

# 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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**E**nhanced Recovery After Surgery (ERAS) is a multimodal, transdisciplinary care improvement initiative to promote recovery of patients undergoing surgery throughout their entire perioperative journey.<sup>1</sup> These programs aim to reduce complications and promote an earlier return to normal activities.<sup>2,3</sup> 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.<sup>4-6</sup> Evidence-based ERAS protocols have been published across multiple surgical specialties.<sup>1</sup> In early studies, the ERAS approach showed promise in cardiac surgery (CS); however, evidence-based protocols have yet to emerge.<sup>7</sup>

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 evidence-based CS ERAS practices.

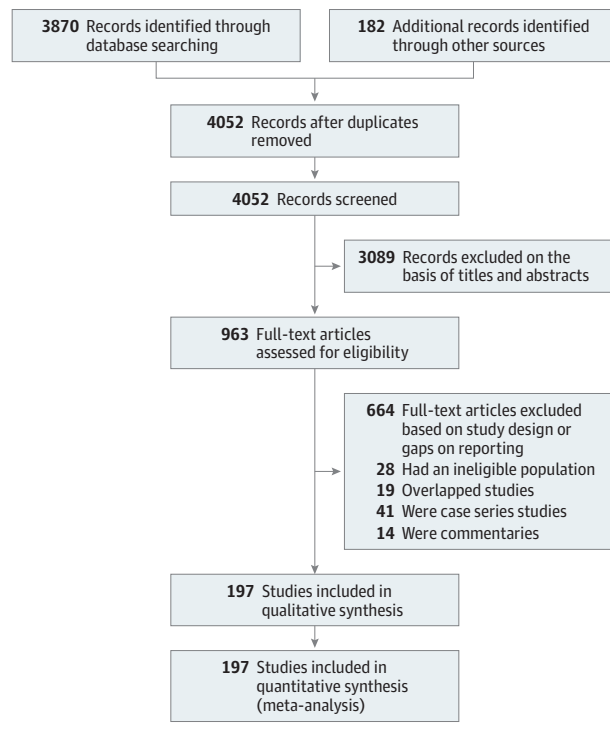
## Methods

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.<sup>8</sup> 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.<sup>9</sup> 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 non-author) screened the abstracts considered for topics. Prospective randomized clinical trials, meta-analyses, 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.<sup>10</sup> 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.<sup>11</sup> 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

Figure. PRISMA Flow Diagram



Heart Association clinical 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 1. 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.<sup>13,14</sup> 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.<sup>15</sup> Despite this recommendation, approximately 25% of patients undergoing CS have hemoglobin A<sub>1c</sub> levels greater than 7%, and 10% have undiagnosed diabetes, indicating a failure to apply current evidence-based recommendations for preoperative diabetes management.<sup>16</sup> A recent retrospective review demonstrated that preadmission glycemic control, as assessed by hemoglobin A<sub>1c</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-

### 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

- A
  - 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
- C-LD
  - 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.)

quality evidence, we recommend preoperative measurement of hemoglobin A<sub>1c</sub> 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

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.<sup>31</sup> In a 2003 Cochrane review<sup>30</sup> of patients undergoing CS, carbohydrate loading reduced postoperative insulin resistance and hospital length of stay. In a large randomized clinical trial<sup>29,30</sup> 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.<sup>33,34</sup> 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.<sup>35</sup> 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.<sup>36,37</sup> 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<sup>37</sup> (class IIa, level C-LD).

**Table 1. Classification of Recommendation and Level of Evidence**

LOE by COR	Recommendation
<b>I</b>	
A	Tranexamic acid or epsilon aminocaproic acid during on-pump cardiac surgical procedures
B-R	Perioperative glycemic control
B-R	A care bundle of evidence-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
<b>IIa</b>	
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
<b>IIb</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
<b>III (No Benefit)</b>	
A	Stripping or breaking the sterile field of chest tubes to remove clots.
<b>III (Harm)</b>	
B-R	Hyperthermia (>37.9°C) while rewarming on cardiopulmonary bypass.

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.

**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

**Table 2. Surgical Site Infection Bundle, Including Classification of Recommendation and Level of Evidence**

LOE by COR	Recommendation
I	
A	Perform topical intranasal decolonization prior to surgery
A	Administer intravenous cephalosporin prophylactic antibiotic 30-60 min prior to surgery
C	Clipping (as opposed to shaving) immediately prior to surgery
IIb	
C	Use a chlorhexidine-alcohol-based solution for skin preparation before surgery
IIa	
C	Remove operative wound dressing after 48 h

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

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.<sup>57,58</sup> 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.<sup>60-62</sup> Two studies validate the reduction of such infections in patients receiving mupirocin.<sup>58,63</sup>

Level IA data exists suggesting that weight-based cephalosporins should be administered fewer than 60 minutes before the skin incision and continued for 48 hours after completion of CS. When the surgery is more than 4 hours, antibiotics require redosing.<sup>64,65</sup> Clarity on the preferability of continuous vs intermittent dosing of cefazolin requires further data.<sup>66</sup> A meta-analysis of skin preparation and depilation protocols indicates that clipping is preferred to shaving.<sup>67</sup> 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.<sup>69,70</sup>

In summary, we recommend the implementation of a care bundle to include topical intranasal therapies to eradicate staphylococcal colonization, weight-based cephalosporin infusion fewer 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 is summarized in Table 2 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.<sup>71-73</sup> Any postoperative hyperthermia within 24 hours after coronary artery bypass grafting has been associated with cognitive dysfunction at 4 to 6 weeks.<sup>71</sup> Rewarming on CPB to normothermia should be combined with continuous surface warming.<sup>74</sup> 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.<sup>75</sup>

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.<sup>75,76</sup> 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.<sup>76</sup> 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<sup>77-79</sup> 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.<sup>80,81</sup> 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.<sup>82,83</sup> 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, cost-effectiveness, 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.<sup>84</sup> Higher dosages, however, appear to be associated with seizures.<sup>85,86</sup> 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).<sup>95,97,98</sup> 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 safest 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 8 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  $\alpha$ -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 in-hospital 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 forced-air 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.<sup>146,147</sup> 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.<sup>148</sup>

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 nonrandomized 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.<sup>155,156</sup> 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.<sup>157-159</sup> Prophylactic anticoagulation for vascular thrombotic events should be considered on the first postoperative day and daily thereafter.<sup>160</sup> A recent medium-quality meta-analysis suggested that chemical prophylaxis could reduce vascular thrombotic event risk without increasing bleeding or cardiac tamponade.<sup>161</sup> 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.<sup>174-176</sup> 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 insulin-like growth factor-binding protein 7) can identify patients as early as 1 hour after CPB who are at increased risk of developing AKI.<sup>177,178</sup>

In a randomized clinical trial after CS, patients with positive urinary biomarkers who were assigned to an intervention algorithm had reductions in subsequent AKI.<sup>179,180</sup> 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.<sup>182</sup> 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.<sup>183</sup> 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.<sup>184-188</sup> 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.<sup>190</sup> 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.<sup>191</sup> This may contribute to postoperative renal dysfunction and suggests that goal-directed 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.<sup>192</sup> Early postoperative enteral feeding and mobilization after surgery are other essential components of ERAS surgical protocols.<sup>1</sup> 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.

