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Expert consensus on the use of human serum albumin in adult cardiac surgery

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Introduction

Albumin, which is a 65-kDa liver-synthesized protein, accounts for nearly 50% of total plasma protein and contributes to approximately 80% of intravascular oncotic pressure. Albumin helps maintain microvascular integrity, functions as an antioxidant, and transports hormones, fatty acid, bile salts, bilirubin, electrolytes (e.g., calcium, magnesium, copper, zinc, *et al*.), and drugs.[1–3] Human serum albumin (HSA) is a sterile, liquid albumin product derived from large pools of human plasma by fractionation and pasteurization. The medical use of HAS could date back to approximately the time of World War II.[4]

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Cardiac surgery inevitably causes major changes, such as surgical trauma, blood loss, hemodilution, and a systemic inflammatory response, in patients.[5–7] HSA has been widely used in adult patients undergoing cardiac surgery for fluid resuscitation, pump priming, or correction of hypoalbuminemia, etc.[8,9] However, evidence and practice guidelines are still lacking regarding the use of HSA in cardiac surgical patients. There is notable interhospital variation in terms of how HSA is used. Inappropriate clinical use of HSA is not uncommon,

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which may cause enormous waste, and increase the burden of healthcare.[3]

Our goal was to develop an expert consensus on the use of HSA in adult patients who underwent cardiac surgery. We aimed to help understand the roles of HSA infusion in perioperative treatment and improve patients' care by systemically evaluating available evidence in the literature. This consensus was written collaboratively by a multidisciplinary team consisting of cardiac surgeons, anesthesiologists, intensivists, perfusionists, and other healthcare providers who care for cardiac surgical patients.

Methodology

According to the recommendation of developing expert consensus statements,[10] a committee was initiated in August 2022 and consisted of 25 experts in cardiac surgery, anesthesiology, critical care, and perfusion. Three sections were developed, including volume replacement, pump priming, and correction of hypoalbuminemia. We searched the PubMed, Ovid, MEDLINE, and Cochrane Library databases from 1990 until August 2022, and reviewed the retrieval results. After the review, drafted recommendations were proposed on the basis of existing evidence in the literature, and by discussion and consensus among the experts. The class of recommendation and the level of evidence of each recommendation were weighed and graded according to predefined scales[11] [Tables 1 and 2]. The class of recommendation (COR) specified the strength of recommendation, including the estimated magnitude and certainty of benefit compared with risk. The level of evidence (LOE) was used to assess the quality of scientific evidence supporting the recommendation, graded by the type, quantity, and consistency of the data from clinical trials and other researches.

A draft of the recommendations was then submitted for voting among committee members. To approve a specific recommendation, a 75% consensus rate was required with 80% participation to ensure the validity of voting. This process was repeated for each section. Controversies were discussed and resolved by regular online video meetings and re-voting, following the Delphi method process.[12] The final draft was approved with high levels of consistency achieved for each recommendation.

SECTION 1: Volume Replacement

Volume replacement is a crucial component of perioperative cardiac surgical care. Volume replacement is often initiated in response to signs of inadequate tissue perfusion or intravascular volume, such as hypotension, oliguria, or hyperlactatemia. Balanced crystalloids, synthetic colloids, and HSA are the most frequently used fluids to maintain or restore circulating plasma volume during and after cardiac surgery.[13,14] Recently published data from randomized, clinical trials (RCTs), meta-analyses,

Table 1: Class of recommendations (COR) and corresponding definition.

COR	Definition
Class I (strong)	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, and effective. (Benefit ≫ Risk)
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
Class IIa (moderate)	Weight of evidence/opinion is in favor of usefulness/efficacy. (Benefit >Risk)
Class IIb (weak)	Usefulness/efficacy is less well established by evidence/opinion. (Benefit ≥Risk)
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.
Class III: No benefit	Benefit = Risk
Class III: Harm	Benefit <Risk

Table 2: Level of evidence (LOE) and corresponding definition.

