



CLINICAL PRACTICE GUIDELINES

National Heart Center Perfusion Guidelines

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ABSTRACT

Objectives: To establish the first national standards and guidelines for best practice in perfusion for patients undergoing cardiothoracic surgery in Saudi Arabia. Cardiopulmonary bypass (CPB) enables complex cardiac surgeries; however, it poses risks of potential complications.

Methods: We used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to develop these guidelines and assess the certainty of evidence through a collaborative process. A panel of 16 Cardiovascu-

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lar perfusion experts across Saudi Arabia formulated 22 key clinical questions relevant to local practice. PubMed, Scopus, and Embase databases were searched for each question to identify relevant systematic reviews, randomized controlled trials (RCTs), non-randomized trials, post hoc analyses, and pooled analyses published from 2010 to 2024. The guideline panel voted for every question using the GRADEpro system, requiring a minimum consensus of 70% for approval.

Results: A total of 16 conditional recommendations and 6 good practice statements were finally approved, categorized into 5 key domains. Of these, 4 addressed guidelines, protocols, and general practices; 2 focused on surgical techniques; 8 covered heart-lung machine hardware; 3 centered on cardioplegia and Priming Solutions; and 5 emphasized monitoring and perioperative management. Six statements were based on expert opinion due to insufficient supporting evidence. Using a standardized pre-bypass checklist to enhance safety and implementing perioperative glycemic management to control glucose levels and reduce complications were strongly recommended by the panel. Conditional recommendations focus on pump selection, biocompatible oxygenators, and continuous cerebral oxygenation monitoring. Anticoagulation, myocardial protection, and transfusion management were also highlighted.

Conclusion: These Saudi guidelines provide evidence-based recommendations to enhance the care of patients undergoing cardiac surgery with CPB, offering clear guidance for clinicians to achieve optimal outcomes. Nevertheless, future locally relevant research and regular updates are essential to bridge existing evidence gaps.

Keywords: Cardiopulmonary bypass, Cardiac surgery, Perfusion, Saudi Arabia

Introduction

Cardiovascular disease (CVD) is a global health burden and a prominent cause of death, projected to increase the world's mortality to 23 million by 2030 [1]. The invention of DeBakey's roller pump and its inclusion in the Cardiopulmonary Bypass (CPB) machine by Gibbon has revolutionized the field of cardiac surgery. Since then, rapid improvement and refinement accelerated the CPB technology, such as the establishment of hollow membrane fiber oxygenators followed by the advancements seen with Heparin-coated circuits, real-time monitoring, and the innovative cardioplegia and its delivery techniques derived by evolutions of computer chips and biomaterial manufacturing [2].

The CPB works by extracorporeal pumping of venous blood to gas exchange device and filter, regulate its temperature then returning it to the patient's arterial system to maintain blood supply to other organs during heart surgery [3]. Due to its complexity and time sensitivity, CPB requires highly trained perfusionists and expert cardiac surgeons, and anesthesiologists [4].

Many factors contribute to the clinical success of CPB, such as blood transfusion management, hemodynamic support of the extracorporeal circulation, and pharmacotherapy strategies management, as well as perioperative control of electrolytes and blood glucose levels [5, 6]. Despite decades of advancements in CPB regarding optimal hemodilution, heparin adjustments, and pH regulation, CPB has been linked to recognized incidence of complications [7]. This is mainly because of blood exposure to foreign surfaces used in the CPB circuit [8]. Moreover, CPB consequences may lead to an increased likelihood of fluid overload after surgery, inflammation, micro-embolic, and immune-related damage [9, 10].

Several societies have developed standards and guidelines for CPB to ensure safe and effective patient care. To enhance the outcomes of patients undergoing heart surgery, a task force composed of experts in the field was formed to create evidence-based guidelines for CPB practice by the European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Cardiothoracic Anesthesiology (EACTA), and the European Board of Cardiovascular Perfusion (EBCP) [11]. The guidelines for blood, transfusion, anticoagulation, and temperature management during CPB in cardiac surgeries were established in 2007 with the collaboration of the Society of Cardiovascular Anesthesiologists (SCA) and then enhanced and revised by the American Society of Extracorporeal Technology (AmSECT), International Consortium for Evidence-Based Perfusion Committee republished in 2011 [12, 13].

In Saudi Arabia, continuous efforts by the medical society have been made to enhance CPB management; Mohanlall et al. [14], conducted a randomized, controlled clinical study at the Northwest Armed Forces Military Hospital in Tabuk, Saudi Arabia. They compared 2 types of modified ultrafiltration systems: conventional arteriovenous modified ultrafiltration (AVMUF) and a custom-designed Veno-arterial modified ultrafiltration (VAMUF) system. The study found that VAMUF was a more physiologically appropriate technique, showing significantly greater reductions in creatinine, serum lactate, and uric acid over time.

Another observational study by Soliman et al. [15], investigates the impact of hemofiltration during CPB on lactate levels in adult patients undergoing cardiac surgery at the Prince Sultan Cardiac Center in Riyadh. They found that hemofiltration led to

hemoconcentration, elevated lactate levels, and a need for increased inotropic support. They also recommended using hemofiltration for patients with impaired renal function, positive fluid balance, or extended bypass times, more than 2 hours, minimizing fluid administration to preserve adequate cardiac output, cutting priming volumes, and performing hemofiltration either before weaning from or after CPB, rather than continuously during the procedure.

Additionally, a trial conducted at King Faisal Specialist Hospital and Research Center (KFSH&RC) by Khouqeer et al. [16], investigated the validity and efficacy of adding a hemoconcentrator reservoir collection bag to the CPB circuit in 13 cardiac surgery patients. The aim of blood transfusion reduction was noticed in the 60% improvement of non-transfusion rates, reinfusing about 292 mL of salvaged blood, and maintaining stable hemoglobin levels.

In the field of cardiothoracic surgery, this is the first publication of national standards and guidelines for best practice in perfusion for patients in Saudi Arabia, introducing invaluable resources to perfusionists, clinicians, cardiac anesthesiologists and surgeons, intensive care specialists, researchers, and medical care providers for improving patient outcomes during and after cardiovascular surgery. These offer pertinent knowledge of CPB and extracorporeal life support during surgery and in non-surgical situations, advising on practical clinical applications from experts in the field.

Scope and purpose

These guidelines provide evidence-based recommendations for the clinical practice of managing patients requiring cardiac perfusion care in Saudi Arabia. They focus on the monitoring and management of patients with ischemic heart diseases, heart failure, and other related conditions requiring cardiac perfusion interventions. These guidelines also address special considerations for certain patients undergoing surgical cardiac perfusion procedures.

The aim is to provide evidence-based recommendations to guide healthcare professionals in managing patients undergoing cardiac perfusion interventions in Saudi Arabia, supplemented by expert consensus where appropriate.

Guidelines scope

The guideline's scope was determined through expert consensus, which includes: guidelines, protocols, and general practices: Addressing the framework for safe and effective CPB practices, highlighting optimal procedure methods. We also address the Heart-Lung Machine Hardware, providing guidance

on equipment usage and maintenance, Cardioplegia and Priming Solutions, focusing on myocardial protection and preparation of the bypass circuit, Monitoring and Perioperative Management, covering some of the strategies for intraoperative and postoperative patient care.

Objectives

The Saudi clinical practice guidelines for cardiac perfusion aim to:

- AServe as a national reference for cardiac perfusion clinical practice to suit the specific demographic needs of local populations in Saudi Arabia.
- Optimize guidance for various treatment modalities for managing cardiac perfusion needs in different clinical scenarios.
- Improve patient outcomes related to management, procedural success rates, and overall quality of life.
- Guide identification and management strategies to minimize the impact of cardiac perfusion-related conditions on patients' lives.

End-users

These guidelines will benefit perfusionists, anesthesiologists, cardiac surgeons, intensivists, cardiologists, general practitioners, and clinical pharmacists in Saudi Arabia. They offer valuable insights into cardiac perfusion management for healthcare decision-makers, researchers, and guideline developers. In addition, end-users might also include patients requiring cardiac perfusion interventions and their caregivers.

How do we use these guidelines?

The Ministry of Health of Saudi Arabia aims to provide clinicians and their patients with guidelines for managing and treating conditions requiring cardiac perfusion among patients of all genders. Clinicians, patients, third-party payers, institutional review committees, and other stakeholders should interpret these recommendations as broad guidance, not absolute mandates, and definitely do not substitute sound clinical judgment and experience.

In this guideline, we used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to state the recommendations. However, as discussed in other guidelines that follow the GRADE approach, no guideline or recommendation can encompass all the unique and often compelling aspects of individual clinical situations. Consequently, those responsible for assessing

clinicians' actions should avoid applying these recommendations rigidly or uniformly without assessing the context of the scenario.

Recommendations are accompanied by statements that take into account values and preferences, resource use, feasibility, equity, acceptability, and other relevant factors. It is crucial to consider that these statements are essential for understanding the context of the recommendations. While the guideline provides valuable guidance, exercising sound clinical judgment in individual cases is essential. Clinicians should tailor their approach to unique needs and circumstances, considering the potential benefits and risks of different management strategies in their patients' overall health and well-being.

Guidelines updating

We recommend a systematic review and update of the existing guidelines one year after their publication, followed by updates every 2 years to ensure they remain relevant, accurate, and aligned with current best practices and stakeholder feedback. To enhance robustness, we also advocate for integration with a national audit registry, along with the creation of a data repository for input from end-users for collecting concerns, issues, and recent advancements pertinent and relevant to the perfusion practice in Saudi Arabia that should be addressed with the coming updates.

Methods

These guidelines were developed using the GRADE approach [17]. The GRADE approach was chosen for its robust framework in assessing the certainty of evidence and the strength of recommendations. By systematically evaluating the quality of evidence, it ensures transparency, consistency, and reproducibility in guideline development. Subsequently, it offers the healthcare personnel well-informed clinical decision-making, balancing benefits and risks while considering patient cases and resource availability.

Panel composition

The panel, composed of 16 experts, focuses on cardiac diseases and cardiac perfusion techniques.

Group interaction and process

The guidelines were created through a collaborative process utilizing the GRADE method, which promoted transparent communication, agreement among specialists, and the consideration of various viewpoints. This method aided in minimizing bias and guaranteed that the recommendations were

founded on the best available evidence. The panel was actively engaged along with the contribution authors in writing up the broad knowledge base, followed by experts' meetings to pose pertinent PICO questions and create guidelines for carrying out the review, consolidating the evidence, evaluating its dependability, and developing recommendations.

Selection of questions and outcomes' prioritization

The guideline panel conducted a thorough review of recently released guidelines to pinpoint key research inquiries [11]. Following this, the panel deliberated on which population, intervention, comparator, and outcome (PICO) questions are vital to complement clinical practice in Saudi Arabia. Additionally, the panel had the opportunity to propose new PICO questions. After thoughtful consideration, the panel formulated 22 questions that were deemed most pertinent to clinical practice in Saudi Arabia. The guideline panel assessed and authorized the finalized list of PICO questions. For each PICO, we utilized the GRADE framework to categorize outcomes as critical, important, or not important [18]. The prioritized outcomes included pertinent clinical data.

Evidence synthesis

The methodologists conducted a systematic literature review to update the evidence supporting previously published guidelines. They meticulously searched medical databases (PubMed and Scopus) using tailored search terms for each specific research question, with the support of experts in research methodology and medical literature. The search terms employed for each question are detailed in the supplementary of tables. All relevant systematic reviews, individual randomized controlled trials (RCTs), non-randomized trials, post hoc analyses, and pooled analyses published from 2010 to 2024 were extracted from the databases, **Figure S1**. If there were no relevant ones, we included articles published before 2010. Case reports, narrative reviews, and clinical guidelines were excluded from the articles that will be applied to the GRADEpro system. When there were insufficient direct articles that could answer the PICO questions, the experts depended on their clinical experience.

Two authors independently examined the titles and abstracts of the collected citations and included studies that satisfied the inclusion criteria for each PICO question. The same reviewers reviewed titles and abstracts and recognized potentially suitable articles.

We focused on incorporating recent meta-analyses and systematic reviews in our search. However, in cases where relevant systematic reviews were

Table 1. Implications of the recommendation's strength.

Strength of recommendation	Definition	Implications for stakeholders
Strong recommendation	There is clear and consistent evidence showing that the benefits significantly exceed the risks.	Healthcare providers are expected to follow this recommendation in most cases. Patients can trust that this option is safe and effective.
Conditional recommendation	The benefits are greater than the risks, but the supporting evidence is limited or uncertain.	Healthcare providers should consider this option, but decisions should be tailored to each patient's specific situation and values. Patients should be aware of the uncertainty and be part of the decision-making process.
No recommendation	There is not enough reliable evidence to support or oppose the intervention.	Healthcare providers must rely on their clinical judgment and patient preferences. More research is needed to evaluate the intervention's impact.
Weak recommendation against	The risks seem to outweigh the benefits, but the supporting evidence is weak.	Healthcare providers should usually avoid this option, though it may still be appropriate in specific cases. Patients should be informed about the possible harms.
Strong recommendation against	Strong and reliable evidence shows the intervention does more harm than good.	Healthcare providers should avoid this intervention entirely. Patients should be clearly informed that the evidence strongly discourages its use.

unavailable or published prior to 2010, we included RCTs that related to our research questions. To evaluate the quality of these RCTs, we employed the established criteria from the Cochrane risk of bias tool to assess potential biases [19]. For non-RCTs, the evaluation was conducted using the Newcastle & Ottawa scale [20]. For every outcome, we applied the GRADE approach to evaluate the certainty of the evidence. The certainty of the evidence was categorized as high, moderate, low, or very low based on several domains: study design, risk of bias, publication bias, consistency of findings, indirectness of evidence, and imprecision of the estimate [21].

Assessing the certainty of evidence

For each PICO question, we utilized the GRADEpro guideline development tool [18] to create evidence profiles that included evaluations of critical and important outcome absolute and relative effects, as well as certainty assessments. We applied the GRADE methodology to assess the reliability of the evidence when formulating clinical practice recommendations for cardioperfusion techniques. The GRADE method is widely used to evaluate the certainty of evidence utilized in clinical practice guidelines. This method examines 5 elements to determine the overall reliability of the evidence: “study design,” “risk of bias,” “publication bias,” “imprecision,” “inconsistency,” and “indirectness.” We displayed the outcomes and the reliability assessment of the evidence through evidence profiles.

After evaluating the 5 domains of GRADE, the certainty of evidence was rated as very low, low, moderate, and high [22]. High certainty indicates a strong assurance that the actual effect is near the estimated effect. Moderate certainty suggests a reasonable level of confidence, with the true effect likely being sim-

ilar. Low certainty signifies that the effect estimate is limited, and the true effect may vary significantly. Very low certainty denotes that the effect estimate is highly uncertain, indicating a need for additional research to diminish this uncertainty.

Each suggestion was made considering the risk-to-benefit balance, the quality of the evidence for each intervention, and the clinical expertise of the panel. The suggestions were updated during virtual meetings. The updated recommendations were submitted to the expert panel for voting using the GRADEpro system, requiring a minimum consensus of 70% to be approved.

The suggestions may either support or oppose the intervention. Furthermore, the recommendations' strength is classified as either strong or conditional. Recognizing the significance of the strength of the recommendation is essential for making informed decisions, as shown in Table 1.

Chapter 1: Cardiovascular perfusion

Cardiovascular perfusion can temporarily bypass the heart and lungs through artificial extracorporeal circulation, providing their physiological functions, including oxygenation, ventilation, and delivering blood all over the body [23]. CPB is a subset of cardiovascular perfusion that is performed by a perfusionist, a key player in the surgical team [24]. Perfusionists are responsible for operating the heart-lung bypass machine during heart surgery, providing stable circulation through the procedure [25]. Additionally, they maintain tissue viability through various tasks, including measuring the components of blood and ensuring appropriate mechanical, pharmacological, and thermal manipulation, consulting cardiac surgeons and anesthesiologists whenever needed [25]. Therefore, they are required to understand the patho-

physiology of both the respiratory and circulatory systems well to make sure they are capable of handling such complex machines proficiently [26, 27]. In addition to that, the stressful conditions of this work necessitate the perfusionist to develop coping strategies, pay attention to details, communicate well with the surgical team, and be updated with the developments in the field [28]. They can also be incorporated into other administrative duties, such as supply chain management and succession planning [29].

Multidisciplinary roles of the cardiovascular perfusion team

High-quality and cost-effective patient care in the modern healthcare system depends on many factors, including patient needs, doctors' experience, and robust hospital structure [30]. One major contributor is an effective multidisciplinary team, which can ensure good management regarding complex and challenging tasks through team collaboration toward shared goals [31]. In high-risk settings such as the cardiac operating room (OR), this collaboration can be life-saving when encountering unexpected events, minimizing catastrophic outcomes [32]. Therefore, a dynamic environment, including perfusionists, surgeons, anesthesiologists, nurses, and other skilled professionals, could lead to quick decision-making and technical excellence [31, 33]. Additionally, optimizing surgical efficiency and reducing errors alongside patient outcome enhancement can be achieved through good teamwork training alongside continuous process improvement measures such as briefings, debriefings, and root cause analyses [30]. In addition to that, this success can be sustained by persistent education and efforts to keep high team performance [32].

Perfusion general practice staffing

Perfusionist staffing levels play a key role in patients' quality of care and outcomes after cardiac surgery with CPB [34].

Principles of perfusionist staffing levels

These principles are responsible for ensuring optimal patient care and outcomes in cardiac surgery with CPB, including: I) Maintaining a safe minimum number of full-time equivalent accredited clinical perfusionists is needed to optimize patient care. While $N + 1$ is the recommended standard number of perfusionists, where N equals the number of operating theaters at any given time, $N + 2$ is recommended when the number of operating rooms exceeds or equals 4, excluding trainees from the minimum safe number [34]. II) On-call shifts should be customized

not to exceed one in every 4 rotations to avoid overworking the staff. As such, 1 in 3 could lead to fatigue and reduced performance. Furthermore, staff should not proceed to regular day work the next day after on-call. Instead, they should get adequate rest to prevent burnout [34–36]. III) Vacation periods, sick leaves, and national holidays should be considered to ensure good coverage all the time. Comfortable accommodations in the on-call rooms and staff lounges should also be provided to increase staff readiness and well-being. Subsequently, this could result in better care for patients, depending on the expected less fatigued and higher-performance staff [37].

The recommended full-time equivalent (FTE) for perfusion services in the Saudi workplace, as endorsed by the Ministry of Health (MOH) of Saudi Arabia is shown in detail in Table 2.

Perfusion role definitions (Saudi MOH framework)

1) Technician: A staff member with foundational training in perfusion-related tasks, often assisting in setup and monitoring under supervision. 2) Specialist: A licensed clinical perfusionist responsible for independently managing CPB cases and extracorporeal systems. 3) Senior Specialist: An experienced perfusionist who takes a supervisory role, mentors junior staff, and handles complex cases or emergencies. 4) Consultant: The highest-level expert in perfusion services with leadership responsibilities, including program development, training, research, and strategic planning (Saudi Commission for Health Specialties [SCFHS], 2015).

Perfusion school in Saudi Arabia

There is a significant gap regarding perfusion schools in Saudi Arabia nowadays. Although they are absent now, they were represented by the Perfusion Undergraduate Diploma Program at the Prince Sultan Cardiac Center (PSCC) and the King Faisal Specialist Hospital (KFSH) program. The PSCC was discontinued in 2016 despite the graduation of 37 perfusionists. Additionally, the KFSH program had 22 technicians who graduated before it ended in 2012. Subsequently, the number of Saudi perfusionists is lacking today, representing only 28% of the current workforce in the country. Numerous cardiac centers are also under development, putting more burden on educating and training more perfusionists to cover these centers, alongside supporting other related services dependent on perfusion technology.

One to 4 years are required to complete training in perfusion centers, educating perfusionists with the necessary knowledge, skills, and techniques. These programs are accredited based on meeting essential

Table 2. Standard of perfusion manpower.

Cardiac catheterization centers				
Type of service	Technician	Specialist	Senior specialist	Consultant
Intra-aortic balloon pump in the cath Lab (IABP)	1	1	–	–
For centers performing fewer than 15 open-heart surgeries per month with one open-heart surgery room.				
Type of service	Technician	Specialist	Senior specialist	Consultant
IABP - open heart surgery	2	3	–	–
For centers performing 30 or fewer than 30 open-heart surgeries per month with one open-heart surgery room.				
Type of Service	Technician	Specialist	Senior specialist	Consultant
IABP - Open Heart Surgery	3	3	1	–
Portable Artificial heart – ECMO	4	6	2	–
For centers performing more than 30 open-heart surgeries per month with two active open-heart surgery rooms.				
Type of Service	Technician	Specialist	Senior specialist	Consultant
IABP - Open Heart Surgery	4	6	2	–
IABP - Open Heart Surgery – ECMO	6	10	2	1
IABP- Open Heart Surgery – ECMO - Left Ventricular Assist Device (LVAD) - HIPIC.	6	12	3	2

HIPEC: Hyperthermic Intraperitoneal Chemotherapy, Definition: Pump for chemical or chemotherapy treatment within the peritoneal membrane.

standards, such as facilities and supervision. Additionally, they should be based on curriculum, such as ensuring good coverage of physiology, biochemistry, applied anatomy, pharmacology, and pathology. They should also care for soft skills, enhance team dynamics and communication, and cope with stress. After completing the program, the trained personnel should be evaluated for their knowledge, skills, and attitude by decisive tools, granting them finally the accreditation of being clinical perfusionists. Certification maintenance requires a minimum annual caseload of 75 cases and continuous professional development. Recertification can be done through the Saudi Commission for Health Specialties (SCFHS) after ensuring compliance with international standards. In addition to that, certified perfusionists must operate within a quality management framework that emphasizes standard operating procedures, risk assessments, peer reviews, and audits.

To address this gap, we recommend re-establishing structured national training programs in partnership with universities and cardiac centers, incorporating simulation-based education and mentorship pathways. A centralized framework under the SCFHS could standardize curricula, ensure sustainability, and align training with international best practices.

Guidelines, protocols, and general practice

1. Should National standards guidelines versus (vs.) No standardized guidelines be used for cardiovascular

surgery patients to improve patient outcomes, reduce complications, and enhance care quality?

Ungraded statement

For patients undergoing cardiovascular surgery, we advise using standard guidelines rather than not using them to improve patient outcomes, reduce complications, and enhance care quality (Good practice statement).

Rationale

This ungraded statement is based on expert opinion due to the lack of sufficient evidence on this topic. Guidelines take their evidence following a hierarchy, with the meta-analysis on top, followed by RCTs, and ending with expert opinion in areas with literature gaps. RCTs compare the intervention and control groups unbiased, such as ensuring the 2 groups have similar characteristics or applying blinding. Subsequently, they neglect confounding factors and provide the true effect of the intervention. This evidence is even more robust when conducting a meta-analysis of RCTs.

Therefore, having standardized guidelines can result in better practice because they provide clinicians with evidence-based recommendations that deal with various clinical situations, including cardiovascular surgery. Upon following these recommendations, it is expected to see improvement in patient outcomes and care quality along with a reduction of

complications. For example, Young et al. [38] followed over 5 years the implementation of a thoracic enhanced recovery program (ERP). They revealed a reduction in hospital stays, costs, and opioid use. The findings of this study pointed out the value of using a structured approach to practice medicine. Not only will the patient benefit, but the health-care resources will be well-optimized, including staff time, equipment, and medications. Regarding cardiovascular surgery, the high costs associated with complications and prolonged hospital stays necessitate following guidelines because they can prevent wrong interventions and provide more cost-effective care for patients.

