

# Pain management and opioid stewardship in adult cardiac surgery: Joint consensus report of the PeriOperative Quality Initiative and the Enhanced Recovery After Surgery Cardiac Society

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## ABSTRACT

**Background:** Opioid-based anesthesia and analgesia is a traditional component of perioperative care for the cardiac surgery patient. Growing enthusiasm for Enhanced Recovery Programs (ERPs) coupled with evidence of potential harm associated with high-dose opioids suggests that we reconsider the role of opioids in cardiac surgery.

**Methods:** An interdisciplinary North American panel of experts, using a structured appraisal of the literature and a modified Delphi method, derived consensus recommendations for optimal pain management and opioid stewardship for cardiac surgery patients. Individual recommendations are graded based on the strength and level of evidence.

**Results:** The panel addressed 4 main topics: the harms associated with historical opioid use, the benefits of more targeted opioid administration, the use of nonopioid medications and techniques, and patient and provider education. A key principle that emerged is that opioid stewardship should apply to all cardiac surgery patients, entailing judicious and targeted use of opioids to achieve optimal analgesia with the fewest potential side effects. The process resulted in the promulgation of 6 recommendations regarding pain management and opioid stewardship in cardiac surgery, focused on avoiding the use of high-dose opioids, as well as encouraging more widespread application of foundational aspects of ERPs, such as the use of multimodal nonopioid medications and regional anesthesia techniques, formal patient and provider education, and structured system-level opioid prescription practices.

**Conclusions:** Based on the available literature and expert consensus, there is an opportunity to optimize anesthesia and analgesia for cardiac surgery patients. Although additional research is needed to establish specific strategies, core principles of pain management and opioid stewardship apply to the cardiac surgery population. (*J Thorac Cardiovasc Surg* 2023; ■:1-12)

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No human subject research occurred, and thus Institutional Review Board approval was not required.

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	PREOP Clinic	PREOP Unit	INTRAOOP	ICU/Wards	Home
General		Education, Patient Engagement & Setting Pain Management Expectations			Optimizing Education, Pain Assessment & Reinforcement of Pain Expectations
Analgesics			Scheduled nonopioid Scheduled gabapentinoid (preoperatively)		NSAIDs as needed (selective)
Local			Regional, neuraxial, paravertebral, local nerve block		
Adjuvants			Atenolol infusion Dexamethasone infusion		
Opioids				Short-acting Opioids based on opioid stewardship principles	

○ Recommended □ May Consider

**Recommendations for pain management and opioid stewardship in cardiac surgery.** © PeriOperative Quality Initiative.

## CENTRAL MESSAGE

This document provides core principles, comprehensive strategies, and graded recommendations regarding pain management and opioid stewardship in adult cardiac surgery.

## PERSPECTIVE

A joint conference between the PeriOperative Quality Initiative and Enhanced Recovery After Surgery Cardiac Society convened to appraise the literature and provide guidance on pain management in the cardiac surgery population. Core principles emerged that support opioid stewardship in cardiac surgery, including the use of nonopioid medications and techniques, patient and provider education, and structured system-level opioid prescription practices.

See Commentary on page XXX.

**Abbreviations and Acronyms**

ERAS	= Enhanced Recovery After Surgery
ERP	= Enhanced Recovery Program
IV	= intravenous
LOE	= level of evidence
NSAID	= nonsteroidal anti-inflammatory drug
ORADE	= opioid-related adverse drug event
PO	= per os
POU	= persistent opioid use
POQI	= PeriOperative Quality Initiative



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The opioid-based cardiac anesthetic technique originated in the late 1960s, when high-dose intravenous (IV) morphine was demonstrated to be a remarkably hemodynamically stable primary anesthetic agent for a series of patients undergoing open heart surgery.<sup>1</sup> As a result, the approach was broadly accepted as commonplace and continues to be promoted in anesthesiology textbooks. As the chapter in *Clinical Anesthesia* titled “Anesthesia for Cardiac Surgery” states, “Opioids lack negative inotropic effects in the doses used clinically and have thus found widespread use as the primary agents for cardiac surgery.”<sup>2</sup> Since the original description of a morphine-based technique, synthetic opioids, including fentanyl, sufentanil, and remifentanyl, have become the primary opioids in use, coupled with other elements of balanced anesthesia to comprise the modern-day cardiac anesthetic—one that remains largely based on opioid administration for analgesia.

Enhanced Recovery Programs (ERPs) involve the bundled provision of evidence-based interventions throughout the surgical encounter to reduce the surgical insult and improve postoperative recovery.<sup>3</sup> Principles of ERP, originally described in non-cardiac surgery patients,

have now been applied to cardiac surgery patients as well.<sup>4,5</sup> A core goal is to optimize pain management through the use of multimodal analgesics, reducing reliance on opioids.<sup>6,7</sup> Existing guidelines either provide pain management recommendations that are not specific for cardiac surgery patients<sup>6,7</sup> or do not provide specific recommendations for pain management techniques. To address this issue, as well as the growing interest in perioperative pathway development and mounting evidence of the potential issues associated with opioid-based techniques, a joint conference between the PeriOperative Quality Initiative (POQI) and Enhanced Recovery After Surgery (ERAS) Cardiac Society was convened to appraise the available literature and provide guidance on pain management and opioid use in the cardiac surgery population. We hypothesized that a formal review and appraisal of the existing literature would reveal strategies to both reduce opioid administration and optimize pain management in the cardiac surgery population.

