Enhanced recovery after cardiac surgery protocol reduces perioperative opioid use

Chelsea M. Loria, MD,[a] Kirsten Zborek, MD,[a] James B. Millward, PA-C,[a] Matthew P. Anderson, BS,[a] Cynthia M. Richardson, RN,[a] Niharika Namburi, MHA,[a] Zainab Faiza, MBBS,[a] Lava R. Timsina, PhD,[a] and Lawrence S. Lee, MD, MBA[a,b]

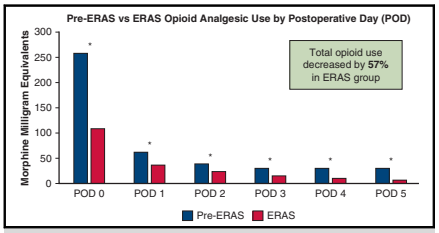
ABSTRACT

Objective: Enhanced Recovery After Surgery protocols are relatively new in cardiac surgery. Enhanced Recovery After Surgery addresses perioperative analgesia by implementing multimodal pain control regimens that include both opioid and nonopioid components. We investigated the effects of an Enhanced Recovery After Surgery protocol at our institution on postoperative outcomes with particular focus on analgesia.

Methods: Single-center retrospective study comparing perioperative opioid use before and after implementation of an Enhanced Recovery After Surgery protocol at our institution. Subjects were divided into 2 cohorts: Enhanced Recovery After Surgery (study group from year 2020) and pre–Enhanced Recovery After Surgery (control group from year 2018). Baseline and perioperative variables including total opioid use from the day of surgery to postoperative day 5 were collected. Opioid use was calculated as morphine milligram equivalents and compared between the 2 cohorts.

Results: A total of 466 patients were included: 250 in the Enhanced Recovery After Surgery group and 216 in the pre–Enhanced Recovery After Surgery group. Both groups had similar baseline characteristics, but the Enhanced Recovery After Surgery group had significantly more subjects with intravenous drug use history ($P < .0001$), endocarditis ($P < .0001$), and liver disease ($P = .007$) compared with the pre–Enhanced Recovery After Surgery group. Every day from the day of surgery to postoperative day 5, the Enhanced Recovery After Surgery group had significant reduction (57%) in opioid use compared with the pre–Enhanced Recovery After Surgery group. Total opioid use for the entire length of stay was 259 morphine milligram equivalents in the Enhanced Recovery After Surgery group versus 452 morphine milligram equivalents in the pre–Enhanced Recovery After Surgery group ($P < .0001$). Subgroup analysis of subjects with intravenous drug use history did not demonstrate a significant reduction in opioid use.

Conclusions: Enhanced Recovery After Surgery protocols with an emphasis on multimodal pain management throughout perioperative care are associated with a significant reduction in the postoperative use of opioid analgesics. (JTCVS Open 2022;12:280-96)



Reduction in opioid use by postoperative day in cardiac surgery patients.

CENTRAL MESSAGE

ERAS protocols with an emphasis on multimodal analgesia are associated with significantly reduced perioperative opioid use in cardiac surgery patients.

PERSPECTIVE

Standardized ERAS protocols can help optimize postoperative outcomes, particularly with respect to perioperative analgesia. A multimodal analgesic regimen consisting of both opioid and nonopioid approaches used throughout all phases of care is associated with significantly reduced perioperative opioid analgesic use in cardiac surgery patients.

See Commentary on page 297.

From the [a]Division of Cardiothoracic Surgery, Indiana University School of Medicine, Indianapolis, Ind; and [b]Division of Cardiac Surgery, Tufts Medical Center, Tufts University School of Medicine, Boston, Mass.

Institutional Review Board Approval: The Institutional Review Board of Indiana University approved this retrospective study on 9/25/2020 (IRB #2009811102). Informed written consent was obtained by all patients who were included in this study.

Read at the 101st Annual Meeting of The American Association for Thoracic Surgery: A Virtual Learning Experience, April 30-May 2, 2021.

Received for publication April 27, 2021; revisions received July 7, 2022; accepted for publication July 26, 2022; available ahead of print Sept 27, 2022.

Address for reprints: Lawrence S. Lee, MD, MBA, Lahey Hospital and Medical Center, 41 Mall Rd, Suite 5 East, Burlington, MA 01805 (E-mail: LLee79@gmail.com).

2666-2736

https://doi.org/10.1016/j.xjon.2022.08.008

Abbreviations and Acronyms

ERAS = Enhanced Recovery After Surgery
IVDU = intravenous drug use
MME = morphine milligram equivalent
NIVDU = nonintravenous drug use
NSAID = nonsteroidal anti-inflammatory drug

To view the AATS Annual Meeting Webcast, see the URL next to the webcast thumbnail.

Enhanced Recovery after Surgery (ERAS) is a multimodal, multidisciplinary perioperative management strategy with the goal of optimizing patient recovery and outcomes.[1] The first ERAS protocol was developed in 2001 to standardize outcomes in colorectal surgery and was largely built on the principles established by Henrik Kehlet in the 1990s surrounding "fast-track surgery."[2] One major aspect of ERAS addresses postoperative analgesia by implementing multimodal pain control regimens. The use of multimodal pain management protocols has been associated with reduction in opioid analgesic use, patient discomfort, and hospital length of stay across multiple surgical subspecialties.[3,4] ERAS protocols remain a relatively new paradigm in cardiac surgery where patients face unique challenges, including multiple incision sites, chest tube drainage, and invasive lines and catheters, which all contribute to patient discomfort.[4] The goal of this study was to investigate the effects of a novel ERAS protocol at our institution on postoperative outcomes. Although we intend to report other outcomes of our protocol, this review focuses on perioperative opioid analgesic use (Figure 1).

METHODS AND MATERIALS

Enhanced Recovery After Surgery Protocol Development

Our institution convened a multidisciplinary group of individuals to develop an ERAS protocol. Every discipline that interacted with cardiac surgical patients was included, with each discipline having an "ERAS Champion" to serve as a liaison to other providers within their respective fields. Our protocol was based on the Guidelines for Perioperative Care in Cardiac Surgery Enhanced Recovery After Surgery Society Recommendations and was tailored with consideration of institutional resources, feasibility of successful implementation, and the needs of our patient population.[3] After multiple iterations of the protocol, final approval was granted by unanimous agreement by the multidisciplinary champions. ERAS was implemented on all patients who underwent nonemergency cardiac surgery via median sternotomy starting in January 2020. Data variables were collected prospectively into an ERAS database, and an ERAS Leadership Team met regularly to monitor for adverse effects and logistic hurdles. This also allowed the team to identify and address challenges as they arose.

Enhanced Recovery After Surgery Protocol Components

The ERAS protocol addressed all phases of care: preoperative, intraoperative, and postoperative. Key components of the protocol included multimodal pain management, patient education, high protein nutritional supplementation, goal-directed intraoperative fluid and hemodynamic management, early postoperative mobilization and chest tube removal, and delirium screening (Figure 2). Although the entire ERAS protocol encompassed all of these areas, for the purposes of this manuscript we focus on the analgesic aspect of the protocol. The multimodal analgesic components included preoperative acetaminophen and gabapentin, intraoperative topical anesthetic with liposomal bupivacaine and encouragement of reduced intravenous (IV) opioid use, and postoperative opioids in combination with nonopioids such as gabapentin, nonsteroidal anti-inflammatory drugs (NSAIDs), and lidocaine patches (Table 1).

Of note, opioid analgesics were not intentionally withheld or limited in the postoperative period; various narcotics were ordered for all patients and administered when requested by patients or deemed necessary to achieve adequate analgesia by nursing or physician staff. Furthermore, clinical staff were instructed that the goal was not to specifically reduce opioid use but rather that the intent with ERAS analgesia was to achieve adequate pain control to allow for enhanced overall patient recovery. Patients were also administered a 3-question survey (all using Likert scale grading) on the day of discharge, with one of the questions focused on the patient's perception of their perioperative analgesia: "How satisfied are you with how your pain was controlled in the hospital after surgery?" The 5-point Likert scale response options were "very dissatisfied," "dissatisfied," "neutral," "satisfied," or "very satisfied."

