AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE: *Exploring the Role of Pharmacologic Preconditioning in Improving Post-Operative Outcomes*

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More than one million cardiac surgeries are performed annually worldwide, creating a need to devise strategies to reduce morbidity and mortality and improve patient outcomes. Operative interventions employing cardiopulmonary bypass (CPB) trigger systemic and tissue-derived inflammation and oxidative stress which, can incite organ dysfunction and lead to post-operative complications. In spite of attempts to mitigate post-operative complications through improvements in surgical techniques and post-operative care, inflammation and oxidant stress continue to adversely impact clinical outcomes (e.g., acute kidney injury, atrial fibrillation, and vasoplegia).1

Although translational research has explored several approaches to protect against surgically-induced systemic inflammation and oxidative stress, a clinically meaningful impact on patient outcomes has yet to be realized.2 Remote ischemic preconditioning was one approach that has shown great promise, yet, despite promising early clinical results, its place in clinical practice has not been adequately defined.3

**CRYO NERVE BLOCK AS ADJUNCTIVE PAIN CONTROL IN FULL STERNOTOMY DURING CARDIAC SURGERY**

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Significant post-operative pain can occur after sternotomy, which can result in pulmonary and respiratory complications. The recent ERAS Cardiac Society consensus report recommends perioperative opioid stewardship and a multi-modal, non-opioid analgesic approach for cardiac surgery patients.1

**VISCOELASTIC TESTING IN THE CARDIAC OR**

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Patient blood management (PBM) is a patient centered, individualized, team approach based upon the belief that the “best” blood is the patient’s own blood.1 PBM is a perfect fit for ERAS in that it enhances the patient experience, reduces complications, involves the patient in their own decision making, reduces medical care costs, and enhances public health.2 One of the key pillars of PBM, as outlined in the seminal World Health Organizations call to action for all 192 nations to adopt PBM, is the concept of individualized coagulation care.3 Individualized coagulation care/monitoring is endorsed in the cardiac surgery guidelines (since 2007) through universal utilization of viscoelastic testing (VET) as point of care (POC) decision making (Level I B evidence).4 Whole blood coagulation
architecture. In an effort to assist with implementation of cardiac enhanced recovery after surgery (ERAS), we have created sample ERAS turnkey order sets (TKOs). These order sets have been translated by subject matter experts using accumulated evidence, peer-reviewed literature, and current enhanced recovery practices. In these manuscripts Table 1 will provide an overview of existing Class I and IIA recommendations from relevant guidelines and consensus statements. Table 2 translates recommendations into a turnkey order set (TKO). Orders derived from Class I or IIA recommendations across all referenced guidelines and consensus manuscripts appear in the TKO in bold type. Selected orders that were inconsistently Class I or IIA, Class IIB, or supported by evidence in published in peer-reviewed journals, were also included in italicized type. Decisions regarding order inclusion have been made based on estimated benefit, risk, cost, implementation complexity, and generalizability. Each of these orders should be considered based on local institutional priorities, resources, practices, and expertise. Although a genuine turnkey order set that works for all institutions is impractical, we are attempting to provide an outline of the basic activities needed to achieve excellent outcomes. Our hope is that these sample order sets can be modified locally to allow widespread implementation of the ERAS principles of care. Digital and hard copies of the order sets will be available to attendees at the conclave.

Follow this link to a publication summarizing the 2022 AATS ERAS Cardiac Conclave: State of the Art: Proceedings of the AATS Enhanced Recovery after Cardiac Surgery Summit

TACKLING PERIOPERATIVE ANXIETY

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Patients facing cardiac surgery often experience fear, nervousness, and worry which can contribute to anxiety. This can increase stress hormones release, resulting in increased heart rate, blood pressure, and postoperative pain. Strategies to lessen anxiety prior to surgery may positively impact patients' functional recovery. 1 Alleviating preoperative anxiety is considered a key component of pre-habilitation, however, providing patients with interventions that support anxiety reduction can be challenging. 2 Baystate Medical Center has tackled the challenge of perioperative anxiety for cardiac surgery patients by partnering with a collaborative partner to build a digital patient engagement platform (DPEP). This platform provides patients with detailed education and customized videos to help prepare them for each phase of their surgical journey. 3 The DPEP has recently been enhanced to include access to self-directed complementary alternative medicine (CAM) resources. Patients are given instructions on how to perform numerous CAM practices including breathing techniques, guided imagery, meditation, and to how to download a customized music playlist. Patients are encouraged to directly contact healthcare professionals that specialize in emotional and spiritual support if they so desire. The foundation of Enhanced Recovery After Surgery (ERAS) is to provide standardized, evidence-based, patient-centered best practice that cumulatively mitigates surgical stress and optimizes patient recovery. Reducing perioperative anxiety is an example of an additional important and often neglected layer of care that will likely enhance recovery.