In the context of CPB, the guideline panel recommends using standardized protocols for perfusionists to get the best organ perfusion practice and minimize complications. They concluded that using such guidelines is likely acceptable and feasible, with no impact on equity.

2. Should the transfusion trigger protocol vs. customary sound judgment be used for patients undergoing CPB?

Ungraded statement

For patients undergoing CPB, we advise using either the transfusion trigger protocol or customary sound judgment (Good Practice statement).

Rationale

This statement relies on the experts' opinion due to the lack of direct evidence comparing the transfusion trigger protocol with the customary sound judgment. The dynamic nature of CPB prevents definite recommendations for a transfusion trigger protocol. While protocols may reduce unnecessary transfusion rates, they do not consider patients' clinical profiles and the complexities of surgeries. Additionally, they can adopt liberal or restrictive strategies, reflecting variable decisions based on clinical scenarios. For example, the liberal protocol may be used in anemic patients where they can benefit from transfusion at a high threshold, such as if Hb is <9.5 g/dl, to avoid the expected anemia symptoms. In contrast, restrictive strategies may be tolerated until Hb is 7 g/dl to avoid volume overload and transfusion complications such as autoimmune reactions and infection. Additionally, the European recommendation with CPB advised for transfusion if the Hb value is <6.0 g/dl and the possibility of transfusion if hematocrit (HCT) values are between 18% and 24% based on tissue perfusion and oxygenation. However, they advised against transfusion of the HCT is $>24\%$ [11]. Factors

such as nadir HCT during CPB and history of coronary surgery, alongside weighing the risk/benefits anticipated with anemia, have been identified as crucial triggers for transfusion decisions [39].

On the other side, sound judgment of surgical teams enables learning and provides flexibility, especially in situations that require a quick response. The guideline panel agrees with the European recommendations on patient blood management for adult cardiac surgery, stating that the key aspect of importance is patient status along with oxygen delivery and extraction, not the hemoglobin (Hb) threshold [40]. Therefore, they advised using protocols or customary judgment in the best interest of the patient. They highlighted that blood transfusion during CPB primarily relies on the perfusionist's clinical assessment of Hb levels during the procedure. While individual hospitals may have established protocols, the final decision still rests with the clinicians in the team (the surgeons and the anesthesiologists) based on the specific circumstances of each case. More trials that compare the 2 approaches are needed.

3. Should Continuous glucose monitoring and insulin therapy vs. Standard glucose management be used for patients undergoing CPB to improve glucose control and reduce postoperative complications?

Recommendation

For patients undergoing CPB, we suggest using continuous glucose monitoring over Standard glucose management to improve glucose control and reduce postoperative complications. (**Table S1**) (conditional recommendation, very low certainty evidence).

Rationale

This recommendation is based on a meta-analysis ($n = 6129$) investigating the impact of perioperative glucose-insulin-potassium (GIK) infusion versus standard glucose management on early outcomes after cardiac surgery. The main outcome of MI was found to be significantly in favor of GIK across 32 RCTs (OR 0.66, 95% CI 0.48 to 0.89; low certainty, **Table S1**). Additionally, the study revealed significant improvement in terms of hemodynamics, including a higher cardiac index in the GIK-treated group across 14 studies (MD 0.43 L/min, 95% CI 0.29 to 0.57; very low certainty, **Table S1**), as well as reduced hyperglycemia noticed in 20 trials (MD -29.84 mg/dL, 95% CI -46.63 to -13.06 ; very low certainty, **Table S1**). Furthermore, the pooled estimate of AKI in 7 RCTs was lower with GIK infusion (OR 0.57; 95% CI: 0.4, 0.82, very low certainty, **Table S1**). Additionally, a shorter stay in the hospital and

ICU was found when pooling the results of 19 and 20 studies, respectively (MD -0.89 days; 95% CI: -1.63 , -0.16 , very low certainty, and MD 5.17 ; 95% CI: 7.35 , 2.99 , very low certainty, **Table S1**). The study also revealed that the cardioprotective effect of GIK was achieved when the insulin dosage exceeded 2 mUI/kg/min. This may be attributed to the shifting of energy production the insulin does from free fatty acid oxidation to glucose oxidation, which is a better pathway, thus improving adenosine triphosphate (ATP) storage in the myocardium, particularly in ischemic events. Additionally, the results were clearer in patients who underwent coronary artery bypass surgery (CABG). In a prospective study, the continuous intravenous insulin infusion effectively managed glucose levels in patients who underwent elective cardiovascular surgery, but subcutaneous insulin injections needed improvement. High glycemic variability during subcutaneous insulin treatment was associated with an increased risk of surgical site infections and AF in some patients [41].

Therefore, the guideline panel recommended the use of continuous glucose monitoring over Standard glucose management in cardiac surgeries with CPB conditionally because of their potential improvement over early postoperative outcomes and the minimization of hospital resource utilization. They also deemed the intervention to be probably feasible and acceptable. However, further research is necessary to solidify the evidence and standardize the timing and composition of GIK solutions.

4. Should perioperative glycemic management vs. routine post-operative care be used for patients undergoing CPB who present for elective cardiac surgery?

Ungraded statement

For patients undergoing CPB who present for elective cardiac surgery, we strongly advise perioperative glycemic management over routine post-operative care (Good practice statement).

Remarks

- Target glucose levels of 80 – 150 mg/dL in the perioperative setting.
- Diabetic patients may require individualized glycemic targets based on their baseline glucose levels and insulin sensitivity.
- Insulin infusion to be started in all diabetic patients the night of surgery. Patients with blood sugar above 150 should start insulin infusion even if not diabetic, according.

- Blood sugar should be measured in all diabetic patients undergoing cardiac surgery every 30 – 60 minutes according to cardiac risk assessment in non-cardiac surgery.
- To boost patient satisfaction while keeping up the high standard of frequent monitoring, we recommend the use of continuous glucose monitoring devices from the night of surgery until discharge or 7 days (KAMC ERACS protocol).
- Avoid dextrose-containing diluents or fluids in the perioperative setting.

Rationale

This ungraded statement is based on expert opinion due to the lack of sufficient evidence on this topic. CPB has been correlated with postoperative hyperglycemia and insulin consumption in patients undergoing cardiac surgery, adding to the risk of morbidity and mortality [42]. Perioperative insulin administration in patients with high glucose levels and continuous monitoring can minimize the risks associated with elective cardiac surgery. Bláha et al. evaluated glucose control pre- and postoperatively across 2383 patients undergoing cardiac surgery. In terms of adverse events, they observed a major reduction in complications, particularly with nondiabetic patients [43]. Similarly, A prospective cohort study of 100 diabetic patients undergoing cardiac surgery revealed that targeted control of blood glucose levels between 80 and 110 mg/dL could result in better cardiac and neurological outcomes compared to less strict management [44].

Therefore, the guideline panel in consensus strongly underscores the great desirable effect resulting from perioperative glucose control. They also acknowledged the large savings probably resulting from decreasing hospital resources utilization after complications reduction, along with the increase in equity among the population and the feasibility and acceptability of this protocol. More robust research is needed to support the guideline experts' statement.

5. Should liraglutide vs. Perioperative management of hyperglycemia by other forms of therapy be used for patients undergoing CPB?

Recommendation

For patients undergoing CPB, we suggest against using liraglutide compared to other perioperative management of hyperglycemia by other forms of therapy (**Table S2**) (Conditional recommendation, moderate certainty evidence).

Table 3. Key components of a cardiopulmonary bypass system.

Component	Primary function
Oxygenator system	Facilitates oxygenation, carbon dioxide removal, and blood temperature regulation (cooling/re-warming).
Hemofilter	Ultrafiltration is a technique used to counteract the rise in total body water and tissue swelling that results from excessive priming volume and the systemic inflammatory response triggered by CPB.
Gas glender and supply line	Provides a controlled gas mixture to the oxygenator.
Arterial Pump	Maintains blood circulation at a set flow rate.
Cardiotomy suction and vents	Collects blood from the surgical field and decompresses the heart.
Arterial line filter	Filters out micro-aggregates and particles larger than 40 μm .
Cardioplegia system	Administers potassium-rich solutions to induce cardiac arrest and protect the myocardium.
Cannulae	Establishes patient connection to the extracorporeal circuit.

Rationale

This recommendation was based on a multicenter randomized controlled trial comparing liraglutide to other forms of perioperative management of hyperglycemia in patients undergoing CPB. For insulin administration requirements, liraglutide demonstrated lower needs for any insulin administration (RR 0.7, 95% CI 0.5 to 0.9, moderate certainty, **Table S2**), resulting in 182 fewer patients per 1,000 requiring insulin. Intraoperative glycemic control showed higher mean blood glucose levels in the liraglutide group (MD 0.66 mmol/L higher, 95% CI 0.39 to 0.93, moderate certainty, **Table S2**). The risk of complications varied, as the results of postoperative nausea and vomiting showed RR 1.25 (95% CI 0.70 to 1.95, moderate certainty, **Table S2**), the results with cardiac complications showing RR 0.93 (95% CI 0.70 to 1.24, moderate certainty, **Table S2**), infectious complications with RR 1.1 (95% CI 0.5 to 2.4, moderate certainty, **Table S2**), and risk of any complications with RR 0.90 (95% CI 0.70 to 1.14, moderate certainty, **Table S2**) (46). For safety outcomes, delirium risk was lower with liraglutide when assessed by ICU + Ward (RR 0.40, 95% CI 0.13 to 1.27; moderate certainty, **Table S2**) and when assessed by CAM-ICU only (RR 0.30, 95% CI 0.06 to 1.40; moderate certainty, **Table S2**). Hemodynamic parameters showed consistent differences, with lower heart rates (MD -10 beats/min, 95% CI -13 to -5.5; low certainty, **Table S2**) and mean arterial pressure (MD -4 mmHg, 95% CI -9 to 0.39, low certainty, **Table S2**) in the liraglutide group [45].

A previous systematic review of cardiac surgery cases reported a 54% rate of the liraglutide group of postoperative nausea and vomiting, which was substantially higher than the rates observed in both study groups; the high incidence of adverse events would support the recommendation of not using liraglutide [46]. In another open-label randomized clinical trial, Initial administration of liraglutide showed an increased incidence of nausea and vomiting, though

these adverse effects subsided after 4-6 weeks of treatment [47].

The guideline panel demonstrated that balancing desirable and undesirable effects favored liraglutide. Additionally, the guideline panel informed that there are large differences in the cost between liraglutide and other interventions. The panel also suggested that there is probably no impact on health equity when using the intervention. The implementation of liraglutide therapy demonstrated limited clinical applicability and feasibility for widespread adoption in the target population [48].

Chapter 2: Cardiopulmonary bypass equipment and disposables

The CPB is a precise technology that is utilized by a multidisciplinary team of surgeons, anesthesiologists, and perfusionists [49]. To get CPB's most benefit, technicians must understand its pathophysiology, weigh the risks, and know the possible side effects if wrongly used [8]. Various equipment are used in CPB, as detailed in **Table 3**.

Principles of perfusion pumps

In extracorporeal circuits, 2 primary types of pumps are used: i) Ones that work by flow production by compressing the tube, expelling the blood through the circuit – roller pump [50]. ii) Ones that exert their function through the pressure gradient created by the impeller, propelling the blood outward by the centrifugal force–centrifugal pumps [51].

Roller pumps

Roller pump technology in CPB

Roller pumps, patented by Dr. DeBakey, have been introduced to the CPB machine since the mid-20th century [52]. They have had a constant design since

then, with 2 opposing rollers that use the peristaltic motion of compressing the tube to move the blood in an anterograde or retrograde manner, as shown in Supplementary **Figure S2** [52]. Circuit resistance does not affect the output of the pump. However, it depends on the tubing diameter and the number of rotations [50]. It can operate through pulsatile and non-pulsatile flow. While the pulsatile flow has the advantage of mimicking the physiologic cardiac cycle, it can lead to hemolysis through the stress shear it exerts on blood cells [53]. Generally, roller pumps also have disadvantages, potentially inducing cavitation upon sudden inflow occlusion. Subsequently, gas bubbles can be formed, causing harm to the patient [54].

Centrifugal pumps

Centrifugal pumps are designed with a cone and a metal bearing enclosed within an outer housing, forming a sealed unit [55]. The pump head is the entrance of the blood and is located on a drive unit. The cone is spun by magnetic force, resulting in negative pressure and a vortex that draws the blood toward the pump. However, blood is expelled outward as the impeller spins at user-set speeds (typically 2000–4000 rpm) [56, 57]. Unlike roller pumps, the outcome of centrifugal pumps is affected by the machine circuit along the patient's own circulation, depending mainly on the pressure gradient and outlet resistance. Additionally, flow meters are used to measure blood velocity, which operate via ultrasonic or electromagnetic methods [56, 57].

Pump heads recommendations

Should Roller pumps (RP) vs. Centrifugal pumps (CP) be used for patients undergoing CPB to reduce hemolysis and improve clinical outcomes?

Recommendation: *For patients undergoing CPB, we suggest using either roller or CP to reduce hemolysis and improve clinical outcomes (Table S3) (Conditional recommendation, high certainty evidence).*

Rationale. This recommendation is based on a meta-analysis of RCTs comparing RP and CP over a group of patients undergoing CPB surgery. They observed hospital transfusions in 243 patients, with 1637 red blood cell units transfused. The meta-analysis found no significant difference in postoperative blood loss, transfusions, hematological variables, neurological outcomes, or mortality between RP and CP [58].

The 2 groups had no significant difference regarding the number of units of transfused RBCs

(Weighted mean difference [WMD] -0.10 units, CI: -0.35 to 0.15 , moderate certainty, **Table S3**). In terms of postoperative blood loss, 11 trials revealed a non-significant difference in mediastinal drainage between the 2 groups at the time of chest tube removal (WMD -10.26 mL, 95% CI: -54.3 to 33.7 , very low certainty, **Table S3**). Additionally, the length of stay, either generally in the hospital or ICU, was reported with non-statistically significant differences between the groups (WMD -0.12 days, 95% CI: -0.37 to 0.12 , high certainty, **Table S3**) and (WMD -0.10 days, 95% CI: -0.29 to 0.09 , moderate certainty, **Table S3**), over 6 and 5 RCTs respectively. Mortality was consistent with other outcomes as no difference was reported between the 2 pumps (OR 1.05 , 95% CI: 0.58 to 1.88 , high certainty, **Table S3**) [58].

However, a previous study found that RP leads to less cognitive decline compared to CP in patients undergoing coronary artery bypass surgery [59]. In an RCT, a reduced inflammatory response was detected in the centrifugal pump used during prolonged CPB and deep hypothermic circulatory arrest compared to the standard roller pump [60].

The guideline panel acknowledged the feasibility of using either pump in patients with CPB surgeries, knowing that the standard care in Saudi Arabia now is RPs and that CPs are increasingly used in ECMO. They agreed on the comparable hematological outcomes and the similarity of safety profiles regarding mortality, postoperative blood loss, and length of stay.

Cardiotomy reservoir and field suction. Components: i) Defoaming Chamber: Equipped with a cardiotomy filter featuring a pore size of 40μ . ii) Storage Chamber: Serves as a reservoir for collected blood. Iii) Macro or Micro Filter: Provides filtration for larger particles or finer debris, respectively [61].

Blood return and Cardiotomy Suction

In CPB, blood may return continuously or intermittently, depending on the setup, to either the venous reservoir (in systems with membrane oxygenators) or directly into the bubble oxygenator [62]. However, while cardiotomy suction is essential for managing blood loss during surgery, it has been linked to several complications, including hemolysis, release of inflammatory mediators, and introduction of particulate microparticles [63]. The structure of the cardiotomy reservoir is illustrated in **Figure S3**.

Strategies to minimize adverse effects of cardiotomy suction

i) Performing Off-Pump procedures: If we avoid CPB, the need for cardiotomy suction will be eliminated [64]. ii) Decrease air aspiration: This can be

achieved through careful suction. Subsequently, it will reduce air-related complications [65]. iii) Blood filtration: By implementing advanced filtration systems [66]. iv) Limit or avoid cardiomy suction usage: Discard shed blood instead of recirculating it. And utilize cell salvage and washing systems to process and return shed blood safely [65]. v) Improve Hemostasis: Implement measures to reduce blood loss, thereby minimizing reliance on cardiomy suction [67].

Cardiac venting

Physiologically, the left ventricle (LV) receives blood from the bronchial and the besian veins during CPB. However, under abnormal conditions, it can receive blood from the left superior vena cava (LSVC), patent ductus arteriosus (PDA) or blalock-taussig (BT) shunt, Ventricular septal defect (VSD and aortic regurgitation (AR) [68, 69]. Therefore, the increased load resulting from the high amount of blood return into the LV can be handled by venting the left heart, minimizing the risk of chamber distension, myocardial ischemia, and inadequate visualization for the surgeon [68, 70–72]. Subsequently, this procedure can serve several purposes, such as: Offer good visualization to the surgeon by providing a bloodless field [70]; prevent chamber distension [68]; minimize myocardial rewarming [70]; and prevent air embolism [72].

The venting cannula can be inserted in many sites, depending on the surgical need and anatomy, having complications mainly because of the site tissue injury. Potential sites of cardiac venting include [70, 72–74]: pulmonary artery (PA); right superior pulmonary vein (RSPV); left atrium (LA); left ventricle (LV); and aortic root cardioplegia cannula.

Additionally, avoiding LV distention during CPB can be achieved through [75–77]: Surgeons' inspection and palpation of the left heart; PA catheter: Any change in LV will be reflected over the pulmonary arteries; LA monitoring: this will serve as a proxy for LV; and transesophageal Echocardiography (TEE): It can provide real-time assessment of LV volume.

Oxygenators

Membrane oxygenator

The membrane oxygenator has a gas-permeable membrane that can separate blood from gas, consisting of an oxygenator unit, a venous reservoir, and a heat exchanger [78, 79]. The material of the membrane can be silicon rubber, which has long durability, or polypropylene with hollow fibers, using each one in different case scenarios based on factors

Table 4. Commonly used oxygenators.

Body Surface Area (BSA)	Oxygenator model
Infant (0.2–0.34 m ²)	Lilliput 1, Lilliput 2 Capiox FX05 Trilly Infant-Pediatric
Children (0.34–0.8 m ²)	Kids D100 Capiox FX15 Trilly Pediatric AF
Adult (0.8–2.2 m ²)	Inspire 6, Inspire 7, Inspire 8 Capiox FX25 Horizon

such as the duration of use and patient-specific needs [78–80].

While silicon rubber is a homogeneous, non-porous material, polypropylene possesses heterogeneous, microporous, and hydrophobic qualities [81]. Additionally, stretching the membrane creates the microporous material that facilitates gas transfer [82]. The diameter of these pores is approximately 0.03 to 0.07 μm and represents about half of the membrane's surface [83]. These pores in their submicron range give the membrane its hydrophobic nature [81, 82]. However, they do not function as a diafilter, even though gas may get forced inside the blood if its pressure is higher than the blood's [78]. A summary of commonly used oxygenators and their alternative models is provided in Table 4.

Hollow fibers

Created from polypropylene, hollow fibers can optimize gas exchange, allowing blood to flow inside or outside according to the configuration [84]. A rupture in any fiber component can have consequences depending on the blood flow [85]. It causes blood to leak into the gas phase, reducing the total surface of oxygen transfer if blood is inside the fiber [86]. Consequently, it leads to impaired performance [86]. Additionally, this could prevent air bubbles visualization during priming [87]. In contrast, a rupture in some of the fibers when blood flows outside leads to the spillage only into the affected area, maintaining the total surface of oxygen transfer and allowing the visualization of air bubbles [86]. This dual configuration underscores the importance of hollow fiber design in ensuring both efficiency and safety in clinical applications [87].

Characteristics of an ideal oxygenator

All oxygenators currently in use meet these requirements to ensure safe and effective operation during CPB: I) Venous blood oxygenation: It must ensure bringing the blood into proximity with the oxygen transfer source safely, through various inlet conditions. II) Removal of Carbon dioxide (CO₂):

Table 5. Comparison of oxygenator types in cardiopulmonary bypass.

Feature	Film oxygenator	Bubble oxygenator	Membrane oxygenator
Reusability	Reusable	Disposable	Disposable
Ease of use	Difficult to use	Easier to assemble	Easiest to assemble
Blood and Gas Interaction	Direct contact of blood and gas	Direct contact of blood and gas	Blood and gas are separated by a porous membrane
Damage to blood cells and protein	Maximum damage	Lesser damage	Minimum damage
Micro air embolism risk	Higher chances	Lesser chances	Minimal chances
Prime volume	Highest	Higher	Lesser
Hemolysis	Maximum	Lesser	Minimum
Cost	Cheapest among oxygenators	Cheaper than a membrane oxygenator	Most expensive
Blood flow through pump head	Oxygenated blood runs through the pump head	Oxygenated blood runs through the pump head	Deoxygenated blood runs through the pump
Gas and blood flow direction	Opposite directions	Same point, same direction	Opposite directions
Independent Control of PO ₂ and PCO ₂	No	No	Yes
Sterilization method	Autoclave	Ethylene oxide (ETO)	Ethylene oxide (ETO)

Avoiding hypercapnia and hypocapnia through efficient CO₂ removal is a must in an ideal oxygenator. III) Minimum trauma to blood: Hence, the design is responsible for the trauma resulting from the direct exposure of gas to blood; a careful design should be considered to minimize blood cells, platelets, and protein damage. IV) Small priming volume: This is necessary to avoid hemodilution, which could lead to cellular and interstitial edema and impair oxygen delivery. V) Safety: The ideal oxygenator should reduce the potential of air embolism. Additionally, it should have easy assembly and operation qualities. VI) Ease of use: Ensuring material transparency provides good visualization and labeling of the ports to prevent confusion. Also, in emergency situations, it should be easily changed [78, 88–90].

Selection of oxygenators

Oxygenators are tailored according to a patient's situation, and they are selected according to the size and type of the patient, their expected cardiac output, and the surgical procedure requirements. Additionally, material biocompatibility is necessary to reduce the potential for inflammatory response and other adverse events. A detailed comparison of oxygenators is available in Table 5 [91–93].

Oxygenators recommendation

Should Biocompatible oxygenators vs. Standard oxygenators be used for patients undergoing CPB to reduce the inflammatory response and organ dysfunction?

Recommendation

For patients undergoing CPB, we suggest using biocompatible oxygenators and circuits over standard

oxygenators to reduce the inflammatory response and organ dysfunction (Table S4) (Conditional recommendation, moderate certainty of evidence).

Rationale. This recommendation is based on a meta-analysis of 36 RCTs, biocompatible oxygenator surfaces resulted in lower packed red cells (PRCs) transfusion, AF rate, and hospital and ICU stay compared to standard oxygenators (Odds ratio [OR] 0.802, 95% CI: 0.692 to 0.929, high certainty, OR 0.76, 95% CI: 0.61 to 0.93, high certainty, mean difference [MD] - 0.552 days, 95% CI: - 0.684 to - 0.42, high certainty and MD - 0.251 hours, 95% CI: - 0.366 to - 0.136, high certainty, Table S4) [94]. However, it did not demonstrate a significant effect on mortality (OR 0.818, 95% CI: 0.558 to 1.199, moderate certainty, Table S4). This may be attributed to the multifactorial contribution that transfusion has, along with the inflammatory nature of AF that could be minimized through a decrease in complement and leukocyte activation and cytokine release. Additionally, it is also believed that the decreased incidence of AF played a key role in shortening hospital and ICU stays [94].