Study Design

The Institutional Review Board of Indiana University approved this retrospective study on 9/25/2020 (IRB #2009811102). Informed written consent was obtained by all patients who were included in this study. Our ERAS prospective database was used to identify the study group, which included all patients who received the ERAS protocol from January to September 2020. An institutional Society of Thoracic Surgeons database was queried to identify the control group: All patients who underwent nonemergency cardiac surgery via median sternotomy from January to September 2018. This time period was chosen as the control group because the surgical attending staff were mostly unchanged (one surgeon from 2018 had departed the group and thus not included in the 2020 study group), and no ERAS components were applied in 2018. Demographic and relevant clinical data were extracted from these registries and from individual medical records. Medication administration records were reviewed, and all sources of opioid analgesic were converted into morphine milligram equivalents (MMEs) using a standardized conversion chart (Table E1).[5]

Statistical Analysis

Patient characteristics were evaluated using frequency and proportion for all categorical variables. All continuous variables were tested for normality using Shapiro–Wilk tests and due to evidence of skewness we used median and inter quartile range for all continuous variables. We also examined the statistical difference in the patient characteristics between the control and ERAS cohorts using chi-square or Fisher exact tests and Wilcoxon rank-sum tests, as appropriate. Bivariate analyses using quantile (median) regressions were done to analyze the relationship between opioid analgesic use by postoperative days in all patients, and this analysis was repeated for 2 subgroup analyses (illicit drug use vs nonillicit drug use). Multivariable quantile regression using 50th percentile (median) of MME was performed at each cross-section of the follow-up time (postoperative day 0 to 5). To account for the panel nature of the study where multiple observations are nested within a study participant, we used multivariable quantile regression with bootstrapped clustered standard error to

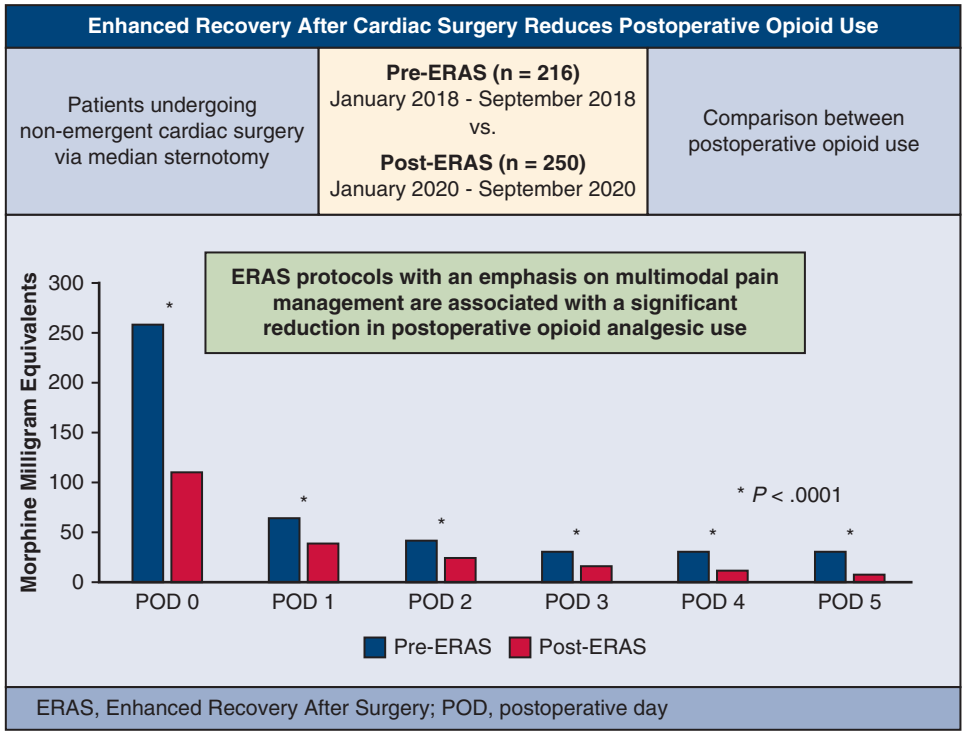


FIGURE 1. ERAS reduces postoperative opioid use. *ERAS*, Enhanced Recovery After Surgery; *POD*, postoperative day.

account for the within subject correlation. Marginal plot of linear prediction of MME over days was also created as a postestimation for the nested study design. The result was consistent with the multivariable quantile regression of MME at each cross-section of the follow-up time. All analyses were done using Stata/MP 16.1.[6]

RESULTS

In total, 466 patients were included and divided into 2 groups: n = 250 in ERAS (study group) and n = 216 in pre-ERAS (control group). Baseline characteristics of the 2 cohorts are listed in Table 2: The 2 groups were similar with the exception that the ERAS group had significantly more patients with endocarditis (n = 60 [24%] vs n = 12 [5.6%], $P < .0001$), a history of intravenous drug use (IVDU) (n = 56 [22%] vs n = 17 [7.9%], $P < .0001$), and liver disease (n = 27 [10.8%] vs n = 9 [4.2%], $P < .007$). These differences between the pre-ERAS and

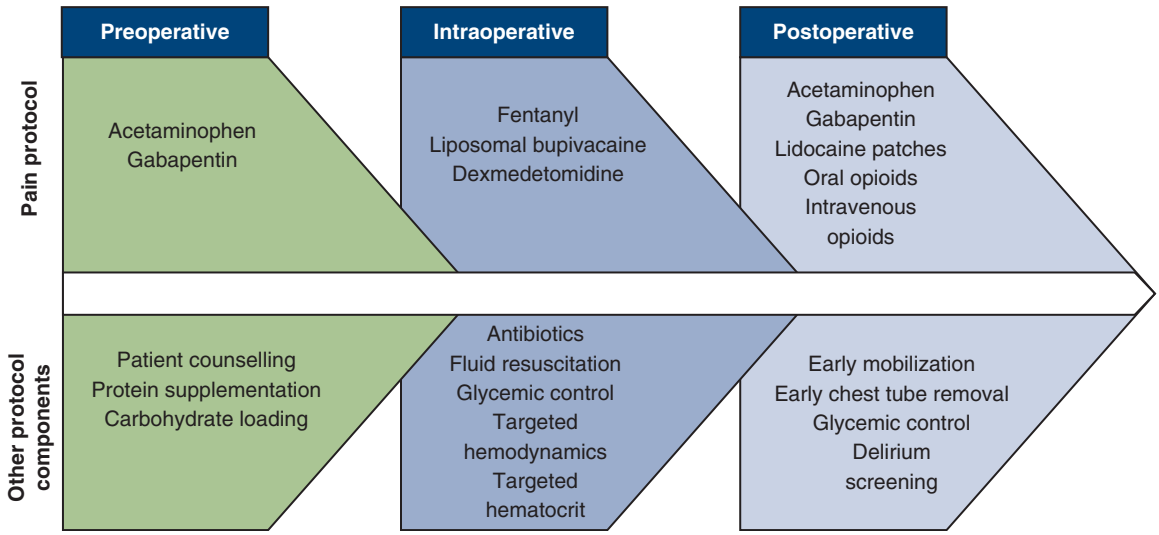


FIGURE 2. ERAS protocol.

TABLE 1. Perioperative multimodal pain regimen

Preoperative
Acetaminophen 1 g 2 h before surgery
Gabapentin 300 mg 2 h before surgery
Intraoperative
Recommend reduced opioid use to < 500 μg fentanyl
Local anesthetic with liposomal bupivacaine
10 mL chest tube sites
15 mL incision
Postoperative
Dexmedetomidine (initiated in OR, continued until extubation)
Acetaminophen 650 mg scheduled every 6 h
Lidocaine 5% transdermal patch, applied to bilateral back or chest
Gabapentin 100 mg TID
100 mg BID if renal impairment
Tramadol 50-100 mg PO every 6 h-PRN for mild pain (every 12 h for CrCl <30, max 200 mg/d)
Oxycodone 5-10 mg PO every 4 h-PRN moderate pain
IV opioids (eg, hydromorphone, fentanyl), PRN severe/breakthrough pain
Dose and drug at provider discretion
Discontinued when chest tubes removed

OR, Operating room; *TID*, ter in die (3 times daily); *BID*, bis in die (2 times daily); *PO*, per os (by mouth); *PRN*, pro re nata (as needed); *CrCl*, creatinine clearance; *IV*, intravenous.