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## REFERENCES

- Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg*. 2017;152(3):292-298. doi:10.1001/jamasurg.2016.4952
- Eskicioglu C, Forbes SS, Aarts MA, Okrainec A, McLeod RS. Enhanced recovery after surgery (ERAS) programs for patients having colorectal surgery: a meta-analysis of randomized trials. *J Gastrointest Surg*. 2009;13(12):2321-2329. doi:10.1007/s11605-009-0927-2
- Lassen K, Soop M, Nygren J, et al; Enhanced Recovery After Surgery (ERAS) Group. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. *Arch Surg*. 2009;144(10):961-969. doi:10.1001/archsurg.2009.170
- Spanjersberg WR, Reurings J, Keus F, van Laarhoven CJ. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database Syst Rev*. 2011;(2):CD007635.
- Stone AB, Grant MC, Pio Roda C, et al. Implementation costs of an enhanced recovery after surgery program in the united states: a financial model and sensitivity analysis based on experiences at a quaternary academic medical center. *J Am Coll Surg*. 2016;222(3):219-225. doi:10.1016/j.jamcollsurg.2015.11.021
- Thiele RH, Rea KM, Turrentine FE, et al. Standardization of care: impact of an enhanced recovery protocol on length of stay, complications, and direct costs after colorectal surgery. *J Am Coll Surg*. 2015;220(4):430-443. doi:10.1016/j.jamcollsurg.2014.12.042
- Fleming IO, Garratt C, Guha R, et al. Aggregation of marginal gains in cardiac surgery: feasibility of a perioperative care bundle for enhanced recovery in cardiac surgical patients. *J Cardiothorac Vasc Anesth*. 2016;30(3):665-670. doi:10.1053/j.jvca.2016.01.017
- Graham R, Mancher M, Miller Wolman D, Greenfield S, Steinberg E, eds. *Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines: Clinical Practice Guidelines We Can Trust*. Washington, DC: US: National Academies Press; 2011.
- Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg*. 2010;8(5):336-341. doi:10.1016/j.ijsu.2010.02.007
- Bakaeen FG, Svensson LG, Mitchell JD, Keshavjee S, Patterson GA, Weisel RD. The American Association for Thoracic Surgery/Society of Thoracic Surgeons position statement on developing clinical practice documents. *J Thorac Cardiovasc Surg*. 2017;153(4):999-1005. doi:10.1016/j.jtcvs.2017.01.003
- Gustafsson UO, Scott MJ, Hubner M, et al. Guidelines for perioperative care in elective colorectal surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations: 2018. *World J Surg*. 2019;43(3):659-695. doi:10.1007/s00268-018-4844-y
- Jacobs AK, Anderson JL, Halperin JL, et al; ACC/AHA TASK FORCE MEMBERS. 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 on practice guidelines. *Circulation*. 2014;130(14):1208-1217. doi:10.1161/CIR.000000000000090
- Narayan P, Kshirsagar SN, Mandal CK, et al. Preoperative glycosylated hemoglobin: a risk factor for patients undergoing coronary artery bypass. *Ann Thorac Surg*. 2017;104(2):606-612. doi:10.1016/j.athoracsur.2016.12.020
- Whang W, Bigger JT Jr; The CABG Patch Trial Investigators and Coordinators. Diabetes and outcomes of coronary artery bypass graft surgery in patients with severe left ventricular dysfunction: results from the CABG Patch Trial database. *J Am Coll Cardiol*. 2000;36(4):1166-1172. doi:10.1016/S0735-1097(00)00823-8
- Wong J, Zoungas S, Wright C, Teede H. Evidence-based guidelines for perioperative management of diabetes in cardiac and vascular surgery. *World J Surg*. 2010;34(3):500-513. doi:10.1007/s00268-009-0380-0
- Halkos ME, Puskas JD, Lattouf OM, et al. Elevated preoperative hemoglobin A1c level is predictive of adverse events after coronary artery bypass surgery. *J Thorac Cardiovasc Surg*. 2008;136(3):631-640. doi:10.1016/j.jtcvs.2008.02.091
- Robich MP, Iribarne A, Leavitt BJ, et al; Northern New England Cardiovascular Disease Study Group. Intensity of glycemic control affects long-term survival after coronary artery bypass graft surgery. *Ann Thorac Surg*. 2019;107(2):477-484. doi:10.1016/j.athoracsur.2018.07.078
- Engelman DT, Adams DH, Byrne JG, et al. Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. *J Thorac Cardiovasc Surg*. 1999;118(5):866-873. doi:10.1016/S0022-5223(99)70056-5
- Kudsk KA, Tolley EA, DeWitt RC, et al. Preoperative albumin and surgical site identify surgical risk for major postoperative complications. *JPEN J Parenter Enteral Nutr*. 2003;27(1):1-9. doi:10.1177/014860710302700101
- Lee EH, Kim WJ, Kim JY, et al. Effect of exogenous albumin on the incidence of postoperative acute kidney injury in patients undergoing off-pump coronary artery bypass surgery with a preoperative albumin level of less than 4.0 g/dl. *Anesthesiology*. 2016;124(5):1001-1011. doi:10.1097/ALN.0000000000001051
- Karas PL, Goh SL, Dhital K. Is low serum albumin associated with postoperative complications in patients undergoing cardiac surgery? *Interact Cardiovasc Thorac Surg*. 2015;21(6):777-786.
- Waitzberg DL, Saito H, Plank LD, et al. Postsurgical infections are reduced with specialized nutrition support. *World J Surg*. 2006;30(8):1592-1604. doi:10.1007/s00268-005-0657-x
- Jie B, Jiang ZM, Nolan MT, Zhu SN, Yu K, Kondrup J. Impact of preoperative nutritional support on clinical outcome in abdominal surgical patients at nutritional risk. *Nutrition*. 2012;28(10):1022-1027. doi:10.1016/j.nut.2012.01.017
- Lauck SB, Wood DA, Achtem L, et al. Risk stratification and clinical pathways to optimize length of stay after transcatheter aortic valve replacement. *Can J Cardiol*. 2014;30(12):1583-1587. doi:10.1016/j.cjca.2014.07.012
- McClave SA, Kozar R, Martindale RG, et al. Summary points and consensus recommendations from the North American Surgical Nutrition Summit. *JPEN J Parenter Enteral Nutr*. 2013;37(5)(suppl):99S-105S. doi:10.1177/0148607113495892
- Yu PJ, Cassiere HA, Dellis SL, Manetta F, Kohn N, Hartman AR. Impact of preoperative prealbumin on outcomes after cardiac surgery. *JPEN J Parenter Enteral Nutr*. 2015;39(7):870-874. doi:10.1177/0148607114536735
- Stoppe C, Goetzenich A, Whitman G, et al. Role of nutrition support in adult cardiac surgery: a consensus statement from an international multidisciplinary expert group on nutrition in cardiac surgery. *Crit Care*. 2017;21(1):131. doi:10.1186/s13054-017-1690-5
- Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Task Force on Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration. *Anesthesiology*. 2017;126(3):376-393. doi:10.1097/ALN.0000000000001452
- Brady M, Kinn S, Ness V, O'Rourke K, Randhawa N, Stuart P. Preoperative fasting for preventing perioperative complications in children. *Cochrane Database Syst Rev*. 2009;(4):CD005285.
- Brady M, Kinn S, Stuart P. Preoperative fasting for adults to prevent perioperative complications. *Cochrane Database Syst Rev*. 2003;(4):CD004423.
- Ljungqvist O. Modulating postoperative insulin resistance by preoperative carbohydrate loading. *Best Pract Res Clin Anaesthesiol*. 2009;23(4):401-409. doi:10.1016/j.bpa.2009.08.004
- Järvellä K, Maaranen P, Sisto T. Pre-operative oral carbohydrate treatment before coronary artery bypass surgery. *Acta Anaesthesiol Scand*. 2008;52(6):793-797. doi:10.1111/j.1399-6576.2008.01660.x
- Feguri GR, de Lima PRL, de Cerqueira Borges D, et al. Preoperative carbohydrate load and intraoperatively infused omega-3 polyunsaturated fatty acids positively impact nosocomial morbidity after coronary artery bypass grafting: a double-blind controlled randomized trial. *Nutr J*. 2017;16(1):24. doi:10.1186/s12937-017-0245-6
- Breuer JP, von Dossow V, von Heymann C, et al. Preoperative oral carbohydrate administration to ASA III-IV patients undergoing elective cardiac surgery. *Anesth Analg*. 2006;103(5):1099-1108. doi:10.1213/01.ane.0000237415.18715.1d
- Hibbard JH, Greene J. What the evidence shows about patient activation: better health outcomes and care experiences; fewer data on costs. *Health Aff (Millwood)*. 2013;32(2):207-214. doi:10.1377/hlthaff.2012.1061
- Oshima Lee E, Emanuel EJ. Shared decision making to improve care and reduce costs. *N Engl J Med*. 2013;368(1):6-8. doi:10.1056/NEJMp1209500