**METHODS**

POQI is a nonprofit organization that assembles international, multidisciplinary groups to develop recommendations on key topics pertinent to perioperative medicine.<sup>8</sup> On October 20 to 22, 2021, the eighth POQI meeting convened in person in conjunction with the ERAS Cardiac Society to address topics relevant to the perioperative management of cardiac surgery patients. A group of experts were identified with clinical backgrounds in anesthesiology, surgery, critical care, pain medicine, and nursing, with a particular focus on cardiac surgery. This report is the result of a subgroup who appraised the literature on pain management and opioid stewardship in the setting of cardiac surgery. Four predetermined topics were addressed by the subgroup and later refined to 4 questions during the conference and subsequent proceedings: (1) are high-dose opioid based techniques harmful to cardiac surgery patients?; (2) how should opioids be used in cardiac surgery patients?; (3) what nonopioid analgesics or regional techniques are available for analgesia in cardiac surgery patients?; and (4) what other interventions facilitate judicious use of opioids in cardiac surgery patients?

The joint POQI/ERAS Cardiac Society conference was a consensus-building initiative using the modified Delphi process (Figure E1), with participants selected to ensure representation of a wide range of backgrounds based on expertise in principles of perioperative pain management for cardiac surgery patients. Questions were refined and recommendations were developed over several days using alternating plenary sessions and small group discussions, and consensus was reached on main issues within each topic. The modified Delphi method used has been previously described in POQI consensus statements<sup>8</sup> and includes iterative steps from an initial literature review to building consensus on questions and recommendations related to the topic. Content refinement continued until

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Received for publication Sept 12, 2022; revisions received Jan 7, 2023; accepted for publication Jan 19, 2023.

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0022-5223

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<https://doi.org/10.1016/j.jtcvs.2023.01.020>

agreement was achieved, resulting in a formal consensus document. Strength of evidence and recommendations were established using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology.<sup>9</sup> Accompanying recommendations were endorsed after large group discussion, with a majority vote representing confirmation. Dissenting votes and associated comments were recorded. For the content included in the document, we performed a scoping review of the literature and searched PubMed from inception to December 2021. All co-authors participated in the literature search and consolidated relevant references to a central repository. The search was limited to human trials and articles published in English. During the conference and thereafter as a writing group, reference applicability to the topic was discussed, and disagreements were resolved by group consensus. Because no human subject research occurred, Institutional Review Board approval was not required.

## RESULTS AND DISCUSSION

This section presents the results and a synopsis of the evidence review and modified Delphi process. Questions and recommendations are summarized in Table 1, and the final voting is provided in Table E1.

### Question 1: Are High-Dose Opioid-Based Techniques Harmful to Cardiac Surgery Patients?

At the end of the 20th century, the cardiac surgery perioperative community recognized the challenges associated with excessive opioid use. High-dose opioids, associated with prolonged mechanical ventilation, contributed to protracted postoperative recovery, including the potential for lengthy intensive care. This led to the adoption of fast-track cardiac surgery, which, among other objectives, endeavored to reduce the absolute amount and duration of opioids administered.<sup>10,11</sup> Fast-track cardiac surgery was associated with shorter duration of mechanical ventilation and intensive care unit length of stay but yielded

inconsistent results regarding postoperative complications and was not found to impact overall length of stay or mortality.<sup>12</sup> Two meta-analyses comparing high-dose (defined in those analyses as fentanyl >20 µg/kg, sufentanil >2 µg/kg, remifentanyl >1.7 mg, and morphine >2 mg/kg) versus low-dose opioids in cardiac surgery found that low-dose opioid administration was associated with shorter postoperative intubation time, but there was no significant difference in the risk of myocardial infarction, stroke, or reintubation between the 2 regimens.<sup>13,14</sup>

The literature is replete with evidence of the multiorgan side effects of opioids, including somnolence, delirium, sleep-disordered breathing, pruritus, nausea/vomiting, constipation, and urinary retention. These side effects are emphasized in noncardiac surgery, particularly among the outpatient and colorectal surgery populations, where the effects most notably impact the overall rate of recovery. In contrast, in cardiac surgery patients, opioid-related adverse drug events (ORADEs) are largely underappreciated. A study of Medicare patients undergoing cardiac surgery suggested that although ORADEs were documented in 0.7% of patients (743 of 110,158), approximately one-third of the patients (32.4%; 35,658 of 110,158) likely experienced 1 of these events during their hospital stay.<sup>15</sup> Although the consequence of numerous potential factors, postoperative nausea and vomiting, a common side effect of opioid-based analgesia, also likely is underrepresented as a complication in cardiac surgery, with the recent literature reporting 60% to 80% of patients experiencing nausea or vomiting within 24 hours of cardiac surgery.<sup>16</sup> ORADEs are more likely with higher opioid doses,<sup>10,11</sup> are associated with longer length of stay and greater healthcare expense, but

TABLE 1. Summary of questions and graded recommendations for pain management in cardiac surgery patients

Question	Recommendation	Strength*	LOE†
1. Are high-dose opioid-based techniques harmful for cardiac surgery patients?	1. We recommend against the routine use of high-dose opioid anesthesia or analgesia for patients undergoing cardiac surgery.	Strong	B
2. How should opioids be used in cardiac surgery patients?	2. We recommend implementation of perioperative opioid stewardship for patients undergoing cardiac surgery.	Strong	B
3. What nonopioid analgesics or regional techniques are available for analgesia in cardiac surgery patients?	3. We recommend the use of multimodal, nonopioid analgesics for patients undergoing cardiac surgery.	Strong	C
	4. We recommend that clinicians consider the use of regional techniques for patients undergoing cardiac surgery.	Weak	C
4. What other interventions facilitate judicious use of opioids in cardiac surgery patients?	5. We recommend that patients and healthcare providers receive formal education on perioperative analgesia for cardiac surgery, including pain management expectations, analgesic options, and potential side effects.	Strong	C
	6. We recommend the development of program-specific multidisciplinary pathways for perioperative pain management.	Strong	C

LOE, Level of evidence. \*Strength of recommendation according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process. †Level of evidence according to the GRADE process.

are not reported to centralized data repositories, including the Society of Thoracic Surgeons Adult Cardiac Surgery Database.