ERAS groups were partially due to the opioid epidemic and were controlled by multivariate analysis (Table E2).[7] Patient compliance was greatest in the postoperative period (Table E3).

Perioperative daily opioid analgesic use was significantly reduced in the ERAS group. In the first 24 hours of care, which included the intraoperative phase of case, median opioid use was 113 MME in ERAS versus 259 MME in pre-ERAS ($P < .0001$). Over the ensuing 5 postoperative days, median MME in the ERAS versus pre-ERAS groups, respectively, were 48 versus 63 MME ($P = .002$), 30 versus 40 MME ($P = .007$), 20 versus 30 MME ($P = .004$), 15 versus 30 MME ($P < .0001$), and 10 versus 30 MME ($P < .0001$). In the multivariable quantile (median) regression, we found a similar pattern of MME by postoperative day (Figure E1, Tables E2 and E4). During the entire hospital length of stay, ERAS patients had a 57% reduction in total opioid use (459 vs 261 MME, $P < .0001$) (Figure 3).

Because a significant portion of the ERAS group (n = 56, 22%) had a history of IVDU, a subgroup analysis was performed to see if this group also benefited from the multimodal pain management protocol. In general, the patients with a history of IVDU were younger (44 vs 64 years, $P < .0001$), with less comorbidities aside from endocarditis (n = 40 [54.8%] vs n = 32 [8.1%], $P < .0001$) and liver disease (n = 28 [38.4%] vs n = 8 [2.0%]) when compared with nonintravenous drug use (NIVDU) (Table E5). For patients with a history of IVDU, those who received the ERAS protocol had a significant reduction in opioid analgesic use on day of surgery (postoperative day zero) compared with pre-ERAS patients (318 MME vs 148 MME, $P < .001$), but there was no difference in the subsequent postoperative days (Figure 4). In contrast, in patients without IVDU history, ERAS patients demonstrated significant reduction in opioid analgesic use compared with pre-ERAS patients throughout the entire length of stay starting with day of surgery to postoperative day 5, respectively: 247 versus 106 MME, 62 versus 40 MME, 40 versus 25 MME, 30 versus 15 MME, 25 versus 10 MME, and 30 versus 5 MME (all days $P < .0001$) (Figure 5).

Other Secondary Outcomes

In addition to reduction in postoperative opioid use, we found that the ERAS group had chest tubes removed earlier (postoperative day 3 vs 4; $P < .0001$) than the pre-ERAS group. There was no significant difference in the following secondary outcomes between pre-ERAS and ERAS groups, respectively: total hospital length of stay (6 vs 6.5 days, $P = .505$), total intensive care unit length of stay (3.3 vs 3.1 days, $P = .302$), initial ventilation duration (4.7 vs 4.9 hours, $P = .540$), 30-day mortality (n = 5 [2.3%] vs n = 8 [3.2%], $P = .779$), and 30-day readmission (n = 17 [7.9%] vs n = 32 [12.8%], $P = .084$). Additionally, there was no difference in postoperative complications, including surgical site infection (n = 1 [0.5%] vs n = 4 [1.6%], $P = .379$), pneumonia (n = 14 [6.5%] vs n = 12 [4.8], $P = .430$), renal failure (n = 6 [2.8%] vs n = 8 [3.2%], $P = .790$), atrial fibrillation (n = 62, [28.7%] vs n = 69 [27.6%], $P = .792$), gastrointestinal side effects (n = 10 [4.6%] vs n = 13 [5.2%], $P = .777$), and stroke (n = 1 [0.5%] vs n = 2 [0.8%], $P > .999$).

Patient Satisfaction

In response to the predischarge survey, 79% of patients stated that they were "satisfied" or "very satisfied" with their pain control after surgery; 2.5% of patients reported being "dissatisfied" with their level of postoperative pain control.

DISCUSSION

This study represents the effects after the implementation of a novel ERAS protocol and its impact on perioperative analgesic use in cardiac surgery patients at our institution.[8] Our objective in developing an ERAS protocol was to create a perioperative management strategy that would optimize patient recovery. Although analgesia is but one component of the ERAS program, we elected to focus on this aspect for purposes of this study because of its immediate and notable impact on the care pathway.

Overall, the ERAS group had a 57% reduction in total opioid requirements during admission when compared with the control group. The primary intent of ERAS was

TABLE 2. Patient characteristics

Characteristic, n (%)	Control (n = 216)	ERAS (n = 250)	Total (n = 466)	*P* value
Procedure type				<.0001
Ascending aortic	47 (21.7)	36 (14.4)	83 (17.8)	
CABG	75 (34.7)	95 (38)	170 (36.5)	
Valve	65 (30.1)	54 (21.6)	119 (25.5)	
Valve + CABG	12 (5.6)	12 (4.8)	24 (5.2)	
Other	17 (7.9)	53 (21.2)	70 (15.0)	
Age, median (Q1, Q3)	64 (57, 70)	62 (51, 70)	63 (55, 70)	.132
Gender				.542
Male	150 (69.4)	167 (66.8)	317 (68.0)	
Female	66 (30.6)	83 (33.2)	149 (32.0)	
Race				.568
White	188 (87.0)	213 (85.2)	401 (86.1)	
Non-White	28 (13.0)	37 (14.8)	65 (14.0)	
Risk factors				
BMI, median (Q1, Q3)	30 (25.9, 34.0)	29 (25.0, 33.8)	29 (25.4, 34.0)	.240
Diabetes	81 (37.5)	93 (37.2)	174 (37.3)	.947
Endocarditis	12 (5.6)	60 (24)	72 (15.5)	<.0001
Cerebrovascular disease	31 (14.4)	52 (20.8)	83 (17.8)	.070
Chronic lung disease	55 (25.5)	62 (24.8)	117 (25.1)	.869
Family history of CAD	9 (4.2)	3 (1.2)	12 (2.6)	.074
Hypertension	180 (83.3)	177 (70.8)	357 (76.6)	.001
Intravenous drug use	17 (7.9)	56 (22.4)	73 (15.7)	<.0001
Last HbA1c, median (Q1, Q3)	6 (5.4, 6.6)	6 (5.6, 7.1)	6 (5.5, 6.9)	.386
Liver disease	9 (4.2)	27 (10.8)	36 (7.7)	.007
Peripheral artery disease	25 (11.6)	38 (15.2)	63 (13.5)	.254
Previous cardiac interventions				
Any	78 (36.1)	95 (38.0)	173 (37.1)	.674
CABG	4 (1.9)	3 (1.2)	7 (1.5)	.709
Valve	20 (9.3)	30 (12.0)	50 (10.7)	.340
Other cardiac surgery	29 (13.4)	35 (14.0)	64 (13.7)	.858
PCI	42 (19.4)	52 (20.8)	94 (20.2)	.716
Preoperative cardiac status				
Prior MI	34 (15.7)	56 (22.4)	90 (19.3)	.120
Heart failure	66 (30.6)	68 (27.2)	134 (28.8)	.425
Cardiogenic shock	1 (0.5)	2 (0.8)	3 (0.6)	.348
Cardiac arrhythmia	48 (22.2)	53 (21.2)	101 (21.7)	.789
Operative				
CPB use	205 (94.9)	244 (97.6)	449 (96.4)	.122
CPB time (min), median (Q1, Q3)	150 (118.5, 190.5)	116.5 (89, 167)	135 (103, 180)	<.0001
Crossclamp time (min), median (Q1, Q3)	108.5 (82, 147)	86.5 (63, 123.5)	94.5 (71, 133)	<.0001
Postprocedure EF	204 (94.4)	237 (94.8)	441 (94.6)	.865

ERAS, Enhanced Recovery After Surgery; *CABG*, coronary artery bypass grafting; *BMI*, Body mass index; *CAD*, coronary artery disease; *HbA1c*, hemoglobin A1c; *PCI*, percutaneous coronary intervention; *MI*, myocardial infarction; *CPB*, cardiopulmonary bypass; *EF*, ejection fraction.

not opioid use reduction per se; rather, the goal was to provide the patient sufficient analgesia that, in turn, could facilitate other aspects of their postoperative recovery such as early mobility and reduction of gastrointestinal and medication adverse effects. Reduction in opioid use has been proposed to enhance patient recovery my minimizing side effects including nausea, constipation, urinary retention, respiratory depression, pruritis, and delirium.[4] Our results demonstrate that the ERAS analgesic protocol successfully achieves this while also reducing opioid consumption.

