Best Practice Multimodal Pain Management

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Disclosures

- I have the following relevant financial relationship(s) with commercial interest(s) involved in products and/or services discussed in this CME activity:

- Consultant for Astute Medical, Zimmer-Biomet, and Edwards Lifesciences
What is Enhanced Recovery After Surgery (ERAS)?

- A research-based approach using selected pre-, intra-, and post-operative interventions in concert to optimize outcomes and the patient experience.

- ERAS programs have been a standard practice in Europe for many years and consist of up to 21 different components.

- These enhanced recovery programs have demonstrated significant reductions in LOS, blood loss, time to ambulation, and complications; and increases in patient satisfaction around pain.

- They are being used in 95% of surgery patients in the UK.
To optimize the perioperative care of cardiac surgical patients through collaborative discovery, analysis, expert consensus, and dissemination of best practices.
ERAS CARDIAC PERIOPERATIVE COMPONENTS

1. Preop Education
2. Prehabilitation
3. Smoking and Alcohol Cessation
4. Nutrition Optimization
5. NPO After Midnight
6. Carbohydrate Clear Drink 2-4 Hours Preop
7. Multimodal Analgesia Initiation

INTRAOPERATIVE COMPONENTS

8. Short-acting Anesthetics
9. Continue Multimodal Analgesia
10. Minimize Crystalloid
11. NO BUGS
   - Normothermia (T > 36°C)
   - Oxygenation (FiO₂ > 0.8)
   - Anti-Biotic drug(s)/timings
   - Underventilation (ETCO₂ > 38)
   - Glycemic control (Glic < 180mg/dL)
   - Skin prep (CHG)/no Shaving
12. PONV Prophylaxis Initiated
13. Postop Sedation Started
14. Continue Multimodal Analgesia

POSTOPERATIVE COMPONENTS

15. Early Extubation
16. Continue PONV Prophylaxis
17. Diet/Bowel Regimen
18. Early Ambulation
19. Line/Drain Removal
20. Priority Discharge

Baystate Medical Center
ERAS Cardiac Surgery
Guidelines

### Class of Recommendation (COR)
- **Class I (Strong)**
- **Class IIa (Moderate)**
- **Class IIb (Weak)**
- **Class III: No Benefit (Moderate)**
- **Class III: No Harm (Strong)**

### Level of Evidence (LOE)
- **Level A**
  - Level B-R (Randomized)
  - Level B-NR (Non-randomized)
- **Level C-LD (Limited Data)**
- **Level C-EO (Expert Opinion)**

### Recommendations

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>A</td>
<td>Tranexamic acid or epsilon aminocaproic acid is recommended during on-pump cardiac surgical procedures.</td>
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<tr>
<td>I</td>
<td>B-R</td>
<td>Perioperative glycemic control is recommended.</td>
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<tr>
<td>I</td>
<td>B-R</td>
<td>A care bundle of evidenced based best practices is recommended to reduce surgical site infections.</td>
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<tr>
<td>I</td>
<td>B-R</td>
<td>Goal directed therapy is recommended to reduce postoperative complications.</td>
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<tr>
<td>I</td>
<td>B-NR</td>
<td>A multimodal, opioid-sparing, pain management plan is recommended postoperatively.</td>
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<tr>
<td>I</td>
<td>B-NR</td>
<td>Persistent hypothermia after CPB should be avoided in the early postoperative period.</td>
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<tr>
<td>I</td>
<td>B-NR</td>
<td>Maintenance of chest tube patency is recommended to prevent retained blood.</td>
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<tr>
<td>I</td>
<td>B-NR</td>
<td>Postoperative systematic delirium screening is recommended at least once per nursing shift.</td>
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<tr>
<td>I</td>
<td>C-LD</td>
<td>Smoking and hazardous alcohol consumption should be stopped 4 weeks before elective surgery.</td>
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<tr>
<td>Level</td>
<td>Grade</td>
<td>Recommendation</td>
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<tr>
<td>IIa</td>
<td>B-R</td>
<td>Early detection of kidney stress and interventions to avoid acute kidney injury are recommended following surgery.</td>
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<tr>
<td>IIa</td>
<td>B-R</td>
<td>Rigid sternal fixation can be useful to improve/accelerate sternal healing and reduce mediastinal wound complications.</td>
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<tr>
<td>IIa</td>
<td>B-NR</td>
<td>Prehabilitation is recommended for patients undergoing elective surgery with multiple comorbidities or significant deconditioning.</td>
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<tr>
<td>IIa</td>
<td>B-NR</td>
<td>An insulin infusion is recommended to treat hyperglycemia in all patients postoperatively.</td>
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<tr>
<td>IIa</td>
<td>B-NR</td>
<td>Strategies to ensure extubation within 6 hours of surgery are recommended.</td>
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<tr>
<td>IIa</td>
<td>C-LD</td>
<td>Patient engagement tools, including online/application-based systems to promote education, compliance, and patient-reported outcomes are recommended.</td>
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<tr>
<td>IIa</td>
<td>C-LD</td>
<td>Chemical thromboprophylaxis is recommended following surgery.</td>
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<tr>
<td>IIa</td>
<td>C-LD</td>
<td>Preoperative measurement of hemoglobin A1c and albumin is recommended.</td>
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<tr>
<td>IIa</td>
<td>C-LD</td>
<td>Preoperative correction of nutritional deficiency is recommended when feasible.</td>
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<tr>
<td>IIb</td>
<td>C-LD</td>
<td>A clear liquid diet may be continued up until 2-4 hours before general anesthesia.</td>
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<tr>
<td>IIb</td>
<td>C-LD</td>
<td>Preoperative carbohydrate loading may be considered before surgery.</td>
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<tr>
<td>III</td>
<td>A</td>
<td>Stripping or breaking the sterile field of chest tubes to remove clot is not recommended.</td>
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<tr>
<td>III</td>
<td>B-R</td>
<td>Hyperthermia (&gt;37.9 C) while rewarming on cardiopulmonary bypass is potentially harmful and should be avoided.</td>
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</table>
CONSEQUENCES OF PAIN