promise in pre-clinical models, but failed in larger clinical trials due to challenges in determining and delivering an ‘effective dose’ of ischemia, and the inconsistency of its impact across various organs. Cumulative evidence does not support the use of ischemic preconditioning as a means of improving post-operative outcomes. Pharmacologic preconditioning, which entails advanced administration of a pharmaceutical agent before surgery that produces predictable, measurable, and effective activation of cytoprotective pathways, is another potential, yet underexplored method for reducing post-operative complications. A recent phase 2, double-blind, randomized, placebo-controlled study evaluated the effect of RBT-1, a preconditioning drug administered 1-2 days prior to cardiac surgery. A statistically significant increase in anti-inflammatory and anti-oxidant proteins (cytoprotective biomarkers) was observed with treatment. More importantly, clinically meaningful improved outcomes (e.g., decreased time on ventilator, ICU and hospital length of stay, 30-day readmission rates, reduced incidence of atrial fibrillation, trend towards reduced mortality) were observed. With an expansive body of experimental work demonstrating the potential benefit of preconditioning, coupled with recent clinical advances, further investigation is warranted to explore the ability of pharmacologic preconditioning to impact the quality and outcomes of cardiovascular surgery.


RBT-1 Improves Postoperative Outcomes in Patients Undergoing Cardiac Surgery

MITT Population

<table>
<thead>
<tr>
<th>Ventilator Days</th>
<th>ICU Days</th>
<th>Hospital Days</th>
<th>AKI</th>
<th>MAKE30</th>
<th>Readmission (Cardiopulmonary)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (N=41)</td>
<td>-1.0</td>
<td>6.00</td>
<td>9.96</td>
<td>19.5%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Combined RBT-1 (N=80)</td>
<td>-2.71</td>
<td>3.29*</td>
<td>-1.27</td>
<td>17.5%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Clinically meaningful</td>
<td>p=0.1071</td>
<td>Clinically meaningful</td>
<td>p=0.0243 vs placebo</td>
<td>p=0.0191 vs placebo</td>
<td>18.4%-72%</td>
</tr>
</tbody>
</table>

AKI: ≥1.5x baseline increase in serum creatinine, oliguria/anuria, or dialysis
MAKE30: Major Adverse Kidney Events at 30 days
CRYO NERVE BLOCK AS ADJUNCTIVE PAIN CONTROL IN FULL STERNOTOMY DURING CARDIAC SURGERY

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Intercostal cryo nerve block (cryoNB) has been described as adjunctive therapy for postoperative analgesia during minimally invasive cardiac surgery. We use this technique bilaterally during heart surgery through a full sternotomy. Here we briefly describe our technique in a case report as recently published.

A 65-year-old man was scheduled for thymoma resection and surgical aortic valve replacement (SAVR) through full sternotomy. At 6-cm from the midline incision, the pleura along the chest wall was incised with electrocautery from T1–T6. Each nerve was cryoablated for two minutes bilaterally. Then, SAVR was performed per standard protocol. The operation took 2 hours 54 minutes with approximately 35 minutes for cryoNB.

Following an intravenous 50-µg (12.5 morphine milligram equivalents [MME]) fentanyl dose administered on arrival to the intensive care unit while the patient was still intubated and sedated and 2 doses of 1000 mg of intravenous acetaminophen on the night of surgery, a total dose of 25-mg (37.5 MME) of oxycodone was administered as needed per postoperative day (POD) 2. The patient was discharged POD4, taking acetaminophen as needed. At 1 month postoperatively, the patient’s sternal incision was well-healed, the sternum was stable, and he reported no use of any pain medication other than acetaminophen. Incision site sensation was normal at 6 months. He is now over 1 year from surgery with no complaints or adverse sequelae.

In summary, bilateral intercostal cryoNB was effectively used to ameliorate pain in open-heart surgery through a full sternotomy. The patient required minimal opioid analgesia as an inpatient, fully recovered without incident, and has returned to normal activity without limitation.