The preoperative administration of acetaminophen and gabapentinoids (gabapentin, pregabalin) is common among ERAS protocols. Administering acetaminophen before

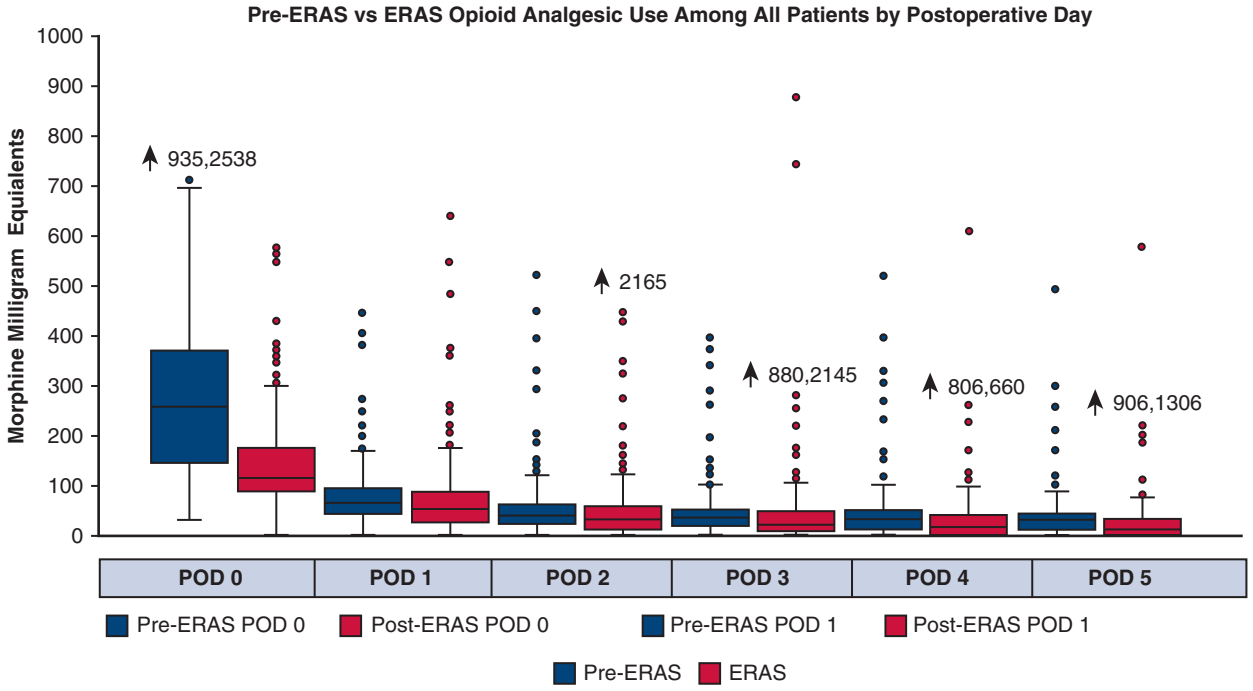


FIGURE 3. Pre-ERAS versus ERAS opioid analgesic use among all patients by postoperative day. *ERAS*, Enhanced Recovery After Surgery; *POD*, postoperative day.

surgery has been associated with reduced pain scores and opioid analgesic use in the immediate postoperative period in noncardiac surgical patients.[9] Likewise, in a randomized study among coronary artery bypass grafting patients, Menda and colleagues[10] found that patients who received gabapentin preoperatively had significant reduction in postoperative morphine requirements. However, the postoperative use of gabapentinoids has been associated with

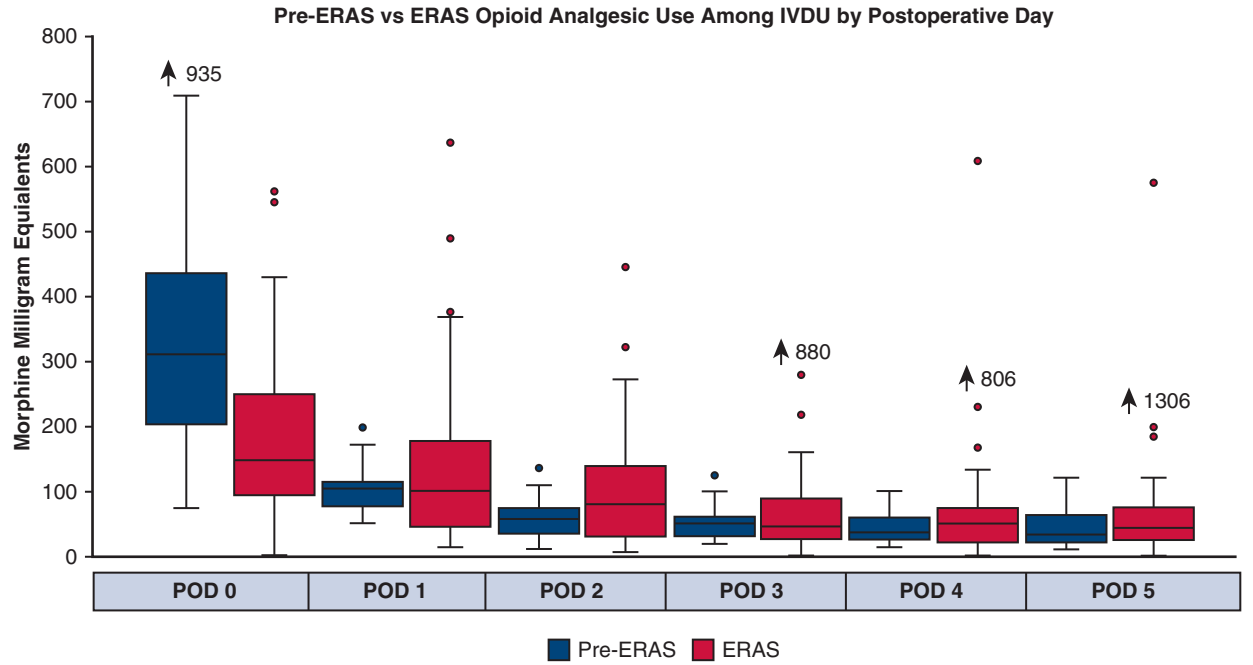


FIGURE 4. Pre-ERAS versus ERAS opioid analgesic use among IVDU by postoperative day. *ERAS*, Enhanced Recovery After Surgery; *IVDU*, intravenous drug use; *POD*, postoperative day.