Perioperative opioid exposure carries an additional risk owing to an association with new persistent opioid use (POU), which is generally defined as previously opioid-naïve patients continuing to fill an opioid prescription 90 to 180 days after surgery. Multiple studies in cardiac surgery patients have found incidence rates of new POU between 5% and 15%,<sup>17,18</sup> in contrast with incidence rates observed in the non-cardiac surgery population of 5.9% after minor surgery and 6.5% after major surgery.<sup>19</sup> The most common predictor of new POU in these studies was the amount of opioids prescribed on discharge,<sup>20</sup> which also is associated with an increased risk of opioid misuse, abuse, or diversion.<sup>21</sup> Patients with new POU after cardiac surgery require more emergency department visits and have higher health care expenditures within the first 6 months postsurgery.<sup>22</sup>

Despite the theoretical benefits of high-dose opioids for cardiac surgery, low-dose opioid regimens have demonstrated similar hemodynamic profiles in addition to improving certain recovery milestones.<sup>14</sup> ORADEs and new POU are underappreciated complications following cardiac surgery and may have costly individual and societal implications. These findings suggest that at best, high-dose opioid-based techniques are not superior to low-dose alternatives and at worst, may be associated with harm.

**Recommendation 1:** *We recommend against the routine use of high-dose opioid anesthesia or analgesia for patients undergoing cardiac surgery (grade: strong; level of evidence [LOE]: B).*

### **Question 2: How Should Opioids Be Used in Cardiac Surgery Patients?**

Opioid stewardship is defined as “the judicious use of opioids to treat surgical pain and optimize postoperative patient outcomes.”<sup>23</sup> Given concerns for ORADEs and POU, there may be a tendency to move toward opioid avoidance. Instead, opioid stewardship calls on providers to use opioids to ensure patient comfort and functional recovery and cautions against an arbitrary reduction of opioids, potentially at the expense of optimal pain management.<sup>6,7</sup> Furthermore, intraoperative providers are appropriately reticent to reduce intraoperative opioid use without the provision of an alternative agent to provide the necessary anesthesia to both avoid recall and meet hemodynamic goals. Opioids provide their greatest value when given in the lowest effective dose for the shortest duration possible. To that end, although reconsideration of their historical role and dosing paradigms is recommended, opioids retain an important role in both acute pain and intraoperative management.

Although opioids are commonly administered during and after cardiac surgery, providers are increasingly favoring

short-acting agents to provide significant pain relief quickly and with easy titratability. Despite this, opioids have been implicated for their potential to induce acute tolerance and hyperalgesia, particularly with short- and ultra-short-acting forms (ie, fentanyl and remifentanyl),<sup>24</sup> contributing to a scenario in which subsequent opioid dosing is rapidly escalated to achieve similar pain control. Tolerance is “unpredictable, with a narrow therapeutic window between desired effects (analgesia) and undesirable side effects.”<sup>24</sup> As a result, there are several examples of the preemptive use of long-acting opioids in the cardiac surgery setting. Murphy and colleagues<sup>25</sup> prospectively compared the use of IV methadone (0.3 mg/kg; maximum dose, 30 mg) to fentanyl (12 µg/kg) for cardiac surgery and reported that the patients who received methadone required less total opioids and had a clinically meaningful reduction in pain scores for 24 hours after surgery, albeit with similar opioid-related complications and recovery milestones. Follow-up suggested lower pain scores throughout the first month as well.<sup>26</sup> A systematic review concluded that 0.1 to 0.3 mg/kg of methadone significantly reduces postoperative opioid use and pain scores compared with shorter-acting alternatives, such as morphine and fentanyl.<sup>27</sup> Intrathecal morphine (5 µg/kg) is associated with an approximate 50% reduction in opioid administration at 24 and 48 hours after surgery, as well as improved visual analog pain scores compared with placebo, although with an increased likelihood of nausea.<sup>28</sup> Based on propensity score-matched analysis, intrathecal morphine is associated with reduced postoperative pulmonary complications compared with IV opioids.<sup>29</sup> Both methadone and intrathecal morphine, as “opioid-sparing opioids,” may reduce rescue opioid requirements, thereby improving pain management and limiting reliance on short-acting alternatives.

Opioid stewardship means the judicious use of opioids, balancing the benefits of optimal analgesia against the side effects and risks of opioid use. The desire to seek opioid-free perioperative care, although noteworthy, does not usually account for the current gaps in understanding regarding the appropriateness of such a strategy in the surgical setting<sup>30,31</sup> or the potential associated risks. It is more advisable to consider opioid-sparing perioperative care, optimizing the delivery of opioids to their greatest potential.