Biocompatible coatings, such as heparin and phosphorylcholine, have also shown benefits in reducing inflammatory markers and oxidative stress compared to uncoated circuits [95]. A novel phosphorylcholine-coated circuit demonstrated significant reductions in inflammatory markers like D-dimer, C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor- α (TNF- α) in patients undergoing aortic valve surgery [96].

These findings suggest that biocompatible CPB circuits may provide advantages in reducing the inflammatory response and potentially improving clinical outcomes in cardiac surgery patients.

The guideline panel consensually agreed on the beneficial effects of biocompatible oxygenators, such

Table 6. Standard tubing sizes in a cardiopulmonary bypass system circuit.

Tubing Size	Application
3/16" (4.5mm)	Used in the cardioplegia section of the blood cardioplegia delivery system. Additionally, it can be an arterial line for neonatal patients.
1/4" (6.0mm)	Employed in suction tubing and the blood section of the cardioplegia delivery system, in addition to serving as a neonatal patient's arterial line.
3/8" (9.0mm)	Functions as the arterial pump line for flow rates below 6.7 L/min and is the primary size for arterial tubing in the extracorporeal circuit.
1/2" (12.0mm)	Serves as the venous drainage line, requiring a larger diameter to facilitate gravity drainage from the patient.

as AF and ICU stay reduction, along with the feasibility of its application in patients undergoing CPB. They also highlighted that biocompatible oxygenators have less contact with blood and reduce the production of inflammatory mediators.

Tubing

The CPB circuit relies on the tubing to connect its components. It is manufactured from several materials, including silicone, latex rubber, and polyvinyl chloride (PVC). These materials are selected according to the needed rate of blood alongside the pressure. The most common material used is PVC, depending on its strength and flexibility upon adding plasticizers. However, in cold temperatures, it turned into a rigid structure, releasing microparticles. Regarding hemolysis, latex rubber came first, followed by PVC, then silicone, which could release more particles than PVC in case of stagnation. Based on the durability of PVC and its average rates of hemolysis among other materials, it is considered the gold standard in tubing, except for the arterial pump boot, which is made of silicone to withstand constant compression [97–100]. Common tubing sizes and their function are summarized in Table 6.

Cannulae

The cannula is chosen depending on various factors, including the anatomy of the patient, the needed flow rates, and the approach to surgery [101]. Insertion of the cannula must be per protocol to ensure securement and avoid dislodgement or trauma to the vasculature [102]. Additionally, monitoring flow rates is crucial to guarantee proper perfusion and prevent excessive shear stress [103].

Venous cannulation

The main purpose of venous cannulation is to transport deoxygenated blood from the patient to the CPB machine [104]. In surgeries like coronary artery bypass grafting (CABG), a 2-stage venous cannula is frequently used where the heart's chambers remain closed [105]. On the other hand, for procedures that require opening the cardiac chambers, bicavalcan-

Table 7. Cannula Size (French) – DLP Metal Tip Right-Angled Venous.

Weight (kg)	SVC (French)	IVC (French)
< 3.5	12	12
3.5–6	12	14
6–8	12	16
8–12	14	16
12–16	14	18
16–22	16	18
22–28	16	20
28–32	18	20
32–40	18	22
> 40	20–22	22–28

nulation is employed [106]. This technique involves placing 2 separate cannulae into the superior and inferior vena cava [106]. These cannulae are then connected with a Y-connector to ensure effective venous drainage during the procedure [107]. Additionally, in complex surgeries, a long single-stage cannula can be inserted into the femoral vein up to the vena cava to ensure proper venous drainage [107].

Types and sizes of cannula

Venous cannulas are classified as either single-stage or double-stage. A double-stage cannula has a wider section with holes intended for placement in the right atrium (RA) and a tapered end that extends into the inferior vena cava (IVC). These cannulas are fabricated from plastic and have wire reinforcement to prevent kinking. They may be either straight or right-angled, with tips formed from plastic or metal to enhance the internal diameter (ID) to outer diameter (OD) ratio for efficient blood flow. The cannula size is selected to facilitate adequate venous drainage, with roughly one-third of the total flow channeled through the superior vena cava (SVC) cannula and 2-thirds through the IVC cannula, Table 7 [107–109]. Venous cannula types examples are provided in Figures S4 and S5.

Arterial cannula

The arterial cannula is responsible for transporting the oxygenated blood from the CPB circuit to the

Table 8. Arterial cannulae flow rates in relation to type/size.

Cannulae	Size French gauge	mm	Flow rate (l/ minute)
DLPangledtip	20	6.7	6.5
	22	7.3	8
	24	8	9
DLP straight tip	21	7	5
	24	8	6
Sarns High flow angled tip	15.6	5.2	3.5
	19.5	6.5	5.25
	24	8	8
	20	6.7	5.9
Sarns straight tip	22	7.3	6
	24	8	6

arteries of the patient, **Figure S6** [62]. Their size is selected based on the size of the targeted vessel and the required blood flow rate [62]. Evaluating the aorta post-sternotomy, the surgeon determines the cannula size, in collaboration with the perfusionist, who may recommend a range of sizes suitable for the required blood flow specific to the patient, surgical technique, and target temperature [110]. Usually, arterial cannulation is performed through the ascending aorta in routine cardiac surgeries, depending on its median sternotomy's easy accessibility and the minimized risk of aortic dissection [111].

A larger internal diameter is present in thin-walled arterial cannulae, making them preferred for use because they offer lower arterial line pressure and resistance, which enhances blood flow [112]. Additionally, angled-tip cannulae can reduce damage to the vessel wall by directing blood toward the aortic arch. Secure attachment of an arterial cannula can be achieved if it has a flange or is reinforced with spirally wrapped wire to prevent kinking and maintain unobstructed flow [24]. Flow rates of arterial cannulae in relation to their type and size are detailed in **Table 8**.

Biocompatible circuits recommendations

1. Should biocompatible tubing vs. non-heparin coated to be used for reducing the inflammatory response and organ dysfunction in patients undergoing CPB?

Recommendation

For patients undergoing CPB, we suggest using biocompatible tubing, such as heparin-coated tubing, instead of non-heparin-coated ones to reduce the inflammatory response and organ dysfunction (**Table S5**) (conditional recommendation, very low certainty of evidence).

Rationale

This recommendation is based on a comparative study by Hanedan et al. between heparin-albumin-coated and non-coated CPB circuits. This study revealed a significant reduction in activated clotting times (ACT) in the heparin-coated group during CPB (355.64 ± 34.12 seconds vs. 560.38 ± 90.20 seconds, very low certainty, **Table S5**). Additionally, biocompatible circuits had better outcomes in terms of hospital stay, postoperative bleeding, and red blood cell transfusion requirements (4.48 ± 3.25 vs. 9.97 ± 6.88 days, very low certainty, 529.11 ± 267.97 vs 660.75 ± 279.73 mL, very low certainty and 1.27 ± 1.32 vs. 2.08 ± 2.28 unit, very low certainty, respectively, **Table S5**). However, comparable outcomes were seen with in-hospital mortality, postoperative stroke rates, and lengths of ICU stay (2.2% vs. 1.9%, very low certainty; 2.2% vs. 1.9%, very low certainty; and 66.70 ± 65.01 vs. 75.07 ± 56.38 hours, very low certainty, respectively, **Table S5**). On the other hand, cross-clamp time was longer in the coated group (58.29 ± 22.49 vs. 51.67 ± 23.56 minutes, very low certainty, **Table S5**). This may be attributed to the complexity of the procedure. However, it did not impact the stroke or mortality rate [113]. This agrees with the meta-analysis by Ranucci et al. [94] and a qualitative, summarized review by Mahmood et al. [114] where they pointed out the comparable findings of biocompatible circuits in some outcomes and the superiority of others.

The guideline panel conditionally recommended the use of biocompatible circuits based on their ability to reduce systemic heparinization while maintaining effective anticoagulation, which could reduce the risk of bleeding and associated complications. Additionally, they acknowledged the moderate required costs along with the acceptability and feasibility of this intervention, calling for larger multicenter trials that consider populations with Heparin-induced thrombocytopenia (HIT) or heparin resistance.

2. Should the SEC-1 coat™ Circuit vs. the heparin-coated Circuit be used for pediatric patients with CPB circuits in pediatric cardiac surgery?

Recommendation

For pediatrics with CPB circuits in pediatric cardiac surgery, we suggest using either SEC-1 coat™ Circuit or heparin-coated Circuit (**Table S6**) (conditional recommendation, very low certainty evidence)

Rationale

This recommendation was based on a randomized controlled pilot study comparing SEC-1 coat™ Circuit to heparin-coated circuits in pediatric cardiac surgery

with CPB [48]. For platelet preservation, the SEC-1 group showed reduced need for platelet transfusion with RR 0.25 (95% CI 0.03 to 1.86; low certainty, **Table S6**). Hematological parameters showed significant differences in Hb with MD 1.3 g/dL lower (95% CI −2.5 to −0.006, low certainty, **Table S6**). While there was no significant difference between SEC-1 coat™ Circuit to heparin-coated circuits regarding white blood cells' reduction (MD $-8.2 \times 10^2/\mu\text{L}$, 95% CI −30.3 to 13.9, very low certainty, **Table S6**) [48]. Coagulation parameters demonstrated insignificant variations in prothrombin-INR (MD −4, 95% CI −2.19 to 1.39, very low certainty, **Table S6**) and fibrinogen levels (MD −16, 95% CI −49 to 17, very low certainty, **Table S6**) between SEC-1 coat™ Circuit to heparin-coated circuits. The same findings were detected in clinical outcomes, including hospital stays (MD −2.3 days, 95% CI −6.6 to 2; very low certainty, **Table S6**) and ICU stays (MD −1 day, 95% CI −3.8 to 1.8, very low certainty, **Table S6**). Inflammatory markers and complement activation products showed lower post-CPB levels in the SEC group, though not reaching statistical significance. The SEC group showed better platelet preservation during CPB with a smaller decline ($81.0 \pm 7.9\%$) compared to the other group ($85.0 \pm 6.9\%$) and maintained significantly higher platelet counts throughout the post-CPB period (low certainty, **Table S6**) [48].

A comprehensive analysis of 14 RCTs demonstrated that using heparin-coated or phosphorylcholine-coated circuits led to improved neurological and pulmonary outcomes after surgery [115]. In addition, research by Fukui et al. [116], showed that SEC-coated and poly-2-methoxyethyl acrylate (PMEA)-coated circuits had comparable biocompatibility profiles, showing similar effects on coagulation and inflammatory responses during CPB.

The guideline panel found no difference when using either SEC-1 coat™ Circuit or heparin-coated Circuit regarding the balance of effects. The guideline panel found that the use of the SEC-1 coat™ Circuit is probably acceptable. They also demonstrated that the studies have shown the feasibility of using the SEC-1 coat™ Circuit, although the sample size is lacking, and more research studies are required.

Gas supply system in the cardiac operating room

Providing the required oxygen and other gases to the CPB oxygenator, the gas supply system is crucial to this procedure, as shown in **Figures S7 & S8**. Therefore, it must meet specific requirements: 1) Standards compliance: The system must adhere to the International Organization for Standardization (ISO) standards to ensure safety and performance. 2) Gas quality and purity: It must be ensured using

medical-grade gases with oxygen purity exceeding 99%. Additionally, gas lines must undergo frequent inspections for pollutants and leakage. 3) Redundant supply: Uninterrupted gas delivery must be ensured in case of failure, thus requiring a backup gas supply, such as reserve tanks, which should be controlled manually or automatically as needed. 4) Pressure monitoring: Abnormal pressure could be indicative of gas leakage or system failure. Therefore, the gas supply system should be equipped with pressure monitors. 6) Flow rate control: It is necessary that the system tailors the flow accordingly, depending on the patient's and surgery requirements. 7) Humidification: Humidifying gases will prevent dehydration of the patient's blood and tissues. 8) Temperature control: Systems that have warming or cooling gas properties could aid in the maintenance of the required patient's body temperature during surgery. 9) Filters and traps: Implementing filters is important to prevent embolism and remove microbubbles. Various types of filters are used in CPB circuits to ensure gas purity, remove microbubbles, and prevent contamination, as summarized in **Table 9**. 10) Fail-safe mechanisms: Fail-safe features must prevent incorrect gas delivery or unsafe pressures and concentrations of the correct gas. 11) Maintenance and testing: It is essential to test the system before each procedure and to follow the regular maintenance schedules to ensure proper functioning. 12) Staff training: Well-trained personnel is necessary to ensure proper function during the operation of the CPB machine. 13) Documentation: Quality control necessitates documentation of the gas supply system's maintenance, testing, and any incidents. 14) Integration with CPB Console: The gas supply system should integrate seamlessly with the CPB machine's console to enable centralized monitoring and control during surgery [11, 12, 117–120].

Heater cooler unit

It is the device that is responsible for regulating the patient's temperature by heating or cooling the blood. Subsequently, they bypassed the physiological thermoregulation, thus leading to vital organs and tissue protection. A heater-cooler unit is a key component in keeping temperatures controlled during surgical procedures [121]. The system incorporates a water tank, a heat exchanger, circulation pumps, temperature control mechanisms, monitoring sensors, and tubing with connectors. The water tank stores and maintains water at the desired temperature, which is subsequently circulated via the system. The heat exchanger facilitates effective heat transmission between the water and the patient's blood circuit while circulation pumps maintain a stable and constant

Table 9. Types of filters used in cardiopulmonary bypass (CPB) circuits.

Filter type	Application and specification
Gas line filter	Removes bacteria from the gas stream, minimizing cross-contamination between the patient and equipment.
Pre-CPB filter	A 0.2 μ m filter used during priming and recirculation to eliminate particulate debris, microbial contaminants, and endotoxins.
Arterial line filter	Removes microemboli larger than 40 μ m from the perfusate during extracorporeal circulation, including gas emboli, fat emboli, and cellular aggregates.
Leukocyte-depletion filter	Reduces leukocyte levels in either the arterial line or cardioplegia system while filtering microemboli >40 μ m.
Cardioplegia Filter	Blood cardioplegia: >40 μ m filter; Crystalloid cardioplegia: >0.2 μ m filter. Designed for low-priming volume solutions and removal of particulates, microbial contaminants, and endotoxins.
Blood transfusion filter	Reduces leukocytes and micro-aggregates from packed red blood cells or whole blood during transfusion.
Cell salvage filter	Filters salvaged blood to remove harmful micro-aggregates, leukocytes, and lipid particles before reinfusion.

flow. The temperature control system carefully manages water temperature, utilizing monitoring sensors to deliver real-time data for precision. Tubing and connectors enable uninterrupted water flow between the heat exchanger and the blood circuit. Maintenance on a regular basis, routine inspections, and personnel training are necessary for safe and successful operation [108, 122, 123].

Chapter 3: Cardiopulmonary bypass circuit setup, safety checks, and priming

Aim

The primary purpose of conducting an efficient CPB setup, priming, and pre-bypass checklist is to prevent potential infection by implementing a sterile environment, thus ensuring patient safety. Additionally, it will lead to better performance regarding perfusion and oxygenation, minimizing complications and risks such as air embolism. Also, priming contributes to maintaining blood components' integrity and balancing acid-base and electrolytes [111, 124, 125].

Policy

Setting up and priming the circuit of CPB should follow standardized protocols, maintain sterility and safety, and ensure the competency of qualified healthcare professionals. Additionally, it must be ensured that all components of the CPB circuit are compatible with the patient's body surface area (BSA) and procedural requirements to optimize circuit performance. The process should be documented, including the used priming solution and medications added, and pre-bypass checklist results. Additionally, regular reviews and updated protocols are needed to match the goal of quality assurance along with the need for

continuous improvement. Adhering to these policies guarantees the safety and efficiency of the setup process [126–129].

Procedure

Setting up and priming the CPB circuit is best performed if it follows specific rules, including: 1) Proper circuit assembly: This could be achieved by carefully checking the CPB component's integrity and expiration date before starting and following a scheme upon assembling. 2) Maintaining septic techniques: Avoid contamination by using sterile gloves and handling the CPB equipment with caution. 3) Priming solution tailoring: The perfusionist and surgeon should collaborate in the selection of the priming solution, considering the requirements of the patient and other important factors such as electrolytes balance and colloid osmotic pressure. Additionally, de-airing the circuit is necessary to prevent air embolism and recirculating the solution to ensure thorough mixing and warming of the priming solution to the target temperature (typically 37°C) before initiating CPB for the prevention of hypothermia. 4) Verifying the components: This entails utilizing a checklist, assessing the oxygenator's functionality, calibrating sensors and monitors, and ensuring the pump operates correctly. All tubing and connectors should be securely fastened and double-checked to avoid disconnections or leaks during CPB. 5) Adhering to safety measures: Safety protocols entail the setup of artery filters to catch debris or air overlooked during priming, as well as the implementation of functioning safety alarms on the CPB machine. 6) Finally, a final inspection for air bubbles in the circuit is conducted, verifying that all clamps are in the correct position and that the bypass circuit is primed and ready for use [124, 125, 127–129].

Hemodilution

Priming with a balanced electrolyte solution is necessary upon starting the CPB process. Tailoring the size of the circuit tubes to patients' BSA and their desired flow is reflected in the volume of the priming solution used. The priming volume and the pre-hematocrit (Hct) are responsible for the resulting Hct. Additionally, target Hct levels should be maintained above 24% or Hb around 80-100 g/dL to ensure adequate oxygen-carrying capacity. Excessive hemodilution may compromise oxygen delivery and contribute to coagulopathy. [130, 131].

Priming solutions

A priming solution could be crystalloid, colloid, or even blood if there is a need to correct the Hct. Considering the relative priming solution tonicity, electrolytes, and the PH to patients' plasma is necessary to prevent RBCs lysis along with shifting of fluid and its consequences [125, 132].

Crystalloid solutions

They are formed from electrolytes and water, such as ringers, lactated ringers, normal saline, and plasma-lyte. They can transport across the vascular membrane, with only a tiny percentage remaining inside the vasculature. Normal saline and lactated ringers are frequently used inside hospitals because of their tonicity and the maintenance of electrolytes. However, they may dilute plasma proteins and increase the risk of fluid overload, particularly in patients with compromised cardiac or renal function [133, 134].

Colloid solution

Unlike crystalloids, colloids are large molecules; thus, they cannot pass through the vascular membrane. Instead, they can be used to maintain the intravascular volume along with edema prevention, opposing the decrease in osmotic pressure that can be seen with priming hemodilution. Subsequently, these solutions, including albumin, gelofusine, dextrans, and starches, can prevent the fluid shift that occurs with oncotic pressure reduction, minimizing the incidence of edema and ensuring proper end-organ perfusion [135–137].

Prime additives

During CPB, various pharmacological agents are added, including heparin, antithrombin III, sodium

bicarbonate, mannitol, albumin, furosemide, vaso-pressors, electrolytes, calcium, and magnesium to maintain renal function, control blood pressure, and maintain heart rhythm [138–140].

Priming solution recommendations

Should priming with colloid solutions vs. priming with crystalloid solutions be used for patients undergoing CPB to improve fluid balance and reduce postoperative edema?

Recommendation

For patients undergoing CPB, we suggest using priming with colloid solutions over priming with crystalloid solutions to improve fluid balance and reduce postoperative edema (**Table S7**) (Conditional recommendation, low certainty evidence).

Rationale

The debate about using crystalloid or colloid fluid in CPB priming has not yet been proven; however, according to the latest meta-analysis performed by Beukers et al., 4 studies compared colloid to crystalloid fluid effects on colloid oncotic pressure (COP) [141]. They narratively discussed the fluid impact on COP to find more decreased COP with crystalloids (9.0 vs.18.4 mmHg) compared to albumin (15.2 vs. 19.3 mmHg) during and after CPB in one trial [142] and no difference in another at 1, 6, and 34 hours postoperatively [143]. Additionally, they noticed a decrease in COP with lactated Ringer's (LR) (delta [D] COP: 8.5 [1.5] mmHg) than gelofusine added to LR (1.5 [2.9] mmHg) during CPB in one RCT [144]. Similarly, they found more decrease against hydroxyethyl starch (HES) by the end of the bypass [145].

Regarding fluid balance, it was found to be decreased in HES more than crystalloid over 6 studies (MD: -960.49 ml, 95% CI: -1105.77 to - 815.21, low certainty, **Table S7**). Similarly, it increased with albumin; however, it did not reach statistical significance ($p = 0.549$). In both colloid groups, fluid requirements were less than crystalloid [141].

These results support the use of colloid priming fluid in CPB because of its ability to maintain COP and decrease fluid leakage and edema. Therefore, they minimize fluid requirements and protect the organs from ischemia. However, it should be used cautiously and with consideration of patients' clinical profiles because of their known allergic reactions and the observations of renal impairment in some studies particularly with HES [146]. This necessitates avoidance of HES in patients with pre-existing renal dysfunction or a risk of acute kidney injury, consistent with international safety warnings [11].

Despite the low certainty evidence, the guideline panel favored colloid use for priming in CPB conditionally, with an agreement on the feasibility and acceptability of its use.

Pre-Bypass Checklist

Perfusionists should complete the pre-bypass checklist, obtaining the surgeon approval to optimize the CPB process and ensure patient's safety [126]. An example of the comprehensive checklist is shown in details in Table 10.

Checklist recommendation

Should a standardized pre-bypass checklist vs. no checklist be used for reducing the incidence of air embolism and improving safety in patients undergoing CPB?

Ungraded statement

For patients undergoing CPB, we strongly advise using a standardized pre-bypass checklist over no checklist for reducing the incidence of air embolism and improving safety (Good Practice statement).

Rationale

The statement provides advice based on expert opinion and widely accepted practices due to the limited direct evidence. The implementation of standardized checklists has significantly reduced errors in high-risk surgeries through a systematic approach that addresses safety issues and enhances team communication [148]. A standardized pre-bypass checklist can prevent complications such as expected air embolism with faulty priming by following all precautions before initiating CPB. It typically encompasses items such as confirming the integrity of the oxygenator, ensuring proper positioning of the canulas, checking the absence of air in the circuit, and confirming the functionality of the equipment [62]. Supported by the low cost and the high impact the checklist exerts, it can be easily integrated into clinical practice [148]. In surgical settings, checklists were proven to improve team coordination and patient outcomes. For example, the Isala Safety Checklist introduced possible interventions to encounter some risk factors systematically, ensuring a safer and more effective surgical approach regarding cardiothoracic surgery [149]. Similarly, the benefits of checklists were evident in a trial by Stents et al., who made 6 checklists and distributed them randomly among 2 or 3 teams performing extracorporeal membrane oxygenation (ECMO) emergencies in simulated sessions [150]. Additionally, full adherence to World

Health Organization (WHO) checklists has also been proven to reduce complications compared to partial compliance [151].

Therefore, the guideline panel strongly advises the use of standardized pre-bypass checklists for patients undergoing CPB to reduce the incidence of air embolism and improve safety.