- Delirium
- Sleep Deprivation
- Anxiety
- Chronic Pain
- Pulmonary Compromise
- Tachycardia
- Anorexia
- Hypertension
- Immunosuppression
- Salt & Water Retention
- Inflammation
- Tissue Edema & Ischemia
- Pro-thrombotic State
- Vasoconstriction
- Immobilization
They’re the most powerful painkillers ever invented.
And they’re creating the worst addiction crisis America has ever seen.

By Massimo Calderone
OPIOID SIDE EFFECTS

- Dizziness
- Sedation
- Hormone Dysfunction
- Nausea
- Respiratory Depression
- Vomiting
- Constipation
- Gastroparesis
- Hyperalgesia
- Immune Suppression
Studied > 18,000 postoperative patients.

Thirty-six percent received no opioids for 24-hr prior to d/c; yet 45% of them were prescribed opioids when they left the hospital.

Opioids are not regularly prescribed in a patient-specific manner to postoperative patients.
Risk of continued opioid use increases at 4-5 days

Likelihood of continuing to use opioids

Percent

Number of days for initial opioid prescription

Source: CDC
Multimodal Analgesia

- Concurrent use of primarily nonopioid analgesics which may have additive, +/- synergistic effects
- Achieves superior analgesia and decreases opioid use and opioid-related adverse effects
- Critical concept of enhanced recovery after surgery (ERAS) programs
With an incidence of 6%, prolonged opioid use (>1 year) may be considered the most common postop-surgical complication. Following surgical procedures, ~44% of patients are discharged with an opioid prescription despite not requiring any opioids within 24-hours of discharge.

Brummett CM. JAMA Surg. 2017;152(6)
Chen EY. JAMA Surg. 2018;153(2)
### Multimodal Analgesia

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<table>
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<tbody>
<tr>
<td><strong>Educate</strong></td>
<td>patients <em>pre-operatively</em> on pain expectations post-surgery</td>
</tr>
<tr>
<td><strong>Decrease</strong></td>
<td>opioid prescribing for pts in ICU</td>
</tr>
<tr>
<td><strong>Decrease</strong></td>
<td>opioid prescribing for pts on telemetry</td>
</tr>
<tr>
<td><strong>Decrease</strong></td>
<td>total opioids on discharge</td>
</tr>
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</table>
Manage Patient Expectations

- 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 (CPOT), behavioral pain scale (BPS), and bispectral index (BIS) monitoring may have a role in this setting.
Opioid Stewardship

- PO: Avoid initiation of long-acting (12-24 hour) agents
- IV: PCAs preferred to protocolized dosing
- Transdermal patch: reserve for chronic pain
- Limit duration (48-hour stop to trigger reassessment)
- Avoid co-prescribing benzodiazepines
- Limit MME < 50 mg/day
OPIOID SPARING STRATEGIES

- Acetaminophen
- Gabapentin
- Tramadol
- Dexmedetomidine
- Ketamine
- Regional Anesthesia
Acetaminophen

- Disadvantages
  - Cost (IV)

- Recommended routinely in ERAS Society guidelines
  - Schedule maximum dose
  - Avoid other acetaminophen-containing products
  - PO vs IV?
Acetaminophen