37. Cook DJ, Manning DM, Holland DE, et al. Patient engagement and reported outcomes in surgical recovery: effectiveness of an e-health platform. *J Am Coll Surg*. 2013;217(4):648-655. doi:10.1016/j.jamcollsurg.2013.05.003
38. Arthur HM, Daniels C, McKelvie R, Hirsh J, Rush B. Effect of a preoperative intervention on preoperative and postoperative outcomes in low-risk patients awaiting elective coronary artery bypass graft surgery: a randomized, controlled trial. *Ann Intern Med*. 2000;133(4):253-262. doi:10.7326/0003-4819-133-4-200008150-00007
39. Sawatzky JA, Kehler DS, Ready AE, et al. Prehabilitation program for elective coronary artery bypass graft surgery patients: a pilot randomized controlled study. *Clin Rehabil*. 2014;28(7):648-657. doi:10.1177/0269215513516475
40. Stammers AN, Kehler DS, Afilalo J, et al. Protocol for the PREHAB study—Pre-operative Rehabilitation for Reduction of Hospitalization After Coronary Bypass and Valvular Surgery: a randomised controlled trial. *BMJ Open*. 2015;5(3):e007250. doi:10.1136/bmjopen-2014-007250
41. Snowden CP, Prentis J, Jacques B, et al. Cardiorespiratory fitness predicts mortality and hospital length of stay after major elective surgery in older people. *Ann Surg*. 2013;257(6):999-1004. doi:10.1097/SLA.0b013e31828dbac2
42. Valkenet K, van de Port IG, Dronkers JJ, de Vries WR, Lindeman E, Backx FJ. The effects of preoperative exercise therapy on postoperative outcome: a systematic review. *Clin Rehabil*. 2011;25(2):99-111. doi:10.1177/0269215510380830
43. Waite I, Deshpande R, Baghai M, Massey T, Wendler O, Greenwood S. Home-based preoperative rehabilitation (prehab) to improve physical function and reduce hospital length of stay for frail patients undergoing coronary artery bypass graft and valve surgery. *J Cardiothorac Surg*. 2017;12(1):91. doi:10.1186/s13019-017-0655-8
44. Orange ST, Northgraves MJ, Marshall P, Madden LA, Vince RV. Exercise prehabilitation in elective intra-cavity surgery: A role within the ERAS pathway? a narrative review. *Int J Surg*. 2018;56:328-333. doi:10.1016/j.ijsu.2018.04.054
45. Barberan-García A, Ubré M, Roca J, et al. Personalised prehabilitation in high-risk patients undergoing elective major abdominal surgery: a randomized blinded controlled trial. *Ann Surg*. 2018;267(1):50-56. doi:10.1097/SLA.0000000000002293
46. Li C, Carli F, Lee L, et al. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. *Surg Endosc*. 2013;27(4):1072-1082. doi:10.1007/s00464-012-2560-5
47. Gillis C, Li C, Lee L, et al. Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. *Anesthesiology*. 2014;121(5):937-947. doi:10.1097/ALN.0000000000000393
48. Reid MC, Fiellin DA, O'Connor PG. Hazardous and harmful alcohol consumption in primary care. *Arch Intern Med*. 1999;159(15):1681-1689. doi:10.1001/archinte.159.15.1681
49. Gaskill CE, Kling CE, Varghese TK Jr, et al. Financial benefit of a smoking cessation program prior to elective colorectal surgery. *J Surg Res*. 2017;215:183-189. doi:10.1016/j.jss.2017.03.067
50. Levett DZ, Edwards M, Grocott M, Mythen M. Preparing the patient for surgery to improve outcomes. *Best Pract Res Clin Anaesthesiol*. 2016;30(2):145-157. doi:10.1016/j.bpa.2016.04.002
51. Tønnesen H, Nielsen PR, Lauritzen JB, Møller AM. Smoking and alcohol intervention before surgery: evidence for best practice. *Br J Anaesth*. 2009;102(3):297-306. doi:10.1093/bja/aen401
52. Sørensen LT. Wound healing and infection in surgery: the pathophysiological impact of smoking, smoking cessation, and nicotine replacement therapy: a systematic review. *Ann Surg*. 2012;255(6):1069-1079. doi:10.1097/SLA.0b013e31824f632d
53. Wong J, Lam DP, Abrishami A, Chan MT, Chung F. Short-term preoperative smoking cessation and postoperative complications: a systematic review and meta-analysis. *Can J Anaesth*. 2012;59(3):268-279. doi:10.1007/s12630-011-9652-x
54. Oppedal K, Møller AM, Pedersen B, Tønnesen H. Preoperative alcohol cessation prior to elective surgery. *Cochrane Database Syst Rev*. 2012;(7):CD008343.
55. Lavallée JF, Gray TA, Dumville J, Russell W, Cullum N. The effects of care bundles on patient outcomes: a systematic review and meta-analysis. *Implement Sci*. 2017;12(1):142. doi:10.1186/s13012-017-0670-0
56. Mutters NT, De Angelis G, Restuccia G, et al. Use of evidence-based recommendations in an antibiotic care bundle for the intensive care unit. *Int J Antimicrob Agents*. 2018;51(1):65-70. doi:10.1016/j.ijantimicag.2017.06.020
57. Lazar HL, Salm TV, Engelman R, Orgill D, Gordon S. Prevention and management of sternal wound infections. *J Thorac Cardiovasc Surg*. 2016;152(4):962-972. doi:10.1016/j.jtcvs.2016.01.060
58. Bode LG, Kluytmans JA, Wertheim HF, et al. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. *N Engl J Med*. 2010;362(1):9-17. doi:10.1056/NEJMoa0808939