Hemoconcentration setup and types

Hemoconcentration is a shared responsibility between the surgeon and the anesthesiologist. Special considerations are required in certain cases, such as patients with sickle cell anemia, where RBCs are fragile. In these situations, lower transmembrane pressures are recommended to minimize the risk of hemolysis [152, 153].

Several locations are suited for the insertion of the hemoconcentrator into the pump circuit. However, using arterial pressure as the driving force with the aid of a Y connector and tubing, the arterial line is best suited for fluid removal [154]. Additionally, the pump flows must be modified to account for the flow redirected to the hemoconcentrator. A pump head may also be employed to regulate the flow via the hemoconcentrator, providing enhanced control while preventing diminished arterial pump output [154]. After CPB, residual blood inside the circuit can be concentrated by cycling it through interconnected arterial and venous lines or an arteriovenous (A-V) bridge, facilitating the hemoconcentrator's filtration of the blood [155].

Types of Hemoconcentration

1) Conventional Ultrafiltration (CUF): During CPB, CUF uses the aorta to revert the hemoconcentrated blood back into the systemic circulation, reducing the fluid in tissues and thus minimizing edema. 2) Modified Ultrafiltration (MUF): Removing the fluid from the pulmonary system, MUF, through the RA, directs the hemoconcentrated blood into the lungs after CPB. It is frequently used in pediatric cases. 3) Zero-Balance Ultrafiltration (Z-BUF): This procedure entails the introduction of a potassium-free replacement fluid (such as normal saline) into the CPB circuit while concurrently extracting an equivalent volume using ultrafiltration. It effectively eliminates compounds such as potassium without inducing fluid imbalance in the patient. 4) Pre-bypass ultrafiltration (PBUF): If primed with packed red blood cells (PRBCs), filtration required to make physiological values for electrolytes, glucose and lactate. After RAP (retrograde autologous priming), PBUF to minimize the priming volume and improve the hematocrit before going on bypass [156–158].

Table 10. The detailed pre-bypass checklist.

Patient verification
☐ Patient identity confirmed ☐ Procedure to be performed confirmed ☐ Blood type and antibodies checked and confirmed ☐ Known allergies reviewed ☐ Blood products and blood bank number verified ☐ Medical record number confirmed ☐ Entire medical chart reviewed for completeness ☐ Participation in surgical safety “time out” to confirm the correct patient, procedure, and site
Sterility and cleanliness
☐ Inspection of all components for intact packaging and current expiration dates ☐ Ensuring the cleanliness of all equipment ☐ Heat exchangers tested for leaks of pump system ☐ Occlusions are properly set according to requirements ☐ Speed controls are operational and responsive ☐ Flow meter correctly oriented and calibration verified ☐ Flow rate indicator checked against patient/tubing size ☐ Rollers and pump head inspected for free rotation and absence of noise ☐ Pump head holders checked for security ☐ Servo-regulation connections tested for proper function Electrical System ☐ All power cords and connections secured and intact ☐ Servo-regulation connections secure and functioning ☐ Batteries confirmed charged and operational cardioplegia system ☐ Cardioplegia system fully debubbled and operational ☐ System integrity maintained after pressurization ☐ Cardioplegia solutions checked for correct composition
Gas supply and management
☐ Secure connection of gas lines and filters ☐ Gas exhaust pathways verified unobstructed ☐ Confirmation of correct gas sources and appropriate connections ☐ Operation of flow meters/gas blenders confirmed ☐ Hoses checked for leaks ☐ Anesthetic gas scavenge system operational Circuit Components ☐ CPB circuit debubbled and ready for use ☐ All connections, stopcocks, and caps secure ☐ Appropriate lines clamped and shunts closed ☐ Correct direction of tubing traced and confirmed ☐ Arterial line and cannula patency verified ☐ Absence of tubing kinks ensured ☐ One-way valves positioned correctly ☐ Pressurization without leaks confirmed Safety Mechanisms ☐ All alarms verified operational, audible, and set ☐ Arterial filter and bubble traps debubbled ☐ Venting of cardiotomy and venous reservoirs checked ☐ Functionality of vent lines confirmed with fluid ☐ Venous line Occluders calibrated and tested ☐ Secure attachment of devices to console
Assisted venous return
☐ Positive-pressure relief valve on cardiotomy reservoir present ☐ Negative-pressure relief valve checked and unobstructed ☐ Vacuum regulator tested and operational Monitoring Systems ☐ Placement of circuit and patient temperature probes verified ☐ Pressure transducers and monitors calibrated to appropriate scales ☐ Inline sensors calibrated as required ☐ Oxygen analyzer calibrated and functional Anticoagulation Control ☐ Heparin administration time and dose confirmed ☐ Adequacy of anticoagulation tested and results documented

(Continued).

Table 10. Continued.

Temperature control systems
– ☐ Connection and operation of water sources confirmed
– ☐ Temperature ranges tested and verified operational
– ☐ Water lines checked for obstructions Supplies and Equipment
– ☐ Adequate supply of tubing clamps on hand
– ☐ Availability of drugs verified and labeling checked
– ☐ Required solutions prepared and available
– ☐ Blood products ready and accessible
– ☐ Sampling syringes and laboratory tubes available
– ☐ Correct anesthetic vaporizer in place
– ☐ Vaporizer checked for operation and filled as necessary
Backup systems
– ☐ Hand cranks available and accessible
– ☐ Duplicate components of the circuit and hardware on standby
– ☐ Emergency lighting and flashlight operational
– ☐ Backup oxygen tank with flow meter ready to use
– ☐ Ice supplies replenished and available emergent restart of bypass
– ☐ Reconfirmation of heparin time and dose
– ☐ Components debubbled as necessary
– ☐ Gas flow to the oxygenator reconfirmed
– ☐ Alarms re-engaged and set
– ☐ Reconnection of water sources termination checklist
– ☐ Venous assist off and venous reservoirs vented
– ☐ Closure of any shunts
– ☐ Vents clamped or removed as appropriate post-bypass checklist
– ☐ Announcement of bypass termination
– ☐ Clamping of arterial and venous lines
– ☐ Arterial circuit checked for air before transfusing perfusate
– ☐ Pump suctions turned off
– ☐ Cell saver re-infusion bags de-aired, labeled, and ready for use
Comments:
Confirmation Signature:
Date:
Time:

Note. Adapted from “Pre-Bypass Checklist,” Perfusion.com (n.d.). Retrieved from <https://perfusion.com/prebypass-checklist/> [147].

Chapter 4: The conduct of CPB

Preoperative planning

Careful planning of CPB is necessary before proceeding with the surgery. All team members in the OR should know the basic steps of venous drainage and arterial cannulation along with the connection between patients’ large vessels and the CPB circuit [49].

Venous drainage

Venous drainage is primarily achieved through a gravity siphon, assisted by low negative pressure. Additionally, vacuum-assisted venous drainage (VAVD), a vacuum in the venous reservoir, augments the venous drainage and is now widely used during CPB procedures, vacuum regulator can be turned on to

a preset pressure of -20 for safe use of VAVD is essential.

To ensure effective drainage: i) The venous reservoir must be positioned below the patient’s level. ii) All tubing must be filled with priming fluid to prevent airlocks, which could impede drainage [159, 160].

Arterial cannulation

Arterial cannulae play a critical role in CPB. They come in various designs in order to optimize blood flow and minimize complications: i) Straight arterial cannulae: This design has the merit of non-turbulent blood flow. Therefore, it is the most frequently used design. However, damaging the aortic wall is a potential risk with the single blood jet. ii) Right-angled cannulae: These cannulae, if correctly positioned, are capable of minimizing the risk of jet-induced aortic

arch damage because they direct blood flow around it. iii) Diffusion cannulae: These are right-angled designs that feature diffusion holes and sealed ends. They modify flow dynamics to reduce the jet effect and decrease the potential for damage to the aortic wall [161–163].

Indications for axillary or femoral cannulation

Axillary or femoral cannulation is preferred in cases like ascending aortic aneurysms, unstable patients before anesthesia induction, alternative access reoperations, complications like antegrade dissection, and minimally invasive cardiac surgeries of unstable patients [164, 165].

Tubing and connectors

It is best to decrease the length of the tubing as possible in order to decrease the volume of priming solution and pressure gradients and prevent blood trauma. Additionally, to prevent leakage of blood upon exposed to positive pressure necessitates tightens the connections [166].

Initiation of the CPB procedure

Initiating CPB is the most important phase because it is where the heart and lung functions are bypassed by the CPB machine. Therefore, team members must communicate well to execute the setup precisely [23]. The initiation process involves several key steps: 1) Low-flow start: Starting the CPB at a low flow rate is necessary until reaching the full flow while taking the venous clamp off slowly to ensure the gradual shift from patient's circulation to the machine. This reduces the change in hemodynamics and provides time for the team to monitor the patient's initial response to the artificial circulation [24, 167]. 2) Monitoring hemodynamic response: The perfusionist and anesthesiologist monitor blood pressure, heart rate, and oxygen saturation, including cerebral and systemic levels, to detect signs of inadequate perfusion or instability, **Figure S9** [6, 168]. 3) Tissue perfusion assessment: Adequate tissue perfusion is confirmed through analysis of arterial and venous blood gases, monitoring cerebral oxygenation by near-infrared spectroscopy (NIRS), and urine output for evaluating renal perfusion [169].

Cerebral oxygenation monitoring recommendation

Should Continuous cerebral oxygenation monitoring using NIRS vs. Standard monitoring without

NIRS be used for patients undergoing CPB to reduce neurological complications and improve cognitive function?

Recommendation

For patients undergoing CPB, we suggest using continuous cerebral oxygenation monitoring using NIRS over standard monitoring without NIRS to reduce neurological complications and improve cognitive function (**Table S8**) (conditional recommendation, very low certainty evidence).

Rationale

Our recommendation is based on a meta-analysis by Serraino et al. (n = 1466), which included ten trials comparing the use of NIRS to standard care. The analysis showed comparable outcomes in mortality, stroke, reoperation for bleeding, red cell transfusion, hospital stay, ICU stay, and MI. The effect size for mortality was (RR 0.76, 95% CI 0.30 to 1.96, very low certainty, **Table S8**), for stroke (RR 1.08, 95% CI 0.40 to 2.91, very low certainty, **Table S8**), for reoperation for bleeding (RR 1.11, 95% CI 0.41 to 3.04, very low certainty, **Table S8**), and for MI (RR 0.90, 95% CI 0.43 to 1.89, very low certainty, **Table S8**). Other outcomes, such as ICU stay (MD 0, 95% CI 0.44 to 0.44, very low certainty, **Table S8**), hospital stay (MD -0.45, 95% CI -0.90 to -0.01, very low certainty, **Table S8**), and red cell transfusion (RR 0.93, 95% CI 0.77 to 1.12, very low certainty, **Table S8**), also showed no significant differences [53].

The potential of NIRS application in CPB has been investigated severely, with no definite conclusive results. Kara et al. [170] conducted RCT over 79 patients undergoing CABG with asymptomatic carotid artery disease. They evaluated cognition using the Montreal Cognitive Assessment Test (MoCA) to find a statistically significant MoCA decrease postoperatively in the non-NIRS group. Additionally, they noticed a higher MoCA in the NIRS group (NIRS: 26.8 ± 1.9 vs. no NIRS: 23.6 ± 2.5 , $p < 0.001$) and correlated it with the use of NIRS statistically ($r = 0.59$, $p < 0.001$). Similarly, NIRS-based algorithms proved to have better cognitive outcomes along with a significant decrease in morbidity and mortality in RCT by Colak et al. [171] performed over 200 CABG patients [171].

Upon this very low-certainty evidence, NIRS routine use for all CPB patients has not been proven yet. However, tailored intervention is based on each case, particularly for individuals with high-risk neurological complications. Additionally, the non-invasive advantage of NIRS can be of significant benefit and

promising feasibility in resource-limited settings if adequate staff training that ensures accurate interpretations is maintained. Therefore, the guideline panel acknowledged the probability of NIRS favor in the balance effect assessment and conditionally recommended it, supporting its probable feasibility and acceptability. However, no data was found regarding its cost and cost-effectiveness, necessitating conducting further well-qualified, larger trials to optimize its role in clinical practice.

Monitoring and maintenance of physiological parameters

The anesthesiologist must monitor and maintain various physiological parameters, including blood pressure, flow rates, temperature management, oxygenation and ventilation, hematocrit and hemoglobin levels, and glucose control. Blood pressure should be maintained between 50-80 mmHg for adequate organ perfusion, with adjustments made through pump flow rates, vasopressors, or vasodilators. Flow rates should be adjusted based on hematocrit, oxygen delivery, and patient temperature. Temperature management should be done using a CPB machine heat exchanger, with a target range of 34-35°C for normothermic procedures and 28-32°C for hypothermic procedures. Oxygenation and ventilation should be maintained with arterial oxygen saturation >95% and partial pressure of oxygen within 100-150 mmHg. Hematocrit and hemoglobin levels should be maintained at 24% or 0.8 g/dL, with red blood cell transfusions as needed. Glucose control should be monitored and maintained within a range of 80-180 mg/dL, using insulin therapy if necessary [11, 172–174].

Anticoagulation management

Heparin administration

A loading dose of heparin should be administered before starting CPB to achieve an activated clotting time (ACT) >480 seconds. An additional dose may be given as needed for ACT maintenance during the whole procedure. Additionally, in cases of insufficient response to heparin, anesthesiologists may consider using fresh frozen plasma (FFP) or antithrombin III (ATIII) to enhance its efficacy. After CPB, the anesthesia team will administer protamine to reverse heparin anticoagulation based on total heparin, time, and ACT values. Monitoring for protamine reaction signs and informing the team if any concerns arise is needed. Additionally, the CPB suction pump should be stopped as soon as half of the protamine dose is given to avoid clot formation in the circuit [175–177].

Alternatives to heparin

For patients with contraindications to heparin, such as type II heparin-induced thrombocytopenia (HIT), direct thrombin inhibitors like bivalirudin and argatroban are recommended [177].

Bivalirudin

Multicenter studies have proven that Bivalirudin can be a safe alternative to unfractionated heparin (UFH) in either CPB or off-pump cardiac surgery [178].

Monitoring

Ecarin clotting time (ECT) is considered the bivalirudin-preferred intraoperative monitoring test. However, ACT can replace ECT if unavailable [178].

Dosing and clearance

The effect of bivalirudin dosing is linear, and its clearance from the system can be achieved through hemodialysis or hemofiltration [177].

Thrombosis prevention

Bivalirudin is crucial to avoid thrombosis and stagnation of blood inside the CPB circuit [177].

Normothermia maintenance

At lower body temperatures, proteolysis could be reduced and thus lead to the residual anticoagulant effect of bivalirudin. Therefore, normothermia should be obtained before separation from CPB to neglect that effect [179].

Anticoagulants recommendation

Should Bivalirudin as an anticoagulant vs. Heparin as an anticoagulant be used for patients undergoing CPB to reduce the incidence of HIT and improve coagulation control?

Recommendation

For patients undergoing CPB, we suggest using Heparin as the standard anticoagulant. Bivalirudin as an anticoagulant vs. Heparin as an anticoagulant should be used for patients undergoing CPB to reduce the incidence of HIT and improve coagulation control

(**Table S9**) (Conditional recommendation, very low certainty evidence).

Remarks

Heparin is the standard of care for all patients. It is the most effective, available, and affordable choice. However, Bivalirudin may be used in specific cases as a life-saving alternative, such as in patients with HIT or other mandated clinical scenarios.

Rationale

This recommendation was based on a systematic review article that investigated this comparison using 2 RCTs and one retrospective study, acknowledging the feasibility, efficacy, and safety of using bivalirudin in adult and pediatric patients [180]. Bivalirudin was associated with lower rates of reoperation or major bleeding (RR 0.89, 95% CI 0.29 to 2.71, very low certainty, **Table S9**) and mortality (RR 0.52, 95% CI 0.13 to 2.10, very low certainty, **Table S9**); however, these results were not statistically significant. Despite the limited studies comparing bivalirudin to heparin in CPB requiring cardiac surgeries, all available studies in the literature showed non-inferiority results with bivalirudin, particularly in patients with HIT or heparin resistance. Dyke et al. [181], one of the included studies, conducted the first RCT over 150 patients undergoing cardiac surgery with CPB and found comparable surgery success rates along with mortality and MI. However, significant blood loss was noticed in patients who received bivalirudin at 2 hours postoperatively. This significance disappeared 24 hours later, with comparable transfusion requirement and reoperation for bleeding findings. Additionally, they observed longer CPB to chest closure time. However, it did not affect the CPB itself, the cross-clamp, or the overall surgery time. Similarly, Hasija et al. [182] confirmed the same findings, conducting RCT over 50 pediatric patients and noticed longer duration from incision to skin closure [182]. The longer duration noticed with the 2 trials may be attributed to the fact that bivalirudin has no antidote like protamine sulfate with heparin. Therefore, it requires strict monitoring postoperatively until a reversal occurs. Additionally, Hasija et al. reported clots in CPB circuits in 2 cases, underscoring also the need for vigilant monitoring in the bivalirudin group. A retrospective study by Carlson et al. [183] compared direct thrombin inhibitors (DTIs), mostly bivalirudin, to heparin in patients with HIT undergoing cardiac surgeries with CPB. They found a significant difference in moderate and severe bleeding outcomes, favoring bivalirudin and lower

rates of mortality and reoperation for bleeding that did not reach significance statistically.

Based on all of that, the guideline panel consensually agreed to the continuous use of heparin as a standard anticoagulant because of its reversal, cost-effectiveness, and long-standing effective use in clinical practice. Additionally, they conditionally recommend bivalirudin in patients with certain clinical profiles, such as in HIT or heparin resistance, calling for good monitoring to avoid circuit clotting and mitigate its lack of a reversal agent.

Use of argatroban

Unlike bivalirudin, argatroban is metabolized hepatically. Therefore, it can be a good alternative for patients undergoing renal replacement therapy (RRT). However, its side effects specially the excessive bleeding requires careful monitoring [184, 185]. The detailed comparison between bivalirudin and argatroban is shown in **Table 11**.

Management of HIT in cardiac surgery

In patients with HIT requiring cardiac surgery, negative confirmatory assays are needed before performing elective procedures, **Table 12**. However, when postponing the surgery is not available, bivalirudin is the preferred anticoagulant in urgent cases because of its efficacy and safety profile. Additionally, alternative strategies such as plasmapheresis, argatroban, or even heparin combined with antiplatelet agents may be considered for patients with significant renal impairment and HIT positivity, though these options carry an increased risk of bleeding and require careful monitoring [186–188].

Steps of initiation CPB. 1) Verify adequate anticoagulation: Ensure that the ACT is within the target range before initiating CPB. 2) Sequential clamp removal: First, remove the arterial clamp, followed by the gradual release of the venous clamp. 3) Controlled flow initiation: Gradually increase the pump flow to prevent hemodynamic instability. 4) Gas flow settings: Start with an initial gas-to-blood flow ratio of 1:1, with an inspired oxygen fraction (FiO₂) of 80% to avoid pumping unoxygenated blood. 5) Heat exchange activation: Initiate water flow through the heat exchanger to regulate temperature and assure warm priming. 6) Indexing flow to BSA: Systemic flow is most often adjusted according to patient size, typically indexed to BSA [62, 168, 189, 190].

Standard flow Indices. i) Normothermic or cooling: 2.2–2.4 L/min/m² or 50–65 mL/kg/min [191]. ii) Higher flow indices are often required in pediatric patients and during rewarming [192].

Table 11. Detailed comparison of Bivalirudin and Argatroban.

Anticoagulant	Initial dosing for HIT-Related thrombosis	Anticoagulant monitoring	Metabolism	Half-life
Bivalirudin	Start without bolus; continuous infusion at 0.15–0.20 mg/kg/h	1.5–2.5 × baseline aPTT	Enzymatic (80%); Renal (20%)	23 min
Argatroban	Start without bolus; continuous infusion at 2 µg/kg/min	1.5–3.0 × baseline aPTT	Hepatobiliary	40–50 min

Table 12. Management of HIT in cardiac surgery.

HIT type	Management approaches
Acute HIT	1. Postpone cardiac surgery for several weeks; afterward, follow guidelines for “Previous HIT.” 2. Administer bivalirudin, provided ecarin clotting time (ECT) monitoring is accessible. 3. Use lepirudin if ECT monitoring is available and renal function is unimpaired. 4. Combine heparin with epoprostenol as an alternative. 5. Utilize tirofiban in conjunction with heparin. 6. Opt for danaparoid if available, ensuring anti-Xa level monitoring can be done.
Subacute HIT	1. Defer surgery for a few weeks, then proceed with the protocol for “Previous HIT.” 2. Off-pump procedures using bivalirudin, lepirudin, or danaparoid can be considered. 3. Heparin may be used if either the washed platelet activation assay yields a negative result or the enzyme immunoassay is negative or only weakly positive. 4. All strategies under “Acute HIT” are also applicable here.
Previous HIT	The numbered approaches listed above serve as individual treatment options. They are generally presented in order of preference, with those listed first typically being more favorable.

Systemic venous drainage

Once CPB is initiated, the heart should be emptied, which can be confirmed by the collapse of the pulmonary artery. This indicates adequate venous drainage and effective bypass [24].

Aortic clamping and cardioplegia administration following the initiation of CPB

Antegrade cardioplegia is delivered after clamping the aorta at a controlled rate of 200 mL/min over several minutes. The heart should not become distended during infusion, and ventricular decompression should be performed if distension occurs. Intermittent delivery of oxygenated cardioplegic solution is required for electromechanical arrest, oxygen delivery, and metabolic waste removal [193, 194].

Venting systems

Testing venting systems before use is necessary to ensure proper suctioning. This can be achieved through brief immersion of the vent tip in saline. However, sometimes a small-gauge needle may be used to relieve pressure and ensure effective decompression in the vent line [195].

CO₂ insufflation for air embolism prevention

CO₂ insufflation was found to be linked to a decrease in the complications associated with air em-

bolism, enhancing the general safety of the patients [196].

Circulatory arrest

To provide a motionless and bloodless surgical field in some complex cardiac procedures, particularly in pediatric surgery and certain adult cases, circulatory arrest may be used in conjunction with CPB. Before stopping the circulation temporarily, CPB cools the patient to a safe temperature, correlating longer and safer circulatory arrest duration to colder temperatures, Table 13. The process involves packing the patient's head in ice to ensure cerebral protection upon arrest. Additionally, EEG, despite not being routinely performed in CPB, is noted to be absent at 15–20°C [197–199].

Preparation for circulatory arrest

Upon scheduling the procedure, the need for circulatory arrest must be explicitly stated. Additionally, it should be confirmed in the preoperative briefing [200].

Key preparatory measures include. 1) Perfusionist readiness: The perfusionist has to predict and deal with the metabolic acidosis linked to circulatory arrest [201]. 2) Pre-arrest alkalosis: Induction mild alkalosis should be performed pre-arrest, often achieved through sodium bicarbonate administration and controlled CO₂ elimination [202]. 3) Use of an A-V bridge: If available, an A-V bridge allows continued circulation through the oxygenator during arrest [203]. 4) Alkalotic blood reintegration: To minimize

Table 13. The correlation between hypothermia levels and the approximate safe circulatory arrest times.