**Recommendation 2:** *We recommend implementation of perioperative opioid stewardship for patients undergoing cardiac surgery (grade: strong; LOE: B).*

### **Question 3: What Nonopioid Analgesics or Regional Techniques Are Available for Analgesia in Cardiac Surgery Patients?**

Pain management is a complex and continuously evolving field and an integral component of perioperative care. Numerous expert groups endorse the use of multimodal analgesic strategies to achieve optimal pain control,

a core tenet of ERPs for both noncardiac and cardiac surgery.<sup>32-34</sup> Multimodal analgesia emphasizes the concurrent use of several mechanistically different agents to provide additive, if not synergistic, analgesic effects.<sup>35</sup> A particular benefit of this is reduced reliance on one medication class (ie, opioids), reducing the likelihood of associated harmful side effects. Although the efficacy and safety of multiple medications has been validated in the noncardiac surgery population,<sup>7,35</sup> similar studies in cardiac surgery are comparatively sparse. This poses a challenge because, although some evidence is readily transferrable, there are circumstances unique to cardiac surgery requiring additional caution when considering certain classes of medications. Table 2 summarizes the typical dosing for key non-opioid medications and specific considerations for cardiac surgery patients. The decision to use a given agent or agents requires consideration of anticipated efficacy (ie, pain control and opioid-sparing potential; Figure 1), individual risk profile, patient- and procedure-specific limitations, availability of alternative techniques, and local workflows and provider expertise.

**Acetaminophen.** Acetaminophen is generally unstudied in cardiac surgery, with the exception of the IV formulation, which has been shown in small, randomized trials to reduce opioid consumption, yield similar pain scores, and

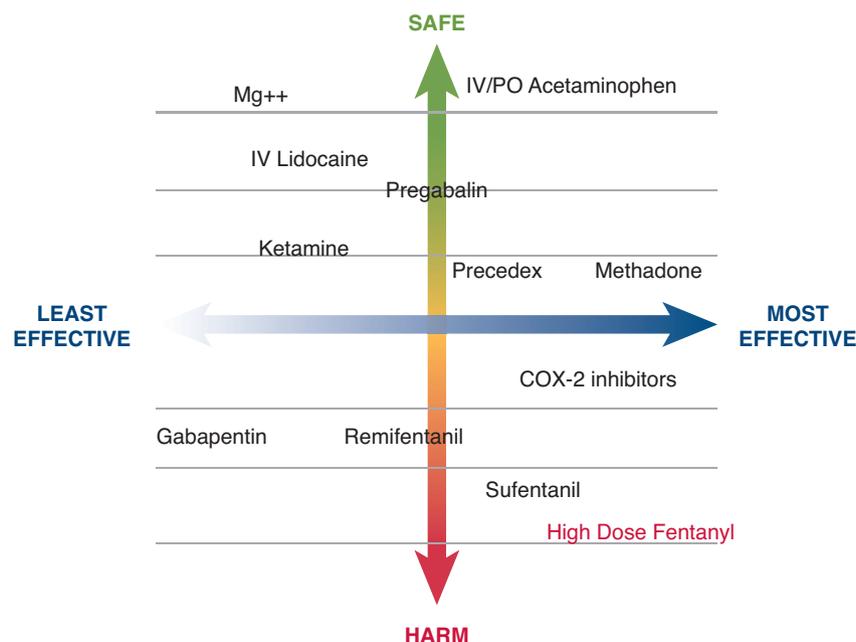
potentially reduce delirium (a possible consequence of poor pain control or opioid side effects) when provided on a standing basis as opposed to an as-needed basis after surgery.<sup>36,37</sup> The relative efficacy versus cost of oral compared with IV administration is controversial,<sup>38</sup> so despite the increased bioavailability of the IV form, scheduled oral acetaminophen is encouraged (maximum dose, 3-4 g/24 hours) unless contraindicated owing to an inability to tolerate oral medications or in the presence of significant liver dysfunction.

**Gabapentinoids.** Several randomized trials in cardiac surgery have investigated the role of gabapentin, a voltage-gated calcium channel inhibitor. In one trial, a single preoperative dose (600 mg) reduced opioid consumption and improved pain scores compared with placebo, but also increased sedation and was associated with a modest increase in postoperative mechanical ventilation.<sup>39</sup> Paradoxically, another trial comparing a larger preoperative dose (1200 mg) followed by scheduled gabapentin (600 mg twice daily) resulted in similar opioid consumption and pain scores with no difference in overall side effects.<sup>40</sup> Gabapentin has been extensively studied in the noncardiac surgery population, with a recent meta-analysis suggesting negligible efficacy in the acute postoperative setting and an association with somnolence and respiratory depression,

**TABLE 2. Nonopioid medications, dosing, and cardiac surgery considerations**

Medication	Mechanism	Dosing	Side effects/limitations to use
Acetaminophen	Unknown	650-1000 mg PO/IV every 6-8 h; maximum 3-4 g/d; duration of 7-14 d	Liver toxicity
Gabapentin	Voltage-gated calcium channel modulator	300-600 mg once, 100-300 mg every 8 h; duration 5-7 d	Sedation and respiratory depression, renal excretion, age-based dose adjustment; questionable efficacy
Pregabalin	Voltage-gated calcium channel modulator	Pregabalin: 50-150 mg (preoperative); 50-150 mg every 8 h; duration 7-14 d	Altered vision, renal excretion, age-based dose adjustment
Ketamine	N-methyl-D-aspartate antagonist	0.1-1.0 mg/kg bolus; 0.1-0.2 mg/kg/h	Tachycardia and questionable efficacy with bolus, hallucinations
Dexmedetomidine	Alpha-2 agonist	0.5-1.5 µg/kg/h	Hypotension, bradycardia
NSAID	Cyclo-oxygenase inhibitor	Ketorolac: 15-30 mg IV every 6-8 h Ibuprofen: 400-800 PO mg every 6-8 h	Platelet dysfunction, gastrointestinal irritation, renal dysfunction; FDA "black-box warning" for CABG
Lidocaine	Voltage-gated sodium channel inhibitor	1 mg/kg bolus; 0.5-2.0 mg/kg/h	Optimal dosage uncertain, local anesthetic toxicity
Regional nerve blocks	Voltage-gated sodium channel inhibitor	TEA/spinal paravertebral and fascial nerve plane block; parasternal, serratus anterior, pectoralis, erector spinae	TEA/spinal: neuraxial hematoma, other neurologic injury, hypotension Other blocks: failure of technique, local anesthetic toxicity, unclear efficacy, wide variation in practice, additional training and expertise required

PO, Per os; IV, intravenous; NSAID, nonsteroidal anti-inflammatory drug; FDA, Food and Drug Administration; CABG, coronary artery bypass grafting; TEA, thoracic epidural analgesia.



