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# Guidelines for Perioperative Care in Cardiac Surgery Enhanced Recovery After Surgery Society Recommendations

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Enhanced Recovery After Surgery (ERAS) evidence-based protocols for perioperative care can lead to improvements in clinical outcomes and cost savings. This article aims to present consensus recommendations for the optimal perioperative management of patients undergoing cardiac surgery. A review of meta-analyses, randomized clinical trials, large nonrandomized studies, and reviews was conducted for each protocol element. The quality of the evidence was graded and used to form consensus recommendations for each topic. Development of these recommendations was endorsed by the Enhanced Recovery After Surgery Society.

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Supplemental content

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nhanced Recovery After Surgery (ERAS) is a multimodal, transdisciplinary care improvement initiative to promote recovery of patients undergoing surgery throughout their entire perioperative journey. These programs aim to reduce complications and promote an earlier return to normal activities. The ERAS protocols have been associated with a reduction in overall complications and length of stay of up to 50% compared with conventional perioperative patient management in populations having noncardiac surgery. Evidence-based ERAS protocols have been published across multiple surgical specialties. In early studies, the ERAS approach showed promise in cardiac surgery (CS); however, evidence-based protocols have yet to emerge.

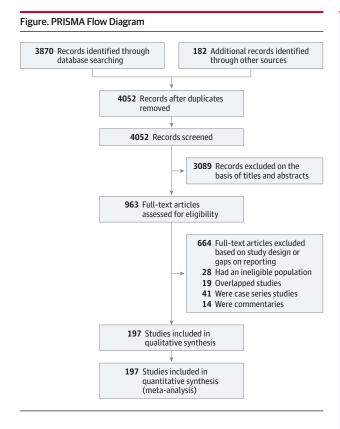
To address the need for evidence-based ERAS protocols, we formed a registered nonprofit organization (ERAS Cardiac Society) to use an evidence-driven process to develop recommendations for pathways to optimize patient care in CS contexts through collaborative discovery, analysis, expert consensus, and best practices. The ERAS Cardiac Society has a formal collaborative agreement with the ERAS Society. This article reports the first expert-consensus review of evidenced-based CS ERAS practices.

# Methods

We followed the 2011 Institute of Medicine Standards for Developing Trustworthy Clinical Practice Guidelines, using a standardized algorithm that included experts, key questions, subject champions, systematic literature reviews, selection and appraisal of evidence quality, and development of clear consensus recommendations. We minimized repetition of existing guidelines and consensus statements and focused on specific information in the framework of ERAS protocols.

As sanctioned by the ERAS Society, we began with a public organizational meeting in 2017 where broad topics of ERAS in CS were discussed, and we solicited public comment regarding appropriate approaches and protocols. A multidisciplinary group of 16 cardiac surgeons, anesthesiologists, and intensivists were identified who demonstrated expertise and experience with ERAS. The group agreed on 22 potential interventions, divided into preoperative, intraoperative, and postoperative phases of recovery.

After selecting topics and assigning group leaders, literature searches were conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Figure), and this included reviews, guideline documents, and studies that were conducted on humans since 2000, published in English, and retrievable from PubMed, Excerpta Medica (Embase), Cochrane, the Agency for Healthcare Research and Quality, and other selected databases relevant to this consensus. 9 Medical Subject Heading terms were used, as were accompanying entry terms for the patient group, interventions, and outcomes. Two independent reviewers (W.B.A. and 1 nonauthor) screened the abstracts considered for topics. Prospective randomized clinical trials, metaanalyses, and well-designed, nonrandomized studies were given preference. When multiple publications had sample overlap, the most recent report was selected. Controversies were discussed and resolved via in-person meetings, conference calls, and discussions. A minimum of 75% agreement on class and level was required for consensus. 10 Consistent with the Institute of Medicine guidelines, panel members with relevant conflicts of interest (COI) were identified and recused from voting on associated recommendations. The structure of the recommendations was modeled after prior published ERAS guidelines. 11 We used the Society of Thoracic Surgeons/ American Association for Thoracic Surgery 2017 updated document "Classification of Recommendations and Level of Evidence," and American College of Cardiology/American Heart Association clini-



cal practice guidelines to grade the consensus class (strength) of recommendation and level (quality) of evidence. <sup>10,12</sup> (**Box**; eAppendix in the Supplement).

## Results

Resulting consensus statements are summarized in **Table 2**. They are organized into preoperative, intraoperative, and postoperative strategies.