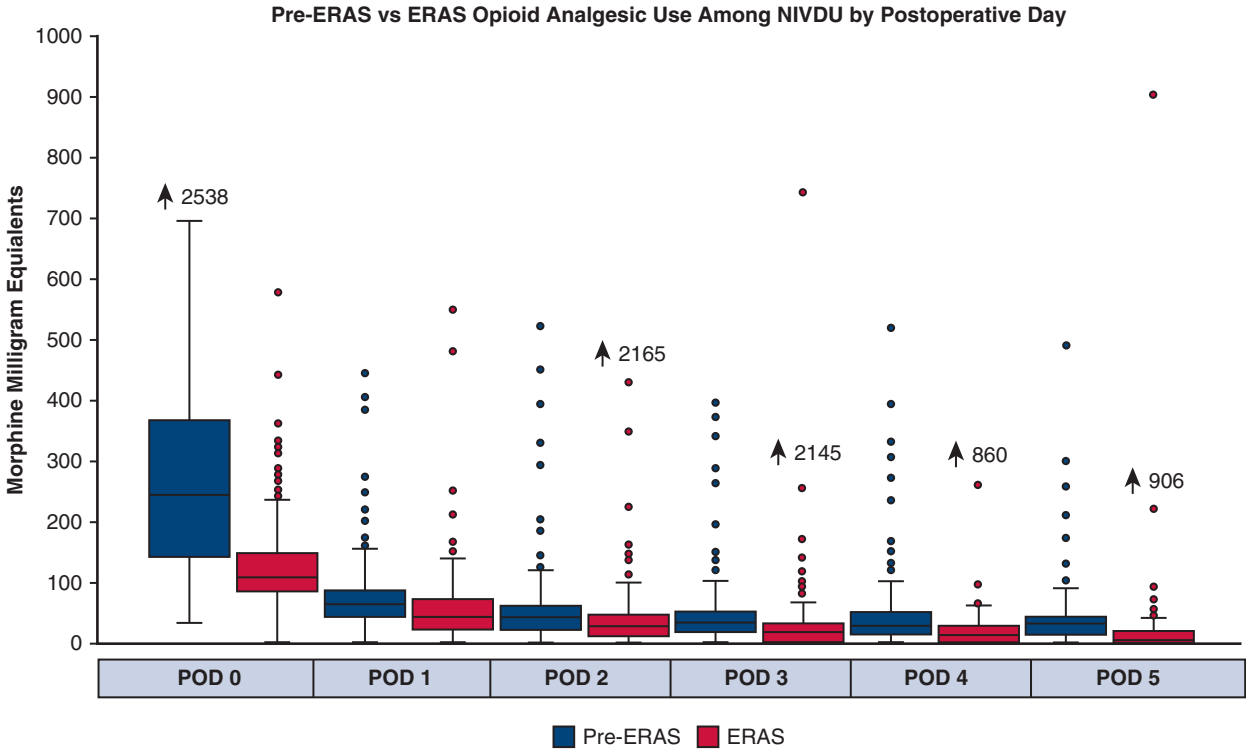


FIGURE 5. Pre-ERAS versus ERAS opioid analgesic use among NIVDU by postoperative day. *ERAS*, Enhanced Recovery After Surgery; *NIVDU*, non-intravenous drug use; *POD*, postoperative day.

oversedation, dizziness, and visual disturbances.[11,12] The use of liposomal bupivacaine at incision and drain sites has also been shown to decrease opioid requirements after laparoscopic abdominal surgeries.[13] However, this analgesic benefit typically diminishes within 24 hours.[11] Dexmedetomidine is a centrally acting α-2 agonist that inhibits the release of norepinephrine and activation of pain signals.[14] This analgesic effect has been linked to decreased opioid requirements in the first 24 hours after surgery, but places patients at risk for bradycardia and potentially hemodynamic instability.[3,6,9] By combining all of these different analgesic modalities, an ERAS protocol aims to combat surgical pain even before the patient arouses from general anesthesia. We also suspect that this regimen contributes to the large reduction in opioid use seen on day of surgery (postoperative day zero). This time period includes the intraoperative phase as well as the first few immediate postoperative hours, during which the patient is often still under effects of general anesthetic. Our protocol also included encouragement of reduced intraoperative reduction of opioid anesthetics and increased use of agents such as dexmedetomidine at the conclusion of surgery rather than agents such as fentanyl infusion.

Over the subsequent 5 postoperative days, the ERAS group consistently used less opioid analgesic than the control group. This continued reduction is likely due to the postoperative multimodal regimen, which included scheduled acetaminophen, gabapentin, lidocaine topical patches, and ketorolac (in patients without contraindication) in addition to as needed tramadol, oxycodone, and hydromorphone. This regimen allowed opioid analgesics to serve as a rescue medication rather than the primary pain regimen.[2] The postoperative administration of scheduled acetaminophen is ubiquitous in ERAS protocols and has been associated with a 20% to 30% decrease in morphine consumption.[13,15] The postoperative use of gabapentinoids has not only been shown to decrease postoperative pain and opioid requirements, but also has the added benefit of reducing anxiety, nausea, and vomiting.[3,16] In cardiac surgery patients, lidocaine patches can be applied to the back or chest to help with pain caused by intraoperative chest wall retraction and chest tube placement. Although the efficacy of lidocaine patches is not well described, they are generally well tolerated by patients and pose limited adverse effect risk.[11,17] The use of tramadol has the benefit of a dual mechanism to address pain, working through both opioid and nonopioid pain pathways and has been

associated with a 25% decrease in opioid analgesic requirement in cardiac surgical patients.[3] Furthermore, tramadol has a favorable safety profile in comparison with other opioid analgesics because it causes less cardiovascular and respiratory depression, is less addictive, and has a lower rate of constipation.[11] Patients should be monitored for onset of postoperative delirium when receiving tramadol because this is one of its most common side effects.[3]

ERAS protocols developed by other surgical subspecialties often emphasize the use of NSAIDs, because evidence suggests that their use in combination with acetaminophen can provide pain control equivalent to opioid analgesics.[17] However, the use of NSAIDs is often limited in cardiac surgery due to the risk of acute kidney injury, bleeding, thromboembolic events, and gastrointestinal complications.[3,12,15,18] In our series, ERAS patients were administered ketorolac followed by ibuprofen starting postoperative day 1. These medications could be withheld at the discretion of the surgeon for renal insufficiency or concerns of platelet dysfunction. In our study, there was no increase in acute kidney injury rates or bleeding seen in those receiving these agents.

Williams and colleagues[19] conducted a retrospective cohort review on the implementation of ERAS protocol in cardiac surgery patients. Their postoperative protocol included scheduled acetaminophen and gabapentin. Oxycodone and fentanyl were provided as needed for pain. The ERAS group had a 30% reduction in IV opioid analgesic use on postoperative day zero. Likewise, in a prospective, observational study of cardiac surgery patients, Fleming and colleagues[20] used a multimodal pain regimen which included the preoperative administration of gabapentin along with postoperative administration of acetaminophen, codeine, and as needed morphine. They demonstrated significantly lower pain scores on postoperative days 1 to 3 in the ERAS group and shorter duration of IV opioid infusion. Our results are similar to these other studies and demonstrate that multimodal pain management is associated with improved pain control and consequently reduces opioid analgesic use after cardiac surgery. It is important to note that our results were not achieved by sacrificing patient perception of pain control. In fact, approximately 80% of our ERAS patients reported being satisfied or very satisfied with their analgesic regimen. Because of the retrospective nature of this study, we were unable to ascertain patient perceptions of the control group. Nonetheless, our results indicate that the pain control achieved with ERAS is well received by patients.

Within our ERAS group, a significant portion of patients (22%) had a history of illicit IVDU. We hypothesized that the nonopioid components of an ERAS protocol would prove beneficial for patients who likely have a tolerance to opioid medications. Although subgroup analysis revealed that although these patients had reduction in opioid analgesic use on postoperative day zero, there was no difference between ERAS and control groups in the subsequent days. Unfortunately, our results reveal that ERAS may not have a notable effect with opioid use in these patients. We continue to use ERAS in IVDU patients, however, because there is some evidence that suggests appropriate treatment of pain and addiction in these patients decreases opioid withdrawal symptoms and the number of patients who leave against medical advice.[21] Similar to ERAS principles, the authors suggest a perioperative strategy to adequately treat postoperative pain and addiction, which begins with consultation of specialists in pain management and addiction medicine on admission.[21] These findings present an opportunity to improve outcomes in patients with a history of addiction and substance use.[21]

Study Limitations

Our study represents a single-center experience and therefore may not be generalizable to other institutions. The retrospective design reduces our ability to understand adjustments or deviations from the ERAS protocol made in real-time by bedside providers. For example, the decision on whether to start, continue, or discontinue ketorolac varied among different surgeons and critical care physicians. In addition, with the current analysis, it is difficult to discern how much of the other ERAS protocol components contributed to the results; the protocol encouraged early chest tube removal, for instance, the final decision on timing of drain removal was left to the discretion of the attending surgeon. Because chest tube removal likely has a beneficial effect on pain control, it is possible that this aspect contributed to differing degrees of opioid use. Although we primarily attribute the reduction in opioid requirements to the multimodal pain protocol, it is possible that a Hawthorne Effect impacted provider's prescribing patterns during the postoperative period. Finally, the predischarge patient surveys were not collected in the control group, and thus we are unable to directly compare patient perception between the ERAS and pre-ERAS groups. Nonetheless, our results demonstrate that an ERAS protocol is associated with a significant reduction in overall opioid use in the perioperative period without compromising patient perception of pain control.

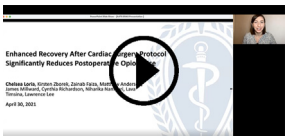
CONCLUSIONS

ERAS protocols with an emphasis on multimodal pain management throughout perioperative care are associated with a significant reduction in the postoperative use of opioid analgesics. Patients with a history of IVDU may not have as pronounced a reduction in opioid use but likely benefit from the nonopioid analgesic regimen. Patients may benefit from future studies analyzing the effects of other

ERAS protocol components beyond pain management aspects.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/21%20AM/AM21_P02/AM21_P02_05.mp4.