59. Paling FP, Olsen K, Ohneberg K, et al. Risk prediction for *Staphylococcus aureus* surgical site infection following cardiothoracic surgery: a secondary analysis of the V710-P003 trial. *PLoS One*. 2018;13(3):e0193445. doi:10.1371/journal.pone.0193445
60. Courville XF, Tomek IM, Kirkland KB, Birhle M, Kantor SR, Finlayson SR. Cost-effectiveness of preoperative nasal mupirocin treatment in preventing surgical site infection in patients undergoing total hip and knee arthroplasty: a cost-effectiveness analysis. *Infect Control Hosp Epidemiol*. 2012;33(2):152-159. doi:10.1086/663704
61. Hong JC, Saraswat MK, Ellison TA, et al. *Staphylococcus aureus* prevention strategies in cardiac surgery: a cost-effectiveness analysis. *Ann Thorac Surg*. 2018;105(1):47-53. doi:10.1016/j.athoracsur.2017.06.033
62. Murphy E, Spencer SJ, Young D, Jones B, Blyth MJ. MRSA colonisation and subsequent risk of infection despite effective eradication in orthopaedic elective surgery. *J Bone Joint Surg Br*. 2011;93(4):548-551. doi:10.1302/0301-620X.93B4.24969
63. Cimochoowski GE, Harostock MD, Brown R, Bernardi M, Alonzo N, Coyle K. Intranasal mupirocin reduces sternal wound infection after open heart surgery in diabetics and nondiabetics. *Ann Thorac Surg*. 2001;71(5):1572-1578. doi:10.1016/S0003-4975(01)02519-X
64. Edwards FH, Engelman RM, Houck P, Shahian DM, Bridges CR; Society of Thoracic Surgeons. The Society of Thoracic Surgeons practice guideline series: antibiotic prophylaxis in cardiac surgery, part I: duration. *Ann Thorac Surg*. 2006;81(1):397-404. doi:10.1016/j.athoracsur.2005.06.034
65. Engelman R, Shahian D, Shemin R, et al; Workforce on Evidence-Based Medicine, Society of Thoracic Surgeons. The Society of Thoracic Surgeons practice guideline series: antibiotic prophylaxis in cardiac surgery, part II: antibiotic choice. *Ann Thorac Surg*. 2007;83(4):1569-1576. doi:10.1016/j.athoracsur.2006.09.046
66. Trent Magruder J, Grimm JC, Dungan SP, et al. Continuous intraoperative cefazolin infusion may reduce surgical site infections during cardiac surgical procedures: a propensity-matched analysis. *J Cardiothorac Vasc Anesth*. 2015;29(6):1582-1587. doi:10.1053/j.jvca.2015.03.026
67. Tanner J, Norrie P, Melen K. Preoperative hair removal to reduce surgical site infection. *Cochrane Database Syst Rev*. 2011;(11):CD004122.
68. Leaper D, Burman-Roy S, Palanca A, et al; Guideline Development Group. Prevention and treatment of surgical site infection: summary of NICE guidance. *BMJ*. 2008;337:a1924. doi:10.1136/bmj.a1924
69. Ban KA, Minei JP, Laronga C, et al. American College of Surgeons and Surgical Infection Society: surgical site infection guidelines, 2016 update. *J Am Coll Surg*. 2017;224(1):59-74. doi:10.1016/j.jamcollsurg.2016.10.029
70. Keenan JE, Speicher PJ, Thacker JK, Walter M, Kuchibhatla M, Mantyh CR. The preventive surgical site infection bundle in colorectal surgery: an effective approach to surgical site infection reduction and health care cost savings. *JAMA Surg*. 2014;149(10):1045-1052. doi:10.1001/jamasurg.2014.346
71. Grocott HP, Mackensen GB, Grigore AM, et al; Neurologic Outcome Research Group (NORG); Cardiothoracic Anesthesiology Research Endeavors (CARE) Investigators of the Duke Heart Center. Postoperative hyperthermia is associated with cognitive dysfunction after coronary artery bypass graft surgery. *Stroke*. 2002;33(2):537-541. doi:10.1161/hs0202.102600
72. Groom RC, Rassias AJ, Cormack JE, et al; Northern New England Cardiovascular Disease Study Group. Highest core temperature during cardiopulmonary bypass and rate of mediastinitis. *Perfusion*. 2004;19(2):119-125. doi:10.1191/0267659104pf7310a
73. Newland RF, Baker RA, Mazzone AL, Quinn SS, Chew DP; Perfusion Downunder Collaboration. Rewarming temperature during cardiopulmonary bypass and acute kidney injury: a multicenter analysis. *Ann Thorac Surg*. 2016;101(5):1655-1662. doi:10.1016/j.athoracsur.2016.01.086
74. Bar-Yosef S, Mathew JP, Newman MF, Landolfo KP, Grocott HP; Neurological Outcome Research Group; CARE Investigators of the Duke Heart Center. Prevention of cerebral hyperthermia during cardiac surgery by limiting on-bypass rewarming in combination with post-bypass body surface warming: a feasibility study. *Anesth Analg*. 2004;99(3):641-646. doi:10.1213/01.ANE.0000130354.90659.63
75. Allen KB, Thourani VH, Naka Y, et al. Randomized, multicenter trial comparing sternotomy closure with rigid plate fixation to wire cerclage. *J Thorac Cardiovasc Surg*. 2017;153(4):888-896.e1. doi:10.1016/j.jtcvs.2016.10.093
76. Allen KB, Thourani VH, Naka Y, et al. Rigid plate fixation versus wire cerclage: patient-reported and economic outcomes from a randomized trial. *Ann Thorac Surg*. 2018;105(5):1344-1350. doi:10.1016/j.athoracsur.2017.12.011