#### **Preoperative Strategies**

Preoperative Measurement of Hemoglobin A<sub>1c</sub> for Risk Stratification Optimal preoperative glycemic control, defined by a hemoglobin A<sub>1c</sub> level less than 6.5%, has been associated with significant decreases in deep sternal wound infection, ischemic events, and other complications. 13,14 Evidence-based guidelines based on poor quality meta-analyses recommend screening all patients for diabetes preoperatively and intervening to improve glycemic control to achieve a hemoglobin A<sub>1c</sub> level less than 7% in patients for whom this is relevant. 15 Despite this recommendation, approximately 25% of patients undergoing CS have hemoglobin  $A_{1c}$  levels greater than 7%, and 10% have undiagnosed diabetes, indicating a failure to apply current evidence-based recommendations for preoperative diabetes management.  $^{16}$  A recent retrospective review demonstrated that preadmission glycemic control, as assessed by hemoglobin A<sub>1ct</sub> is associated with decreased long-term survival.<sup>17</sup> It is unclear whether preoperative interventions in patients undergoing CS will result in improved outcomes. Based on this moderate-quality evidence, we

#### Box. Class of Recommendation and Levels of Evidence<sup>a</sup>

# Class (Strength) of Recommendation

I (strong): benefit many times greater than risk

IIa (moderate): benefit much greater than risk

IIb (weak): benefit greater than risk

III: no benefit (moderate): benefit equal to risk

III: harm (strong): risk greater than benefit

#### Level (Quality) of Evidence

Α

High-quality evidence from more than 1 randomized clinical trial Meta-analysis of high quality randomized clinical trials

One or more randomized clinical trials corroborated by registry studies

B-R

Moderate-quality evidence from 1 or more randomized clinical trial

Meta-analysis of moderate-quality randomized clinical trials

B-NR

Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies or observational studies

CID

Randomized or nonrandomized observational or registry studies with limitations of design or execution

C-EO

Consensus of expert opinion based on clinical experience

<sup>a</sup> Adapted from Jacobs AK, Anderson JL, Halperin JL. The evolution and future of ACC/AHA clinical practice guidelines: a 30-year journey: a report of the American College of Cardiology/American Heart Association Task Force 1099 on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:1373-84. <sup>13</sup> (Reprinted with permission from Elsevier.)

recommend preoperative measurement of hemoglobin  $A_{1c}$  to assist with risk stratification (class IIa, level C-LD).

# Preoperative Measurement of Albumin for Risk Stratification

Low preoperative serum albumin in patients undergoing CS is associated with an increased risk of morbidity and mortality postoperatively (independent of body mass index). <sup>18</sup> Hypoalbuminemia is a prognosticator of preoperative risk, correlating with increased length of time on a ventilator, acute kidney injury (AKI), infection, longer length of stay, and mortality. <sup>19-21</sup> Low-quality meta-analyses support measuring preoperative albumin to prognosticate postoperative CS complications. <sup>21</sup> Based on the moderate quality of evidence, it can be useful to assess preoperative albumin before CS to assist with risk stratification (class IIa, level C-LD).

#### **Preoperative Correction of Nutritional Deficiency**

For patients who are malnourished, oral nutritional supplementation has the greatest effect if started 7 to 10 days preoperatively and has been associated with a reduction in the prevalence of infectious complications in colorectal patients. <sup>22</sup> In patients undergoing CS who had a serum albumin level less than 3.0 g/dL (to convert to g/L, multiply by 10.0), supplementation with 7 to 10 days' worth of intensive nutrition therapy may improve outcomes. <sup>23-26</sup> Currently, however, no adequately powered trials of nutritional therapy initiated early in patients undergoing CS who are considered high risk