Conflict of Interest Statement

The authors reported no conflicts of interest.

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.

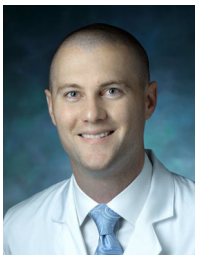
References

1. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg*. 2017;152:292-8.
2. Brown JK, Singh K, Dumitru R, Chan E, Kim MP. The benefits of enhanced recovery after surgery programs and their application in cardiothoracic surgery. *Methodist Debakey Cardiovasc J*. 2018;14:77-88.
3. Engelman DT, Ben Ali W, Williams JB, Perrault LP, Reddy VS, Arora RC, et al. Guidelines for perioperative care in cardiac surgery: enhanced recovery after surgery society recommendations. *JAMA Surg*. 2019;154:755-66.
4. Barr LF, Boss MJ, Mazzeffi MA, Taylor BS, Salenger R. Postoperative multimodal analgesia in cardiac surgery. *Crit Care Clin*. 2020;36:631-51.
5. Centers for Disease Control and Prevention. Calculating total daily dose of opioid for safer dosage [Internet]. Accessed September 11, 2021. https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf
6. StataCorp. *Stata Statistical Software: Release 16*. StataCorp LLC; 2019.
7. Kadri AN, Wilner B, Hernandez AV, Nakhoul G, Chahine J, Griffin B, et al. Geographic trends, patient characteristics, and outcomes of infective endocarditis associated with drug abuse in the United States from 2002 to 2016. *J Am Heart Assoc*. 2019;8:e012969.
8. Lu SY, Lai Y, Dalia AA. Implementing a cardiac enhanced recovery after surgery protocol: nuts and bolts. *J Cardiothorac Vasc Anesth*. 2020;34:3104-12.
9. Echeverria-Villalobos M, Stoicea N, Todeschini AB, Fiorda-Diaz J, Uribe AA, Weaver T, et al. Enhanced recovery after surgery (ERAS): a perspective review of postoperative pain management under ERAS pathways and its role on opioid crisis in the United States. *Clin J Pain*. 2020;36:219-26.
10. Menda F, Köner O, Sayın 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;24:808-13.
11. Wick EC, Grant MC, Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: a review. *JAMA Surg*. 2017;152:691-7.
12. McConnell G, Woltz P, Bradford WT, Ledford JE, Williams JB. Enhanced recovery after cardiac surgery program to improve patient outcomes. *Nursing*. 2018;48:24-31.
13. Tan M, Law LS, Gan TJ. Optimizing pain management to facilitate enhanced recovery after surgery pathways. *Can J Anaesth*. 2015;62:203-18.
14. Simpson JC, Bao X, Agarwala A. Pain management in enhanced recovery after surgery (ERAS) protocols. *Clin Colon Rectal Surg*. 2019;32:121-8.
15. Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, Brunelli A, Cerfolio RJ, Gonzalez M, et al. Guidelines for enhanced recovery after lung surgery: recommendations of the enhanced recovery after surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). *Eur J Cardiothorac Surg*. 2019;55:91-115.
16. Kołodziej T, Maciejewski T, Mendrala K, Darocha T, Węglarzy A, Budziarz B, et al. Enhanced recovery after cardiac surgery. *Kardiochir Torakochirurgia Pol*. 2019;16:32-6.
17. Harvin JA, Green CE, Vincent LE, Motley KL, Podbielski J, Miller CC, et al. Multi-modal analgesic strategies for trauma (MAST): protocol for a pragmatic randomized trial. *Trauma Surg Acute Care Open*. 2018;3:e000192.
18. Gregory AJ, Grant MC, Manning MW, Cheung AT, Ender J, Sander M, et al. Enhanced recovery after cardiac surgery (ERAS cardiac) recommendations: an important first step-but there is much work to be done. *J Cardiothorac Vasc Anesth*. 2020;34:39-47.
19. Williams JB, McConnell G, Allender JE, Woltz P, Kane K, Smith PK, et al. One-year results from the first US-based enhanced recovery after cardiac surgery (ERAS cardiac) program. *J Thorac Cardiovasc Surg*. 2019;157:1881-8.
20. Fleming IO, Garratt C, Guha R, Desai J, Chaubey S, Wang Y, 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;30:665-70.
21. Ray V, Waite MR, Spexarth FC, Korman S, Berget S, Kodali S, et al. Addiction management in hospitalized patients with intravenous drug use-associated infective endocarditis. *Psychosomatics*. 2020;61:678-87.

Key Words: perioperative care, cardiac surgery

Discussion

Presenter: Dr Chelsea M. Loria



Dr Michael C. Grant *(Baltimore, Md)*. I'm excited to get the opportunity to discuss what was a really wonderful presentation by Chelsea. This is quite an undertaking. Obviously, some of the things that you touched on are, I think, really important for everybody to hear about. Oftentimes, we read a study and it just says, "We implemented a bunch of these things, and then we have a certain outcome." But you did a nice job of outlining exactly how the institution went about this, devising the team, putting a protocol together, doing it all together. I think that's effective. One of the things that you obviously alluded to is that you're reducing the number of opioids after surgery. My first question to you is how did you measure opioids? Is this something you typically did on a regular basis? Is this something that you became aware of as part of this project? And then how has it informed your thinking about opioids each day since then?

Dr Chelsea M. Loria *(Indianapolis, Ind)*. Before we instituted the ERAS protocol, we were not routinely tracking how much opioids patients received. So, we had to really put our heads together with our pharmacy colleagues to see what the most effective way would be to track that in patients. What it really came down to was looking at the medication

administration record. Because it doesn't really matter what the patients are prescribed after surgery if they're not actually getting it. That was our way of kind of tabulating how much each patient got. Within the protocol and once people realized that things were being documented, the nursing staff and the prescribers were being more thoughtful about, "How can we really optimize this patient's pain?" And if they see they still have IV medications ordered that they haven't used for days, "Why don't we just go ahead and discontinue that if it's not benefiting the patient?"

Dr Grant. It seems like you touched on 2 really good pieces. One, this idea that there's this now common vernacular among you to think about opioid use and what MMEs actually are. And then maybe that second piece, in some ways a more important piece, that if you can stop the IV options and move to something for a longer duration, something oral, you might get more bang for your buck. I think that's great. You touched on IV drug users, obviously a really challenging group of patients to manage. The other group that we often think about, too, are opioid-tolerant patients, patients who came to surgery having been on opioids previously. Have you guys thought about looking at that subset of patients in the context of your study?

Dr Loria. We did specifically pull out patients who had a history of chronic opioid use for chronic pain, outside of patients with a history of IV drug use. I think that is an important factor because, obviously, they're going to be treated similarly because they are opioid tolerant. So, the management of their pain will be important. Something we found in the IV drug use group is that we need to be more aggressive with their pain control. We commonly involved our addiction colleagues and our palliative care colleagues who are more well trained at addressing chronic pain in patients who are opioid tolerant. That was an important factor, especially in patients with a history of IV drug use, reducing the number of patients who potentially leave against medical advice or have withdrawal symptoms in their postoperative period.

Unidentified Speaker 1. This talk highlighted some important parts. My thought is we need to have better situational awareness in real time of MMEs. We can't have a pharmacist calculating off a Medication Administration Record in real-time. You'll have no idea. We need active de-escalation of MMEs. We need to get rid of the ones that are on the Medication Administration Record but no one's actually taking, so that at 2:00 AM some nurse doesn't give someone a Percocet. We really need to focus on the discharge MMEs. Did you look at that in your study, comparing before and after, the amount of MMEs that were prescribed to that patient on discharge? Because the amount that's prescribed as shown by Dr Grant and associates was prescribed on discharge directly relates to the risk of that patient becoming a new persistent opioid user, which we know in cardiac surgery is up to 11%.

Dr Loria. That's an excellent point. We didn't look in particular at the amount of opioids that patients were prescribed after surgery, but I think that is an important component especially because we obviously have a high percentage of patients with a history of opioid abuse. I think it's important to look at not only the amount that patients are being prescribed after surgery but also what strength and what dose. So, patients going home with tramadol might be a lower risk for addiction than patients going home with a high dose of oxycodone.

