Enhanced Recovery After Surgery Multi-Modality Pain Regimen Performs Similar to PRN Narcotics on Outcomes and Pain Control After Cardiac Surgery: A Quality Improvement Project

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Abstract

Background: While enhanced recovery after surgery (ERAS) pathways have been successfully applied for cardiac surgery, there has been limited research directly comparing ERAS protocols to ad hoc narcotic use after surgery. We hypothesized that a standardized ERAS protocol would provide similar pain management and psycho-emotional outcomes while decreasing the use of opioids in the hospital and after discharge. **Methods**: As part of a 7-month quality improvement project, cardiac surgery patients on a fast tracked to extubate pathway were assigned PRN narcotic pain management for 3 months (n=49). After a 1-month ERAS protocol optimization period, a separate group of patients were given the ERAS protocol (n=34). Clinical outcomes were gathered, and participants completed a quality of recovery survey that allowed for the assessment of pain and symptom control at 4 time-points post-surgery. **Results**: Among 83 participants, 66% were male and the mean age was 53 years. There were no differences in patient characteristics between PRN and ERAS groups (all p>0.244). There were no differences between ERAS and PRN groups for surgery characteristics (all p>0.060), inpatient outcomes (all p>0.658), or after-discharge outcomes (all p>0.397). Furthermore, across all time-point comparisons, there were no supported differences in patient-reported outcome and pain control between the ERAS and PRN narcotic groups (all p>0.075). **Conclusions**: An ERAS protocol demonstrated similar patient outcomes and pain control to traditional opioid use for postoperative cardiac surgery patients. Further research is recommended to further confirm the results of this study.

Introduction

Enhanced recovery after surgery (ERAS) protocols are being used in various surgical areas in an effort to reduce the use of opioids while responding to the trauma of surgery and postoperative pain. This has become increasingly important in the wake of the opioid crisis and the confirmed role that surgeons can play . [1-3] Cardiac surgeons are not without fault in this crisis, with some studies demonstrating that nearly 10% of cardiac surgery patients go on to develop persistent opioid requirements after cardiac surgery [4] Indeed, ERAS protocols are highlighted for their pain managements strategies which the do not rely on opioids, but the benefits extend beyond pain management. These protocols have demonstrated improvement in length of stay and overall postoperative complications in multiple surgical specialties.[5,6] Hirji et al developed a list of objective data elements which could be collected to demonstrate the benefits of ERAS

protocols for cardiac surgery and standardize benchmarks across hospitals.[7] A brief commentary noted the benefits of ERAS protocols for cardiac surgery with early extubation, potentially even in in the operating room immediately after surgery.[8] Williams et al noted in a 1-year study that ERAS protocols for cardiac surgery programs had significantly improved perioperative outcomes including decreased intensive care unit (ICU) stay and hospital length of stay (LOS), decreased incidence of gastrointestinal (GI) complications, and decreased utilization of narcotic pain regimens.[9] Pain management and opioid sparing strategies are only a portion of a comprehensive ERAS protocol. The benefits of these protocols go beyond pain control and are multi-dimensional in their aim to improve the patients' surgical experience. Adequate pain control may lead to patient satisfaction, overall improved attitude towards the postoperative experience, and increased willingness to participate in postoperative care (eg, physical therapy etc). Currently, the ERAS studies in cardiac surgery have focused on many aspects of improving the postoperative course of patients, including faster time to extubation, decreased length of stay, and others. We developed an ERAS protocol as a quality improvement initiative and sought to evaluate its effect regarding pain control. We hypothesized that with a multi-modality pain regimen and limited narcotics administration, patients' pain would be well controlled after cardiac surgery, resulting in improved patient satisfaction.

Methods

Patient Population

The current study was a single-center, IRB approved, prospective, sequentially allocated, non-randomized quality improvement trial. Any patient undergoing either elective or urgent cardiac surgery deemed appropriate for fast track to extubate was eligible for inclusion in the study, including both PRN and ERAS arms. Any patient undergoing non-emergent surgery was eligible for the fast track to extubate pathway.