77. Park JS, Kuo JH, Young JN, Wong MS. Rigid sternal fixation versus modified wire technique for poststernotomy closures: a retrospective cost analysis. *Ann Plast Surg.* 2017;78(5):537-542. doi:10.1097/SAP.0000000000000901
78. Nazerali RS, Hinchcliff K, Wong MS. Rigid fixation for the prevention and treatment of sternal complications. *Ann Plast Surg.* 2014;72(suppl 1):S27-S30. doi:10.1097/SAP.0000000000000155
79. Raman J, Lehmann S, Zehr K, et al. Sternal closure with rigid plate fixation versus wire closure: a randomized controlled multicenter trial. *Ann Thorac Surg.* 2012;94(6):1854-1861. doi:10.1016/j.athoracsur.2012.07.085
80. Christensen MC, Dziejewicz F, Kempel A, von Heymann C. Increased chest tube drainage is independently associated with adverse outcome after cardiac surgery. *J Cardiothorac Vasc Anesth.* 2012;26(1):46-51. doi:10.1053/j.jvca.2011.09.021
81. Dyke C, Aronson S, Dietrich W, et al. Universal definition of perioperative bleeding in adult cardiac surgery. *J Thorac Cardiovasc Surg.* 2014;147(5):1458-1463.e1. doi:10.1016/j.jtcvs.2013.10.070
82. Ferraris VA, Brown JR, Despotis GJ, et al; Society of Thoracic Surgeons Blood Conservation Guideline Task Force; Society of Cardiovascular Anesthesiologists Special Task Force on Blood Transfusion; International Consortium for Evidence Based Perfusion. 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. *Ann Thorac Surg.* 2011;91(3):944-982. doi:10.1016/j.athoracsur.2010.11.078
83. Pagano D, Milojevic M, Meesters MI, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. *Eur J Cardiothorac Surg.* 2018;53(1):79-111. doi:10.1093/ejcts/ezx325
84. Myles PS, Smith JA, Forbes A, et al; ATACAS Investigators of the ANZCA Clinical Trials Network. Tranexamic acid in patients undergoing coronary-artery surgery. *N Engl J Med.* 2017;376(2):136-148. doi:10.1056/NEJMoa1606424
85. Koster A, Faraoni D, Levy JH. Antifibrinolytic therapy for cardiac surgery: an update. *Anesthesiology.* 2015;123(1):214-221. doi:10.1097/ALN.0000000000000688
86. Levy JH, Koster A, Quinones QJ, Milling TJ, Key NS. Antifibrinolytic therapy and perioperative considerations. *Anesthesiology.* 2018;128(3):657-670. doi:10.1097/ALN.0000000000000997
87. Tengborn L, Blombäck M, Berntorp E. Tranexamic acid—an old drug still going strong and making a revival. *Thromb Res.* 2015;135(2):231-242. doi:10.1016/j.thromres.2014.11.012
88. Macisaac RJ, Jerums G. Intensive glucose control and cardiovascular outcomes in type 2 diabetes. *Heart Lung Circ.* 2011;20(10):647-654. doi:10.1016/j.hlc.2010.07.013
89. Moghissi ES, Korytkowski MT, DiNardo M, et al; American Association of Clinical Endocrinologists; American Diabetes Association. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care.* 2009;32(6):1119-1131. doi:10.2337/dc09-9029
90. Selvin E, Marinopoulos S, Berkenblit G, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann Intern Med.* 2004;141(6):421-431. doi:10.7326/0003-4819-141-6-200409210-00007
91. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med.* 2001;345(19):1359-1367. doi:10.1056/NEJMoa011300
92. Gianotti L, Biffi R, Sandini M, et al. Preoperative Oral Carbohydrate Load Versus Placebo in Major Elective Abdominal Surgery (PROCY): a randomized, placebo-controlled, multicenter, phase III trial. *Ann Surg.* 2018;267(4):623-630. doi:10.1097/SLA.0000000000002325
93. Williams JB, McConnell G, Allender JE, et al. One-year results from the first US-based enhanced recovery after cardiac surgery (ERAS cardiac) program. *J Thorac Cardiovasc Surg.* 2018;pii: S0022-5223(18)33225-2.
94. Greisen J, Nielsen DV, Sloth E, Jakobsen CJ. High thoracic epidural analgesia decreases stress hyperglycemia and insulin need in cardiac surgery patients. *Acta Anaesthesiol Scand.* 2013;57(2):171-177. doi:10.1111/j.1399-6576.2012.02731.x
95. Lazar HL, Chipkin SR, Fitzgerald CA, Bao Y, Cabral H, Apstein CS. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. *Circulation.* 2004;109(12):1497-1502. doi:10.1161/01.CIR.0000121747.71054.79
96. Furnary AP, Wu Y. Eliminating the diabetic disadvantage: the Portland Diabetic Project. *Semin Thorac Cardiovasc Surg.* 2006;18(4):302-308. doi:10.1053/j.semctvs.2006.04.005
97. Chaney MA, Nikolov MP, Blakeman BP, Bakhos M. Attempting to maintain normoglycemia during cardiopulmonary bypass with insulin may initiate postoperative hypoglycemia. *Anesth Analg.* 1999;89(5):1091-1095. doi:10.1213/0000539-199911000-00004
98. Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. *Ann Intern Med.* 2007;146(4):233-243. doi:10.7326/0003-4819-146-4-200702200-00002
99. White PF, Kehlet H, Neal JM, Schrickler T, Carr DB, Carli F; Fast-Track Surgery Study Group. The role of the anesthesiologist in fast-track surgery: from multimodal analgesia to perioperative medical care. *Anesth Analg.* 2007;104(6):1380-1396. doi:10.1213/01.ane.0000263034.96885.e1
100. Wick EC, Grant MC, Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: a review. *JAMA Surg.* 2017;152(7):691-697. doi:10.1001/jamasurg.2017.0898
101. Qazi SM, Sindby E, Nørgaard MA. Ibuprofen—a safe analgesic during cardiac surgery recovery? a randomized controlled trial. *J Cardiovasc Thorac Res.* 2015;7(4):141-148. doi:10.1571/jcvtr.2015.31
102. Nussmeier NA, Whelton AA, Brown MT, et al. Complications of the COX-2 inhibitors parecoxib and valdecoxib after cardiac surgery. *N Engl J Med.* 2005;352(11):1081-1091. doi:10.1056/NEJMoa050330
103. Jelacic S, Bollag L, Bowdle A, Rivat C, Cain KC, Richebe P. Intravenous acetaminophen as an adjunct analgesic in cardiac surgery reduces opioid consumption but not opioid-related adverse effects: a randomized controlled trial. *J Cardiothorac Vasc Anesth.* 2016;30(4):997-1004. doi:10.1053/j.jvca.2016.02.010
104. Petring OU, Dawson PJ, Blake DW, et al. Normal postoperative gastric emptying after orthopaedic surgery with spinal anaesthesia and I.M. ketorolac as the first postoperative analgesic. *Br J Anaesth.* 1995;74(3):257-260. doi:10.1093/bja/74.3.257
105. Apfel CC, Turan A, Souza K, Pergolizzi J, Hornuss C. Intravenous acetaminophen reduces postoperative nausea and vomiting: a systematic review and meta-analysis. *Pain.* 2013;154(5):677-689. doi:10.1016/j.pain.2012.12.025
106. Radbruch L, Glaeske G, Grond S, et al. Topical review on the abuse and misuse potential of tramadol and tilidine in Germany. *Subst Abuse.* 2013;34(3):313-320. doi:10.1080/08897077.2012.735216
107. But AK, Erdil F, Yucel A, Gedik E, Durmus M, Ersoy MO. The effects of single-dose tramadol on post-operative pain and morphine requirements after coronary artery bypass surgery. *Acta Anaesthesiol Scand.* 2007;51(5):601-606. doi:10.1111/j.1399-6576.2007.01275.x
108. Joshi SS, Jagadeesh AM. Efficacy of chronic perioperative pregabalin in acute and chronic post-operative pain after off-pump coronary artery bypass surgery: a randomized, double-blind placebo controlled trial. *Ann Card Anaesth.* 2013;16(3):180-185. doi:10.4103/0971-9784.114239
109. Borde DP, Futane SS, Asegaonkar B, et al. Effect of perioperative pregabalin on postoperative quality of recovery in patients undergoing off-pump coronary artery bypass grafting (OPCABG): a prospective, randomized, double-blind trial. *J Cardiothorac Vasc Anesth.* 2017;31(4):1241-1245. doi:10.1053/j.jvca.2016.09.029
110. Menda F, Köner O, Sayin M, Ergenoğlu M, Küçükaksu S, Aykaç B. Effects of single-dose gabapentin on postoperative pain and morphine consumption after cardiac surgery. *J Cardiothorac Vasc Anesth.* 2010;24(5):808-813. doi:10.1053/j.jvca.2009.10.023
111. Khalil MA, Abdel Azeem MS. The impact of dexmedetomidine infusion in sparing morphine consumption in off-pump coronary artery bypass grafting. *Semin Cardiothorac Vasc Anesth.* 2013;17(1):66-71. doi:10.1177/1089253212463969
112. Ji F, Li Z, Young N, Moore P, Liu H. Perioperative dexmedetomidine improves mortality in patients undergoing coronary artery bypass surgery. *J Cardiothorac Vasc Anesth.* 2014;28(2):267-273. doi:10.1053/j.jvca.2013.06.022
113. Liu X, Xie G, Zhang K, et al. Dexmedetomidine vs propofol sedation reduces delirium in patients after cardiac surgery: A meta-analysis with trial sequential analysis of randomized controlled trials. *J Crit Care.* 2017;38:190-196. doi:10.1016/j.jcrc.2016.10.026
114. Cho JS, Shim JK, Soh S, Kim MK, Kwak YL. Perioperative dexmedetomidine reduces the incidence and severity of acute kidney injury following valvular heart surgery. *Kidney Int.* 2016;89(3):693-700. doi:10.1038/ki.2015.306
115. Hudetz JA, Patterson KM, Iqbal Z, et al. Ketamine attenuates delirium after cardiac surgery with cardiopulmonary bypass. *J Cardiothorac Vasc Anesth.* 2009;23(5):651-657. doi:10.1053/j.jvca.2008.12.021
116. Faritous Z, Barzanji A, Azarfarin R, et al. Comparison of bispectral index monitoring with the critical-care pain observation tool in the pain assessment of intubated adult patients after cardiac surgery. *Anesth Pain Med.* 2016;6(4):e38334. doi:10.5812/aapm.38334
117. Gélinas C, Fillion L, Puntillo KA, Viens C, Fortier M. Validation of the critical-care pain