| Table 2  | Classification   | of Docom  | mendation and | م امیره ا | f Evidonco |
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| LOE by<br>COR       |         | Recommendation   |
|---------------------|---------|--|
| Ι                   |         |  |
|                     | A       | Tranexamic acid or epsilon aminocaproic acid during on-pump cardiac surgical procedures  |
|                     | B-R     | Perioperative glycemic control   |
|                     | B-R     | A care bundle of evidenced based best practices to reduce surgical site infections   |
|                     | B-R     | Goal-directed fluid therapy  |
|                     | B-NR    | A perioperative, multimodal, opioid-sparing, pain management plan  |
|                     | B-NR    | Avoidance of persistent hypothermia (<36.0°C) after cardiopulmonary bypass in the early postoperative period.                        |
|                     | B-NR    | Maintenance of chest tube patency to prevent retained blood  |
|                     | B-NR    | Postoperative systematic delirium screening tool use at least once per nursing shift   |
|                     | C-LD    | Stopping smoking and hazardous alcohol consumption 4 weeks before elective surgery   |
| Ш                   | a       |  |
|                     | B-R     | Early detection of kidney stress and interventions to avoid acute kidney injury after surgery  |
|                     | B-R     | Use of rigid sternal fixation to potentially improve or accelerate sternal healing and reduce mediastinal wound complications        |
|                     | B-NR    | Prehabilitation for patients undergoing elective surgery with multiple comorbidities or significant deconditioning                   |
|                     | B-NR    | An insulin infusion to treat hyperglycemia in all patients postoperatively   |
|                     | B-NR    | Strategies to ensure extubation within 6 h of surgery  |
|                     | C-LD    | Patient engagement tools, including online/application-based systems to promote education, compliance, and patient-reported outcomes |
|                     | C-LD    | Chemical or mechanical thromboprophylaxis after surgery  |
|                     | C-LD    | Preoperative measurement of hemoglobin A1c to assist with risk stratification  |
|                     | C-LD    | Preoperative correction of nutritional deficiency when feasible  |
| Ш                   | b       |  |
|                     | C-LD    | Continued consumption of clear liquids up until 2 to 4 h before general anesthesia   |
|                     | C-LD    | Preoperative oral carbohydrate loading may be considered before surgery  |
| III (No<br>Benefit) |         |  |
|                     | Α       | Stripping or breaking the sterile field of chest tubes to remove clots.  |
| III<br>(Harm)       |         |  |
|                     | B-R     | Hyperthermia (>37.9°C) while rewarming on cardiopulmonary bypass.  |
| ۸ ۱                 | brovist | ions: A. A-level evidence: R-P. R-level evidence, randomized studies:  |

Abbreviations: A, A-level evidence; B-R, B-level evidence, randomized studies; B-NR, B-level evidence, nonrandomized studies; C-LD, C-level evidence, limited data; COR, classification of recommendation; LOE, level of evidence.

are available. <sup>27</sup> In addition, this may not be feasible in urgent or emergency settings. Further studies are needed to determine when to delay surgery to correct nutritional deficits. Based on these data, we note that correction of nutritional deficiency is recommended when feasible (class IIa, level C-LD).

#### Consumption of Clear Liquids Before General Anesthesia

Most CS programs mandate that a patient ingest nothing by mouth after midnight for surgery the following day, or at the very least, fast for 6 to 8 hours from the intake of a solid meal before elective cardiac surgery. <sup>28</sup> Several randomized clinical trials have demonstrated, however, that nonalcoholic clear fluids can be safely given up to 2 hours before the induction of anesthesia, and a light meal

can be given up to 6 hours before elective procedures requiring general anesthesia. <sup>28-30</sup> Encouraging clear liquids until 2 to 4 hours preoperatively is an important component of all ERAS protocols outside of CS. <sup>31</sup> However, no large studies have been performed in populations undergoing CS. The supporting evidence is extrapolated from populations having noncardiac surgery. A small study in patients undergoing CS demonstrated that an oral carbohydrate drink consumed 2 hours preoperatively was safe, and no incidents of aspiration occurred. <sup>32</sup> Aspiration pneumonitis has not been reported, although this potential remains in patients undergoing CS who have delayed gastric emptying owing to diabetes mellitus, and transesophageal echocardiography may also increase aspiration risk. Based on the data available on CS, clear liquids may be continued up to 2 to 4 hours before general anesthesia (class IIb, level C-LD).

#### **Preoperative Carbohydrate Loading**

A carbohydrate drink (a 12-ounce clear beverage or a 24-g complex carbohydrate beverage) 2 hours preoperatively reduces insulin resistance and tissue glycosylation, improves postoperative glucose control, and enhances return of gut function. In a 2003 Cochrane review of patients undergoing CS, carbohydrate loading reduced postoperative insulin resistance and hospital length of stay. In a large randomized clinical trial in patients undergoing CS, preoperative carbohydrate administration was found to be safe and improved cardiac function immediately after cardiopulmonary bypass. However, it did not affect postoperative insulin resistance. Si. 33-34 Given the current minimal supportive data in patients undergoing CS, carbohydrate loading is given a weak recommendation at this time (class IIb, level C-LD).

# **Patient Engagement Tools**

Patient education and counseling prior to surgery can be completed in person, through printed material, or through novel online or application-based approaches. These efforts include explanations of procedures and goals that may help reduce perioperative fear, fatigue, and discomfort and enhance recovery and early discharge. Data are emerging that software applications can engage patients, promote compliance, and capture patient-reported outcome measures. They are designed to increase preventive care and encourage patients to perform physical exercise. These platforms have the potential to increase patient knowledge, decrease anxiety, improve health outcomes, and reduce variation in care. Sac Pilot studies in CS have demonstrated the effectiveness of e-health platforms without any evidence of harm. Thus, it is recommended that these efforts be undertaken (class IIa, level C-LD).