LOE	Definition
Level A	• High quality evidence from more than one randomized controlled trial (RCT) • Meta-analysis of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies
Level B-R (randomized)	• Moderate quality evidence from one or more RCTs • Meta-analysis of moderate quality RCTs
Level B-NR (nonrandomized)	• Moderate quality evidence from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analysis of such studies
Level C-LD (limited data)	• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Moderate quality of such studies • Physiological or mechanistic studies in human subjects
Level C-EO (expert opinion)	• Consensus of expert opinion based on clinical experience

and observational studies have shown that synthetic colloids, particularly hydroxyethyl starches, increase the risk of death, acute kidney injury (AKI), and excess bleeding in cardiac surgical patients.[15–18] Therefore, the U.S. Food and Drug Administration and European Medicine Agency recommend suspending all hydroxyethyl starches products unless adequate alternative treatment is unavailable.

HSA remains in the intravascular space for a more extended period than crystalloids when the endothelial glycocalyx is intact because of its large molecular weight.[19,20] With regard to the colloid oncotic effect of albumin, it is believed to provide intravascular volume expansion more sustainably and efficiently than crystalloids. Larger volumes of crystalloids are required to create similar changes in hemodynamic parameters during resuscitation compared with albumin.[21–24] Yanase *et al*[21] monitored hemodynamic parameters (cardiac index, mean arterial pressure, and central venous pressure) after administering 20 g of albumin or 500 ml of crystalloid as fluid bolus therapy after cardiac surgery. They found that both of these achieved a similar immediate increase in the cardiac index and mean arterial pressure, but the improvement in mean arterial pressure was maintained longer by albumin than by crystalloids.

HSA and kidney function

AKI is one of the most common complications after cardiac surgery,[25,26] and preoperative hypoalbuminemia is a risk factor for developing AKI.[27,28] However, the effect of exogenous albumin on renal function is still largely unknown. Frenette *et al*[29] showed a dose-dependent effect of albumin administration on AKI, which raised concern about the safety of albumin on kidney function in patients undergoing cardiac surgery. However, in this study, preoperative albumin concentrations were not matched, and a majority of patients in the albumin group also received other colloids. Therefore, the study's validity is limited by its design, and its results should be interpreted with caution.[30] A prospective, single-center, randomized, controlled study evaluated the effect of preoperative 20% albumin administration on postoperative AKI in 220 patients with preoperative hypoalbuminemia (<4.0 g/dL) undergoing off-pump coronary artery bypass grafting.[31] This study showed that the postoperative incidence of AKI in the albumin group was lower than that in the group without preoperative albumin supplementation (13.7% *vs.* 25.7%, $P = 0.048$), but there was no difference in new-onset dialysis-dependent renal failure.[31] The first large interventional RCT, Albumin in Cardiac Surgery (ALBICS) trial, showed that pump priming and fluid resuscitation with albumin did not increase the risk of AKI compared with crystalloids (3.3% *vs.* 2.6%, $P = 0.43$).[32]

The ALBICS trial randomly assigned 1386 patients into 2 groups who received 4% albumin solution or Ringer acetate for cardiopulmonary bypass (CPB) priming and perioperative 24-h intravenous volume replacement. The investigators examined the incidence of operative complications in the two groups and found that 4% albumin solution did not significantly reduce the risk of major adverse events over 3 months following cardiac surgery. In detail, patients in the albumin group received less volume of fluid replacement (median: 2150 mL *vs.* 3298 mL, $P < 0.001$), had a lower incidence of myocardial injury (risk ratio [RR] 0.44; 95% confidence interval [CI], 0.28–0.68; $P < 0.001$), but had a higher incidence of bleeding (RR, 1.73; 95% CI, 1.12–2.68; $P = 0.01$), re-exploration (RR, 1.85; 95% CI, 1.28–2.68; $P = 0.001$), and infection (RR, 1.45; 95% CI, 1.07–1.97; $P = 0.02$) than the Ringer's group.[32] However, this trial has some limitations. First, the patients in this study had a median EuroSCORE of 1.7, which indicated that only low-risk patients were included, and this trial did not represent the high-risk population who might benefit the most from HSA use. Second, the concentration/dose of HSA used and the criteria for switching from crystalloids to albumin during resuscitation followed in this trial are different from routine practice, which might affect the interpretation of the results.