- May be the safest non-opioid analgesic.
- IV acetaminophen may be better until gut function has recovered postoperatively.
- When added to opioids, acetaminophen produces superior analgesia, an opioid-sparing effect, and independent antiemetic actions.
- Acetaminophen dosing is either enteral or parenteral at 1g every 6 hours.
- Combination acetaminophen preparations with opioids should be discontinued.
Randomized, 3-way, cross-over design in 6 healthy volunteers; efficacy was not assessed

Mean Plasma Values

- The IV route produced a 76% higher mean plasma $C_{\text{max}}$ ($p = 0.0004$) than PO, and 256% higher ($p < 0.0001$) than PR
- The median plasma $T_{\text{max}}$ for the IV route was earlier (0.25h) than PO (1.0h, $p = 0.0018$) or PR (2.5h, $p = 0.0025$)

Note: PR acetaminophen data reflects standardization of the 1300 mg dose to 1000 mg (linear kinetics)

Randomized, 3-way, cross-over design in 6 healthy volunteers; efficacy was not assessed

**Mean Cerebrospinal Fluid Values**

- The mean CSF IV acetaminophen AUC over 6h is 75% higher than the PO group ($p = 0.0099$) and 142% higher than the PR group ($p = 0.0004$).
- Comparing mean CSF $C_{max}$ values, the IV group was 59.7% higher than PO ($p < 0.0001$) and 86.8% higher than PR ($p < 0.0001$).
- The median CSF $T_{max}$ values were 2.0, 4.0 and 6.0h for IV, PO and PR, respectively.

*PR acetaminophen data reflects standardization of the 1300 mg dose to 1000 mg (linear kinetics)*

Gabapentin/Pregabalin

• Within 24-hours of gabapentin/pregabalin initiation, a significant decrease in opioid consumption has been demonstrated.

• Precautions (dose-dependent)
  • Dizziness
  • Drowsiness

Gabapentin

• The precise mechanisms by which it produces its analgesic and actions are unknown.

• Binds to voltage-gated Ca\(^{2+}\) channels

• 600-1200 mg PO 2 hours pre-op followed by 100-600 mg TID post-op
  • Reduced pain, opioid use, & PONV.
  • Increased extubation time & sedation.

• Pregabalin also decreases opioid consumption and is used in postoperative multimodal analgesia.
Tramadol

• Tramadol has dual opioid/non-opioid effects but with a high delirium risk.

• Tramadol produces a 25% decrease in morphine consumption, decreased pain scores, and improved patient comfort postoperatively.
Dexmedetomidine

- An intravenous alpha-2 agonist, reduces opioid requirements.
- A meta-analysis of dexmedetomidine infusion reduced all-cause mortality at 30 days with a lower incidence of postoperative delirium and shorter intubation times.
- Dexmedetomidine may also reduce AKI after cardiac surgery.
Ketamine

- NMDA receptor antagonist with dose-dependent CNS and sympathomimetic effects
  - Anesthetic dose = dissociative state
  - Analgesic dose (≤ 8 mcg/kg/min): reduces post-op pain, opioid hyperalgesia, N/V, opioid consumption

- Favorable hemodynamic profile, minimal respiratory depression, analgesic properties, and reduced delirium incidence.

Schwenk ES. Reg Anesth Pain Med. 2018;43(5):1
Devlin JW. CCM Journal Vol 16.; 2018
Ketamine

- Intraoperative dosing is 50 mg pre-incision (gives you 0.5-1.0 mg/kg for most patients) followed by infusion at .125 mg/kg/hr.

- Turned off once protamine is given, to minimize the Ketamine "stunning" when patients are woken up for extubation in the CVICU.
Regional Anesthesia

Spinal

Epidural/Paravertebral

Parasternal block

Pre-fascial plane infusion for minithoracotomy

Serratus Anterior Block

Cryoanalgesia- intercostal ablation of axon (ganglion preserved)
What is Cryoanalgesia?

- Cryoanalgesia is a procedure used to temporarily block nerve conduction along peripheral nerve pathways; similar to the effect of local anesthetics.
- The procedure, which involves freezing targeted nerves, allows for the complete regeneration of the internal structure and function of the affected nerve.

Cryoanalgesia: Technique / Duration

- Maintain adequate pressure on nerve
  - Blanching of thumb
- Ablation
  - 120 seconds
  - ~-65°C
- Active-defrost
  - Remove probe >0°C
CVICU

- Fentanyl infusion
- Dexmedetomidine or propofol infusion
- Acetaminophen
- PCA pumps
- Early mobility
- Alternative healing services
NSAIDs

- Precautions?