**FIGURE 1.** Perioperative analgesic options for cardiac surgery patients stratified by efficacy and safety. © PeriOperative Quality Initiative. *Mg*, Magnesium; *IV*, intravenous; *PO*, per os; *COX-2*, cyclo-oxygenase inhibitor.

particularly when administered in conjunction with opioids.<sup>41</sup> Pregabalin also modulates voltage-gated calcium channels and reduces opioid consumption, improves pain, and possibly improves the time to extubation with a single preoperative dose (150 mg) followed by scheduled dosing (75 mg twice daily) following cardiac surgery.<sup>42,43</sup> Gabapentinoids are excreted renally and require dosing adjustments according to kidney function.<sup>35</sup>

**NMDA receptor antagonists.** Ketamine has been studied as bolus, as infusion, and in combination. Although early data suggested that ketamine may have a role in the prevention of postoperative delirium, a recent article reported that a single dose of ketamine (0.5-1.0 mg/kg) prior to incision resulted in no difference in delirium, opioid consumption, or pain scores but was associated with a greater incidence of hallucinations and nightmares.<sup>44</sup> Ketamine infusions (0.1-0.5 mg/kg/h) have yielded modest results, with one trial suggesting reduced opioid administration and pain scores but others failing to show similar results.<sup>45,46</sup> This is counter to the finding in noncardiac surgery patients that subanesthetic ketamine reduces rescue analgesics and pain intensity.<sup>47</sup> Magnesium, another NMDA receptor antagonist, also has been investigated, but results are generally conflicting.

**Dexmedetomidine.** IV dexmedetomidine has been the focus of numerous randomized clinical trials and meta-analyses in cardiac surgery, which have reported a variety of benefits, including earlier extubation and reduced arrhythmias, delirium, and lengths of stay.<sup>48,49</sup> It has shown

promise as an analgesic, providing a significant reduction in opioid requirement and improved pain for up to 24 hours after cardiac surgery.<sup>50,51</sup> With bolus or rapidly escalating doses, dexmedetomidine may cause hypotension and bradycardia, potentially limiting its widespread adoption as a primary analgesic.<sup>52</sup>

**Nonsteroidal anti-inflammatory drugs.** One of the most common classes of medications utilized for pain management in noncardiac surgery settings, Nonsteroidal anti-inflammatory drugs (NSAIDs), both cyclooxygenase-2 and nonselective cyclooxygenase inhibitors, are routinely recommended in ERPs as part of the comprehensive analgesic strategy.<sup>32,33</sup> NSAIDs are reasonably well represented in cardiac surgery literature, and several small prospective studies generally support their utility in postoperative pain control and opioid prevention.<sup>53,54</sup> However, concerns for potential kidney injury and gastrointestinal complications limit their widespread use.<sup>55</sup> Even more problematic, the Food and Drug Administration issued a formal warning regarding NSAIDs in patients undergoing coronary revascularization owing to an association with thrombotic cardiovascular complications.<sup>56,57</sup>

**IV and topical lidocaine.** IV lidocaine is generally well-studied in noncardiac surgery patients, particularly in colorectal surgery, for which randomized trials and a recent meta-analysis have shown improved bowel recovery, decreased length of stay, and a modest reduction in pain scores.<sup>58</sup> Transdermal lidocaine is generally considered ineffective for postoperative pain management.<sup>59</sup> Studies

are limited in cardiac surgery. Higher plasma lidocaine concentrations may be associated with neurocognitive side effects.<sup>7</sup>

**Regional nerve block.** Regional nerve block—the targeted injection of local anesthetics to block pain sensation to nerves that correspond to the site of surgical incision or manipulation—has a significant role in multimodal analgesia. Regional nerve blocks must account for nerve distribution in surgical incision and drain sites, so for median sternotomy or thoracotomy, the targets are the perforating branches of the intercostal nerves from the thoracic spine nerves (T1-T11).<sup>60,61</sup> Several studies investigating neuraxial analgesia, as either thoracic epidural analgesia or spinal analgesia, reported reduced perioperative opioid consumption, improved pain control, earlier extubation, and possibly reduced cardiopulmonary complications.<sup>62-67</sup> However, concerns regarding potentially devastating neuraxial hematoma, particularly in the setting of systemic heparinization, as well as the potential for sympathectomy-mediated hypotension, represent barriers to the widespread adoption of neuraxial techniques.<sup>68,69</sup>

Alternative regional nerve blocks have emerged, including paravertebral and fascial plane blocks, allaying concerns associated with neuraxial instrumentation. Paravertebral techniques have similar efficacy as thoracic epidural analgesia with fewer side effects, although hypotension has been reported.<sup>70,71</sup> Ultrasound-guided fascial plane blocks, including erector spinae,<sup>72,73</sup> pectoralis,<sup>74</sup> serratus anterior,<sup>75,76</sup> and parasternal<sup>77,78</sup> nerve blocks, have been described. Studies, generally small, single-center trials or case series, have suggested decreased pain scores and opioid requirements with few side effects. Additional investigation is needed to establish the optimal block timing and dosing and to formally assess the safety profile associated with regional use, especially given the concomitant use of systemic anticoagulation in cardiac surgery, as well as to determine whether one technique is superior for a particular surgical approach (ie, sternotomy vs thoracotomy vs minimally invasive). Infiltrative techniques (ie, wound injection) and intercostal nerve block have shown equivalent results to no intervention and thus are not routinely recommended.<sup>79,80</sup> Overall, regional nerve block for cardiac surgery is promising and a burgeoning area of investigation.