HSA and coagulation

Besides the hemodilution effect from albumin infusion, studies have shown mixed results regarding the effect of albumin on coagulation function and bleeding in patients undergoing cardiac surgery. Albumin inhibits platelet aggregation *in vitro*.[33,34] Niemi *et al*[16] performed thromboelastography (TEG) in patients who underwent cardiac surgery and found that maximum clot firmness, fibrin formation, and fibrinogen-dependent clot strength did not change after albumin infusion. Another RCT showed that albumin infusion during cardiac surgery resulted in weaker clot strength (TEG-maximal amplitude [MA]: 59±6 mm *vs.* 67±6 mm, $P < 0.001$) and slower clot growth in thromboelastography (TEG angle: 69°±5° *vs.* 74°±3°, $P < 0.01$) than those with crystalloids.[35] However, there was no significant difference in postoperative blood loss between these treatments ($P = 0.45$).[35] Skhirtladze *et al*[36] evaluated the effects of 5% albumin solution and lactate Ringer's solution on blood loss and coagulation function in 240 patients after cardiac surgery. Albumin did not increase chest drainage at 24 h after cardiac surgery (835 mL *vs.* 670 mL, $P = 0.085$), but increased the requirement of red blood cell infusion (300 mL *vs.* 0 mL, $P = 0.0015$) at 24 h after cardiac surgery compared with lactate Ringer's solution.[36] A meta-analysis from 21 studies of 1346 patients who underwent cardiac surgery also showed no significant effect of albumin infusion on postoperative blood loss or blood transfusion.[37] However, the ALBICS trial showed a higher risk of major postoperative bleeding in the albumin group than in the crystalloid group (7.5% *vs.* 4.3%; RR, 1.73; 95% CI, 1.12–2.68).[32]

Recommendation 1: A comprehensive multimodality approach by a multidisciplinary team is recommended to minimize hemodilution during cardiac surgery (COR I, LOE C-expert opinion [EO]).

Although hemodilution during CPB was routinely applied to reduce blood viscosity and improve tissue perfusion

during hypothemia,[38] current evidence has shown that excessive hemodilution increases the risk of receiving allogenic blood transfusion, AKI, and positive fluid balance, and thus should be well controlled.[5,39–41] To effectively minimize hemodilution, a multimodality approach is recommended,[42] which should include the following items: (1) restricting intravenous fluid administration before CPB when acute normovolemic hemodilution is not applied; (2) minimizing the circuit prime volume;[43] (3) applying autologous priming techniques, such as retrograde autologous priming and/or venous antegrade priming;[44] and (4) ultrafiltration techniques.[45] This approach has also been recommended by the recent Society of Thoracic Surgeons (STS)/Society of Cardiovascular Anesthesiologists (SCA)/American Society of ExtraCorporeal Technology (AmSECT)/Society for the Advancement of Blood Management (SABM) and European Association for Cardio-Thoracic Surgery (EACTS) clinical practice guidelines regarding blood management in patients with cardiac surgery.[39,43]

Recommendation 2: Goal-directed fluid therapy (GDFT) is recommended to assess the volume status and optimize fluid resuscitation during and after cardiac surgery (COR I, LOE B-nonrandomized [NR]).

GDFT uses comprehensive measures of organ perfusion, such as hemodynamic parameters (e.g., blood pressure, central venous pressure, and the cardiac index), metabolic parameters (e.g., urine output, serum lactate concentrations, and mixed venous oximetry), and monitoring systems (e.g., Vigileo, pulse-induced contour cardiac output [PiCCO], and LiDCO) during and after cardiac surgery. With this approach, intravascular fluid volume, vascular resistance, and cardiac output can be dynamically assessed and addressed. This helps determine the timing and dose of albumin infusion and achieve adequate resuscitation but not over-resuscitation (positive fluid balance).[46–48] A meta-analysis on 5 studies of 699 patients showed that the use of GDFT reduced the postoperative complication rate (odds ratio [OR], 0.33; 95% CI, 0.15–0.73; $P = 0.006$) and the hospital length of stay (mean difference, −2.44 days; 95% CI, −4.03–0.84 days; $P = 0.003$), without a significant reduction in mortality.[49] Johnston *et al*[50] showed that GDFT was associated with a significantly reduced risk of AKI after cardiac surgery (adjusted OR, 0.63; 95% CI, 0.43–0.90).