Degree of Hypothermia	Core body temperature (°C)	Estimated safe arrest duration (minutes)
Mild	37 to 32	Approximately 5 to 10
Moderate	32 to 28	Roughly 10 to 15
Deep	28 to 18	Around 15 to 60
Profound	Below 18	Approximately 60 to 90

post-arrest acidosis, normalizing pCO₂ blood levels should be done by the oxygenator before resuming normal flow [204]. 5) Temperature gradient control: The warming difference between the patient and perfusate should be less than 8°C to avoid the formation of microbubbles and air embolisms that may occur with the release of oxygen upon rapid warming [205].

Pulmonary management during CPB

Lung protection during CPB is critical to reduce postoperative respiratory complications [206].

A. Lung protection strategies. 1) Preventing atelectasis: During CPB, Continuous Positive Airway Pressure (CPAP) can improve postoperative oxygenation despite lasting only 4 hours in the postoperative period. Recruitment strategies, persistent ventilation with physiological positive end-expiratory pressure (PEEP), and decreasing FiO₂ to ambient air concentrations can mitigate atelectasis. However, these measures are transient and temporary [206, 207]. 2) Preventing acute lung injury: The use of biocompatible coatings such as phosphorylcholine and heparin, MUF, continuous ventilation, CPAP, and high-dose dexamethasone may decrease the incidence of ALI by minimizing the risk of inflammation and respiratory failure while enhancing oxygenation. However, more research is required to determine long-term benefits [208, 209].

B. Pulmonary management. Effective weaning from CPB necessitates coordination among anesthesiologists, surgeons, and perfusionists to facilitate an effortless return to autonomous cardiac and pulmonary function. A standardized pre-weaning checklist is advised, and closed-loop communication must verify the return of ventilation before the cessation of CPB. Manual lung inflation is conducted to ensure complete lung expansion, and any retained fluid is evacuated. Mechanical breathing is reestablished with PEEP when confirming lung expansion, and tracheobronchial suctioning is performed to enhance airway patency. Ventilation has to start prior to cardiac ejection of blood in order to avoid systemic arterial hypoxia. Finally, alarms must be reactivated prior to weaning after the silence CPB period to ensure continued patient monitoring and safety [210–213].

Chapter 5: Hormonal activities and electrolyte levels effects of CPB

The CPB techniques, anesthesia, and patients' comorbidities may affect electrolyte levels and hormones. This depends on factors such as the bypass duration, hypothermal degree, and priming solution contents, reflecting on the extent of these alterations. CPB is responsible for the excessive release of stress hormones.

However, the main cause behind these changes has not yet been ascertained. It can be hypothermia, perfusion decrease of hemodilution, anticoagulation, or the change of non-pulsatile perfusion within organs, which alters the levels of hormones, electrolytes, and serum proteins. These endocrine and metabolic responses are usually diluted by analgesia in addition to spinal and epidural anesthesia, decreasing the mortality rate of CPB. Additionally, immunological reactions, plasma protein removal, and blood cell damage may arise from the use of tubing and the pump-oxygenator [214–216].

Potassium levels in plasma are also primarily affected by cardioplegia dosage and components. Priming and its hemodilution effect after the initiation of CPB cause ionized calcium levels to decrease initially before returning to normal in response to the reaction of the parathormone hormone. Therefore, there is no need to take calcium supplements regularly after CPB. In contrast, hypomagnesemia is usually seen after CPB, necessitating intravenous magnesium administration as prophylaxis to minimize the risk of post-CPB atrial and ventricular arrhythmias [217–220].

Glucose regulation is maintained through various hormones, such as glucagon, insulin, and cortisone, which fluctuate upon the impact of CPB along with surgery. In cases of unbalance, blood glucose levels in adults are elevated during CPB, accompanied by hypoinsulinemia due to hypothermia. Therefore, keeping blood glucose levels within the normal range during CPB can be challenging, even if a high insulin dose is administered [221, 222].

Additionally, decreased response of T3 and T4 to the normal thyroid-stimulating hormones (TSH) is seen in CPB, which is called sick euthyroid syndrome. Increasing the risk of myocardial ischemia and

infarction, aggressive preoperative treatment with T3 and T4 is not recommended. However, it is advised to continue thyroid hormone replacement therapy in patients who already use it to maintain metabolic stability.

Having a vital role in regulating metabolism, heart rate, and myocardium, evidence suggested that a prophylactic T3 dose may enhance post-CPB outcomes. Also, the impact of T3 and T4 on cardiac function makes them a choice for intensivists as an adjunct therapy in cases of refractory heart failure [223–225].

Anesthesia and pulsatile perfusion can counteract the CPB effect on the adrenal gland, which secretes high levels of aldosterone, cortisol, and catecholamines. Also, the aldosterone hormone is secreted in response to activating the renin-angiotensin-aldosterone system (RAAS). The biocomponents of this system, including renin, angiotensin II, and aldosterone, are increased during CPB and shortly after. They function as arterial blood pressure regulators, maintaining fluid balance [226, 227]. In addition to that, postoperative pituitary dysfunction has been observed in patients with pituitary adenomas (POMs) despite their rarity and severity. This observation has not been attributed to the effect of CPB itself because pituitary dysfunction does not occur unless there is a pituitary mass. Hormonal disturbances and ocular hypertrophy or even loss of vision can occur as a result to the compression effect of the enlarged pituitary over the adjacent structures. Mass diagnosis is usually achieved by CT or MRI and treated by hormone replacement therapy along with surgery [228].

Antidiuretic hormone (ADH) is responsible for regulating the kidney water flow. It rises and continues its elevation for several hours during and after CPB, influenced by the effect of general anesthesia and some heart surgery medications, such as angiotensin-converting enzyme (ACE) inhibitors. This is reflected in increased vascular resistance and von Willebrand factor (VWF), aiding hemostasis during surgery [229].

A decrease in testosterone hormone is noticed in men after cardiac surgery. However, it rises in women, posing unknown significance until now [230]. Additionally, catecholamines are elevated during CPB, exerting their vasoconstriction peripherally and affecting the organs' blood flow. The increase in epinephrine can reach tenfold due to the hypothermic effect. In contrast, norepinephrine levels do not rise to that extent. However, a contradictory response can occur with deeper levels of hypothermia and anesthesia, decreasing epinephrine and norepinephrine levels within the surgery [231].

Natriuretic peptides, including atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP),

are secreted by the heart and regulate blood pressure, vascular volume, and cardiac remodeling. ANP levels decrease perioperatively, which may contribute to postoperative fluid retention, particularly in patients with atrial fibrillation. Additionally, BNP levels rise in response to ventricular dysfunction and are associated with heart failure and postoperative morbidity. After CPB, BNP levels typically increase, especially in patients with preexisting heart failure [232].

During extracorporeal perfusion, lung bypass alters the concentrations and metabolism of eicosanoids, which play a key role in vascular tone and platelet function. The lungs regulate prostaglandins, including prostacyclin (PGI₂), a vasodilator that inhibits platelet aggregation, and thromboxane A₂ (TXA₂), which promotes vasoconstriction and platelet activation. The protease inhibitor aprotinin used during CPB reduces TXA₂ levels, enhancing platelet function and minimizing the risk of postoperative bleeding. However, it increases the risk of thrombosis and stroke [233, 234].

Additionally, cysteinyl leukotrienes, which contribute to pulmonary dysfunction, rise during CPB, especially in patients with chronic lung disease. In infants undergoing congenital heart surgery, lipid emulsions and medium-chain triglycerides help mitigate inflammation by reducing leukotrienes. Histamine levels may also increase, leading to vasodilation and hypotension, with certain opioids and muscle relaxants contributing to this effect during cardiac surgery [235].

Immune system and inflammatory response to CPB

Various factors contribute to the development of a systemic inflammatory response, such as endotoxemia and contact activation. They exert their effect by activating leukocytes, resulting in cytokines release and complement activation. Depending on the degree of this response, severe clinical manifestations can occur, including systemic inflammatory response syndrome (SIRS), organ dysfunction, and capillary leak syndrome.

To minimize these effects, healthcare providers implement comprehensive strategies that include the preoperative, intraoperative, and postoperative phases: 1) Preoperative management. It involves assessing patients at risk for excessive inflammatory responses, particularly those with comorbidities, and optimizing their chronic conditions to minimize postoperative complications. 2) Intraoperative strategies. Several strategies are implemented within the circuit and surgical approach to minimize the inflammatory response and improve patient outcomes during CPB. It includes utilizing biocompatible coatings on

the CPB circuit that can enhance the compatibility with circulating blood components. Additionally, incorporating leukocyte filters and anti-inflammatory agents in the prime solution can further minimize inflammatory activation. Careful temperature regulation, whether maintaining normothermia or inducing mild hypothermia, plays a crucial role in reducing metabolic demands and protecting against ischemia-reperfusion injury. Furthermore, myocardial protection techniques, including specialized cardioplegic solutions and strategies to minimize myocardial stress, are essential for preserving cardiac function during surgery. 3) Pharmacologic interventions. Anesthesiologists administer corticosteroids to mitigate the SIRS. However, timing and dosage are still under investigation to identify their optimum. Additionally, antifibrinolytics and antibiotics are used to prevent fibrinolysis and infections that can occur with inflammation. 4) Postoperative management. Postoperative care includes strict monitoring and attention to symptoms and signs of inflammation and organ dysfunction. Additionally, Supportive measures may be necessary to manage complications, including organ-specific treatments such as RRT for kidney impairment or ventilatory support for respiratory insufficiency [236–239].

Neurologic effects of CPB

The CPB can lead to various neurological complications, ranging from mild cognitive impairment to severe brain injury. Patients may experience cognitive dysfunction, including memory deficits, difficulty concentrating, and slower mental processing. Stroke can occur due to embolism or cerebral perfusion reduction, while transient ischemic attacks (TIAs) occur when there are temporary disruptions in cerebral blood flow. In more severe cases, extensive cerebral hypoperfusion may lead to hypoxic-ischemic encephalopathy. Additionally, postoperative delirium, characterized by acute disorientation and variable degrees of consciousness, is a common neurological concern following CPB [240].

Intraoperative cerebral monitoring

Intraoperative cerebral monitoring plays a crucial role in ensuring brain protection during CPB. Transcranial Doppler (TCD) is used to assess cerebral blood flow and detect micro-emboli that may contribute to neurological complications. NIRS provides real-time feedback on cerebral oxygen saturation, helping to maintain adequate brain oxygenation. Electroencephalography (EEG) is utilized to mon-

itor brain activity, allowing for early detection of ischemic events. Additionally, cerebral oximetry measures regional oxygen saturation, serving as an important indicator of potential hypoxia and guiding interventions to optimize cerebral perfusion [241–243].

Intraoperative neuroprotective strategies

Several strategies are employed during CPB to protect brain function and minimize the risk of neurological complications. Maintaining hemodynamic stability is crucial for ensuring adequate cerebral perfusion, which involves regulating blood pressure and flow. Additionally, optimizing blood gas levels, particularly the partial pressure of carbon dioxide (PaCO₂), is important for controlling cerebral vasodilation and enhancing oxygen delivery to the brain.

De-airing techniques are used to prevent air embolism by carefully removing any air from the circuit before discontinuing CPB. Temperature management, whether through hypothermia or normothermia, is adjusted according to the specific procedure and the patient's needs in order to reduce ischemic damage.

Pharmacological interventions, including agents such as thiopental, propofol, steroids, and mannitol, may provide neuroprotection by decreasing inflammation and metabolic demand. Furthermore, aortic filtration captures embolic debris in the arterial line, which further reduces the risk of cerebral embolism [244–247].

Postoperative management

Effective postoperative care focuses on early detection and intervention to minimize neurological complications. Regular neurological assessments are essential for promptly identifying any emerging deficits. If changes are observed, postoperative imaging with CT or MRI is conducted to evaluate potential brain injury. For patients experiencing neurological impairments, a multidisciplinary rehabilitation approach involving physical, occupational, and speech therapy is crucial for optimizing recovery and functional outcomes [248].

Kidney function and CPB

Renal dysfunction, including acute kidney injury (AKI), is a common complication of CPB. Various preventive strategies have been developed to minimize this risk, focusing on preoperative evaluation, intraoperative optimization, and postoperative monitoring.

Preoperative assessment

1) Risk evaluation: Identify high-risk patients, such as those with comorbidities, like chronic kidney disease (CKD), diabetes, hypertension, heart failure, or advanced age. 2) Baseline renal function: Assessing kidney function and detecting preexisting impairment can be achieved through serum creatinine levels and glomerular filtration rate (GFR). 3) Hydration Optimization: It is crucial to confirm adequate volume status before surgery to support renal perfusion.

Intraoperative management

1) Hemodynamic stability: Preserving renal perfusion can be achieved through adequate blood pressure and cardiac output. 2) Minimize CPB duration: Shortening bypass time whenever possible is crucial because longer durations are associated with a higher risk of AKI. 3) Avoid nephrotoxic agents: Reduce exposure to harmful substances such as contrast dyes, NSAIDs, and nephrotoxic antibiotics. 4) Renal protection strategies use: Implement measures like maintaining optimal hematocrit levels, considering prophylactic RRT, and using renoprotective agents.

Postoperative management

1) Renal function monitoring: Detecting early signs of AKI must be ensured through regular assessment of serum creatinine and urine output. 2) Fluid and electrolyte balance: Carefully regulate fluid intake and electrolyte levels to prevent overload and imbalances. 3) Early intervention: In cases of AKI development, early intervention aims to optimize hemodynamics promptly, avoid additional nephrotoxic exposure, and initiate RRT if necessary [249–252].

Pharmacodynamics and Pharmacokinetics during CPB

Effects of CPB

The establishment of CPB significantly affects the plasma concentration, distribution, and metabolism of administered drugs. Several key factors contribute to these changes: 1) Hemodilution: Adding the priming solution leads to the patient's blood dilution and consequently reduces the overall concentration of free drugs in circulation. 2) Altered plasma protein binding: By decreasing plasma protein levels, hemodilution increases the free or unbound components of the drugs, which are the active ones. 3) Hypotension: Minimizing blood perfusion to vital organs, such as the kidney and the liver, impacts drug metabolism

and clearance. 4) Hypothermia: Lower body temperature decreases the removal of drugs by reducing renal perfusion, GFR, and tubular secretion. 5) Pulsatile vs. non-pulsatile flow: The redistribution of previously sequestered drugs in poorly perfused tissues after CPB cessation and the return of pulsatile blood flow may alter systemic drug levels. 6) Lung isolation and drug sequestration: During CPB, the lungs are bypassed. Therefore, it may serve as a reservoir that allows the release of sequestered drugs when normal circulation is back [253–255].

Inhalation anesthetic agents

This category includes volatile anesthetics such as sevoflurane and isoflurane, which require specialized vaporizers, as well as nitrous oxide (NO), a weak anesthetic gas.

Pharmacokinetics

The onset of action of each anesthetic is dependent on its solubility, with rapid induction occurring with lower solubility agents and vice versa. Hypothermia increases the solubility of volatile anesthetics during the cooling phase of CPB. Subsequently, this decreases anesthetic potency. On the other hand, rewarming increases the potency of the anesthetics by reducing their solubility. Additionally, HCT levels can impact solubility. While hemodilution lowers solubility, hemoconcentration increases it. The countereffects of both temperature and Hct result in a state of balanced effect over anesthetic levels.

Pharmacodynamics

Volatile agents can cause hypotension through their vasodilatation effect. NO can induce air bubbles because of its blood insolubility. Therefore, using this agent during and after CPB may lead to bad neurological outcomes related to the expansion of gaseous emboli. Additionally, it exerts several effects on the CVS after CPB, such as hypotension, bradycardia, and reduction of cardiac output [256–258].

Intravenous agents

This category includes Propofol, opioids (Fentanyl, Remifentanyl), and Benzodiazepines (midazolam).

Pharmacokinetics

Hemodilution reduces the overall concentration of intravenous anesthetic drugs due to hemodilution. However, certain agents, such as propofol and

opioids, can avoid this effect due to their highly bound-to-protein nature. The hemodilution effect on plasma proteins can explain this outcome because a reduction in plasma proteins equals freer and more active biocomponents of the agents, balancing the initial impact. Additionally, hypothermia decreases intravenous agent clearance because of hepatic and renal hypoperfusion, raising the levels of propofol and opioids.

Pharmacodynamics

Intravenous agents exert similar pharmacodynamic effects to volatile anesthetics; Propofol may cause hypotension by vasodilation [254, 259–261].

Muscle relaxants

Pharmacokinetics 1) Effect of Cooling: Hypothermia during CPB reduces acetylcholine mobilization, leading to impaired neuromuscular transmission and altered muscle function. 2) Impact of Hemodilution: The dilution of blood caused by CPB lowers the overall concentration of muscle relaxants. However, since these drugs are highly protein-bound, the reduction in plasma proteins (such as albumin) increases the proportion of unbound, pharmacologically active drug, partially counteracting the effects of hemodilution. 3) Influence of Hypothermia on Drug Clearance: Hypothermia slows the hepatic metabolism of steroidal neuromuscular blocking agents, such as rocuronium, which primarily rely on liver clearance. However, it may enhance renal elimination, contributing to variable effects on the duration of action of these agents [254, 259, 260, 262].

Chapter 6: Myocardial protection - (cardioplegia)

Myocardial protection is a vital step during CPB because it has a higher risk of morbidity and mortality [263].

Cardioplegic solutions

Cardioplegia solution may be prepared by some cardiac centers according to their own preference, getting the advantages of being cheaper and immediately available with simple components, including: Dextrose 5% in Water 1000ml; Potassium Chloride Injection 80 mEq; Magnesium Sulfate 500mg; Sodium Bicarbonate 8.4%, 2.5mEq; Sodium Chloride (2.5 mEq/ml) 27mEq; and Methylprednisolone 500mg.

However, this kind of preparation may lack quality and the benefit of ongoing research over the years.

Table 14. Component of Del Nido cardioplegia.

Ingredient	Quantity used
Plasma-Lyte A	1000 mL
20% Mannitol solution	16.3 mL
50% Magnesium sulfate	4 mL
8.4% Sodium bicarbonate	13 mL
Potassium chloride (2 mEq/mL)	13 mL
1% Lidocaine	13 mL

Additionally, it is exposed to errors during preparation and does not adhere to sterility standards and composition uniformity. Even though it is a lifesaving technique, particularly with experience build-up and the ability to conduct other blood mixing techniques [264–266].

Cardioplegia delivery system

1. *Antegrade Infusion.* Blood cardioplegia is given initially in adults at a dose of 15 ml/kg, followed by 5 ml/kg. However, it is administered at a 40 ml/kg dose, followed by 20 ml/kg in children. Histidine-tryptophan-ketoglutarate (HTK) solution, also known as Custodiol, is the most commonly used crystalloid cardioplegic solution. It is usually administered at 30-50 mL/Kg, lasting 2-3 hours. The infusion pressure is optimally 125-150 mmHg, except with coronary occlusion, which needs higher pressure (250 mmHg), so the cardioplegia gains the ability to reach distant vascular regions [267, 268].
2. *Retrograde Infusion.* Retrograde administration is performed by inserting a cannula into the coronary sinus, passing through the right atrium, while monitoring infusion pressure. It requires about 35-50 mmHg to ensure adequate delivery [269].

Del Nido Cardioplegia

Del Nido cardioplegia solution was initially designed for children by Pedro Del Nido, but it is now expanding into adult cardiac surgery. Usual cardioplegic solutions have a 4:1 blood to crystalloid ratio. In contrast, Del Nido cardioplegia is reversed, having a 1:4 ratio. Additionally, it comprises the typical components, inducing cardiac arrest by potassium while using bicarbonate as a buffer. Additionally, mannitol provides oncotic support and acts as a free radical scavenger, whereas magnesium and lidocaine help stabilize the myocyte membrane, Table 14. Del Nido is typically induced at a 20 ml/kg rate, lasting up to 90 minutes, followed by 10 mg/kg whenever needed, and maintains a pressure of 80 - 100 mmHg. A hemocentrator is also suggested to minimize the effect of hemodilution [270–273].

Del Nido Cardioplegia Recommendation

Should Del Nido cardioplegia solution vs. Standard blood cardioplegia solution be used for patients undergoing cardiac surgery with CPB to improve myocardial protection and reduce ischemic damage?

Recommendation

For patients undergoing CPB, we suggest using the Del Nido cardioplegia solution or standard blood cardioplegia solution to improve myocardial protection and reduce ischemic damage (**Table S10**) (Conditional recommendation, moderate certainty evidence). It is imperative to know the limitations of any of these strategies and avoid implementations that can result in HARM (especially with repeating the dose of Del Nido cardioplegia).

Rationale

Myocardium protection from ischemic damage in cardioplegia requiring surgeries can be achieved through arrest induction by crystalloid or blood-based cardioplegic solutions. Del Nido's cardioplegic solution is a 4-crystalloid to one-part blood, unlike the conventional cardioplegic solution, which is 1 to 4. The del Nido solution has Plasma-Lyte A or alternative fluids such as Ringer's Lactate in addition to the mixture of potassium Chloride (KCl), magnesium Sulfate, lidocaine, sodium Bicarbonate, dextrose, and mannitol. The comparison between the del Nido and standard cardioplegic solution has been debated since each of them has different qualities. For example, del Nido was first designed for the pediatric population and given as a single dose that could provide 60 to 90 minutes of protection. On the other hand, the conventional cardioplegic solution is used for adult patients and repeated every 20 to 30 minutes as a cold or warm solution. Therefore, it is best used for complex or long-duration surgeries. A retrospective study investigated these 2 solutions in 118 patients who underwent aortic surgery with CPB, comparing their operative and postoperative outcomes. The results were in favor of del Nido solution achieving desirable outcomes, including lowering significantly the need for inotropic support and comparable IABP requirement (20/54 (37.0%) vs. 36/65 (55.4%), very low certainty and 2/54 (3.7%) vs. 3/65 (4.6%), very low certainty, **Table S10**). Additionally, they noticed a comparable decrease in cerebrovascular accident (CVA) and AF (1/54 (1.9%) vs. 2/65 (3.1%), very low certainty, and 6/54 (11.1%) vs. 8/65 (12.3%), very low certainty, **Table S10**). Undesirable outcomes included higher bleeding and lower mortality in both groups (3/54 (5.6%) vs. 4/65 (6.2%), very low cer-

Table 15. Components of the histidine-tryptophan-ketoglutarate Solution.

Substance	Approximate Concentration	Unit
Na ⁺	15	mmol/L
K ⁺	9	mmol/L
Mg ²⁺	4	mmol/L
Ca ²⁺	0.015	mmol/L
Histidine	198	mmol/L
Tryptophan	2	mmol/L
Ketoglutarate	1	mmol/L
Mannitol	30	mmol/L
Glucose	–	mmol/L
Lidocaine	–	mg
pH	7.02–7.20	–

tainty, and 2/54 (3.7%) vs. 2/65 (3.1%), very low certainty, **Table S10**) [274].

Therefore, upon this very low certainty evidence, the guideline panel conditionally recommended either the intervention or the comparison, with a recommendation of using del Nido solution in valve-based procedures where there is no need for redosing because of the surgery's short duration. Additionally, they believed that using traditional cardioplegia in CABG would be more protective, whereas ischemic protection is crucial because of the coronary grafting nature and longer surgery. Further and larger studies are needed to confirm the benefits observed in this study and solidify the evidence.

