systemic inflammatory response syndrome, together with ischemia-reperfusion injury, operative trauma, and non-pulsatile blood flow as the principal mechanisms leading to increased vascular permeability and tissue edema, including myocardial swelling. Increased cardiac tissue water may have led to a decrease in left ventricular compliance and diastolic dysfunction, prompting the clinicians to administer more fluids. In light of these considerations, positive fluid balance could be identified as an epiphenomenon secondary to abnormal vascular permeability. In an associated editorial, Ricci et al remarked on the importance of appropriate hemodynamic monitoring (discussed in the following) aimed at optimizing the management of hemodynamic instability and possibly reducing fluids administration in favor of vasoactive therapy.[36] In 2011, Cannesson et al published an interesting survey aimed at evaluating hemodynamic management practices among North American and European anesthesiologists.[37] Most of the practitioners treated high-risk surgery patients, with 13.8% of American respondents and 10.3% of European respondents treating cardiac surgery patients. The survey clearly showed that hemodynamic monitoring used during the management of high-risk patients was pressure based (arterial blood pressure or CVP) in almost 80% to 90% of the cases, and only 35% of the practitioners based their decisions on flow measures (CO). The major limitation of the study, in the present context, was that data from cardiac surgery