	PREOP Clinic	PREOP Unit	INTRAOP	ICU/Wards	Home
<b>General</b>	Education, Patient Engagement & Setting Pain Management Expectations			Ongoing Education, Pain Assessment & Reinforcement of Pain Expectations	
<b>Analgesics</b>		Scheduled acetaminophen		Scheduled gabapentinoids (pregabalin)	
				NSAIDs as needed ( <i>selective</i> )	
<b>Local</b>		Regional: <i>neuraxial, paravertebral, fascial nerve block</i>			
			Lidocaine infusion		
<b>Adjuncts</b>			Ketamine infusion		
			Dexmedetomidine infusion		
<b>Opioids</b>			Short-acting Opioids based on opioid stewardship principles		
			Methadone		
			Intrathecal Morphine		

○ Recommended    ◌ May Consider

**FIGURE 2.** Potential components of a comprehensive multimodal perioperative analgesic plan for cardiac surgery patients. © PeriOperative Quality Initiative. ICU, Intensive care unit; NSAIDs, nonsteroidal anti-inflammatory drugs.

PM

**Comprehensive perioperative multimodal approach.**

Observational studies provide details on comprehensive multimodal cardiac anesthetic and/or perioperative analgesic strategies.<sup>4,5,81</sup> Figure 2 provides a potential outline of components of a multimodal approach to pain management for the cardiac surgery encounter. Uniformly, programs that have published their accounts report a strong association between the use and number of nonopioid agents and techniques, with reductions in opioid administration, opioid-related side effects, time to extubation, and overall length of stay. Specific elements may be applied in a highly selective fashion based on procedure- or patient-related factors, for example, in elderly patients or those with renal dysfunction. Individual programs are encouraged to tailor pain regimens based on local constraints, including medication formulary, subspecialty expertise, resources, and clinical workflow. Multimodal analgesia is a core tenet of perioperative care for the cardiac surgery population, and its use should be balanced against associated risks. In addition, opioid-based analgesia has its greatest potential benefit when given after exhausting the various alternative multimodal options, provided that its use adheres to the previously described principles of opioid stewardship.

**Recommendation 3:** *We recommend the use of multimodal nonopioid analgesics for patients undergoing cardiac surgery (grade: strong; LOE: C).*

**Recommendation 4:** *We recommend that clinicians consider the use of regional techniques for patients undergoing cardiac surgery (grade: weak; LOE C).*

**Question 4: What Other Interventions Facilitate the Judicious Use of Opioids in Cardiac Surgery Patients?**

Multidisciplinary, system-level interventions have been shown to optimize perioperative analgesia and improve opioid stewardship. ERPs for cardiac surgery optimize pain management and reduce opioid requirements. A foundational aspect of a successful ERP is patient and provider education.<sup>6,7</sup> Studies specific to cardiac surgery are lacking, but when a multimodal opioid-sparing pain regimen was coupled with patient and provider education for noncardiac procedures, postoperative pain management consistently

reduced opioid consumption with similar, if not superior, patient satisfaction related to pain control.<sup>82,83</sup> Shared patient-provider decision making sets expectations around anticipated pain intensity and standardized pain management and reinforces the role of opioids and structured feedback in the adequacy of pain control.<sup>6,84</sup> Formal education for physicians and other providers, specifically on utility of nonopioid medications, proper opioid prescribing practices, and principles of opioid stewardship, is also integral,<sup>85-87</sup> aligning patients' and providers' education on nonopioid pain management and opioid prescribing and empowering physicians to increase adherence to opioid education and safe opioid prescribing.

Other examples of system-level interventions include procedure-specific opioid prescriptions limiting the number of tablets prescribed at discharge,<sup>88</sup> patient-specific protocols tailoring discharge prescriptions to opioid requirements in the 24 to 48 hours prior to discharge,<sup>89</sup> and transitional programs monitoring pain control and opioid use.<sup>90</sup> Establishing opioid-sparing pain management plans without organized phase of care transitions can undermine both pain management and opioid reduction goals,<sup>91</sup> and thus programs should couple pain management protocols with patient and provider education and reinforcement of principles of opioid stewardship.

**Recommendation 5:** *We recommend that patients and healthcare providers receive formal education on perioperative analgesia for cardiac surgery, including pain management expectations, analgesic options, and potential side effects (grade: strong; LOE: B).*

**Recommendation 6:** *We recommend the development of program-specific multidisciplinary pathways for perioperative pain management (grade: strong; LOE: B).*