#### Prehabilitation

Prehabilitation enables patients to withstand the stress of surgery by augmenting functional capacity. <sup>38-40</sup> Preoperative exercise decreases sympathetic overreactivity, improves insulin sensitivity, and increases the ratio of lean body mass to body fat. <sup>41-43</sup> It also improves physical and psychological readiness for surgery, reduces postoperative complications and the length of stay, and improves the transition from the hospital to the community. <sup>38,39</sup> A cardiac prehabilitation program should include education, nutritional optimization, exercise training, social support, and anxiety reduction, although current existing evidence is limited. <sup>41-44</sup> Three non-CS studies <sup>45-47</sup> have successfully demonstrated the benefits of 3 to 4

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weeks of prehabilitation in the context of ERAS. Prehabilitation interventions prior to CS must be further examined to advance this area of research. The small number of studies and the diversity of validation tools used limits the strength of the recommendation. In addition, this may not be feasible in urgent and emergency settings (class IIa, level B-NR).

#### **Smoking and Hazardous Alcohol Consumption**

Screening for hazardous alcohol use and cigarette smoking should be performed preoperatively. <sup>48</sup> Tobacco smoking and hazardous alcohol consumption are risk factors for postoperative complications and present another opportunity for preoperative interventions. They are associated with respiratory, wound, bleeding, metabolic, and infectious complications. <sup>23,49-51</sup> Smoking cessation and alcohol abstinence for 1 month are associated with improved postoperative outcomes after surgery. <sup>51-53</sup> Only a small number of studies are available, and further CS-specific studies are needed. However, given the low risk of this intervention, patients should be questioned regarding smoking and hazardous alcohol consumption using validated screening tools, and consumption should be stopped 4 weeks before elective surgery. <sup>54</sup> However, this may not be feasible in urgent or emergency settings (class I, level C-LD).

#### Intraoperative Strategies

#### **Surgical Site Infection Reduction**

To help reduce surgical site infections, CS programs should include a care bundle that includes topical intranasal therapies, depilation protocols, and appropriate timing and stewardship of perioperative prophylactic antibiotics, combined with smoking cessation, adequate glycemic control, and promotion of postoperative normothermia during recovery. Moderate-quality meta-analysis have concluded that care bundles of 3 to 5 evidence-based interventions can reduce surgical site infections. <sup>55,56</sup> This topic has been reviewed extensively with class of recommendation and level of evidence in an expert consensus review by Lazar et al. <sup>57</sup>

Evidence supports topical intranasal therapies to eradicate staphylococcal colonization in patients undergoing CS. 57,58 From 18% to 30% of all patients undergoing surgery are carriers of Staphylococcus aureus, and they have 3 times the risk of S. aureus surgical site infections and bacteremia.<sup>59</sup> It is recommended that topical therapy be applied universally. 60-62 Two studies validate the reduction of such infections in patients receiving mupirocin. 58,63 Level IA data exists suggesting that weight-based cephalosporins should be administered fewer than 60 minutes before the skin incision and con $tinued for 48\,hours\,after\,completion\,of\,CS.\,When\,the\,surgery\,is\,more$ than 4 hours, antibiotics require redosing. 64,65 Clarity on the preferability of continuous vs intermittent dosing of cefazolin requires further data. 66 A meta-analysis of skin preparation and depilation protocols indicates that clipping is preferred to shaving. 67 Clipping using electric clippers should occur close to the time of surgery.<sup>68</sup> A preoperative shower with chlorhexidine has only been demonstrated to reduce bacterial counts in the wound and is not associated with significant levels of efficacy.<sup>57</sup> Postoperative measures including sterile dressing removal within 48 hours and daily incision washing with chlorhexidine are potentially beneficial. 69,70

In summary, we recommend the implementation of a care bundle to include topical intranasal therapies to eradicate staphylococcal colonization, weight-based cephalosporin infusion fewer

Table 3. Surgical Site Infection Bundle, Including Classification of Recommendation and Level of Evidence

| LOE by<br>COR | Recommendation  |  |  |  |  |
|---------------|---|--|--|--|--|
| 1             |   |  |  |  |  |
| Α             | Perform topical intranasal decolonization prior to surgery                              |  |  |  |  |
| А             | Administer intravenous cephalosporin prophylactic antibiotic 30-60 min prior to surgery |  |  |  |  |
| С             | Clipping (as opposed to shaving) immediately prior to surgery                           |  |  |  |  |
| Ilb           |   |  |  |  |  |
| С             | Use a chlorhexidine-alcohol-based solution for skin preparation before surgery          |  |  |  |  |
| lla           | lla   |  |  |  |  |
| С             | Remove operative wound dressing after 48 h  |  |  |  |  |