Recommendation 3: It is reasonable to administer HSA following crystalloid resuscitation in patients who need further volume replacement during and after cardiac surgery to avoid excessive positive fluid balance (COR IIb, LOE B-NR).

Volume replacement in cardiac surgical patients is challenging because hemodynamic parameters during and after cardiac surgery can be affected by multiple factors, such as blood loss, post-bypass vasoplegia, and low cardiac output syndrome.[51,52] In fact, accurately assessing intravascular volume is usually difficult. Therefore, over-resuscitation is relatively common in patients undergoing cardiac surgery.[19,53] Recent studies have shown that volume overload is independently associated with an increased risk of morbidity (e.g., pulmonary edema, AKI, and congestive heart failure) and mortality in patients who undergo cardiac surgery.[54–56]

As a colloid, HSA is believed to remain in the intravascular space for a more extended period and thus provide intravascular volume expansion more efficiently than crystalloids.[57] Less volume of HSA can achieve more durable hemodynamic improvement than crystalloids during and after cardiac surgery.[21–23] In a sequential, open-label pilot study, Wigmore *et al*[58] included 100 patients who required fluid resuscitation during the first 24 h after cardiac surgery. They treated the first 50 patients with crystalloid fluid bolus (control group) and the following 50 patients with up to 200 ml of 20% HSA, which were followed by crystalloid fluid bolus if required (intervention group). The intervention group was associated with a less positive fluid balance (median: 1100 mL *vs.* 1970 ml, $P = 0.001$), fewer episodes of fluid bolus therapy (median: 3 *vs.* 5, $P < 0.0001$), and a lower volume of fluid bolus therapy (median: 700 mL *vs.* 1500 mL, $P < 0.0001$) than the control group. The intervention was also associated with a decreased median overall dose of norepinephrine (median: 19 *vs.* 47, $P = 0.025$) and a shorter median time to cessation of norepinephrine (median: 17 h *vs.* 28 h, $P = 0.002$).[13,58,59] Another retrospective study by Thang *et al*[60] included 8136 cardiac surgical patients and showed that 4444 (54.6%) patients who received HSA during the first 24 h of intensive care unit admission had significantly lower adjusted mortality than patients who did not (OR, 0.68; 95% CI, 0.48–0.97; $P < 0.05$). As a result, there is a growing interest in the utility of HSA to avoid over-resuscitation and an excessive positive fluid balance in patients undergoing cardiac surgery.[32,58,61]

Recommendation 4: HSA infusion might be helpful to maintain intravascular volume and arterial pressure when aggressive diuresis is given to relieve fluid overload and interstitial edema after cardiac surgery. Hypertonic (20% or 25%) HSA is preferred in this setting (COR IIb, LOE C-limited data [LD]).

Once the acute phase of fluid resuscitation is passed, patients often gain a positive fluid balance and present with interstitial salt and water overload (e.g., weight gain, and pedal or pulmonary edema, etc.). The excretion of excessive salt and water by diuresis is the first sign of recovery and convalescence in patients who undergo cardiac surgery.[62] However, these patients may also have an inadequate intravascular volume. Aggressive diuresis can often worsen the deficiency of intravascular volume and cause systemic hypotension. In this population, HSA infusion helps avoid diuresis-induced hypotension by expanding the circulating plasma volume to maintain adequate preload.[63] In addition, HSA is also believed to help recovery of the endothelial glycocalyx,[20] which creates an osmotic gradient that promotes interstitial fluid to shift from the extravascular space to the intravascular space.[19,64,65] However,

adding HSA to diuresis does not appear to help with the diuretic effect.[65,66]

Notably, postoperative interstitial salt and water overload are usually more evident in high-risk patients with impaired heart function, a long pump run, or a complicated procedure. Future studies need to investigate whether HSA provides more benefit in this specific patient population.