- observation tool in adult patients. *Am J Crit Care*. 2006;15(4):420-427.
- 118.** Payen JF, Bru O, Bosson JL, et al. Assessing pain in critically ill sedated patients by using a behavioral pain scale. *Crit Care Med*. 2001;29(12):2258-2263. doi:10.1097/00003246-200112000-00004
- 119.** Rijkenberg S, Stijlma W, Bosman RJ, van der Meer NJ, van der Voort PHJ. Pain measurement in mechanically ventilated patients after cardiac surgery: comparison of the Behavioral Pain Scale (BPS) and the Critical-Care Pain Observation Tool (CPOT). *J Cardiothorac Vasc Anesth*. 2017;31(4):1227-1234. doi:10.1053/j.jvca.2017.03.013
- 120.** Arenson BG, MacDonald LA, Grocott HP, Hiebert BM, Arora RC. Effect of intensive care unit environment on in-hospital delirium after cardiac surgery. *J Thorac Cardiovasc Surg*. 2013;146(1):172-178. doi:10.1016/j.jtcvs.2012.12.042
- 121.** Barr J, Fraser GL, Puntillo K, et al; American College of Critical Care Medicine. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2013;41(1):263-306. doi:10.1097/CCM.0b013e3182783b72
- 122.** European Delirium Association; American Delirium Society. The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer. *BMC Med*. 2014;12:141. doi:10.1186/s12916-014-0141-2
- 123.** McPherson JA, Wagner CE, Boehm LM, et al. Delirium in the cardiovascular ICU: exploring modifiable risk factors [correction published in *Crit Care Med*. 2013;41(4):e41]. *Crit Care Med*. 2013;41(2):405-413. doi:10.1097/CCM.0b013e31826ab49b
- 124.** Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients. *Crit Care Med*. 2004;32(4):955-962. doi:10.1097/01.CCM.0000119429.16055.92
- 125.** Rudolph JL, Inouye SK, Jones RN, et al. Delirium: an independent predictor of functional decline after cardiac surgery. *J Am Geriatr Soc*. 2010;58(4):643-649. doi:10.1111/j.1532-5415.2010.02762.x
- 126.** Rudolph JL, Jones RN, Grande LJ, et al. Impaired executive function is associated with delirium after coronary artery bypass graft surgery. *J Am Geriatr Soc*. 2006;54(6):937-941. doi:10.1111/j.1532-5415.2006.00735.x
- 127.** Maldonado JR. Neuropathogenesis of delirium: review of current etiologic theories and common pathways. *Am J Geriatr Psychiatry*. 2013;21(12):1190-1222. doi:10.1016/j.jagp.2013.09.005
- 128.** Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med*. 2001;27(5):859-864. doi:10.1007/s001340100909
- 129.** Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA*. 2001;286(21):2703-2710. doi:10.1001/jama.286.21.2703
- 130.** Siddiqi N, Harrison JK, Clegg A, et al. Interventions for preventing delirium in hospitalised non-ICU patients. *Cochrane Database Syst Rev*. 2016;3:CD005563.
- 131.** Young J, Murthy L, Westby M, Akunne A, O'Mahony R; Guideline Development Group. Diagnosis, prevention, and management of delirium: summary of NICE guidance. *BMJ*. 2010;341:c3704. doi:10.1136/bmj.c3704
- 132.** Page VJ, Ely EW, Gates S, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial. *Lancet Respir Med*. 2013;1(7):515-523. doi:10.1016/S2213-2600(13)70166-8
- 133.** van den Boogaard M, Slooter AJC, Brüggemann RJM, et al; REDUCE Study Investigators. Effect of haloperidol on survival among critically ill adults with a high risk of delirium: the REDUCE randomized clinical trial. *JAMA*. 2018;319(7):680-690. doi:10.1001/jama.2018.0160
- 134.** Sessler DI. Perioperative heat balance. *Anesthesiology*. 2000;92(2):578-596. doi:10.1097/0000542-200002000-00042
- 135.** Karalipillai D, Story D, Hart GK, et al. Postoperative hypothermia and patient outcomes after elective cardiac surgery. *Anaesthesia*. 2011;66(9):780-784. doi:10.1111/j.1365-2044.2011.06784.x
- 136.** Karalipillai D, Story D, Hart GK, et al. Postoperative hypothermia and patient outcomes after major elective non-cardiac surgery. *Anaesthesia*. 2013;68(6):605-611. doi:10.1111/anae.12129
- 137.** Campbell G, Alderson P, Smith AF, Warrtig S. Warming of intravenous and irrigation fluids for preventing inadvertent perioperative hypothermia. *Cochrane Database Syst Rev*. 2015;(4):CD009891.
- 138.** Engelen S, Himpe D, Borms S, et al. An evaluation of underbody forced-air and resistive heating during hypothermic, on-pump cardiac surgery. *Anaesthesia*. 2011;66(2):104-110. doi:10.1111/j.1365-2044.2010.06609.x
- 139.** Grocott HP, Mathew JP, Carver EH, Phillips-Bute B, Landolfo KP, Newman MF; Duke Heart Center Neurologic Outcome Research Group. A randomized controlled trial of the Arctic Sun temperature management system versus conventional methods for preventing hypothermia during off-pump cardiac surgery. *Anesth Analg*. 2004;98(2):298-302. doi:10.1213/01.ANE.0000096242.06561.C0