Custodiol (HTK) solution

Custodiol solution, firstly created to preserve transplanted organs, contains a small amount of potassium, calcium, and sodium, exerting its effect intracellularly. Additionally, it has magnesium to stabilize the membrane and is based on the HTK formulation, **Table 15**. It is initially administered at 80–100 mmHg perfusion pressure, maintained at 40–60 mmHg, with an optimum temperature of 4–8 °C. Perfusion time also should not be less than 6 minutes, having a total dose of 30–50mL/kg. The heart has the ability to tolerate cold ischemia for 3–4 hours. Additionally, hyponatremia and acidosis can represent issues with HTK. Hemoconcentration is also suggested for excess fluid removal [275, 276].

Histidine-tryptophan-ketoglutarate solution recommendation

Should the HTK solution vs. Multidose cardioplegia be used for myocardial protection in cardiac surgeries? Recommendation. For myocardial protection in cardiac surgeries, we suggest using either HTK solution or multi-dose cardioplegia (**Table S11**) (Conditional recommendation, very low certainty evidence).

Remarks

The HTK intracellular cardioplegia solution provides myocardial protection for an extended period of 3-4 hours with a single infusion dose, whereas extracellular conventional blood cardioplegia requires re-dosing every 20-30 minutes. Consequently, each cardioplegia type is selected based on specific procedural needs, with HTK suited to longer procedures like organ transplants and long, complex, and congenital heart surgery. In comparison, extracellular solutions are appropriate for shorter, simpler cases with intermittent protection like CABGs. Different surgeons' preferences for specific cardioplegia are taken into consideration.

Rationale

This recommendation was based on a systematic review and meta-analysis of RCTs ($n = 1327$) comparing HTK solution to multidose cardioplegia [277]. Procedural outcomes showed minimal differences in CPB time (MD -1.98 minutes, 95% CI 4.31 to 0.35 , very low certainty, **Table S11**) and aortic cross-clamping time (MD 1.51 minutes, 95% CI 1.58 to 4.6 , very low certainty, **Table S11**). Cardiac parameters revealed differences in cardiac arrest beginning time (MD 4.87 seconds, 95% CI -5.01 to 14.76 , very low certainty, **Table S11**), with a similar number of grafts (MD -0.04 , 95% CI -0.25 to 0.17 , very low certainty, **Table S11**). Clinical outcomes in the HTK solution group showed higher postoperative inotropic support requirements (MD 1.11 , 95% CI 0.95 to 1.28 ; very low certainty, **Table S11**), minimal EF changes (MD -0.11 , 95% CI -0.86 to 0.64 ; low certainty, **Table S11**), and increased ECG changes (MD 0.81 , 95% CI 0.61 to 1.09 ; very low certainty, **Table S11**) [277]. There was a higher incidence of postsurgical AF (MD 0.82 , 95% CI 0.61 to 1.1 ; very low certainty, **Table S11**). Length of stay outcomes showed reduced hospital stays (MD -0.51 days, 95% CI 0.71 to -0.31 ; low certainty, **Table S11**) and slightly shorter ICU stays (MD -0.09 days, 95% CI 0.15 to -0.03 ; very low certainty, **Table S11**). Cardiac biomarkers showed variations with CK level (MD 15.01 , 95% CI -62.21 to 92.23 ; very low certainty, **Table S11**), CK-MB level (MD -3.35 , 95% CI 5.69 to -1.02 ; very low certainty, **Table S11**), and Tn-I level (MD -0.03 , 95% CI -0.62 to 0.56 ; very low certainty, **Table S11**) [277].

The prospective study made by Cvetković et al. demonstrated comparable outcomes between HTK and cardioplegia solutions regarding their safety profile, effectiveness, and hemodynamic parameters [278].

The Guideline panel deemed HTK ideal for longer procedures like organ transplants and complex con-

genital surgeries, while extracellular solutions, requiring re-dosing every 20-30 minutes, are preferred for shorter cases like CABGs, considering surgeon preferences. They demonstrated that the application of the HTK solution will result in moderate costs. The panel showed that health equity would probably be increased when using the HTK solution. The use of the HTK solution was found to be feasible and probably acceptable according to the guideline panel.

Chapter 7: Autologous blood salvage

Intraoperative cell salvage (ICS) allows the return of shed blood during surgery after its processing, minimizing blood loss. It is recommended in certain cases, such as when significant blood loss is anticipated (> 1 L) or with patients who refuse transfusion of blood. In contrast, it is not recommended for cancer or surgeries with contaminated fields to avoid dissemination [279, 280].

Cell saver preparation

To prepare the setup, the cell saver machine and the disposable kit are needed: *Components of a disposable kit*: i) Reservoir: It collects the shed blood for processing. ii) Aspiration and anticoagulant (A&A) line: It prevents coagulation along with facilitating blood aspiration. iii) Vacuum Line: It aids blood collection through suction; Processing Set: Enables filtration and separation of red blood cells. iv) Postoperative set: It enables processed blood reinfusion blood after surgery. v) Sequestration set: Isolates specific blood components as needed [281, 282].

Anticoagulation bag

Anticoagulants like heparin are needed for adequate cell salvage of extracorporeal circulation. A recommendation for mixing aspirated blood and 30,000 units of heparin contained in 1 L of 0.9 saline has been suggested by the American Association of Blood Banks guideline at a rate of 15 ml per 100 ml of collected blood [283].

Installing the cell salvage components

It is important to ensure the validity and suitability of the cell salvage set before the use. This could be achieved by checking the expiration date of all the one time use components, reading the set label and searching for any kinks in the tubes that could obstruct the flow. Additionally, all caps and connections should be intact and secured. Lastly, a set examination for contamination and deficits should be

Table 16. Filters utilized in intraoperative cell salvage.

Filter type	Filtration medium	Primary function: Removes
Standard Blood Administration Set	200-micron screen	Blood components and other particulate matter
Microaggregate Filter	40-micron mesh	Small blood clots (microaggregates) and non-blood debris
Lipid Reduction Filter	40-micron mesh	Microaggregates, lipids, complement protein C3a, and some leukocytes
Leukocyte Depletion Filter	Affinity-based filter	White blood cells, lipids, bacteria, and tumor cells

performed to ensure both safety and efficiency are maintained [281, 284, 285].

Priming the reservoir

The A&A line packaging should be opened carefully using an aseptic technique. Secondly, the sterile inner-wrapped line is transferred into the sterile field. After that, the plastic suction wand is attached to the A&A line before passing the opposite end back out to the device. In addition to that, the A&A line should be connected to the reservoir securely and positioned within the tubing support. Finally, selecting the Suction function will activate suction. If manual suction is used, ensure it is set to a minimal acceptable level, not exceeding 200 mmHg [283, 285].

Process and equipment

Three stages are involved in the process of cell salvage, including collection, processing, and reinfusion.

Collection

The surgical team performs this stage, aiming to collect a viable and suitable amount of red cells without contaminants.

Processing

Before reinfusion, red cell is separated in this stage by centrifugation and then washed with a sterile 0.9% saline solution.

Reinfusion

The optimum time for reinfusion is in the theatre within 6 hours of the first collection to ensure that red cells function well. Additionally, for the fear of air embolism, salvaged blood should not be reinfused under pressure.

Filters

During intraoperative cell salvage, various filters are used to remove unwanted components from salvaged blood before reinfusion, Table 16 [281–283, 285, 286].

Clinical considerations and postoperative management

Upon reinfusion, the patient's Hb level and overall condition should be assessed, confirming reinfusion orders by the anesthesiologist or intensivist if the patient is in the ICU. Cost-effectiveness should also be considered, in light of the surgery and the anticipated loss of blood.

Postoperatively, patients need strict monitoring for complications such as coagulopathy and fluid overload. Also, the effectiveness of cell salvage and its impact should be assessed by reviewing transfusion rates and postoperative hemoglobin levels [286, 287].

Cell saver recommendation

Should the use of a cell saver for autologous blood salvage vs. the use of a cell saver be used for patients undergoing cardiac surgery with CPB to reduce the need for allogeneic blood transfusions and improve postoperative recovery?

Recommendation

For patients undergoing cardiac surgery with CPB, we suggest either cell saver usage/or not for autologous blood salvage to reduce the need for allogeneic blood transfusions and improve postoperative recovery (Table S12) (Conditional recommendation, very low certainty evidence).

Rationale

Cell savers can prevent many risks associated with the loss of blood inside the chest cavity because this blood can get activated and coagulated based on the availability of coagulating factors and excess thrombin [288]. This consumption can increase the risk of allogeneic blood transfusion, which adds to the risks of immune reaction and systemic inflammation. Additionally, reinfused unprocessed blood contains fat particles, cellular debris, and inflammatory cytokines that can lead to neurological and lung injury. Cell savers through the collection, filtration, and reinfusion of the shed blood can prevent this sequence [289]. However, the literature has some contradic-

tory findings that do not conclusively acknowledge the superiority of autologous blood salvage.

This recommendation is based on a meta-analysis of RCTs involving 4781 patients and investigating the efficacy of the cell saver system against standard care [290].

They revealed a significant decrease in transfused units and the number of transfused patients (Standardized mean difference [SMD] – 0.42, 95 % CI – 0.83 to – 0.02, very low certainty, and RR 0.71, 95 % CI 0.60 to 0.84, very low certainty, **Table S12**, respectively). On the other hand, comparable findings were observed regarding hospital and ICU stay, the reoperation number, and platelet transfused units and individuals (SMD 0.09, 95 % CI - 0.23 lower to 0.05, very low certainty, SMD 0, 95 % CI 0.08 to 0.9, very low certainty, RR 1.08; 95 % CI: 0.75 to 1.54, very low certainty, SMD –0.10, 95 % CI: –0.33 to 0.12, very low certainty and RR 1.08, 95 % CI: 0.79 to 1.49, very low certainty, **Table S12**, respectively) [290].

The effectiveness of cell salvage may depend on when it is used during surgery, with better results observed when used for shed blood and/or residual blood throughout the entire operative period [291].

Given the high risk of bias included in the meta-analysis, which results in very low certainty evidence, the guideline panel conditionally recommends the use of either the cell saver system or none, reflecting the need for individualized decision-making based on patient characteristics such as body surface area (BSA), preoperative HCT, Hb and platelet count along with surgical factors and institutional resources. This individualized approach matches the European recommendation of returning the shed blood directly unprocessed to the patient or processed with plasma supplement if an excessive amount is present because of the fear of large plasma and coagulation factors loss and of using a cell saver if a moderate amount is lost, whereas small amounts are best discarded as waste [11]. Additionally, they agreed on the feasibility, acceptability, and moderate savings that cell savers provide. However, definite superiority is not yet well-established, and high-quality trials are being called for to solidify the evidence.

Chapter 8: Emergency procedures of CPB

Air embolism

Immediate and coordinated action is critical to minimize complications in the event of an air embolism during CPB. The following steps should be taken: 1) Alert the surgical team: The surgical team should be informed immediately to take corrective actions

without delay. 2) Cease circulation and secure lines: The pump must stop instantly, along with clamping all lines and shunts. Also, each action taken should be declared to coordinate among the team. Ventilate the patient as necessary. 3) Identify and eliminate the air source: This is achieved through inspecting and resolving potential issues by recirculating ports in the cardioplegia circuit and arterial filter, checking for any loose or cracked connectors, ensuring the oxygenator's gas outlet vent is clear, and repriming or briefly recirculating the circuit if possible. 4) Manage Air Embolism in the Patient: If an air embolism occurs, patients should be positioned in a deep Trendelenburg position (head-down), followed by compressing the carotid arteries and preparing for hypothermic retrograde cerebral perfusion (RCP) if the surgeon approves. Until the surgeon confirms air evacuation and decides to stop, retrograde perfusion should be continued for several minutes. Then, the surgeon restores the original circuit and cannula orientation, reinitiating the bypass with increased flow and pressure and rewarming gradually. Additionally, mannitol or other edema treatments, such as thiopental or methylprednisolone, should be considered, with the consultation of the surgeon and anesthesiologist. 4) Reporting the event: This incident needs to be reported through the institution's reporting [292–294].

Water-to-blood leak

Early recognition of oxygenator leak is needed to ensure proper intervention and minimize adverse events. Several indicators may point to a water-to-blood leak, including an unjustified increase in circuit volume, progressive decline in blood pH, reduced HCT levels, and evidence of hemolysis, such as hemoglobinuria. However, other causes should also be excluded, such as suction of irrigating fluids, pleural effusions, or inadvertent addition of crystalloid solutions that can be a cause of volume increase. Therefore, oxygenator replacement is needed as an immediate corrective action once this problem is discovered to avoid further complications [295–297].

Oxygenator failure

Oxygenator failure is known by a decreased arterial partial pressure of oxygen (PaO₂) or venous saturation in spite of the 100% FiO₂ and the high flow or high transmembrane pressure. If confirmed, oxygen lines need to be checked for their connection, along with the oxygen analyzer and FiO₂ delivery check for leaks. Additionally, the transfer formula is suggested to assess oxygen transfer if the failure is gradual, replacing the oxygenator if there is a must [298, 299].

Oxygenator change out

Reasons for change out: An oxygenator may need to be replaced due to failure, blood leakage, or leaks in the heat exchanger, leading to water-to-blood contamination.

Replacement procedure

If failure is gradual, follow steps 1–4; for urgent cases, start at step 5.

- 1) Inform the surgeon about the need for replacement.
- 2) Collect the needed equipment.
- 3) Tailor the new oxygenator priming and temperature according to the case if there is time. Additionally, consider ventilating and coming off the bypass for an oxygenator change if the heart is still ejecting adequately.
- 4) Transition off bypass.
- 5) Disconnect water lines.
- 6) Detach the oxygen (O₂) line.
- 7) Clamp the blood inlet and outlet lines, ensuring enough length for reconnection.
- 8) Clamp any additional blood lines, such as cardioplegia or recirculation lines.
- 9) Cut the lines using sterile scissors.
- 10) Remove the old oxygenator and salvage blood if possible.
- 11) Secure the new oxygenator in place.
- 12) Reconnect the blood inlet, cardioplegia, and recirculation lines.
- 13) Pump blood slowly through the oxygenator to remove air (skip if pre-primed).
- 14) Connect the outlet line and use a recirculation loop or A-V bridge to eliminate air, followed by reconnecting the O₂ and water lines and resuming bypass [299, 300].

Oxygenator failure recommendation

Should implementation of emergency protocols for oxygenator failure vs. No specific emergency protocols be used for patients undergoing CPB to reduce mortality and improve management of oxygenator failure?

Ungraded statement

For Patients undergoing CPB, we advise the implementation of emergency protocols for oxygenator failure to reduce mortality and improve the management of oxygenator failure (**good practice statement**).

Rationale

This ungraded statement provides advice based on expert opinion and good practice due to the lack of direct evidence. Although oxygenator failure during CPB is a limited condition, occurring in 0.02-0.04% of cases, it can lead to lethal complications such as oxygen delivery failure, which may be associated with patient injury or death if not addressed rapidly [298, 301]. Oxygenator thrombosis remains a concern, occurs in 50-133 cases annually in the United States, even with modern heparin-coated circuits, and requires CPB cessation and replacement of the oxygenator [302]. Emergency protocols can facilitate prompt and systematic responses to manage life-threatening conditions [301].

Implementing emergency protocols for oxygenator failure during CPB can significantly improve patient outcomes [303]. Existing clinical practice guidelines and expert consensus strongly acknowledge the beneficial impact of protocol implementation to avoid CPB complications. They typically include steps for early failure identification and alternative solutions.

The guideline panel highlighted that oxygenator failure may occur at any time during surgery, recommending informing the complete team and changing the oxygenator as early as possible. They recommended the availability of another oxygenator in the operating room along with trained staff to prevent prolonged hypoxia in this situation.

A previous study emphasized the importance of training healthcare professionals on safety algorithms and drills for managing oxygenator failures effectively and other CPB emergencies and minimizing risks [302].

Given the risks involved in oxygenator failure and the existing body of knowledge supporting the value of structured emergency management in critical care, the guideline panel advised the implementation of emergency protocols for patients undergoing CPB to reduce mortality and improve the handling of oxygenator failure. Further studies are needed to validate these benefits.

Power supply failure

This is the nightmare of the operating team. All perfusionists should be well-versed in managing such a disaster. It is recommended that the team should have an explicit, itemized, and detailed protocol that is handy by the CPB machine, which is easily accessible with clear instructions to execute smoothly and effectively during the disaster. Multiple drills are of enormous value for the practicing team [304–306].

Power supply failure during CPB

In case of power supply during CPB, immediate actions are required, including informing the surgical team, activating emergency backup, and strictly monitoring patient condition. Additionally, switching to the manual backup system, if available, is suggested. Off-pump surgery should also be considered if there are high risks or prolonged duration of failure, such as releasing the aortic cross-clamp early [307].

Power supply failure after aortic cross-clamp removal

Alternative bypass methods should be prepared for a power failure after aortic cross-clamp removal. Portable bypass machines or ECMOs are valid alternatives in case backup power is unavailable. Additionally, venous return and circulation management are essential, involving preventing the flow back to the reservoir via venous line clamping and sustaining the circulation by manual pumping. The weaning process requires some adjustments from the surgical team, such as regulating the venous clamping, maintaining hand-cranking, and blood pressure stabilization with inotropic. CPB discontinuation is initiated after stabilizing the circulation and achieving a core temperature of 35°C [305, 307, 308].

****Exemplary emergency protocol: power failure management**

A. Power supply failure during CPB

1. Notify the surgical team immediately. Request assistance from a second perfusionist.
2. Activate emergency backup power to resume the pump and oxygenator function.
3. Assess the patient's condition, including vital signs, cerebral oxygenation (if monitored), and arterial pressure.
4. Switch to manual mode (hand-crank) if available. Alternate with another perfusionist if necessary to maintain flow.
5. Communicate continuously with anesthesia and surgery teams.
6. Evaluate urgency: If prolonged downtime is expected, the surgeon may need to consider early aortic cross-clamp release or "damage control" strategies to limit operative duration.

B. Power supply failure after cross-clamp removal

1. Notify the surgical and anesthesia teams immediately.
2. Activate backup power if available.
3. Monitor the patient's hemodynamics and oxygenation closely.

4. Prepare for transition to a portable pump or ECMO if required.
5. Clamp the venous line to prevent backflow into the reservoir.
6. Initiate hand-cranking to sustain blood flow and maintain reservoir volume.
7. Adjust venous return manually to balance reservoir levels.
8. Continue manual circulation while preparing for weaning.
9. Administer inotropes to support native cardiac output.
10. Once the patient is stable and normothermic ($\geq 35^{\circ}\text{C}$), proceed with CPB discontinuation [304–306, 309].

Chapter 9: Prolonged mechanical circulatory support

Extracorporeal membrane oxygenation (ECMO) in adults

Prolonged mechanical circulatory support can be achieved through ECMO in critically ill patients. ECMO therapy can serve as a bridge in the following scenarios: 1) Bridge to Recovery: Temporary support until heart or lung function improves. 2) Bridge to Mechanical Assist Device: Transition to left ventricular assist device (LVAD), right ventricular assist device (RVAD), or biventricular assist device (BiVAD) based on ventricular function 3) Bridge to Transplant: Support until a suitable organ for transplantation becomes available. 4) Bridge to Decision: Temporary stabilization while determining the next course of action [310–312].

Types of ECMO

Veno arterial (VA) ECMO and Veno venous (VV) ECMO. In certain situations, it is necessary to convert from VV ECMO to VA ECMO support, typically when there is hemodynamic compromise while on VV ECMO [313].

Types of Cannulations

Three cannulation types are involved in accessing the major vessels for ECMO: 1) Surgical central cannulation: The surgeon connects the arterial cannula to the heart's major vessels directly in the operating room. The chest is left open if the cannula is connected to the aorta. However, in certain cases, when the cannula is connected to a proximal major branch of the aorta, such as the right axillary artery, the

chest is closed. 2) Surgical peripheral cannulation: If central cannulation can not be done, a closed chest method of peripheral cannulation is used, inserting the cannula into peripheral blood vessels, such as the femoral artery and vein, through a small surgical incision. 3) Percutaneous cannulation: This is a minimally invasive bedside technique that is performed in emergency settings. A needle and guidewire are used to connect the cannula to blood vessels, typically through the femoral or jugular veins [314–316].

The ECMO selection criteria and indications

The ECMO has various indications, including patients with severe cardiac or respiratory failure who are unresponsive to conventional management. The following conditions may indicate the need for ECMO support:

Respiratory indications

Respiratory indications include acute respiratory distress syndrome (ARDS), severe pulmonary edema, massive pulmonary embolism, respiratory failure due to infections, and thoracic trauma with lung contusion.

Cardiac indications

Cardiac indications include refractory cardiogenic shock, cardiomyopathy, cardiac arrest, cardiac trauma, drug overdose, and severe hypothermia with cardiac instability.

Post-surgical and procedural indications

Post-surgical and procedural indications include failure to wean from CPB, postoperative cardiac support after high-risk surgery, bridge to heart transplantation, and procedural support for complex interventions [316–318].

Patient eligibility criteria

For patients who usually have reversible lung disease with non-response to all medical treatments, ECMO is considered an alternative that can provide a good chance of survival. The exclusion criteria include patients who have intracranial hemorrhage and severe chromosomal or genetic malformations. In these conditions, ECMO may be used on a compassionate basis after obtaining a written explanation for its use from the physician [317].

The ECMO Qualifying Criteria

A patient is eligible for ECMO if they meet at least one of the following criteria, despite receiving optimal medical treatment: Severe Hypoxemia: $\text{PaO}_2 < 50$ mmHg for ≥ 2 hours; Impaired Gas Exchange: A-a gradient > 605 for ≥ 4 hours; High Oxygenation Index (OI): $\text{OI} > 35$ for ≥ 4 hours; Acute Deterioration: $\text{PaO}_2 < 40$ mmHg or sudden cardiovascular collapse; Severe Acidosis & Hypotension: $\text{pH} < 7.25$ with persistent low blood pressure for ≥ 2 hours; and Refractory Hypotension: Systolic, mean, and diastolic BP below the 5th percentile for weight for ≥ 2 hours despite fluid resuscitation and medication [319, 320].

Exclusionary criteria for respiratory ECMO support

A patient is ineligible for respiratory ECMO if any of the following conditions apply:

- Severe metabolic crisis: Serum lactate > 25 at any point.
- Terminal illness: Advanced-stage lethal disease.
- Life-threatening complications: Fatal condition with a critical complication.
- Prolonged cardiac arrest: History of arrest lasting > 60 minutes.
- Recent CNS hemorrhage: Intracranial bleeding within the past 7 days [321].

VV ECMO Contraindications. VV ECMO is not recommended for patients with:

- Irreversible lung disease without transplant eligibility.
- Severe pulmonary hypertension with right heart failure.
- Terminal cancer or other advanced malignancies.
- Chronic dysfunction of major organs.
- Lung failure due to bone marrow transplantation.
- Inability to tolerate anticoagulation therapy.
- Recent spinal cord or CNS trauma/bleeding [322–324].

VA ECMO contraindications. VA ECMO is unsuitable for patients with:

- End-stage heart disease not eligible for transplant or VAD.
- Severe aortic pathology, including regurgitation or dissection.
- Cardiac arrest without witnessed resuscitation.
- Advanced malignancies or progressive organ failure.
- Recent CNS or spinal trauma/hemorrhage.
- Contraindications to anticoagulation [325–327].