- Place in therapy?
## Precautions: NSAIDs in CV Surgery

### Pro

**Postoperative Analgesia With Ketorolac Is Associated With Decreased Mortality After Isolated Coronary Artery Bypass Graft Surgery in Patients With Kidney Disease**

Milo Engoren, MD, Jonathan Hadaway, MD, Thomas A. Schwann, MD, and Robert H. Habib, PhD

Department of Anesthesiology, Mercy St. Vincent Medical Center, Toledo; Departments of Anesthesiology and Cardiothoracic Surgery, University of Toledo College of Medicine, Toledo, Ohio; Department of Anesthesiology, University of Florida College of Medicine, Gainesville.

**Objective:** In 2005, after the identification of cardiovascular safety concerns with the use of nonsteroidal anti-inflammatory drugs (NSAIDs), the FDA issued a black box warning recommending against the use of NSAIDs following cardiac surgery. The goal of this study was to assess the postoperative safety of ketorolac, an intravenously administered NSAID, after cardiac surgery.

**Design:** Retrospective observational study.

**Participants:** A total of 1,309 cardiac surgical patients (78.1% coronary bypass, 20.8% valve) treated between 2006 and 2012.

**Interventions:** A total of 488 of these patients received ketorolac for postoperative analgesia within 72 hours of surgery.

**Measurement and Main Results:** Ketorolac-treated patients were younger, had better preoperative renal function, and underwent less complex operations compared with non-ketorolac patients. Ketorolac was administered, on average, 8.7 hours after surgery (mean doses: 3.1). Postoperative outcomes for ketorolac-treated patients were similar to those expected using Society of Thoracic Surgery database risk-adjusted outcomes. In unadjusted analysis, patients who received ketorolac had similar or better postoperative outcomes compared with patients who did not receive ketorolac, including gastrointestinal bleeding (1.2% vs. 1.3%; p = 1.0), renal failure requiring dialysis (0.4% vs. 3.0%; p = 0.001), perioperative myocardial infarction (1.0% vs. 0.6%; p = 0.51), stroke or transient ischemic attack (1.0% vs. 1.7%; p = 0.47), and death (0.4% vs. 5.8%; p < 0.0001). With adjustment in a multivariate model, treatment with ketorolac was not a predictor for adverse outcome in this cohort (odds ratio: 0.72; p = 0.23).

**Conclusions:** Ketorolac appears to be well-tolerated for use when administered selectively after cardiac surgery. Although a black box warning exists, the data highlights the need for further research regarding its perioperative administration.

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**KEY WORDS:** analgesia, postoperative, cardiac surgery, safety, ketorolac, NSAIDs

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### Con

**The Effect of the COX-2 Inhibitors celecoxib and diclofenac sodium on postoperative pain and respiratory outcomes after cardiac surgery**

Andrew A. Whelton, M.D., Mark T. Brown, M.D., C.A., Andreas Hoeft, M.D., Joel L. Parlow, M.D., M.D., and Kenneth M. Verburg, Ph.D.

**ABSTRACT**

Celecoxib and diclofenac sodium are nonsteroidal anti-inflammatory drugs (NSAIDs) that are commonly used for the treatment of postoperative pain. However, neither of these agents is currently approved by the Food and Drug Administration for the treatment of perioperative pain in patients undergoing coronary artery bypass graft (CABG) surgery. This study aimed to evaluate the safety and efficacy of these agents in this clinical setting.

Celecoxib is CONTRAINDICATED for the treatment of peri-operative pain in coronary artery bypass graft (CABG) surgery (see WARNINGS).
NSAIDs

- All NSAIDs are not created equal

- Precautions
  - CV events (COX-2 > COX-1)
  - Bleeding (COX-1 > COX-2)

- Place in therapy
  - Non-CABG
  - Younger, low bleed risk

Liu G. *Am J Cardiol*. 2014;114(10):1523-1529
Devlin JW. *CCM Journal* Vol 16.; 2018
NSAIDs: Not Created Equal

CV events (COX-2 > COX-1)  Bleeding (COX-1 > COX-2)

Figure 2  Relative COX selectivity of non-steroidal anti-inflammatory drugs displayed by the concentration of the drugs (IC$_{80}$) required to inhibit COX-1 and COX-2 activity by 80%.

Opioid-Sparing Effect of Cannabinoids: A Systematic Review and Meta-Analysis

“In summary, pre-clinical studies provide robust evidence of the opioid-sparing effect of cannabinoids”

Neuropsychopharmacology (2017) 42, 1752-1765; doi:10.1038/npp.2017.51
Summary

Although no single pathway exists for multimodal opioid-sparing pain management, the consensus ERAS Cardiac panel concluded there is sufficient evidence to recommend that programs consider:

- Acetaminophen
- Tramadol
- dexmedetomidine
- pregabalin/Gabapentin, based on formulary availability in developing individual ERAS® protocols.