Dr Grant. Alex, you have thoughts?

Unidentified Speaker 2. Just quickly with the perspective of someone who has run an acute and a chronic pain in inpatient service. I almost wanted to say that your results on the IV drug users, you might be able to look at those as successful because we all know that both IV drug users and, as Mike alluded to, the chronic opioid users will always have a baseline requirement of opioid needs for pain reasons. So the fact that you didn't see a rebound of extra opioids in days 2 and 3, and those stayed low relative to the NVIDU population, and you showed that the multimodal approach you took actually just kept them at their baseline opioid needs, and then their surgical pain was well controlled by what you had done. That might be successful.

Dr Grant. Tom, other thoughts?

Unidentified Speaker 3. That was a great talk and comment by Alex because those patients usually have a lot of pain. My question is, when you did your ERAS bundle, did you rigid–just to our earlier discussion, were you plating everybody, and did everybody get the [inaudible]—

Dr Loria. Oh, yeah, that's—

Unidentified Speaker 3. –as part of the [inaudible]?

Dr Loria. Yeah, that's [inaudible].

Unidentified Speaker 3. Is that routine?

Dr Loria. We don't routinely do rigid sternal fixation. Most of our staff use traditional sternal wires. I've only seen the rigid sternal fixation in patients who they think are at high risk for sternal wound infections or who have a history of poor external healing if it's a redo. The use of liposomal bupivacaine or Exparel was routine. Toward the beginning of the study, it wasn't something that the surgeons were used to incorporating on a routine basis, but by the end of the study, everyone was routinely making it a habit that, "Hey, we're getting ready to close. Is the Exparel on the field? Can we go ahead and administer that?" Anecdotally this isn't something that we looked at, but as someone who is a bedside provider, I found that a lot of times the first day after surgery, patients weren't reporting incisional pain. They're reporting back pain associated with their chest tubes. I thought that was kind of a testament to using that local anesthetic.

Unidentified Speaker 3. Yeah, we [infiltrate?] with Marcaine, and I just have been battling with the pharmacy to get

liposomal Marcaine. I'll go back to the battle. I think if you could publish your results, that might help. The more literature we get out there about that will help.

Dr Grant. Couldn't agree more with that.

Unidentified Speaker 4. Same thing with Exparel. It's hard to get it on formulary.

Dr Grant. I think Exparel in many ways is going to go the route that we've seen with dexmedetomidine. The idea that perhaps we're waiting for the day when the costs just simply come down. But the data on this right now are still limited to small case studies, case series, some randomized data, but this is a real challenge. Amanda, thoughts?

Unidentified Speaker 5. I have one comment regarding pain and chest tubes. You had commented that once you use the Exparel. You noticed that maybe they were expressing more about back pain related to chest tubes. Typically, in your practice, when do you normally take out chest tubes? The ERAS protocols clearly outline early removal of tubes. I think that helps with ambulation and getting patients up quicker, as well as reduction in pain. Some of the caveat to that is potentially more plural effusions that could crop up if you're getting them out sooner. I'd like to hear your comments on those questions.

Dr Loria. I think an important point is that chest tube removal enhances patients' recovery: They get up faster and have less pain, and they're taking less pain medications. They obviously benefit from that because they're less sedated and have early return of bowel function. At our institution, primarily the chest tube management, a lot of it is staff dependent. We're trying to go toward more of a protocolized system where especially if chest tube output is frankly serous that they're discontinued at that time. I don't want to say regardless of the output, but if they're higher output and serous, we are more comfortable pulling them. In our study, I didn't present this, but we did find that chest tubes were removed earlier, which was a significant difference from before we instituted our ERAS protocol. I think that also could have contributed to the reduction in postoperative opioid requirement.

Dr Grant. I'll admit we could talk about this for a longer period of time, but we should turn it back over for the rest of the session to Helen-Marie and Thomas.

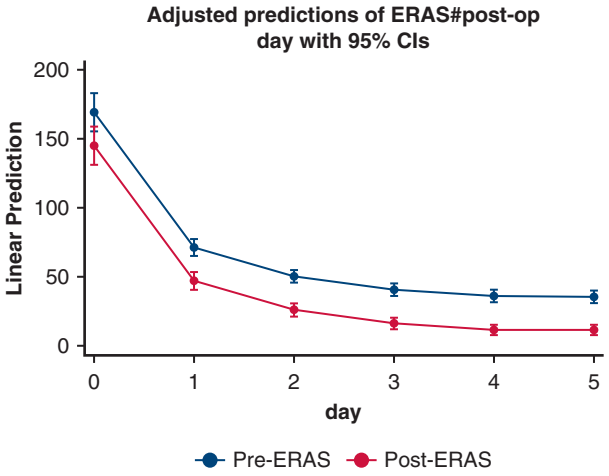


FIGURE E1. Repeated-measures analysis. *ERAS*, Enhanced Recovery After Surgery; *CI*, confidence interval.

TABLE E1. Morphine milligram equivalent conversion factors for common opioid medications

Opioid	Conversion factor
Codeine	0.15
Fentanyl (IV)	0.1
Hydrocodone	1
Hydromorphone	4
Morphine	1
Oxycodone	1.5

IV, Intravenous.

TABLE E2. Pre–Enhanced Recovery After Surgery versus Enhanced Recovery After Surgery multivariable quantile (median) regression analysis by postoperative day

	Morphine milligram equivalents by POD					
	POD 0	**POD 1**	**POD 2**	**POD 3**	**POD 4**	**POD 5**
Pre- (Ref) vs Post-ERAS, (95% CI, *P* value)	–148.8 (–183.8 to –113.8), <.0001	–25.6 (–36.7 to –14.6), <.0001	–17.6 (–25.6 to –9.6), <.0001	–16 (–23.1 to –8.9), <.0001	–15.9 (–23 to –8.9), <.0001	–21.6 (–28.4 to –14.9), <.0001
Patient characteristics (95% CI, *P* value)						
Procedure type						
Ascending aortic	**Ref**	**Ref**	**Ref**	**Ref**	**Ref**	**Ref**
CABG	–18.1 (–85.4-49.1), .597	0.3 (–21-21.6), .977	–7.5 (–22.9-7.8), .336	–3.8 (–17.5-9.9), .584	–2.6 (–16.5-11.3), .714	–5.1 (–18.2-7.9), .438
Valve	–11.6 (–68.2-45), .687	–6.4 (–24.2-11.4), .483	–13.3 (–26.2-0.4), .043	–15.6 (–27- –4.1), .008	–5.2 (–16.6-6.1), .362	–3.7 (–14.2-6.8), .487
Valve + CABG	–27.0 (–108-54.0), .512	8.7 (–17-34.5), .505	5.9 (–12.7-24.6), .531	3.6 (–13.3-20.5), .674	–9.1 (–25.6-7.3), .277	–5.4 (–21.2-10.4), .504
Other	–21.4 (–89.2-46.4), .535	4.3 (–17.2-25.8), .697	8.7 (–6.8-24.1), .272	11 (–2.7-24.7), .117	14.3 (0.8-27.7), .038	7.3 (–4.7-19.3), .232
No endocarditis (Ref) vs endocarditis	3.2 (–54.2-60.7), .912	6.8 (–11.4-4.9), .464	28.8 (15.7-42), <.0001	7.6 (–4-19.3), .199	7.8 (–3.5-19.1), .175	6.6 (–3.5-16.7), .199
No hypertension (Ref) vs hypertension	17.7 (–24.1-59.6), .405	–10.4 (–23.9-3), .127	–5.1 (–14.7-.5), .300	–7.7 (–16.3-0.8), .075	–7.9 (–16.3-0.4), .063	–5.8 (–13.6-2.1), .152
NIVDU (Ref) vs IVDU	53.7 (–0.4-107.7), .052	34.9 (17.9-51.9), <.0001	12.1 (–0.4-24.5), .057	15.5 (4.3-26.8), .007	15.6 (4.7-26.5), .005	20.2 (10.2-30.1), <.0001
No liver disease (Ref) vs Liver disease	–6.0 (–76.6-64.6), .868	17.4 (–4.8-39.5), .125	5.8 (–10.3-21.8), .483	4.9 (–9.4-19.2), .505	1.0 (–13.7-13.8), .992	–0.9 (–13.2-11.4), .886
Cardiac presentation						
Anginal equivalent	**Ref**	**Ref**	**Ref**	**Ref**	**Ref**	**Ref**
Stable angina	52.0 (–106.5-210.5), .519	–14.9 (–65.2-35.4), .561	–4.2 (–40.3-32), .821	–11.7 (–43.8-20.3), .472	13.6 (–27.1-54.2), .513	27.1 (–8.4-62.7), .134
Unstable angina	39.6 (–105.5-184.8), .592	–7 (–52.5-38.6), .763	2.8 (–30.3-35.8), .869	–0.3 (–29.6-29), .986	22.7 (–15.3-60.7), .242	20 (–12.5-52.6), .227
Non-ST elevation	49.6 (–120.2-219.5), .566	6.4 (–46.9-59.7), .813	6 (–32.6-44.6), .760	2.6 (–31.6-36.8), .882	23.5 (–18.4-65.5), .271	28.8 (–7.4-65), .119
ST-elevation MI	71.4 (–169.3-312.1), .560	–4.2 (–79.6-71.3), .913	–0.8 (–55.5-53.9), .978	–10.7 (–59.2-37.8), .665	13.6 (–44.3-71.5), .645	22.5 (–39-84.1), .472
Asymptomatic	31.5 (–117.4-180.5), .677	–14.3 (–61-32.3), .546	–5.7 (–39.6-28.2), .741	–11.5 (–41.5-18.6), .453	17.3 (–20.7-55.3), .372	15.4 (–17.6-48.4), .359
Other	39.4 (–100.5-179.4), .580	–12 (-55.9-31.9), .591	–2.9 (–34.8-28.9), .856	0.1 (–28.1-28.4), .993	20.2 (–16.1-56.5), .274	17.3 (–13.6-48.1), .271
Intraoperative times (min)						
CPB	–0.2 (–0.6-0.3), .487	–0.02 (–0.2-0.1), .775	–0.03 (–0.1-0.1), .672	0.01 (–0.1-0.1), .862	0.01 (–0.1-0.1), .875	0.03 (–0.1-0.1), .545
Crossclamp	0.1 (–0.5-0.8), .655	0.04 (–0.2-0.2), .719	–0.03 (–0.2-0.1), .721	–0.03 (–0.2-0.1), .620	–0.01 (–0.1-0.1), .863	–0.1 (–0.2-0.1), .347