The ECMO recommendations

Should VA-ECMO with and without an Intra-Aortic Balloon Pump (IABP) vs. no VA-ECMO with and without an IABP be used for patients undergoing CPB who developed post-cardiotomy hemodynamic compromise?

Ungraded statement

For patients undergoing CPB who developed post-cardiotomy hemodynamic compromise, we advise using either VA-ECMO with and without IABP or no VA-ECMO with and without IABP (Good Practice statement).

Remarks

Combining both for mainly cardiogenic shock complicating acute myocardial infarction (AMI) may be used with restrictions. We need to keep an eye on recent emerging developments in this regard with other devices.

Rationale

This recommendation was based on the clinical experience of the experts due to the lack of direct evidence. Patients who develop AMI may suffer from cardiogenic shock, resulting in impaired tissue perfusion and severe hemodynamic compromise. MCS, including VA-ECMO and IABP, has been suggested as cardiac support. Patients with severe cardiac conditions were usually approached with VA-ECMO, by which they can bypass the heart and lung function [328]. However, because of the retrograde return of the blood into the artery, there will be an increase in the afterload and, consequently, the left ventricle end-diastolic pressure (LVEDP), resulting in the worsening of the condition after an increase in oxygen demand. To unload the left ventricle, the addition of IABP to VA-ECMO has been suggested, by which inflation and deflation can happen synchronously with systole and diastole, mimicking and strengthening the physiological action of the heart. This hypothesis was investigated by Meertens et al., who performed a meta-analysis on the comparison of VA-ECMO plus IABP against VA-ECMO alone in 5063 patients with cardiogenic shock due to AMI. They revealed a statistically significant decrease in mortality along with increased odds of successful weaning. However, these results should be treated cautiously because of the absence of RCTs. Additionally, limited evidence is present about the comparison against the use of IABP alone despite the theoretical advantage of its less invasive nature [328].

The guideline panel acknowledged the use of either the intervention or the comparison according to the patient's clinical condition. While the VA-ECMO plus IABP strategy can be used in severely compromised patients despite the potential risk, complexity, and high cost it carries, IABP can be used with mild and moderate cases. Prospective research is needed to validate this comparison and create reality-based evidence.

Priming procedure

In adults, the ECMO circuit is primed with a clear fluid (e.g., Ringer's lactate, Plasma-Lyte, or normal saline) and maintained for immediate deployment. The primed circuit expires after 30 days, and the date, time, and initials of the primer must be labeled on the oxygenator. In pediatrics, the circuit is first primed with clear fluid, followed by blood priming using packed red blood cells (PRBCs) prepared with heparin (150 units), sodium bicarbonate (10 mEq), 25% albumin (40 mL), fresh frozen plasma (FFP) (30 mL) and calcium chloride (150 mg) [329].

The ECMO equipment checklist

The essential components are pump module; rotaflow/cardiohelp hand crank and holder; ECMO pack; 2x isotonic crystalloid solutions; and 2x tubing clamps [329]. While the additional items for patient care are the following: ECMO operating notes, troubleshooting guide, and observation chart; 4 sterile tubing clamps and sterile heavy scissors; heparin-bonded connectors; ACT machine and tubes; heater-cooler unit; and cable ties and a gun [329].

Steps for priming the ECMO circuit:

1. Assemble the circuit by connecting the venous line, centrifugal pump, oxygenator, arterial line, and priming bag.
2. Attach the gas line and heater-cooler system. Perform a leak test before priming.
3. Start priming with clear fluid using gravity flow.
4. Once the circuit is filled and air is removed from the pump head, activate the pump.
5. Maintain continuous circulation until the circuit is entirely air-free [329].

ECMO management parameters

Key laboratory parameters for ECMO patients

Strict monitoring of blood gases, hemoglobin levels, and lactate clearance is required during ECMO to maintain adequate oxygenation and organ perfusion, Table 17 [330].

Table 17. Optimal blood gas and hemoglobin levels in extracorporeal membrane oxygenation patients.

Parameter	Target value
SaO ₂	> 90%
SvO ₂	> 70%
PaO ₂	150–200 mmHg
Hb	10–12 mg/dL
HCT	30–40%
Lactate	< 5 mmol/L
Hgb (ABG)	80–140 mg/dL

Anticoagulation and blood gas monitoring protocol

Monitoring anticoagulation in ECMO is essential to balance the risks of thrombosis and bleeding, [Table 18](#). The ACT is the most commonly used test across ECMO centers due to its rapid bedside availability. However, it has limitations such as variability and susceptibility to multiple influencing factors, like thrombocytopenia and coagulopathy. The target ACT range is typically adjusted based on patient-specific risks of bleeding or clotting. Activated Partial Thromboplastin Time (aPTT) is also widely used, particularly for titrating unfractionated heparin (UFH) and direct thrombin inhibitors (DTIs). However, it may be unreliable in critically ill or pediatric patients due to developmental differences in coagulation and interference from inflammatory markers. The anti-factor Xa assay has gained prominence as a more precise measure of heparin activity, correlating better with clinical outcomes like reduced blood product use and longer circuit life. However, it may be affected by antithrombin (ATIII) deficiency, requiring supplementation in some cases. Thromboelastography (TEG) and thromboelastometry (ROTEM) provide a comprehensive assessment of clot formation, platelet function, and fibrinolysis, helping guide anticoagulation adjustments in cases of excessive bleeding or clotting. Antithrombin (AT) levels are also monitored since AT deficiency, common in neonates and critically ill patients, can lead to heparin resistance. AT can be replenished with fresh frozen plasma (FFP) or AT concentrates, though the latter is costly and should be avoided in actively bleeding patients. A structured anticoagulation monitoring schedule typically includes frequent ACT (hourly to bi-hourly), aPTT, anti-factor Xa assays, and AT levels, with blood product transfusion guided by platelet and fibrinogen thresholds. Given the high prevalence of hemorrhagic and thrombotic complications in ECMO, individualized anticoagulation management is critical, often requiring interdisciplinary consultation with hematology specialists [\[331–335\]](#).

Daily Investigations.

1. Imaging: Chest x-ray.

2. Lab Tests: Liver and renal profile, coagulation profile (APTT/INR, D-dimers on alternate days) [\[336\]](#).

The ECMO circuit management and blood flow targets

Maintaining optimal blood flow and gas exchange is critical to ECMO function [\[337\]](#). [Table 19](#) summarizes the recommended circuit settings:

Assessing circuit pressures and performance

Circuit pressures are key indicators of circuit performance. Elevated pressures may indicate clot formation, membrane failure, or mechanical obstruction [\[338\]](#). [Table 20](#) lists acceptable pressure limits:

Hemodynamic stability and perfusion goals

To assess cardiovascular stability, specific arterial pressures, central venous pressure (CVP), and left atrial pressure (LA) should be maintained within these ranges, [Table 21](#) [\[339\]](#):

The ECMO team roles and responsibilities

A multidisciplinary team must monitor the ECMO circuit, manage complications, and adjust ventilatory support [\[340\]](#). [Table 22](#) outlines key roles and responsibilities.

The ECMO weaning and termination

V-A ECMO weaning

V-A ECMO weaning involves cardiac surgeons and ICU consultants making decisions, assessing heart function via ECHO, adding heparin, and turning off oxygenator gas flow if respiratory function is stable.

V-V ECMO weaning

V-V ECMO weaning requires no circuit flow reduction or heparin addition, complete ventilation re-established, and oxygen flow to the oxygenator turned off and clamped.

Decannulation procedure

The decannulation procedure involves a cardiac surgeon surgically removing arterial cannulas, applying 20 minutes of compression for vein cannula removal, and conducting a post-decannulation Doppler study to check for DVT.

Table 18. The recommended laboratory monitoring schedule during cardiopulmonary bypass or extracorporeal membrane oxygenation.

Test	Recommended frequency
Activated clotting time (ACT)	Every 1–2 hours
Activated partial thromboplastin time (aPTT)	Every 6–12 hours
Anti-factor Xa assay	Every 6 hours
Platelet count	Every 6–12 hours
International normalized ratio (INR)	Every 6–12 hours
Fibrinogen level	Every 12–24 hours
Complete blood count (CBC)	Every 6–12 hours
Antithrombin III Level	Daily or as needed (PRN)
Thromboelastography (TEG/ROTEM)	Daily or as needed (PRN)
Circuit arterial blood gases (ABG)	Every 8 hours (pre- & post-oxygenator)

Table 19. Recommended extracorporeal membrane oxygenation circuit settings and blood flow ratios.

Parameter	Target range
Blood flow	2.0–2.4 L/min/m ²
Blood: gas flow ratio	Initially 1:0.5 (maximum)

Table 20. Acceptable circuit pressure limits to prevent malfunction.

Pressure location	Target value
Pre-pump	< 0–80 mmHg
Pre-membrane	< 350 mmHg
Post-membrane	< 300 mmHg
Transmembrane pressure drop	< 150 mmHg

Table 21. Target hemodynamic parameters for extracorporeal membrane oxygenation patients.

Parameter	Target range
Arterial pressure (systolic)	< 120 mmHg
Arterial pressure (mean)	> 60 mmHg
Central venous pressure (CVP)	4–6 mmHg
Left atrial pressure (LA)	4–6 mmHg

The ECMO reinitiation

The surgeon, cardiologist, intensivist, and perfusionist collaborate to decide to restart ECMO if patient instability occurs post-weaning [341–345].

Complications

Advancements in ECMO technology have significantly reduced the risk of mechanical complications; however, patients remain susceptible to a range of unique challenges that must be anticipated and mitigated. Potential complications include vascular injury, cardiac dysfunction, severe bleeding, infections, heparin-induced thrombocytopenia (HIT), intracranial hemorrhage or infarction, aortic thrombosis, persistent hypoxia, thrombocytopenia, and coagulopathy. Also, lung ischemia and machine-related

failures—such as pump malfunction, hemolysis, air embolism, circuit thrombosis, oxygenator dysfunction, circuit rupture, and unintended decannulation—can pose serious risks and require prompt intervention [346–348].

Standby ECMO circuit protocol

A wet-primed ECMO circuit is recommended on standby for up to 30 days to optimize resource utilization and reduce waste, provided sterility is preserved. An aseptic environment must be ensured upon circuit assembly to minimize the risk of infection, and each circuit must be labeled with the assembly date and the perfusionist's name. Key sterility measures include disinfecting surfaces before assembly, verifying sterile packaging, performing antiseptic handwashing, and following aseptic techniques during assembly. Components should be carefully connected, with all outlet ports securely capped before storage. If a primed ECMO circuit is not used within 30 days, it must be discarded. Additionally, water in heater-cooler machines should be replaced weekly to maintain optimal function and infection control [349–352].

The ECMO Recommendation

Should venoarterial ECMO (VA-ECMO) vs. venovenous ECMO (VV-ECMO) be used for patients requiring prolonged mechanical circulatory support (MCS) to improve survival rates and reduce complications?

Recommendation

For patients requiring prolonged mechanical circulatory support, we suggest using VA-ECMO over VV-ECMO to improve survival rates and reduce complications (Conditional recommendation, very low certainty evidence).

Table 22. Multidisciplinary team involvement in extracorporeal membrane oxygenation (ECMO) management.

Role	Responsibility
On-call resident	Maintains hemodynamics, arranges blood products
Perfusionist	ECMO circuit management and troubleshooting
Respiratory therapist	Manages ventilator settings
Nurses	Patient care
On-call cover team	Available 24/7 for ECMO-related decisions

Rationale

The data regarding the comparison between VA-ECMO and VV-ECMO in the literature are scarce. The key difference between them is their primary use. While VA-ECMO is primarily used in cases that need cardiac and respiratory support, such as cardiogenic shock or cardiac arrest cases, VV-ECMO is used for respiratory failure support in acute respiratory distress syndrome (ARDS) cases where there is adequate cardiac function. This precise distinction underscores the importance of treating each patient individually based on their clinical condition and needs. However, VA-ECMO poses several complications in the literature. A meta-analysis by Shoskes et al. pointed out the higher neurological complications of VA-ECMO compared to VV-ECMO in 9056 patients across 53 studies, represented by higher rates of ischemic stroke and brain death along with low survival (9% in VA vs. 1% in VV, 10% in VA vs. 1% in VV, and 51% in VA vs. 64% in VV, respectively) [353]. There was no significant difference in the prevalence of intracranial hemorrhage between VA-ECMO and VV-ECMO [353].

Additionally, the HECTIC Study noticed a higher percentage of thrombin generation and consumptive coagulopathy represented by low platelet count and fibrinogen, underscoring the pro-coagulant state of cases treated with VA-ECMO compared with VV-ECMO [354]. These 2 trials call for vigilant monitoring and strict consideration regarding VA-ECMO, outweighing the benefits and complications, particularly in patients with high-risk neurological or hematological complications. These complications may be attributed to the underlying severity of VA-ECMO cases and their more invasive nature, pointing out the different roles of each intervention and calling for outcome-predictive models. In this context, the Survival After Veno-Arterial Extracorporeal Membrane Oxygenation (SAVE) score was developed by Amin et al. to predict the survival rate of each VA-ECMO-treated case and compare it with the actual observation over 7 years. This model resulted in higher scores with the survivors and good discrimination between the survivors and non-survivors. However, the calibration represented by comparing

the predictive numbers with the observed ones was lower regarding classes II–V, which could deny them support based on their high-risk [355].

The guideline panel acknowledged the distinction of each intervention and the importance of tailoring use based on patients' clinical profiles. They also agreed on the large beneficial effects of VA-ECMO in severe cases with prolonged mechanical circulatory support, along with the feasibility and acceptability of this intervention. In addition, they acknowledged the consideration of patients' needs, recommending VA ECMO as the best option when both the heart and lungs are affected. They also highlighted the importance of focusing on the recent emerging developments in this regard with other devices. Further experimental trials are needed in order to strengthen the evidence.

Chapter 10: Additional practices

Minimal invasive extracorporeal circulation (MiECC)

The MiECC is an advanced perfusion technique designed for minimally invasive cardiac surgery (MICS). It integrates specialized circuit modifications to improve biocompatibility, reduce inflammatory responses, and optimize anticoagulation management. The ideal MiECC setup consists of coated surfaces, closed-circuit designs, targeted anticoagulation strategies, shed blood separation systems, and reduced priming volumes to minimize hemodilution and improve patient outcomes. While some hospitals utilize standardized commercial MiECC circuits, others customize their CPB setups by integrating different components based on institutional preferences [356–358].

Anticoagulation strategy for MiECC

MiECC generates less thrombin compared to traditional CPB, allowing for a reduced heparin dosage with a shorter ACT. To ensure proper anticoagulation, heparin dosing should be individualized using heparin dose–response monitoring systems. However, if the MiECC circuit includes an open component,

Table 23. Cannulation techniques and cannula sizes in minimal invasive extracorporeal circulation.

Cannulation Type	Cannula size (Fr)	Purpose
Arterial Cannulation	15, 16, 17, 19	Delivers oxygenated blood from the CPB circuit to the arterial system.
Retrograde limb perfusion shunt	5, 6, 7	Maintains blood flow to the lower limb, preventing ischemia during femoral artery cannulation.
Venous cannulation	21, 23, 25	Drains deoxygenated blood into the CPB circuit; multistage design ensures better venous drainage.
Jugular cannulation	15, 16, 17, 19	Alternative/additional venous drainage site for right atrial decompression and improved venous return.

anticoagulation management should align with conventional CPB protocols, often requiring higher ACT levels as per institutional guidelines [359–361].

Cannulation in MiECC

Multiple access points are involved in the MiECC cannulation to optimize circulation and ensure effective perfusion, Table 23 [358, 362].

MiECC Recommendation

Should MiECC vs. conventional extracorporeal circulation (CECC) be used for patients undergoing minimally invasive cardiac surgery to reduce postoperative recovery time and complications?

Recommendation

For patients undergoing minimally invasive cardiac surgery, we suggest using either MiECC or CECC to reduce postoperative recovery time and complications (Table S13) (Conditional recommendation, moderate certainty evidence).

Rationale

This recommendation is based on a recent multicenter RCT that compared both procedures across patients undergoing CABG, aortic valve replacement (AVR), or both. The trial demonstrated risk reduction in favor of MiECC for the primary outcome encompassing major complications such as reintubation, reoperation, mechanical ventilation >48 hours, and stage 3 acute kidney injury (AKI) (Risk ratio [RR] 0.73, 95% Confidence interval [CI]: 0.56 to 0.96, moderate certainty, Table S13). However, there was no risk difference that was small (-3.5%, 95% CI: -7.0% to 0.3%) and did not reach statistical significance ($p = 0.073$). The most frequent events were reintubation (2.5% vs 5.0 % in the MiECC and CECC groups, respectively), reoperation (3.3% and 4% in the MiECC and CECC groups, respectively), mechanical ventilation >48 h (2.5% vs. 2.7% in the MiECC

and CECC groups, respectively), and stage 3 AKI (1.9% and 2.5% in the MiECC and CECC groups, respectively) [363].

In addition to that, comparable results were found regarding secondary outcomes, including mortality (RR 0.80, 95% CI: 0.36 to 1.74, moderate certainty, Table S13), non-primary serious adverse events (SAEs) (RR 0.79, 95% CI: 0.53 to 1.18, moderate certainty, Table S13), and length of stay in hospital or ICU (Intensive care unit) (Hazard ratio [HR] 1.05, 95% CI: 0.93 to 1.19 and HR 0.98, 95% CI: 0.87 to 1.11, moderate certainty, respectively, Table S13). In addition, the trial revealed similar results in terms of RBC transfusion in both approaches (RR 0.84, 95% CI: 0.70 to 1.01, moderate certainty, Table S13) [363].

Multiple studies have found that MiECC significantly reduces postoperative arrhythmias, blood loss, and transfusion requirements. MiECC also demonstrated shorter hospital and intensive care unit stays [364, 365]. MiECC had shorter operative times and a lower incidence of postoperative atrial fibrillation (AF) than CECC [366].

However, other studies found comparable findings between CECC and MiECC related to outcomes for emergency and mortality in patients undergoing reoperation for isolated CABG [366, 367].

Given this moderate certainty evidence, the guideline panel acknowledged the potential advantages of MiECC in some outcomes while being comparable to CECC in most others. They voted for a conditional recommendation for either MiECC or CECC in patients undergoing minimally invasive cardiac surgery, allowing flexibility based on institutional expertise, patient factors, and resource availability. They also judged both approaches as feasible and acceptable with moderate cost.

Conversion from off-pump to on-pump surgery

To ensure patient safety and optimal outcomes, the surgeon decides to convert from off-pump to CPB when complications arise. Additionally, the perfusionist is responsible for the preoperative evaluation of the patients, CPB machine preparation, and

ensuring readiness for a potential transition, and of course, it would be best to have it documented in a protocol with frequent drills to assure proficiency. The surgeon's preference determines whether or not to use priming in off-pump procedures. Also, collaboration with anesthesia is a paramount necessity to administer anticoagulation in a timely fashion and to monitor ACT levels, with a target of over 400 seconds before initiating bypass [368–370].

Pump recommendation

Should On-pump CPB vs. Off-pump CPB be used for perioperative safety and efficacy in patients undergoing CABG?

Recommendation

For perioperative safety and efficacy in patients undergoing CABG, we suggest using either on-pump CPB or off-pump CPB (**Table S14**) (Conditional recommendation, very low certainty evidence).

Rationale

The choice of using on or off-pump CPB in patients undergoing CABG has been debated since they have different safety qualities and perioperative outcomes. This recommendation is based on a real-world study retrieved from 1621 patients over 10 10-year duration by Koster et al., comparing both ways in terms of efficacy and safety profiles. Outcomes of stroke and hemofiltration were slightly higher in on-pump CPB (RR 1.68, 95% CI: 1.01 to 2.79, very low certainty, and RR 1.53, 95% CI: 1.17 to 2.02, very low certainty, **Table S14**, respectively). No significant difference was detected regarding mediastinitis, 30-day and one-year mortality (RR 0.78, 95% CI: 0.34 to 1.82, low certainty, RR 1.68, 95% CI: 0.97 to 2.91, low certainty and RR 1.10, 95% CI: 0.85 to 1.41, low certainty, **Table S14**, respectively). Additionally, readmission for wound infection and thoracic wound infection were lower in on-pump CPB (RR 0.42, 95% CI: 0.24 to 0.72, very low certainty, and RR 0.25, 95% CI: 0.12 to 0.54, very low certainty, respectively) [371].

Perioperative outcomes came in favor of off-pump CPB in terms of outcomes such as no red blood cell transfusion, mechanical ventilation >24 hours, and ICU stay >48 hours (RR 0.08, 95% CI 0.06 to 0.16, very low certainty, RR 1.34, 95% CI 1.03 to 1.73, very low certainty and RR 1.19, 95% CI 1.02 to 1.38, very low certainty, **Table S14**, respectively) [371].

These findings revealed comparable results regarding SAEs, such as mortality, while pointing out the superiority of each intervention in one aspect or an-

other, such as on-pump with BIMA (Bilateral internal mammary artery) or off-pump with transfusion.

The debate between on-pump and off-pump CABG remains inconclusive. Several studies have found no significant differences in short-term outcomes between the 2 techniques [372, 373]. However, off-pump CABG has been associated with reduced rates of blood transfusion, acute kidney injury, and respiratory complications [372]. Conversely, on-pump CABG has demonstrated better long-term outcomes, including higher graft patency rates and fewer repeat revascularizations [372]. The choice between techniques may depend on patient characteristics, with off-pump CABG potentially benefiting high-risk patients [374]. However, in elderly patients (≥ 75 years), no significant differences were observed between the 2 methods in composite outcomes at 30 days and 12 months post-surgery [373]. Ultimately, the decision should be based on the surgeon's expertise and individual patient factors [372].

Therefore, the guideline panel recommended either a conditional intervention based on factors related to patient profile, complexity of surgery, or surgeon expertise. They also acknowledged the large savings resulting from off-pump CABG procedures, calling for more RCTs that compare both ways in a more unbiased approach.

Intra-aortic balloon counter-pulsation therapy (IABP)

The IABP therapy is a catheter with a helium-driven balloon and a control console that synchronizes inflation and deflation based on the aortic pressure waveform or ECG signal. The balloon inflates during diastole to enhance coronary perfusion and deflates before systole to reduce afterload, improving myocardial oxygen supply and decreasing cardiac workload [375].

1. *Indications and contraindications.* It is primarily used in cardiogenic shock, refractory angina, post-cardiopulmonary bypass low cardiac output states, and high-risk percutaneous interventions. It also serves as a bridge to definitive therapies in severe heart failure or ventricular arrhythmias. However, it is contraindicated in severe aortic regurgitation, aortic aneurysms, advanced peripheral vascular disease, and uncontrolled bleeding disorders [375, 376].
2. *Complications.* Complications include vascular ischemia, thrombosis, infection, arterial dissection, embolization, thrombocytopenia, and balloon rupture. The risk of sepsis increases with prolonged use. Proper catheter positioning is crucial to avoid renal or subclavian artery occlusion [377].