- 140.** Karimov JH, Gillinov AM, Schenck L, et al. Incidence of chest tube clogging after cardiac surgery: a single-center prospective observational study. *Eur J Cardiothorac Surg*. 2013;44(6):1029-1036. doi:10.1093/ejcts/ezt140
- 141.** Shalli S, Saeed D, Fukamachi K, et al. Chest tube selection in cardiac and thoracic surgery: a survey of chest tube-related complications and their management. *J Card Surg*. 2009;24(5):503-509. doi:10.1111/j.1540-8191.2009.00905.x
- 142.** Balzer F, von Heymann C, Boyle EM, Wernecke KD, Grubitzsch H, Sander M. Impact of retained blood requiring reintervention on outcomes after cardiac surgery. *J Thorac Cardiovasc Surg*. 2016;152(2):595-601.e4. doi:10.1016/j.jtcvs.2016.03.086
- 143.** Boyle EM Jr, Gillinov AM, Cohn WE, Ley SJ, Fischlein T, Perrault LP. Retained blood syndrome after cardiac surgery: a new look at an old problem. *Innovations (Phila)*. 2015;10(5):296-303.
- 144.** Tauriainen TKE, Morosin MA, Airaksinen J, Biancari F. Outcome after procedures for retained blood syndrome in coronary surgery. *Eur J Cardiothorac Surg*. 2017;51(6):1078-1085. doi:10.1093/ejcts/ezx015
- 145.** St-Onge S, Perrault LP, Demers P, et al. Pericardial blood as a trigger for postoperative atrial fibrillation after cardiac surgery. *Ann Thorac Surg*. 2018;105(1):321-328. doi:10.1016/j.athoracsur.2017.07.045
- 146.** Day TG, Perring RR, Gofton K. Is manipulation of mediastinal chest drains useful or harmful after cardiac surgery? *Interact Cardiovasc Thorac Surg*. 2008;7(5):888-890. doi:10.1510/icvts.2008.185413
- 147.** Halm MA. To strip or not to strip? physiological effects of chest tube manipulation. *Am J Crit Care*. 2007;16(6):609-612.
- 148.** Boyacıoğlu K, Kalender M, Özkaynak B, Mert B, Kayalar N, Erentuğ V. A new use of Fogarty catheter: chest tube clearance. *Heart Lung Circ*. 2014;23(10):e229-e230. doi:10.1016/j.hlc.2014.04.255
- 149.** Grieshaber P, Heim N, Herzberg M, Niemann B, Roth P, Boening A. Active chest tube clearance after cardiac surgery is associated with reduced reexploration rates. *Ann Thorac Surg*. 2018;105(6):1771-1777. doi:10.1016/j.athoracsur.2018.01.002
- 150.** Maltais S, Davis ME, Haglund NA, et al. Active clearance of chest tubes reduces re-exploration for bleeding after ventricular assist device implantation. *ASAIO J*. 2016;62(6):704-709. doi:10.1097/MAT.0000000000000437
- 151.** Perrault LP, Pellerin M, Carrier M, et al. The PleuraFlow Active chest tube clearance system: initial clinical experience in adult cardiac surgery. *Innovations (Phila)*. 2012;7(5):354-358.
- 152.** Sirch J, Ledwon M, Püski T, Boyle EM, Pfeiffer S, Fischlein T. Active clearance of chest drainage catheters reduces retained blood. *J Thorac Cardiovasc Surg*. 2016;151(3):832-838.e2. doi:10.1016/j.jtcvs.2015.10.015
- 153.** St-Onge S, Ben Ali W, Bouhout I, et al. Examining the impact of active clearance of chest drainage catheters on postoperative atrial fibrillation. *J Thorac Cardiovasc Surg*. 2017;154(2):501-508. doi:10.1016/j.jtcvs.2017.03.046
- 154.** Gercekoglu H, Aydin NB, Dagdeviren B, et al. Effect of timing of chest tube removal on development of pericardial effusion following cardiac surgery. *J Card Surg*. 2003;18(3):217-224. doi:10.1046/j.1540-8191.2003.02020.x
- 155.** Edelman JJ, Reddel CJ, Kritharides L, et al. Natural history of hypercoagulability in patients undergoing coronary revascularization and effect of preoperative myocardial infarction. *J Thorac Cardiovasc Surg*. 2014;148(2):536-543. doi:10.1016/j.jtcvs.2013.10.028
- 156.** Parolari A, Mussoni L, Frigerio M, et al. Increased prothrombotic state lasting as long as one month after on-pump and off-pump coronary surgery. *J Thorac Cardiovasc Surg*. 2005;130(2):303-308. doi:10.1016/j.jtcvs.2004.11.002
- 157.** Hill J, Treasure T. Senkung des Risikos für venöse Thromboembolien bei stationären Patienten: Zusammenfassung der NICE-Leitlinien. *Praxis (Bern)*. 2010;99(16):977-980. doi:10.1024/1661-8157/a000221
- 158.** Kakkos SK, Caprini JA, Geroulakos G, et al. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism. *Cochrane Database Syst Rev*. 2016;9:CD005258.
- 159.** Sachdeva A, Dalton M, Lees T. Graduated compression stockings for prevention of deep vein thrombosis. *Cochrane Database Syst Rev*. 2018;11:CD001484.
- 160.** Dunning J, Versteegh M, Fabbri A, et al; EACTS Audit and Guidelines Committee. Guideline on antiplatelet and anticoagulation management in cardiac surgery. *Eur J Cardiothorac Surg*. 2008;34(1):73-92. doi:10.1016/j.ejcts.2008.02.024
- 161.** Ho KM, Bham E, Pavey W. Incidence of venous thromboembolism and benefits and risks of thromboprophylaxis after cardiac surgery:

- a systematic review and meta-analysis. *J Am Heart Assoc*. 2015;4(10):e002652. doi:10.1161/JAHA.115.002652
162. Ahmed AB, Koster A, Lance M, Faraoni D; ESA VTE Guidelines Task Force. European guidelines on perioperative venous thromboembolism prophylaxis: cardiovascular and thoracic surgery. *Eur J Anaesthesiol*. 2018;35(2):84-89.
163. Rajakaruna C, Rogers CA, Angelini GD, Ascione R. Risk factors for and economic implications of prolonged ventilation after cardiac surgery. *J Thorac Cardiovasc Surg*. 2005;130(5):1270-1277. doi:10.1016/j.jtcvs.2005.06.050
164. Barker J, Martino R, Reichardt B, Hickey EJ, Ralph-Edwards A. Incidence and impact of dysphagia in patients receiving prolonged endotracheal intubation after cardiac surgery. *Can J Surg*. 2009;52(2):119-124.
165. Camp SL, Stamou SC, Stiegel RM, et al. Can timing of tracheal extubation predict improved outcomes after cardiac surgery? *HSR Proc Intensive Care Cardiovasc Anesth*. 2009;1(2):39-47.
166. Camp SL, Stamou SC, Stiegel RM, et al. Quality improvement program increases early tracheal extubation rate and decreases pulmonary complications and resource utilization after cardiac surgery. *J Card Surg*. 2009;24(4):414-423. doi:10.1111/j.1540-8191.2008.00783.x
167. Cheng DC, Karski J, Peniston C, et al. Morbidity outcome in early versus conventional tracheal extubation after coronary artery bypass grafting: a prospective randomized controlled trial. *J Thorac Cardiovasc Surg*. 1996;112(3):755-764. doi:10.1016/S0022-5223(96)70062-4
168. Cheng DC, Wall C, Djajani G, et al. Randomized assessment of resource use in fast-track cardiac surgery 1-year after hospital discharge. *Anesthesiology*. 2003;98(3):651-657. doi:10.1097/0000542-200303000-00013
169. Guller U, Anstrom KJ, Holman WL, Allman RM, Sansom M, Peterson ED. Outcomes of early extubation after bypass surgery in the elderly. *Ann Thorac Surg*. 2004;77(3):781-788. doi:10.1016/j.athoracsur.2003.09.059
170. Konstantakos AK, Lee JH. Optimizing timing of early extubation in coronary artery bypass surgery patients. *Ann Thorac Surg*. 2000;69(6):1842-1845. doi:10.1016/S0003-4975(00)01248-0
171. London MJ, Shroyer AL, Coll JR, et al. Early extubation following cardiac surgery in a veterans population. *Anesthesiology*. 1998;88(6):1447-1458. doi:10.1097/0000542-199806000-00006
172. Flynn BC, He J, Richey M, Wirtz K, Daon E. Early extubation without increased adverse events in high-risk cardiac surgical patients. *Ann Thorac Surg*. 2019;107(2):453-459. doi:10.1016/j.athoracsur.2018.09.034
173. Meade MO, Guyatt G, Butler R, et al. Trials comparing early vs late extubation following cardiovascular surgery. *Chest*. 2001;120(6)(suppl):445S-453S. doi:10.1378/chest.120.6\_suppl.445S
174. Hu J, Chen R, Liu S, Yu X, Zou J, Ding X. Global incidence and outcomes of adult patients with acute kidney injury after cardiac surgery: a systematic review and meta-analysis. *J Cardiothorac Vasc Anesth*. 2016;30(1):82-89. doi:10.1053/j.jvca.2015.06.017
175. Kuitunen A, Vento A, Suojäranta-Ylinen R, Pettilä V. Acute renal failure after cardiac surgery: evaluation of the RIFLE classification. *Ann Thorac Surg*. 2006;81(2):542-546. doi:10.1016/j.athoracsur.2005.07.047
176. Xie X, Wan X, Ji X, et al. Reassessment of acute kidney injury after cardiac surgery: a retrospective study. *Intern Med*. 2017;56(3):275-282. doi:10.2169/internalmedicine.56.7638
177. Kashani K, Al-Khafaji A, Ardiles T, et al. Discovery and validation of cell cycle arrest biomarkers in human acute kidney injury. *Crit Care*. 2013;17(1):R25. doi:10.1186/cc12503
178. Mayer T, Bolliger D, Scholz M, et al. Urine biomarkers of tubular renal cell damage for the prediction of acute kidney injury after cardiac surgery: a pilot study. *J Cardiothorac Vasc Anesth*. 2017;31(6):2072-2079. doi:10.1053/j.jvca.2017.04.024
179. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract*. 2012;120(4):c179-c184.
180. Meersch M, Schmidt C, Hoffmeier A, et al. Prevention of cardiac surgery-associated AKI by implementing the KDIGO guidelines in high risk patients identified by biomarkers: the PrevAKI randomized controlled trial. *Intensive Care Med*. 2017;43(11):1551-1561. doi:10.1007/s00134-016-4670-3
181. Göcze I, Jauch D, Götz M, et al. Biomarker-guided intervention to prevent acute kidney injury after major surgery: the prospective randomized BigpAK study. *Ann Surg*. 2018;267(6):1013-1020. doi:10.1097/SLA.0000000000002485
182. Vanmassenhove J, Kielstein J, Jörres A, Biesen WV. Management of patients at risk of acute kidney injury. *Lancet*. 2017;389(10084):2139-2151. doi:10.1016/S0140-6736(17)31329-6
183. Thomson R, Meeran H, Valencia O, Al-Subaie N. Goal-directed therapy after cardiac surgery and the incidence of acute kidney injury. *J Crit Care*. 2014;29(6):997-1000. doi:10.1016/j.jcrr.2014.06.011
184. Osawa EA, Rhodes A, Landoni G, et al. Effect of perioperative goal-directed hemodynamic resuscitation therapy on outcomes following cardiac surgery: a randomized clinical trial and systematic review. *Crit Care Med*. 2016;44(4):724-733.
185. Dalfino L, Giglio MT, Puntillo F, Marucci M, Brienza N. Hemodynamic goal-directed therapy and postoperative infections: earlier is better, a systematic review and meta-analysis. *Crit Care*. 2011;15(3):R154. doi:10.1186/cc10284
186. Sun Y, Chai F, Pan C, Romeiser JL, Gan TJ. Effect of perioperative goal-directed hemodynamic therapy on postoperative recovery following major abdominal surgery—a systematic review and meta-analysis of randomized controlled trials. *Crit Care*. 2017;21(1):141. doi:10.1186/s13054-017-1728-8
187. Goepfert MS, Richter HP, Zu Eulenburg C, et al. Individually optimized hemodynamic therapy reduces complications and length of stay in the intensive care unit: a prospective, randomized controlled trial. *Anesthesiology*. 2013;119(4):824-836. doi:10.1097/ALN.0b013e31829bd770
188. Aya HD, Cecconi M, Hamilton M, Rhodes A. Goal-directed therapy in cardiac surgery: a systematic review and meta-analysis. *Br J Anaesth*. 2013;110(4):510-517. doi:10.1093/bja/aet020
189. Baron DM, Hochrieser H, Posch M, et al; European Surgical Outcomes Study (EuSOS) group for Trials Groups of European Society of Intensive Care Medicine; European Society of Anaesthesiology. Preoperative anaemia is associated with poor clinical outcome in non-cardiac surgery patients. *Br J Anaesth*. 2014;113(3):416-423. doi:10.1093/bja/aeu098
190. Muñoz M, Acheson AG, Auerbach M, et al. International consensus statement on the peri-operative management of anaemia and iron deficiency. *Anaesthesia*. 2017;72(2):233-247. doi:10.1111/anae.13773
191. Lannemyr L, Bragadottir G, Hjärpe A, Redfors B, Ricksten SE. Impact of cardiopulmonary bypass flow on renal oxygenation in patients undergoing cardiac operations. *Ann Thorac Surg*. 2019;107(2):505-511. doi:10.1016/j.athoracsur.2018.08.085
192. Zamani MM, Najafi A, Sehat S, et al. The effect of intraoperative lung protective ventilation vs conventional ventilation, on postoperative pulmonary complications after cardiopulmonary bypass. *J Cardiovasc Thorac Res*. 2017;9(4):221-228. doi:10.15171/jcvtr.2017.38
193. Engelman RM, Rousou JA, Flack JE III, et al. Fast-track recovery of the coronary bypass patient. *Ann Thorac Surg*. 1994;58(6):1742-1746. doi:10.1016/0003-4975(94)91674-8
194. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth*. 1997;78(5):606-617.