Abbreviations: COR, classification of recommendation; LOE, level of evidence.

than 60 minutes before skin incision, with redosing for cases longer than 4 hours, skin preparation, and depilation protocols with dressing changes every 48 hours to reduce surgical site infections (class I, level B-R). The bundle of recommendations to reduce surgical site infections are summarized in **Table 3** with the classification of recommendations and level of evidence per Lazar et al.<sup>57</sup>

#### Hyperthermia

Moderate-quality prospective studies have demonstrated that when rewarming on cardiopulmonary bypass (CPB), hyperthermia (core temperature >37.9°C) is associated with cognitive deficits, infection, and renal dysfunction. Any postoperative hyperthermia within 24 hours after coronary artery bypass grafting has been associated with cognitive dysfunction at 4 to 6 weeks. Rewarming on CPB to normothermia should be combined with continuous surface warming. Thus, we recommend avoiding hyperthermia while rewarming on cardiopulmonary bypass (class III, level B-R).

#### **Rigid Sternal Fixation**

Most cardiac surgeons use wire cerclage for sternotomy closure because of the perceived low rate of sternal wound complications and low cost of wires. Wire cerclage brings the cut edges of bone back together by wrapping a wire or band around or through the 2 portions of bone, then tightening the wire or band to pull the 2 parts together. This achieves approximation and compression but does not eliminate side-by-side movement, and thus rigid fixation is not achieved with wire cerclage. 75

In 2 multicenter randomized clinical trials, sternotomy closure with rigid plate fixation resulted in significantly better sternal healing, fewer sternal complications, and no additional cost compared with wire cerclage at 6 months after surgery. Patient-reported outcome measures demonstrated significantly less pain, better upper-extremity function, and improved quality-of-life scores, with no difference in total 90-day cost. Limitations of these studies include a sample size designed to test the primary end point of improved sternal healing but not the secondary end points of pain and function; in addition, the studies were limited by unblinded radiologists. Additional research demonstrated decreased mediastinitis, painful sternal nonunion relief after median sternotomy, and superior bony healing when compared with wire cerclage. Based on these studies, the consensus concluded that rigid sternal fixation has

benefits in patients undergoing sternotomy and should be especially considered in individuals at high risk, such as those with a high body mass index, previous chest wall radiation, severe chronic obstructive pulmonary disorder, or steroid use. Rigid sternal fixation can be useful to improve or accelerate sternal healing and reduce mediastinal wound complications (class IIa, level B-R).

#### Tranexamic Acid or Epsilon Aminocaproic Acid

Bleeding is a common occurrence after CS and can adversely affect outcomes. 80,81 Publications on patient blood management are typically focused on reducing red blood cell transfusions through identification and treatment of preoperative anemia, delineation of safe transfusion thresholds, intraoperative blood scavenging, monitoring of the coagulation system, and data-driven algorithms for appropriate transfusion practices. This has been an area of focus in previously published, large, comprehensive, multidisciplinary, multisociety clinical practice guidelines. 82,83 The inclusion of all aspects of patient blood management are beyond the scope of these recommendations, although we encourage the incorporation of these existing guidelines within a local ERAS framework. This includes education, audit, and continuous practitioner feedback. Owing to the near-universal accessibility, low-risk profile, costeffectiveness, and ease of implementation, we did evaluate  $antifibrinolytic \, use \, with \, tranexamic \, acid \, or \, epsilon \, aminocaproic \, acid.$ In a large randomized clinical trial of patients undergoing coronary revascularization, total blood products transfused, and major hemorrhage or tamponade requiring reoperation were reduced using tranexamic acid. 84 Higher dosages, however, appear to be associated with seizures. 85,86 A maximum total dose of 100 mg/kg is recommended.<sup>87</sup> Based on this evidence, tranexamic acid or epsilon aminocaproic acid is recommended during on-pump cardiac surgical procedures (class I, level A).

# **Postoperative Strategies**

## Perioperative Glycemic Control

Interventions to improve glycemic control are known to improve outcomes. Multiple randomized clinical trials <sup>88-91</sup> with diverse patient cohorts support intensive perioperative glucose control. Preoperative carbohydrate loading has resulted in reduced glucose levels after abdominal surgery and CS. <sup>92,93</sup> Epidural analgesia during CS has been shown to reduce hyperglycemia incidence. <sup>94</sup> After CS, hyperglycemia morbidity is multifactorial and attributed to glucose toxicity, increased oxidative stress, prothrombotic effects, and inflammation. <sup>14,15,89,91,95</sup> Perioperative glycemic control is recommended based on randomized data <sup>96</sup> not specific to populations undergoing CS and high-quality observational studies (class I, level B-R).