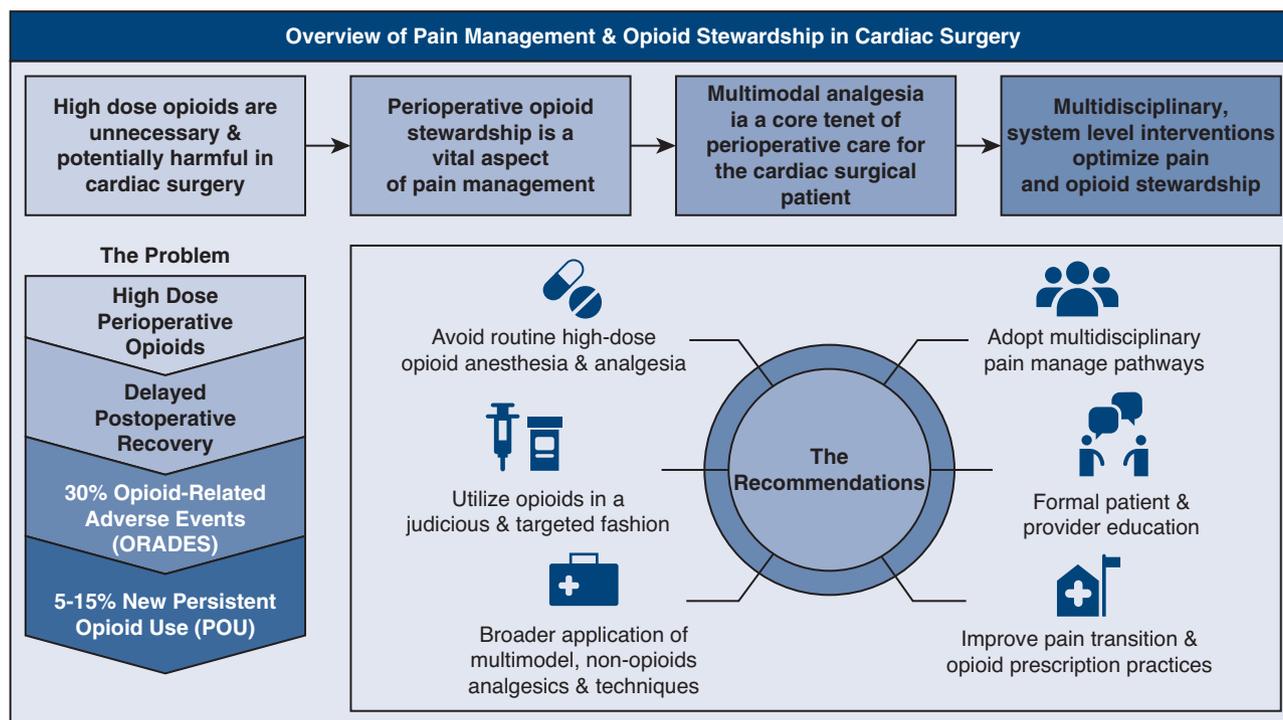
**SUMMARY, FUTURE DIRECTIONS, AND LIMITATIONS**

Pain management and opioid stewardship are integral to optimal perioperative care for cardiac surgery patients. Based on the available literature and expert consensus, a number of principles emerged, as itemized in Table 3. Pain management in the cardiac surgery setting is a growing

**TABLE 3. Principles of pain management for cardiac surgery**

1	Pain management is a core component of ERPs for cardiac surgery
2	Opioid stewardship involves the judicious use of opioids to optimize pain management and improve postoperative outcomes.
3	Although minimizing opioids and their side effects are foundational to ERPs, the rote avoidance of opioids at the expense of optimal pain management is inappropriate.
4	There are many analgesic (medication and regional) combinations that provide efficacy, and their use is tailored to local service line constraints.
5	Pain management protocols require adaptation based on procedure and patient-specific considerations.
6	Pain management protocols should be coupled with patient and provider education, involve shared decision making, and be accompanied by phase-of-care transition support.

ERP, Enhanced recovery pathway.

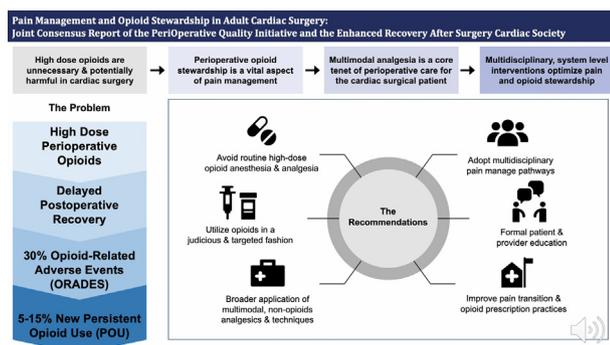


**FIGURE 3.** Overview of the recommendations for pain management and opioid stewardship in cardiac surgery. © Perioperative Quality Initiative.

area and appears to be underinvestigated compared to noncardiac procedures. Although prior guidelines support the adoption of an opioid-sparing, multimodal pain management plan,<sup>34</sup> the recommendations provided here outline the rationales, key considerations, and systems-level interventions necessary to achieve this goal. The guidance provided by this document has some inherent limitations, however. These include the potential of uncaptured published or unpublished data on certain interventions due to the scoping, rather than systematic, nature of the literature review. Observations are largely isolated to practice patterns in North America and reflect the expertise and

experience of the authors and members of the working group, even though discussions focused on establishing pragmatic recommendations grounded in the available evidence. Additional trials are needed to establish the benefits and risks of individual nonopioid medications, especially those with side effects that represent risks in cardiac surgery patients, as well as bundled interventions, focusing on clinically meaningful improvements in recovery metrics. Investigations using randomized controlled design as well as large database analyses are likely to continue to add to our understanding of the role of pain management in cardiac surgery patients. These include trials designed to assess the outcomes associated with varying strategies for more judicious or targeted postoperative opioid administration. Regional analgesia requires further study to establish optimal timing, dosing, and strategies to ensure methodologic consistency and enhance our understanding of various safety profiles in the cardiac surgery setting. Comprehensive methods to mitigate the risk of new POU must be identified. Finally, patients with preoperative opioid tolerance or chronic opioid use remain a particularly challenging group to address, and although guidance is available for patients in the noncardiac surgery setting, it is unclear how those concepts relate to the cardiac surgery population and is an unmet need.