Recommendation 5: HSA is not routinely recommended as the first-line choice of fluid resuscitation during and after cardiac surgery (COR III: No Benefit, LOE B-randomized [R]).

The choice between crystalloids and colloids for fluid resuscitation has been studied extensively for decades. Despite the efficacy of crystalloids in volume expansion, no consistent evidence has shown that resuscitation with albumin improves operative outcomes in patients undergoing cardiac surgery.[58,60,67,68] As mentioned above, the ALBICS trial failed to demonstrate any significant benefits by HSA infusion as the first-line choice of fluid resuscitation regarding major morbid outcomes in patients who underwent cardiac surgery compared with crystolloids.[32] In addition, the University of Maryland Medical Center restricted its albumin use in 2015 only to patients requiring more than 3 liter of crystalloid infusion in the first 24 h after cardiac surgery, hypoalbuminemia (serum albumin concentrations <30 g/L), or patients considered to have fluid overload (central venous pressure >5 mmHg, pulmonary artery diastolic pressure >20 mmHg, and pulmonary edema). A study from this center compared 440 patients who received restricted albumin use with 961 patients in whom albumin was used without restriction. This study showed that a significant reduction in albumin use (mean: 101 doses monthly *vs.* 280 doses monthly, P <0.001) after albumin restriction resulted in similar mortality and morbidity. This study suggested that albumin restriction in postoperative care of cardiac surgical patients is feasible and safe.[69] Therefore, considering the high cost and limited availability of albumin, it is not recommended as the first-line choice for fluid replacement.

Recommendation 6: Using HSA for fluid resuscitation in patients with hemorrhagic shock and uncontrolled bleeding is not recommended (COR III: No Benefit, LOE C-EO).

The strategy to manage cardiac surgical patients with active bleeding and hemorrhagic shock should focus on timely control of surgical bleeding, targeted correction of coagulopathy, and adequate fluid resuscitation.

In patients who are complicated with massive bleeding or hemodynamically unstable, appropriate blood products such as red blood cells, fresh frozen plasma, platelets, and cryoprecipitate should be initially provided to replace blood components on the basis of hemodynamic parameters, the rate of bleeding, and point-of-care hemostasis testing.[39] In addition, balanced crystalloid should serve as the first-line choice after blood products for fluid resuscitation owing to its availability and safety profile on coagulation. To date, no studies have investigated the safety and effectiveness of albumin use in cardiac surgical patients complicated by hemorrhagic shock and uncontrolled bleeding. However, avoiding albumin and choosing a safer fluid, such as crystalloids, are reasonable choices in hemorrhagic shock because of its possible effect on coagulation.

Recommendation 7: HSA infusion is reasonable to supplement prior volume and albumin loss in patients with bleeding-controlled hemorrhagic shock (COR IIa, LOE C-EO).

Patients in hemorrhagic shock during or after cardiac surgery will usually have been resuscitated with crystalloids and blood transfusion. After the active bleeding has been controlled, these patients often require ongoing volume resuscitation and have an intravascular oncotic deficit from prior bleeding-caused albumin loss. In addition, postoperative bleeding and blood transfusion usually exacerbate the systemic inflammation and damage of the endothelial glycocalyx in cardiac surgical patients.[20,42] In this situation, HSA infusion is indicated to help with volume replacement, limit positive fluid balance, restore microvascular integrity, and reduce systemic inflammation.

SECTION 2: Pump Priming

Regarding CBP, HSA is currently used for pump priming, replacing volume loss, and relieving a drop in oncotic pressure.

Recommendation 8: Pump priming with HSA for optimizing blood management might be reasonable (COR IIb, LOE B-NR).

Recommendation 9: Pump priming with HSA might be considered in specific cardiac surgical populations, such as those undergoing heart transplantation, pulmonary thromboembolectomy, and deep hypothermic circulatory arrest (COR IIb, LOE C-EO).