POD, Postoperative day; *ERAS*, Enhanced Recovery After Surgery; *CI*, confidence interval; *CABG*, coronary artery bypass grafting; *NIVDU*, nonintravenous drug use; *IVDU*, intravenous drug use; *MI*, myocardial infarction; *CPB*, cardiopulmonary bypass.

TABLE E3. Enhanced Recovery After Surgery multimodal pain medication patient compliance

Medications	Compliance, n (%)
Preoperative	
Acetaminophen	152 (60.8)
Gabapentin	152 (60.8)
Intraoperative	
Liposomal bupivacaine	214 (85.6)
Postoperative	
Dexmedetomidine	176 (70.4)
Acetaminophen	248 (99.2)
Lidocaine patches	248 (99.2)
Gabapentin	228 (91.2)
Tramadol	235 (94.0)
Oxycodone	245 (98.0)
IV fentanyl/hydromorphone	246 (98.4)

IV, Intravenous.

TABLE E4. Patient characteristics in intravenous drug user (IVDU) versus nonintravenous drug user (NIVDU)

Characteristics, n (%)	NIVDU (393)	IVDU (73)	*P* value
Procedure type			<.0001
Ascending aortic	75 (19.08)	8 (10.96)	
CABG	153 (38.93)	17 (23.29)	
Valve	107 (27.23)	12 (16.44)	
Valve + CABG	23 (5.85)	1 (1.37)	
Other	35 (8.91)	35 (47.95)	
Age, median (Q1, Q3)	64 (57, 71)	44 (34, 60)	<.0001
Gender			.008
Male	277 (70.48)	40 (54.79)	
Female	116 (29.52)	33 (45.21)	
Race			.16
White	342 (87.02)	59 (80.82)	
Non-White	51 (12.98)	14 (19.18)	
Risk factors			
BMI, median (Q1, Q3)	29.85 (26.02, 34.27)	25.77 (22.77, 30.94)	.0001
Diabetes	161 (40.97)	13 (17.81)	<.0001
Endocarditis	32 (8.14)	40 (54.79)	<.0001
Cerebrovascular disease	67 (17.05)	16 (21.92)	.318
Chronic lung disease	102 (25.95)	15 (20.55)	.328
Family history of CAD	11 (2.80)	1 (1.37)	.701
Hypertension	326 (82.95)	31 (42.47)	<.0001
Last HbA1c level, median (Q1, Q3)	6 (5.5, 7)	5.7 (5.4, 6.5)	.0282
Liver disease	8 (2.04)	28 (38.36)	<.0001
Peripheral artery disease	57 (14.50)	6 (8.22)	.149
Previous cardiac interventions			
Any	145 (36.90)	28 (38.36)	.813
CABG	6 (1.53)	1 (1.37)	>.999
Valve	36 (9.16)	14 (19.18)	.011
Other cardiac surgery	52 (13.23)	12 (16.44)	.465
PCI	83 (21.12)	11 (15.07)	.237
Preoperative cardiac status			
Prior MI	78 (19.85)	12 (16.44)	.687
Heart failure	121 (30.79)	13 (17.81)	.024
Cardiogenic shock	2 (0.51)	1 (1.37)	.401
Cardiac arrhythmia	89 (22.65)	12 (16.44)	.237
Operative times (min)			
CPB, median (Q1, Q3)	138 (105, 184)	117 (86, 155)	.0043
Crossclamp, median (Q1, Q3)	97 (74, 136)	82 (61, 117)	.0027

CABG, Coronary artery bypass grafting; *BMI*, body mass index; *CAD*, coronary artery disease; *HbA1c*, hemoglobin A1c; *PCI*, percutaneous coronary intervention; *MI*, myocardial infarction; *CPB*, cardiopulmonary bypass.

TABLE E5. Pre–Enhanced Recovery After Surgery versus Enhanced Recovery After Surgery (ERAS) opioid analgesic use by repeated measures multivariable design

	MME over time (95% CI, *P* value)
Pre-ERAS (Reference) vs Post-ERAS	–24.4 (–29.2-19.5), <.0001
Morphine equivalents (0-5 d)	
Day 0	**Ref**
Day 1	–98 (–112 to –84), <.0001
Day 2	–118.9 (–132.6 to –105.2), <.0001
Day 3	–128.4 (–142.2 to –114.7), <.0001
Day 4	–133.3 (–147 to –119.7), <.0001
Day 5	–133.7 (-147.3 to –120.1), <.0001
Procedure type	
Ascending aortic	**Ref**
CABG	–4.3 (–13.8-5.2), 0.377
Valve	–4.7 (–11.6-2.2), 0.180
Valve + CABG	1.6 (–14.6-17.7), 0.851
Other	7.3 (–4.6-19.2), 0.227
No endocarditis (Ref) vs ENDOCARDITIS	8 (–1.3-17.2), 0.091
No hypertension (Ref) vs Hypertension	–7 (–13.9 to –0.03), 0.049
NIVDU (Ref) vs IVDU	22.9 (11.8-34.1), <.0001
No liver disease (Ref) vs liver disease	4.8 (–12.3-21.9), 0.584
Cardiac presentation	
Anginal equivalent	**Ref**
Stable angina	–2.6 (–22.5-17.3), 0.796
Unstable angina	1.9 (–18.2-22), 0.854
Non-ST elevation MI	6.1 (–19.3-31.5), 0.636
ST-elevation MI	2.3 (–28.7-33.3), 0.886
Asymptomatic	–6.7 (–27.3-14), 0.526
Other	–3.1 (–23.1-17), 0.765
Intraoperative times (min)	
CPB	0.01 (–0.1-0.1), 0.804
Crossclamp	–0.03 (–0.1-0.1), 0.551

MME, Morphine milligram equivalent; *CI*, confidence interval; *CABG*, coronary artery bypass grafting; *NIVDU*, nonintravenous drug user; *IVDU*, intravenous drug user; *MI*, myocardial infarction; *CPB*, cardiopulmonary bypass.