This document provides several strategies to comprehensively address pain management and ensure opioid stewardship for the cardiac surgery patient, as illustrated in [Figure 3](#)



**VIDEO 1.** Summary of recommendations for pain management and opioid stewardship in cardiac surgery resulting from the 8th Perioperative Quality Initiative. Video available at: [https://www.jtcvs.org/article/S0022-5223\(23\)00089-2/fulltext](https://www.jtcvs.org/article/S0022-5223(23)00089-2/fulltext).

and described in Video 1. Foundational elements include patient and provider education, application of multimodal nonopioid medications including consideration of regional anesthesia, avoidance of high-dose opioids, and selective use of opioids to achieve optimal perioperative analgesia.

### Conflict of Interest Statement

M.C.G. receives salary support from the Agency for Healthcare Research and Quality and is a nonremunerated executive board member of the ERAS Cardiac Society; D.C. receives honoraria from Edwards Lifesciences and Medtronic; T.J.G. receives honoraria from Acacia, Baudax, Edwards and Medtronic; T.E.M. receives honoraria from Edwards Lifesciences and Baxter; and J.L.B. is a nonremunerated board member of the Society of Cardiovascular Anesthesiologists.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

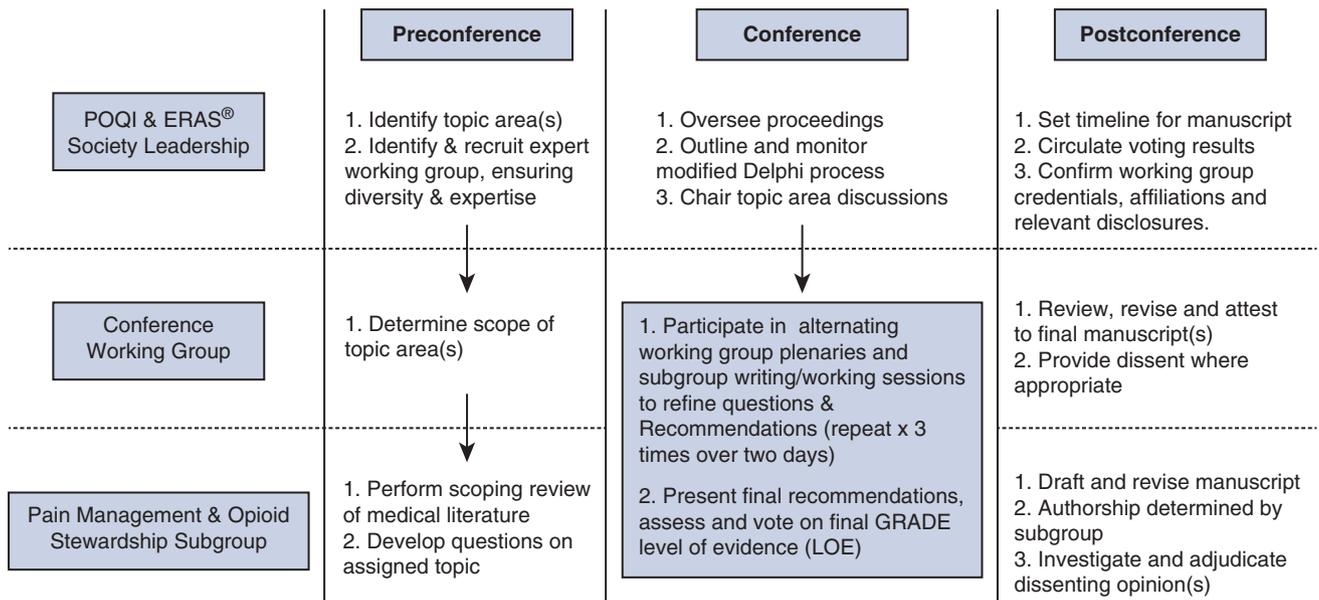
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**Key Words:** enhanced recovery programs, cardiac surgery, pain management, opioids, opioid adverse events, opioid stewardship, perioperative, anesthesia



**FIGURE E1.** Perioperative pain management working group workflow during different phases of modified Delphi process. *POQI*, PeriOperative Quality Initiative; *ERAS*, Enhanced Recovery After Surgery.



TABLE E1. Results of final voting on pain management and opioid stewardship recommendations

Question	Recommendation	Strength*	LOE†	For	Against	Comment
1. Are high-dose opioid-based techniques harmful to cardiac surgery patients?	1. We recommend against the routine use of high-dose opioid anesthesia or analgesia for patients undergoing cardiac surgery.	Strong	B	19	0	Majority decision (10-9) for LOE
2. How should opioids be used in cardiac surgery patients?	2. We recommend implementation of perioperative opioid stewardship for patients undergoing cardiac surgery.	Strong	B	19	0	N/A
3. What nonopioid analgesics or regional techniques are available for analgesia in cardiac surgery patients?	3. We recommend the use of multimodal, nonopioid analgesics for patients undergoing cardiac surgery.	Strong	C	19	0	N/A
	4. We recommend that clinicians consider the use of regional techniques for patients undergoing cardiac surgery.	Weak	C	19	0	Majority decision (15-4) for strength
4. What other interventions facilitate the judicious use of opioids in cardiac surgery patients?	5. We recommend that patients and healthcare providers receive formal education on perioperative analgesia for cardiac surgery, including pain-management expectations, analgesic options, and potential side effects.	Strong	C	19	0	N/A
	6. We recommend implementation of program-specific multidisciplinary pathways for perioperative pain management.	Strong	C	19	0	N/A

LOE, Level of evidence; N/A, not available. \*Strength of recommendation according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process. †Level of evidence according to the GRADE process.