Pump priming usually takes approximately 1.0 L to 1.5 L of fluid and induces considerable hemodilution.[38] This priming may lead to a fall in colloid oncotic pressure (COP) and extravascular fluid shift, which further cause interstitial salt and water overload, as well as postoperative weight gain.[70] Colloids are usually used as priming fluid to help maintain oncotic pressure. However, because of the concern regarding AKI and the bleeding risk mentioned above, the use of synthetic colloids has declined over the last decade. Fresh frozen plasma is also not recommended as priming fluid in the adults because of the risk of blood transfusion.[39] However, some centers commonly use HSA as a pump priming fluid. According to two surveys, HSA is used for CPB priming by approximately 30% of healthcare responders in the United States and approximately 8.7% in European countries.[61,71] Studies have shown that priming with HSA attenuates an on-pump fall in COP and reduces positive fluid balance.[72,73]

In addition, shear stress and a pressure drop across the pump boot may release inflammatory mediators and

initiate a systemic inflammatory response, which may further cause the breakdown of endothelial permeability.[74] HSA has been postulated to help protect the endothelial glycocalyx and microvascular integrity.[9]

Furthermore, blood contact with roller pumps and the foreign inner surface of oxygenator and extracorporeal circuits induces bound fibrinogen, which may cause platelet adhesion on fibrinogen via glycoprotein IIb/IIIa receptor, fibrin deposition, and platelet consumption.[75,76] Albumin from pump priming coats the surface of the circuit and oxygenator, which prevents fibrinogen binding during bypass and helps protect from platelet adhesion and likely the consumption of other coagulation factors.[9,77]

A meta-analysis of 1346 patients from 21 studies compared platelet counts, COP, on-bypass fluid balance, and postoperative weight gain. Compared with crystalloid priming, albumin priming significantly reduced the drop in the postoperative platelet count (-23.8×10^9/L; 95% CI, -42.8×10^9/L to -4.7×10^9/L), minimized the decline in COP (−3.6 mmHg; 95% CI, −4.8 mmHg to −2.3 mmHg) during bypass, and caused a less positive fluid balance (−584 mL, 95% CI: −819 mL to −348 mL) and less postoperative weight gain (−1.0 kg; 95% CI, −1.3 kg to −0.6 kg).[37]

Despite the benefits mentioned above, pump priming with HSA has failed to translate into an improvement in the outcome in the general cardiac surgery population.[9,32] In the ALBICS trial, the group with pump priming of 60 g of HSA did not show reduced morbid outcomes compared with the group of priming with crystalloid.[32] However, HSA is currently widely used for high-risk patient populations, such as those with a low body weight, heart transplantation, pulmonary thromboembolectomy, deep hypothermic circulatory arrest, advanced age, reoperations, thrombocytopenia, impaired heart function, and a long pump run. Future studies should investigate the benefit of HSA priming in these patients and provide evidence for this practice.

SECTION 3: Correction of Hypoalbuminemia

Recommendation 10: HSA infusion is reasonable to correct preoperative hypoalbuminemia in normovolemic patients (COR IIb, LOE B-NR).

Hypoalbuminemia is defined as serum albumin concentrations <35 g/L. Preoperative hypoalbuminemia is common among cardiac surgical patients, and is usually caused by cardiac-related malnutrition, liver dysfunction, and chronic consumption.[78] Preoperative hypoalbuminemia is strongly associated with early and late adverse outcomes,[79–82] especially infection,[81] AKI,[27] and delirium.[83] Baseline albumin concentrations have been used to help assess the operative risk in cardiac surgical patients. However, whether exogenous HSA supplementation can improve operative outcomes is still controversial. A meta-analysis of nine controlled, clinical trials on critically ill non-cardiac surgical patients was performed. This analysis showed that HSA infusion significantly reduced the incidence of postoperative complications in patients whose preoperative albumin concentration was corrected to higher than 30 g/L.[84] However, limited evidence is available in cardiac surgical patients. A single-center, parallel-arm RCT of 220 patients who underwent off-pump coronary artery bypass grafting with preoperative albumin concentrations <4.0 g/L showed that preoperative administration of 20% albumin solution reduced the risk of postoperative AKI (albumin *vs.* control group: 13.7% *vs.* 25.7%, $P = 0.048$), but there was no significant effect on mortality or other major morbidities.[31] Notably, hypoalbuminemia often occurs in preoperative patients with congestive heart failure, and HSA infusion, especially hypertonic HSA, should be avoided in such patients who are intolerant of hypervolemia.