3. *Insertion and console setup.* The IABP is inserted percutaneously, usually via the femoral artery, with the balloon placed in the descending aorta. The console setup requires ECG and arterial pressure monitoring, ensuring optimal timing for inflation and deflation [378].
4. *Weaning.* Weaning is initiated when the patient demonstrates hemodynamic stability by gradually reducing augmentation frequency. Complete removal follows after ensuring adequate cardiac function, normal coagulation parameters, and stable perfusion. Post-removal monitoring is essential to detect complications like bleeding or limb ischemia [379].
5. *Troubleshooting.* Common troubleshooting issues include trigger loss, inadequate pressure tracing, helium leaks, and balloon rupture, requiring immediate intervention to prevent hemodynamic instability [378, 380].

Isolated limb perfusion (ilp)

The ILP is a treatment for malignancies in localized regions, commonly those confined to the extremities, like melanoma and soft tissue sarcoma. It is achieved by administering a high dose of chemotherapeutics, with low systemic exposure. A tourniquet is used to isolate the limb, while extracorporeal circulation is responsible for area perfusion [381, 382].

1. *Circuit configuration.* In ILP, hemodilution is minimized by utilizing pediatric circuits, implementing appropriately sized oxygenators and filters. The treated limb controls the tubing size, selecting 1/4-inch arterial and 1/4-inch venous tubing for arm perfusion and 1/4-inch arterial and 3/8-inch venous tubing with leg perfusion. Additionally, residual chemotherapeutic agents are drained through the Y-connector, which delivers them from the venous line to the waste collection bag at the end of the procedure. A separate cardiectomy reservoir is used to compensate for fluid loss in the process of drug clearance. In addition to that, limb perfusion resistance is monitored using perfusion pressure measurements [383, 384].
2. *Cannulation techniques.* Vascular isolation can be done by single or double-Cuff Techniques, which are placed proximal or proximal and distal to the cannulation site, respectively. This results in limb isolation and minimizes systemic exposure to chemotherapeutics in the case of the double technique [385, 386].
3. *Priming solution.* The needed prime volume is determined by the “Rule of Nines” upon the perfused limb, with the arm representing approximately 9% and the leg approximately 18% of the total body surface area. The base of the priming fluid is dependent on a balanced electrolyte solution, such as Ringer’s, while agents like 5,000 units of heparin and 25 mEq/L of sodium bicarbonate are commonly used as additives to prevent clot formation or buffer metabolic acidosis. Additionally, adequate oxygen delivery can be maintained when HCT is above 15% during the procedure [384, 387, 388].
4. *Conduct of ILP.* First, patient is fully heparinized with a dose of 300 units/kg, ensuring adequate ACT before initiating bypass. Systemic circulation limb access is occluded through a tourniquet, such as an Esmarch band with a Steinmann pin. Additionally, patient stability is ensured by applying invasive monitoring, including arterial pressure line, ECG, oxygen saturation, and CVP. The pump flow rate (PFR) is calculated based on a percentage of the patient’s cardiac output (CO), typically using the formula: $PFR = \text{Limb \%} \times CO$. In addition to that, pump resistance (PR) is calculated using the equation: $PR = (\text{limb perfusion pressure (LPP)} \times 80) / \text{pump flow (PF)}$. Transfusion test is used before initiating full perfusion to ensure that the cannula is correctly placed. After that, a gradual increase in perfusion is performed, reaching the calculated target flow and maintaining $FiO_2 \geq 80\%$ and PaO_2 above 400 mmHg in the perfused limb. Oxygenator’s heat exchanger and a warming blanket are actively utilized to warm the limb, with a range of 38–40°C, using temperature probes as a monitor of limb temperature [383, 384, 386–388].
5. *Leak detection and management.* Tourniquets are used to isolate the limb vasculature, ensuring non-exposure of systemic circulation to cytotoxic agents. They are preferred over a single bone, such as the humerus or femur, because this allows for a tighter seal than those achieved with the dual-bone, which are also prone to leaks. The perfusionist is responsible for monitoring the volume in the oxygenator continuously, where a volume decrease is indicative of systemic leak, and a volume increase is associated with leakage into the limb. Systemic leakage risk can be minimized through several maneuvers, including keeping the perfusate pressure below the patient’s diastolic pressure, pump flow adjustment, and administering vasodilators, which collectively aim to maintain optimal perfusion pressure. Additionally, leak localization can be

done through the fluorescein dye that is viewed under a black lamp, having above tourniquets dye as indicative of systemic leakage [389–392].

Robotic surgery

Proper planning is required in robotic cardiac surgery to ensure myocardial protection and optimal circulatory support. Peripheral cannulation is the preferred method over other types in robotic surgery, accessing the femoral artery and vein in addition to jugular cannulation as an additional drainage site when needed. The surgical table should have certain tools, including a femoral insertion kit, a male-to-1/4 connector, an extra piece of 3/8-inch tubing, and a Y-connector (3/8-inch). Robotic procedures typically use femoral arterial cannulae ranging from 15 to 19 Fr, retrograde limb perfusion shunts between 5 and 7 Fr, multistage venous femoral cannulae from 21 to 25 Fr, and jugular vein cannulae between 15 and 19 Fr, selected based on patient size and surgical requirements. Anticoagulation is initiated with partial heparinization during jugular vein cannulation, transitioning to full bypass as managed by anesthesia. Suction and venting lines are designated for blood removal, de-airing, and cardioplegia delivery. Myocardial protection strategies include standard cardioplegia or fibrillatory arrest in redo cases, maintaining cooling at 32°C to optimize right atrial drainage. Additionally, cerebral protection during robotic procedures can involve retrograde or selective antegrade cerebral perfusion, ensuring adequate brain perfusion while minimizing embolic risk [393–395].

Cerebral perfusion strategies

1. *Retrograde Cerebral Perfusion (RCP)*. The RCP is used to protect the brain during aortic surgery or in cases of arterial air embolism. It is delivered through the SCV using either a single venous cannula or a retrograde cardioplegia cannula. The setup involves placing a male-to-male pressure line and ensuring the cardioplegia system delivers cold blood only, without potassium. The perfusate temperature is maintained around 18°C. The perfusionist monitors central venous or jugular pressure closely, keeping it between 20 and 25 mmHg. Adequate retrograde flow is confirmed by observing blood exiting from the open aorta [396–398].
2. *Selective Antegrade Cerebral Perfusion (SACP)*. The SACP delivers oxygenated blood directly through the innominate and left common carotid arteries to maintain cerebral circulation

during circulatory arrest. Flow is usually set between 8 to 12 mL/kg/min, with right radial arterial pressure closely maintained within 50 to 70 mmHg. The total SACP flow accounts for 15–20% of the full CPB flow. It is adjusted according to cerebral oximetry readings and arterial pressure trends to ensure adequate brain perfusion throughout the procedure [399–401].

3. *Circulatory arrest*. Patients are cooled to <18°C to enable safe arrest. Agents like sodium pentothal and insulin are used for neuroprotection. EEG is monitored to confirm cerebral inactivity. Controlled rewarming (gradient <8°C) is critical. Blood may be recirculated through an A-V bridge during arrest.

Temperature classification:

- Mild: 32–37°C
- Moderate: 28–31°C
- Deep: 18–28°C
- Profound: <18°C

Safe arrest durations;

- 32°C: <10 min
- 28°C: 10–15 min
- 18°C: 16–45 min

1. <18°C: 46–60 min [402–405].

Non-cardiac applications of CPB

The CPB is used in various non-cardiac surgeries, including neurosurgery, urologic surgery, pulmonary bypass, hepatic surgery, and venovenous bypass. In neurosurgery, CPB allows DHCA during complex aneurysm repairs or tumor resections. In urologic surgery, CPB ensures safe circulatory management using profound hypothermia. In pulmonary bypass, it is used in cases of pulmonary embolism or tumor invasion into the heart. CPB also assists in major hepatic procedures, especially those involving the IVC. Venovenous bypass, which operates at lower pressure and does not use an oxygenator, is often preferred due to its simplicity. Common complications include hypothermia, low arterial pressure, and elevated CVP. Heparin is avoided unless used for extracorporeal CO2 removal [406–408].

Aortic aneurysm and dissection repair

Cannulation and monitoring

Arterial cannulation is performed distal to the aneurysm; innominate artery cannulation is preferred for arch repairs due to procedural advantages. Venous

return is obtained via the RA, femoral vein, or SVC. Arterial monitoring is conducted via right radial and femoral lines; left radial may be used if dissection is suspected [409–411].

Left Heart Bypass

Left heart bypass is applied during clamping of the descending thoracic aorta to preserve blood flow to distal organs and protect the spinal cord from ischemia. Blood is diverted from the left atrium and returned to the femoral artery using a centrifugal pump, allowing targeted perfusion around the clamped segment. Minimal heparinization is required, typically 100 IU/kg, with ACT levels maintained near 200 seconds. Bioactive circuit surfaces help reduce the need for full anticoagulation. The perfusionist maintains flow at around 75% of the calculated target, ensuring distal aortic pressure stays above 60 mmHg. Continuous radial pressure monitoring above the clamp is essential to guide flow and maintain adequate upper body perfusion [412–414].

Chapter 11: Pediatric cardiac surgery

A. Myocardial protection in neonates and infants. Myocardial protection is ensured through the collective impact of electromechanical cardiac arrest and cardioplegia. The cardioplegic solution, either crystalloid or blood, is used widely in combination with temperature optimization, minimizing ischemic insults and enhancing cardiac recovery [415, 416].

Types of cardioplegia in pediatrics:

1. Blood Cardioplegia: It is a mixture of blood with a crystalloid solution, such as in Del Nido Cardioplegia, providing prolonged myocardial protection with improved oxygen delivery.
2. Crystalloid Cardioplegia: It causes membrane depolarization, leading to electromechanical arrest, similar to Bretschneider's HTK solution, which is the most common type used in pediatric procedures [263, 417].

Ventricular venting and venous drainage

After aortic cross-clamping, venting of the LV is usually performed via the right superior pulmonary vein to prevent distension and optimize myocardial protection. The risk of air embolism is minimized if vent removal is controlled. Additionally, PA venting has been associated with lower left heart pressures within CPB [418, 419].

B. Neuroprotection in infant cardiac surgery. Cardiac surgery in neonates can lead to neurological impair-

ment influenced by preoperative, intraoperative, and postoperative factors. Neuroprotection protocols are implemented in order to optimize perfusion and minimize inflammatory reactions, using comprehensive neuromonitoring [420, 421].

Neuromonitoring techniques:

1. NIRS: It continuously measures cerebral oxygen saturation, detecting inadequate oxygen delivery during cardiac surgery. A significant drop in the NIRS value ($> 20\%$ from baseline or below 40%) necessitates intervening with of cannulation, bypass flows, or perfusion pressures [422].
2. EEG: It monitors brain activity during cardiac surgery, detecting hypoxia with slow or loss of signals, particularly with deep hypothermic circulatory arrest (DHCA). Additionally, it assesses burst suppression, a protective state induced by deep hypothermia to reduce metabolic demand and minimize the risk of ischemic injury during circulatory arrest [423, 423].
3. TCD: It is a non-invasive ultrasound technique that employs its ability to assess cerebral blood flow velocity and autoregulation in real-time to detect the change in cerebral perfusion in cardiac surgery [424].

C. Optimizing perfusion and metabolic parameters. Adequate perfusion pressure and oxygen delivery (DO_2) are ensured in pediatric cardiac surgery through venous oxygen saturation (SvO_2) and ABG analysis. Inflammatory reactions associated with CPB is minimized by the use of steroids, leukocyte-depleting filters, and heparin-coated circuits. Additionally, at or below normothermic temperatures, pH-stat management is needed to enhance cerebral oxygenation. Keeping Hct level $\geq 30\%$ in infants and $\geq 25\%$ in older children is necessary to ensure that there is adequate DO_2 to vital organs, minimizing ischemic events [425, 426].

The DHCA Considerations

The DHCA is used in complex pediatric cardiac surgery for its ability to provide clear bloodless fields while preserving organ function. It requires adequate cooling for at least 20 minutes to achieve uniform cerebral and systemic hypothermia, reducing metabolic demand and protecting the brain. Additionally, it is recommended to perform hyperoxygenation prearrest to improve cerebral oxygen reserves and minimize ischemia. Also, a limit of 40 DHCA minutes is set to prevent ischemia associated with prolonged arrest. However, adjunctive techniques such as intermittent cerebral perfusion or antegrade/retrograde cerebral perfusion can be used

if there is a need for prolonged arrest to get favorable outcomes [427–429].

The NIRS recommendation in pediatrics

Should NIRS vs. Standard monitoring without NIRS be used for Neonates and infants undergoing cardiac surgery to reduce the incidence of brain injury and improve neuroprotective outcomes?

Recommendation

For neonates and infants undergoing cardiac surgery, we suggest using NIRS over Standard monitoring without NIRS to reduce the incidence of brain injury and improve neuroprotective outcomes (Conditional recommendation, very low certainty evidence).

Rationale

There is insufficient evidence regarding the use of NIRS for neonates and infants undergoing cardiac surgery with CPB. This recommendation was based on a meta-analysis by Serraino et al., which highlighted a significant lack of experimental trials in the pediatric population. The analysis revealed no clinical benefits regarding morbidity and mortality associated with the use of NIRS in adults undergoing cardiac surgery with CPB [430].

Daubeney et al. identified in an observational study pre- and early post-bypass periods as hypoxemia periods through monitoring cerebral oxygenation with NIRS across 18 children undergoing cardiac surgery [431]. Similarly, a cohort of 115 neonates suggested the use of NIRS to avoid the noted reduction in cerebral regional oxygen saturation after cardiac surgery with circulatory arrest and the associated neurodevelopment impairment [432]. A systematic review conducted in 2017 found insufficient evidence to support or refute the benefits of NIRS-guided interventions in preventing cerebral injury in preterm infants [433].

Given this rarity, contradicted and the very low certainty evidence, the guideline panel recommended the use of NIRS conditionally as a promising tool for oxygen optimization saturation in neonates and infants, particularly because of their physiologic vulnerability and cerebrovascular autoregulation immaturity that could lead to serious neurological complications. They also underscore the vital need for interventional trials on this population to stand on the real benefits behind NIRS application in neonates and infants.

Disussion

The development of these current national CPB guidelines would mark a crucial advancement in Saudi Arabian cardiac surgical practice, as we encompassed 16 conditional recommendations and 6 good practice statements organized across 5 key categories: Guidelines and Protocols, Heart-Lung Machine Hardware, Monitoring and Perioperative Management, Cardioplegia and Priming Solutions, and Surgical Techniques.

In the realm of Guidelines and Protocols, our recommendations achieved notably high consensus, particularly regarding standardized pre-bypass checklists and emergency protocols, with our panel showing different agreement levels and some questions reaching an agreement level of 100%. The Heart-Lung Machine Hardware-related recommendations demonstrated strong support for biocompatible components, including oxygenators and circuits, reflecting the growing emphasis on reducing inflammatory responses and improving clinical outcomes.

About the Monitoring and Perioperative Management recommendations, this national guideline highlighted the importance of continuous cerebral oxygenation monitoring and glycemic control, with conditional recommendations supporting NIRS implementation for both adult and pediatric populations. The Cardioplegia and Priming Solutions category addressed critical aspects of myocardial protection, offering evidence-based comparisons between various solutions, including HTK, Del Nido, and conventional cardioplegia. Surgical Techniques recommendations provided balanced guidance on choosing between on-pump and off-pump approaches, as well as minimally invasive options when available within the hospital. If not available, there will be slight differences when using the conventional ways.

Our study has several strengths; the methodological approach integrated systematic evidence evaluation with expert clinical experience, specifically made to match the Saudi healthcare environment and be suitable for the Saudi Arabian population. Furthermore, the recommendations draw from multiple levels of evidence, prioritizing high-quality sources such as systematic reviews and meta-analyses when available while also incorporating data from RCTs and observational studies. Notably, this guideline is the first pioneering effort to provide comprehensive national CPB guidelines in Saudi Arabia.

Several limitations warrant consideration. Evidence certainty varied significantly across recommendations, ranging from very low to moderate, particularly in areas such as cardioplegia selection and mechanical circulatory support. A notable limitation

is the lack of high-quality research specific to the Saudi population, which could impact the generalizability of some recommendations. Additionally, implementation challenges may arise from resource variability across Saudi healthcare facilities and the need for specialized training in newer technologies.

To address these limitations, we propose establishing a structured review mechanism for regular updates, which is especially important given the rapid evolution of CPB technology. Additionally, we recommend developing tiered implementation protocols that can accommodate different resource levels while maintaining essential safety standards.

To ensure successful implementation, there is a critical need for the presence of a multidisciplinary team in each healthcare center to adapt these guidelines into local protocols. Furthermore, we will require a comprehensive educational strategy, including practical workshops and continuing medical education programs. Parameters related to adherence and outcomes should be assessed through a defined set of Key Performance Indicators (KPIs), such as pre-bypass checklist compliance, transfusion rates, and incidence of stroke. Additionally, we call for a national registry or periodic audits to collect the data prospectively and evaluate the impact of these guidelines on patient outcomes.

Conclusion

These national CPB guidelines for Saudi Arabia provide evidence-based recommendations to enhance patients' cardiac surgery involving CPB, marking a pivotal step in improving the quality and consistency of cardiac surgical care across the country. Nevertheless, future locally relevant research and regular updates are essential to bridge existing evidence gaps.

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Appendix

Summary of recommendations and evidence.

Summary of Recommendations

- Guidelines and Protocols: Using standardized guidelines, emergency protocols, and pre-bypass checklists is strongly advised to improve patient outcomes, reduce complications, and enhance care quality.
- Surgical Techniques: Both MiECC and CECC are recommended conditionally for minimally invasive cardiac surgery, while on-pump and off-pump CPB are options for CABG.
- Heart-lung Machine Hardware: The choice between roller and centrifugal pumps, biocompatible vs. standard circuits, and cell saver use should be tailored according to patient needs and institutional practices. VA-ECMO is preferred over VV-ECMO for long-term mechanical support.
- Cardioplegia and Priming Solutions: Colloid solutions are preferred over crystalloid for priming, and myocardial protection can be enhanced with various cardioplegia solutions (Del Nido, HTK).
- Monitoring and Perioperative Management: NIRS monitoring, continuous glucose control, and perioperative glycemic management are recommended to improve neurological outcomes. Heparin remains the standard anticoagulant, whereas Bivalirudin can be used for patients at risk of HIT.

Summary of evidence

- The recommendations are primarily based on expert consensus, with varying levels of certainty of evidence (ranging from high to very low).
- Good Practice Statements support key recommendations are based on strong expert agreement because of limited formal grading of evidence.
- Conditional recommendations are based on moderate to very low evidence certainty, particularly for surgical techniques, heart-lung machine hardware, and monitoring strategies.
- Most recommendations are supported by high agreement levels (70-100%) among experts. The detailed strength and level of evidence for all recommendations are summarized in [Table 24](#).

Table 24. Strength and level of evidence used in the text above.

Strength and level of evidence for the recommendations for guidelines, protocols, and general Practice.			
Recommendations	Strength of recommendation	Certainty of evidence	Percentage of panel agreement
For patients undergoing cardiovascular surgery, we advise using standard guidelines rather than not using them to improve patient outcomes, reduce complications, and enhance care quality.	Good practice statement		89%
For Patients undergoing CPB, we advise the implementation of emergency protocols for oxygenator failure to reduce mortality and improve the management of oxygenator failure.	Good practice statement		100%
For patients undergoing CPB, we strongly advise using a standardized pre-bypass checklist over no checklist for reducing the incidence of air embolism and improving safety.	Good practice statement		100%
For patients undergoing CPB, we advise using either transfusion trigger protocol or customary sound judgment.	Good practice statement		70%
Strength and level of evidence for the recommendations for Surgical techniques and approaches.			
For patients undergoing minimally invasive cardiac surgery, we suggest using either MiECC or CECC to reduce postoperative recovery time and complications.	Conditional	Moderate	100%
For perioperative safety and efficacy in patients undergoing CABG, we suggest using either on-pump CPB or Off-pump CPB.	Conditional	Very low	100%

(Continued.)

Table 24. Continued.

Recommendations	Strength of recommendation	Certainty of evidence	Percentage of panel agreement
Strength and level of evidence for the recommendations for heart-lung machine hardware.			
For patients undergoing CPB, we suggest using either roller or centrifugal pumps to reduce hemolysis and improve clinical outcomes.	Conditional	High	89%
For patients undergoing CPB, we suggest using biocompatible oxygenators and circuits over standard oxygenators to reduce the inflammatory response and organ dysfunction.	Conditional	Moderate	89%
For patients undergoing cardiac surgery with CPB, we suggest either cell saver usage/or not for autologous blood salvage to reduce the need for allogeneic blood transfusions and improve postoperative recovery.	Conditional	Very low	78%
For patients requiring prolonged mechanical circulatory support, we suggest using VA-ECMO over VV-ECMO to improve survival rates and reduce complications.	Conditional	Very low	100%
For patients undergoing CPB, we suggest using biocompatible tubing such as heparin-coated tubing instead of using non-heparin-coated ones to reduce the inflammatory response and organ dysfunction.	Conditional	Very low	89%
For patients undergoing CPB who developed post-cardiotomy hemodynamic compromise, we advise using either VA-ECMO with and without IABP or no VA-ECMO with and without IABP.	Good Practice Statement		89%
For pediatrics with cardiopulmonary bypass circuits in pediatric cardiac surgery, we suggest using either SEC-1 coat™ Circuit or heparin-coated Circuit.	Conditional	Very low	100%
Strength and level of evidence for the recommendations for cardioplegia and priming solutions			
For patients undergoing CPB, we suggest using priming with colloid solutions over priming with crystalloid solutions to improve fluid balance and reduce postoperative edema.	Conditional	Low	89%
For patients undergoing CPB, we suggest using the Del Nido cardioplegia solution or standard blood cardioplegia solution to improve myocardial protection and reduce ischemic damage.	Conditional	Moderate	78%
For myocardial protection in cardiac surgeries, we suggest using either a histidine-tryptophan-ketoglutarate solution or multi-dose cardioplegia.	Conditional	Very low	78%
Strength and level of evidence for the recommendations for monitoring and perioperative management.			
For patients undergoing CPB, we suggest using continuous cerebral oxygenation monitoring using NIRS over standard monitoring without NIRS to reduce neurological complications and improve cognitive function	Conditional	very low	100%
For patients undergoing CPB, we suggest using Heparin as the standard anticoagulant. Bivalirudin as an anticoagulant vs. Heparin as an anticoagulant should be used for patients undergoing CPB to reduce the incidence of HIT and improve coagulation control	Conditional	very low	89%
For patients undergoing CPB, we suggest using continuous glucose monitoring over Standard glucose management to improve glucose control and reduce postoperative complications.	Conditional	very low	100%
For neonates and infants undergoing cardiac surgery, we suggest using NIRS over Standard monitoring without NIRS to reduce the incidence of brain injury and improve neuroprotective outcomes.	Conditional	very low	100%
For patients undergoing CPB who present for elective cardiac surgery, we strongly advise perioperative glycemic management over routine post-operative care.	Good practice statement		100%
For patients undergoing CPB, we suggest against using Liraglutide compared to other perioperative management of hyperglycemia by other forms of therapy.	Conditional	Moderate	78%

CPB: Cardiopulmonary bypass, CABG: Coronary Artery Bypass Grafting, CECC: Conventional extracorporeal circulation, MiECC: Minimally invasive extracorporeal circulation, VA-ECMO: Veno-arterial extracorporeal Membrane Oxygenation, IABP: Intra-aortic balloon pump.