## Insulin Infusion

Treatment of hyperglycemia (glucose >160-180 mg/dL [to convert to mmol/L, multiply by 0.0555]) with an insulin infusion for the patient undergoing CS may be associated with improved perioperative glycemic control. Postoperative hypoglycemia should be avoided, especially in patients with a tight blood glucose target range (ie, 80-110 mg/dL). P5.97,98 Randomized clinical trials support insulin infusion protocols to treat hyperglycemia perioperatively; however, more high-quality, CS-specific studies are needed (class IIa, level B-NR).

#### Pain Management

Until recently, parenteral opioids were the mainstay of postoperative pain management after CS. Opioids are associated with multiple adverse effects, including sedation, respiratory depression, nausea, vomiting, and ileus. <sup>99</sup> There is growing evidence that multimodal opioid-sparing approaches can adequately address pain through the additive or synergistic effects of different types of analgesics, permitting lower opioid doses in the population receiving CS. <sup>100</sup>

Nonsteroidal anti-inflammatory drugs are associated with renal dysfunction after CS. <sup>101</sup> Selective *COX-2* inhibition is associated with a significant risk of thromboembolic events after CS. <sup>102</sup> The safeest nonopioid analgesic may be acetaminophen. <sup>103</sup> Intravenous acetaminophen may be better absorbed until gut function has recovered postoperatively. <sup>104</sup> Per a medium-quality meta-analysis, when added to opioids, acetaminophen produces superior analgesia, an opioid-sparing effect, and independent antiemetic actions. <sup>105</sup> Acetaminophen dosing is 1 g every 6 hours. Combination acetaminophen preparations with opioids should be discontinued.

Tramadol has dual opioid and nonopioid effects but with a high delirium risk. <sup>106</sup> Tramadol produces a 25% decrease in morphine consumption, decreased pain scores, and improved patient comfort postoperatively. <sup>107</sup> Pregabalin also decreases opioid consumption and is used in postoperative multimodal analgesia. <sup>108</sup> Pregabalin given 1 hour before surgery and for 2 postoperative days improves pain scores compared with placebo. <sup>109</sup> A 600-mg gabapentin dose, 2 hours before CS, lowers pain scores, opioid requirements, and postoperative nausea and vomiting. <sup>110</sup>

Dexmedetomidine, an intravenous α-2 agonist, reduces opioid requirements. <sup>111</sup> A medium-quality meta-analysis of dexmedetomidine infusion reduced all-cause mortality at 30 days with a lower incidence of postoperative delirium and shorter intubation times. <sup>112,113</sup> Dexmedetomidine may reduce AKI after CS. <sup>114</sup> Ketamine has potential uses in CS owing to its favorable hemodynamic profile, minimal respiratory depression, analgesic properties, and reduced delirium incidence; further studies are needed in the CS setting. <sup>115</sup>

Patients should receive preoperative counseling to establish appropriate expectations of perioperative analgesia targets. Pain assessments must be made in the intubated patient to ensure the lowest effective opioid dose. The Critical Care Pain Observation Tool, Behavioral Pain Scale, and Bispectral Index monitoring may have a role in this setting. <sup>116-119</sup> Although no single pathway exists for multimodal opioid-sparing pain management, there is sufficient evidence to recommend that CS programs use acetaminophen, Tramadol, dexmedetomidine, and pregabalin (or gabapentin) based on formulary availability (class I, level B-NR).

## Postoperative Systematic Delirium Screening

Delirium is an acute confusional state characterized by fluctuating mental status, inattention, and either disorganized thinking or altered level of consciousness that occurs in approximately 50% of patients after CS. <sup>120-125</sup> Delirium is associated with reduced inhospital and long-term survival, freedom from hospital readmission, and cognitive and functional recovery. <sup>126</sup> Early delirium detection is essential to determine the underlying cause (ie, pain, hypoxemia, low cardiac output, and sepsis) and initiate appropriate treatment. <sup>127</sup> A systematic delirium screening tool such as the Confusion Assessment Method for the Intensive Care Unit or the In-

tensive Care Unit Delirium Screening Checklist should be used. <sup>128,129</sup> The perioperative team should consider routine delirium monitoring at least once per nursing shift. <sup>121</sup>

Owing to the complexity of delirium pathogenesis, it is unlikely that a single intervention or pharmacologic agent will reduce the incidence of delirium after CS. <sup>127</sup> Nonpharmacologic strategies are a first-line component of management. <sup>130,131</sup> There is no evidence that prophylactic antipsychotic use (eg, haloperidol) reduces delirium. <sup>132,133</sup> Based on moderate-quality, nonrandomized studies in patients receiving noncardiac surgery, delirium screening is recommended at least once per nursing shift to identify patients at risk and facilitate implementation of prevention and treatment protocols (class I, level B-NR).