Recommendation 11: Correcting postoperative hypoalbuminemia by HSA infusion in normovolemic patients might be beneficial (COR IIb, LOE C-EO).

In cardiac surgical patients, baseline hypoalbuminemia, operative loss, leakage to the extravascular space, and considerable hemodilution often lead to postoperative hypoalbuminemia. An observational study of 2818 patients who underwent cardiac surgery showed that 61.5% of patients had serum albumin concentrations <30 g/L postoperatively.[85] Studies have shown that postoperative hypoalbuminemia is associated with adverse outcomes.[85,86] HSA is commonly used to replace an albumin deficit during the postoperative period, aiming to maintain oncotic pressure, relieve tissue edema, and maintain microvascular integrity and metabolism, etc. In the future, studies should be carried out to determine whether exogenous HSA improves the clinical outcome of patients who have postoperative hypoalbuminemia, but do not require volume replacement.[87]

Conclusions

HSA can be used for volume replacement, pump priming, and correcting hypoalbuminemia in cardiac surgical patients. We summarized the recommendations for use of human serum albumin (HSA) in adult cardiac surgery in Table 3. However, more evidence is required to justify this practice, especially regarding the improvement of clinical outcomes. This expert consensus will serve to guide the decisions regarding the use of HSA during and after cardiac surgery.

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Conflicts of interest

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Table 3: Recommendations for use of human serum albumin (HSA) in adult cardiac surgery.

No.	Recommendations	COR	LOE	References
Section 1. Volume replacement				
1	A comprehensive multimodality approach by a multidisciplinary team is recommended to minimize hemodilution during cardiac surgery.	I	C-EO	5, 39–45
2	Goal-directed fluid therapy is recommended to assess the volume status and optimize fluid resuscitation during and after cardiac surgery.	I	B-NR	46–50
3	It is reasonable to administer HSA following crystalloid resuscitation in patients who need further volume replacement during and after cardiac surgery to avoid excessive positive fluid balance.	IIb	B-NR	13, 19, 21–23, 32, 51–59, 61
4	HSA infusion might be helpful to maintain intravascular volume and arterial pressure when aggressive diuresis is given to relieve fluid overload and interstitial edema after cardiac surgery. Hypertonic (20% or 25%) HSA is preferred in this setting.	IIb	C-LD	19,20,62–66
5	HSA is not routinely recommended as the first-line choice of fluid resuscitation during and after cardiac surgery.	III: No Benefit	B-R	32, 58, 60, 67–69
6	Using HSA for fluid resuscitation in patients with hemorrhagic shock and uncontrolled bleeding is not recommended.	III: No Benefit	C-EO	None
7	HSA infusion is reasonable to supplement prior volume and albumin loss in patients with bleeding-controlled hemorrhagic stroke.	IIa	C-EO	None
Section 2. Pump priming				
8	Pump priming with HSA for optimizing blood management might be reasonable.	IIb	B-NR	9, 32, 37–39, 61, 70–76
9	Pump priming with HSA might be considered in specific cardiac surgical populations, such as those undergoing heart transplantation, pulmonary thromboembolectomy, and deep hypothermia circulatory arrest.	IIb	C-EO	None
Section 3. Correction of hypoalbuminemia				
10	HSA infusion is reasonable to correct preoperative hypoalbuminemia in normovolemic patients.	IIb	B-NR	31, 77–83
11	Correcting postoperative hypoalbuminemia by HSA infusion in normovolemic patients might be beneficial.	IIb	C-EO	None

COR: Class of recommendations; EO: Expert opinion; LD: Limited data; LOE: Level of evidence; NR: Nonrandomized; R: Randomized.

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