Figure 1: Positioning of cryoprobe in the intercostal space (right side)

Figure 2: Cryoablation of the intercostal nerve

Figure 3: Active defrost and safe removal from tissue
analysis with VET (clot shear modulus over time) encompasses all elements of clot formation, stabilization and lysis with the exception of live interaction with an endothelium. VET has been demonstrated to be a better predictor of coagulopathies and the need for transfusion than standard laboratory testing. The use of VET demonstrated reductions in transfusion rates, complications and mortality. Prior to the last 3 years, when VET advanced to true POC, blood samples obtained in the operating rooms were sent to central laboratories for VET analysis, resulting in long turnaround times for results. Today, advances in VET automated with ultrasound technology allows samples to be run in the ORs either by the anesthesiology team or the perfusionists. Decision making in as little as 12 minutes allow the cardiac teams to hone their usage of plasma (FFP), platelets (PLT) and cryoprecipitate (Cryo) as well as to make informed judgements regarding expensive pro-coagulant pharmaceuticals. FFP and PLT concentrates are linked more closely to ARDS, TRALI and prolonged ventilation than packed red blood cells. PLT are linked to increases in stroke rate and mortality, so appropriate usage, only when VET demonstrates that deficit in conjunction with active bleeding, is good PBM practice for coagulation care. Instituting POC VET testing in recent publications show that morbidity, mortality and costs are reduced when these technologies are embraced. PBM coagulation individualized care is now possible in every cardiac operating room. Patient care improves when teams embrace ERAS. The new POC coagulation technologies further that end goal.

PBM IS A PERFECT FIT FOR ERAS IN THAT IT ENHANCES THE PATIENT EXPERIENCE, REDUCES COMPLICATIONS, INVOLVES THE PATIENT IN THEIR OWN DECISION MAKING, REDUCES MEDICAL CARE COSTS, AND ENHANCES PUBLIC HEALTH.


Disclosure: Dr Spiess discloses that he is medical director of HemoSonics, Durham, NC.
RECENT ERAS® CARDIAC PUBLICATIONS:


UPCOMING MEETINGS:

9th World Congress of the Enhanced Recovery After Surgery Society, Lisbon, Portugal, May 31 - June 2
EBPOM World Congress of Prehabilitation Medicine, London, England, July 4-6

European Association For Cardio-Thoracic Surgery 37th Annual Meeting, Vienna, Austria, October 4-7
European Association of Cardiothoracic Anaesthesiology and Intensive Care 37th Annual Meeting, Budapest, Hungary, October 11-13
American Society of Anesthesiologists Annual Meeting, San Francisco, CA, October 13-17

To learn more about our organization, including our board members and upcoming meetings: www.erascardiac.org
Who We Are

The ERAS® Cardiac Society is an international non-profit organization comprised of experts from around the world, including participation from all members of the healthcare team. Led by an executive board, an advisory board, and a pool of subject matter experts, our members strive to implement enhanced recovery principles at their local institutions while advancing improved patient care internationally through collaboration, education, and dissemination of up-to-date knowledge regarding optimal perioperative care.

ERAS® Society

The ERAS® Society is an international organization with enhanced recovery guidelines for several surgical sub-specialties. Beginning as the ERAS® Study Group in 2001, team leaders Professor Ken Fearon (University of Edinburgh) and Professor Olle Ljungqvist (Karolinska Institutet) spearheaded the developments made in multimodal surgical care. The ERAS® Study Group soon discovered that there were a variety of local traditions in practice, as well as an inconsistent application of evidence-based best practices. This prompted the group to examine the process of change from tradition to best-practice. Since its inception, the ERAS® Society has expanded to include several subspecialties, emphasized the benefits of standardized best-practices across the continuum of the perioperative period, highlighted the importance of data-driven self-evaluation, and promoted the improvement of patient care.

Our Organizational Structure

Our ERAS® Cardiac Society is made up of experts from around the world, including participation from all members of the healthcare team. Our members strive to implement enhanced recovery principals at their local institutions while advancing improved patient care internationally through collaboration, education, and dissemination of up-to-date knowledge regarding optimal perioperative care. Our organization is divided into an Executive Board, Advisory Board, and a pool of Subject Matter Experts.
Corporate financial support will be used to promote the mission of the ERAS® Cardiac Society. We are committed to standardizing best practice surrounding the preoperative and perioperative care of cardiac surgical patients through expert consensus, review of the literature and open communication. This unrestricted support does not represent the ERAS® Cardiac Society’s support or agreement to promote any pharmaceutical, device, or technology related to the sponsors.

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