#### Persistent Hypothermia

Postoperative hypothermia is the failure to return to or maintain normothermia (>36°C) 2 to 5 hours after an intensive care unit (ICU) admission associated with CS. <sup>134</sup> Hypothermia is associated with increased bleeding, infection, a prolonged hospital stay, and death. Large registry observational studies suggest if hypothermia is of short duration, outcomes can be improved. <sup>135,136</sup> Based on this evidence, we recommend prevention of hypothermia by using forcedair warming blankets, raising the ambient room temperature, and warming irrigation and intravenous fluids to avoid hypothermia in the early postoperative period <sup>71,137,139</sup> (class 1, level B-NR).

#### Chest Tube Patency

Immediately after CS, most patients have some degree of bleeding. <sup>81</sup> If left unevacuated, retained blood can cause tamponade or hemothorax. Thus, a pericardial drain is always necessary after CS to evacuate shed mediastinal blood. <sup>80</sup> Drains used to evacuate shed mediastinal blood are prone to clogging with clotted blood in up to 36% of patients. <sup>140,141</sup> When these tubes clog, shed mediastinal blood can pool around the heart or lungs, necessitating reinterventions for tamponade or hemothorax. <sup>142-144</sup> Retained shed mediastinal blood hemolyzes and promotes an oxidative inflammatory process that may further cause pleural and pericardial effusions and trigger postoperative atrial fibrillation. <sup>143,145</sup>

Chest tube manipulation strategies that are commonly used in an attempt to maintain tube patency after CS are of questionable efficacy and safety. One example is chest-tube stripping or milking, in which the practitioner strips the tubes toward the drainage canister to break up visible clots or create short periods of high negative pressure to remove clots. In meta-analyses of randomized clinical trials, chest-tube stripping has been shown to be ineffective and potentially harmful. Another technique used to maintain patency is to break the sterile field to access the inside of chest tubes and use a smaller tube to suction the clot out. This technique may be dangerous, because it can increase infection risk and potentially damage internal structures. 148

To address the unmet need to prevent chest-tube clogging, active chest-tube clearance methods can be used to prevent occlusion without breaking the sterile field. This has been demonstrated to reduce the subsequent need for interventions to treat retained blood compared with conventional chest tube drainage in 5 non-randomized clinical trials of CS. <sup>149-153</sup> Active chest-tube clearance has also been shown to reduce postoperative atrial fibrillation, suggesting that retained blood may be a trigger for this common problem. <sup>145</sup>

While there are no standard criteria for the timing of mediastinal drain removal, evidence suggests that they can be safely removed as soon as the drainage becomes macroscopically serous. <sup>154</sup> Based on these clinical trials, maintenance of chest tube patency without breaking the sterile field is recommended to prevent retained blood complications (class I, level B-NR). Stripping or breaking the sterile field of chest tubes to remove clot is not recommended (class IIIA, level B-R).

#### Chemical Thromboprophylaxis

Vascular thrombotic events include both deep venous thrombosis and pulmonary embolism and represent potentially preventable complications after CS. Patients remain hypercoagulable after CS, increasing vascular thrombotic event risk. 155,156 All patients benefit from mechanical thromboprophylaxis achieved with compression stockings and/or intermittent pneumatic compression during hospitalization or until they are adequately mobile to reduce the incidence of deep-vein thrombosis after surgery even in the absence of pharmacological treatment. 157-159 Prophylactic anticoagulation for vascular thrombotic events should be considered on the first postoperative day and daily thereafter. 160 A recent medium-quality metaanalysis suggested that chemical prophylaxis could reduce vascular thrombotic event risk without increasing bleeding or cardiac tamponade. 161 Based on this evidence, pharmacological prophylaxis should be used as soon as satisfactory hemostasis has been achieved (most commonly on postoperative day 1 through discharge)<sup>160-162</sup> (class IIa, level C-LD).

#### **Extubation Strategies**

Prolonged mechanical ventilation after CS is associated with longer hospitalization, higher morbidity, mortality, and increased costs. <sup>163</sup> Prolonged intubation is associated with both ventilator-associated pneumonia and significant dysphagia. <sup>164</sup> Early extubation, within 6 hours of ICU arrival, can be achieved with time-directed extubation protocols and low-dose opioid anesthesia. This is safe (even in patients at high risk) and associated with decreased ICU time, length of stay, and costs. <sup>165-172</sup> A meta-analysis demonstrated that ICU times and length of stay were reduced; however, no difference in morbidity and mortality occurred, likely because of disparate study design and statistical underpowering. <sup>173</sup> Thus, studies have shown early extubation to be safe, but efficacy in reducing complications has not been conclusively demonstrated. Based on this evidence, we recommend strategies to ensure extubation within 6 hours of surgery (class IIa, level B-NR).

#### Kidney Stress and Acute Kidney Injury

Acute kidney injury (AKI) complicates 22% to 36% of cardiac surgical procedures, doubling total hospital costs. 174-176 Strategies to reduce AKI involve assessing which patients are at risk and then implementing therapies to reduce the incidence. Urinary biomarkers (such as tissue inhibitor of metalloproteinases-2 and insulinlike growth factor-binding protein 7) can identify patients as early as 1 hour after CPB who are at increased risk of developing AKI. 177,178

In a randomized clinical trial after CS, patients with positive urinary biomarkers who were assigned to an intervention algorithm had reductions in subsequent AKI. The algorithm included avoiding nephrotoxic agents, discontinuing angiotensin-converting enzyme inhibitors and angiotensin II antagonists for 48 hours, close

monitoring of creatinine and urine output, avoiding hyperglycemia and radiocontrast agents, and close monitoring to optimize volume status and hemodynamic parameters. Similar results have been reported in a randomized clinical trial after surgery in a population who received noncardiac surgery. <sup>181</sup>

Although many risk scores for AKI after CS have been published, these scoring systems have good discrimination in assessing low-risk groups but relatively poor discrimination in patients at moderate to high risk. This would suggest that all patients undergoing CS may benefit from detection of modifiable early kidney stress to prevent AKI. Based on these studies, biomarkers are recommended for early identification of patients at risk and to guide an intervention strategy to reduce AKI (class IIa, level B-R).

#### **Goal-Directed Fluid Therapy**

Goal-directed fluid therapy uses monitoring techniques to guide clinicians with administering fluids, vasopressors, and inotropes to avoid hypotension and low cardiac output. 183 While many clinicians do this informally, goal-directed fluid therapy uses a standardized algorithm for all patients to improve outcomes. Quantified goals include blood pressure, cardiac index, systemic venous oxygen saturation, and urine output. Additionally, oxygen consumption, oxygen debt, and lactate levels may augment therapeutic tactics. Goal-directed fluid therapy trials consistently demonstrate reduced complication rates and length of stay in surgery overall and specifically in CS. 184-188 Based on this, we recommend goal-directed fluid therapy to reduce postoperative complications (class I, level B-R).

# Other Important, Ungraded ERAS Elements

Preoperative anemia is common and associated with poor outcomes in patients undergoing noncardiac surgery. <sup>189</sup> Patients scheduled for CS may have multifactorial causative mechanisms for anemia, including acute or chronic blood loss, vitamin B12, or folate

deficiency, and anemia of chronic disease. 190 If time permits, all causes of anemia should be investigated, but data supporting improved outcomes in the literature on CS is weak. Intraoperative anesthetic and perfusion considerations are also important ERAS elements. Impaired renal oxygenation has been demonstrated during CPB and is ameliorated by an increase in CPB flow. 191 This may contribute to postoperative renal dysfunction and suggests that goaldirected perfusion strategies need to be considered. Other anesthetic considerations may include a comprehensive protective lung ventilation strategy. Multiple studies have established that clinicians should use a low tidal volume strategy for mechanical ventilation in CS. 192 Early postoperative enteral feeding and mobilization after surgery are other essential components of ERAS surgical protocols. We recommend that programs tailor these recommendations to achieve these goals working with staff with expertise in nutrition, early cardiac rehabilitation, and physical therapy.

#### Conclusions

In CS, a fast-track project to improve outcomes was first initiated by bundling perioperative treatments. <sup>193</sup> The ERAS pathway was initiated in the 1990s by a group of academic surgeons to improve perioperative care for patients receiving colorectal care, but it is now practiced in most fields of surgery. <sup>1,194</sup> Although ERAS is relatively new to CS, we anticipate that programs can benefit from these recommendations as they develop protocols to decrease unnecessary variation and improve quality, safety, and value for their patients. Cardiac surgery involves a large clinician group working in concert throughout all phases of care. Patient and caregiver education and systemwide engagement (facilitated by specialty champions and nurse coordinators) are necessary to implement best practices. A successful introduction of ERAS protocols is possible, but a broad-based, multidisciplinary approach is imperative for success.

# ARTICLE INFORMATION

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