Data were collected over a 7-month period in 2019. For the first 3 months of the study, any eligible participant received the traditional PRN narcotic regimen which included medications such as hydrocodone/acetaminophen and oxycodone/acetaminophen PRN. These patients are denoted as the "PRN" group. The ERAS protocol was then introduced for all eligible patients at a single medical center. Following a 1-month protocol optimization period, eligible patients were treated using the ERAS pain management protocol over the subsequent 3 months. These participants are denoted as the "ERAS" group. The full pre- and post-operative ERAS protocols are shown in **Figures 1 and 2** .

Clinical Characteristics

Clinical metrics assessed included: aortic cross-clamp time and cardiopulmonary bypass time during the operation, ICU and in-hospital LOS, rates of postoperative atrial fibrillation, wound infection, stroke, prolonged ventilation, and 30-day mortality and readmission rate.

Quality of Recovery

Participants were given a 40-item quality of recovery survey (QoR-40) at four time points during the study: (i) at 48 hours post-extubation, (ii) at transfer from ICU to non-ICU, (iii) at hospital discharge, and (iv) at a 2-week in-person clinic follow-up visit. We assessed various dimensions of recovery via item-level symptom reports of pain (7 questions), physical comfort (8 questions), emotional state (6 questions), and psychological support (1 question).[10] Each participant was asked "Have you had any of the following in the last 24 hours?" They were then asked to grade these symptoms on a 5-point Likert scale: "None of the time", "Some of the time", "Usually", "Most of the time", and "All of the time". **(Instrument included in Supplementary Materials).**

Statistical Analysis

Summary statistics were calculated using standard methods. Multivariable mixed effects ordered logistic models were employed using self-reported frequencies across symptom categories. The primary modeling framework included an interaction of peri-surgical time point and pain management protocol, adjusted for age, race, gender, body-mass index (BMI), history of intravenous (IV) drug use, and use of pain medications

at home around the surgical window. Graphs were drawn using marginal estimates from fully adjusted models. Due to limited data in some response categories, results were presented for participants reporting "none" or "some" symptom occurrences at each time point. Furthermore, for some outcomes, absence of variation in the data would not allow for model convergence, so these outcomes are omitted from reported results. There was no reason to assume missing data were not missing at random (NMAR). The missing at random (MAR) assumptions of the mixed models utilized in analyses were deemed valid. All statistical analyses were completed using Stata v16.1.

Results

There were 83 participants, 49 in the PRN narcotic group and 34 assigned to ERAS. Sixty-six percent were male and the mean age was 53 years (**Table 1**). There were no differences in patient characteristics between PRN and ERAS groups; this includes no significant different in age (54.37±13.56 PRN vs 51.76±14.83; p=0.41), history of IV drug use (n=4 PRN vs. n=2 ERA; p=0.69) or prevalence of prior pain medication prescriptions (n=11 PRN vs n=10 ERA; p=0.47) The type of operations included was heterogeneous and included coronary artery bypass grafting (CABG) alone (n=27; 32%), valve surgery alone (n=15; 18%), CABG + valve (n=3; 4%), CABG + other (n=2;2%), Valve + other (n=13;16%), and other procedures (n=23; 28%), with the vast majority of these procedures consisting of thoracic aortic repair. All procedures were performed via median sternotomy. Surgical characteristics are described in **Table 2** . There was no difference in hospital mortality (n=1 PRN vs n=1ERA; p=0.79), hospital length of stay (16.8 days PRN vs. 15.35 days ERAS; p=0.66), or ICU length of stay (6.88 days PRN vs 6.88 days ERAS; p=0.99). There was a trend toward significant for operative cardiopulmonary bypass times (145.41 minutes PRN vs. 114.85 minutes ERAS; p=0.06) but no difference in aortic cross clamp times (97 minutes PRN vs 75.82 minutes ERAS; p=0.11).

There were no supported differences in patient-reported outcome and pain control between the ERAS protocol and traditional narcotic PRN-only pain medications (**Table 3**). As an illustrative example of patient-reported trajectories at the 4 time points, **Figure 3**shows percentage of patients reporting headache either none of the time (green) or some of the time (orange) for both ERAS (solid lines) and PRN (dashed lines). For this particular outcome, headache remained stable across time, with those on the ERAS protocol displaying a higher proportion of having no headache. Trajectory relationships for other outcomes are shown in **Figures 4 and 5** . Low-level presence of almost all patient reported adverse outcomes and pain was observed across the full battery of symptoms reported (**Figures 3-5**), with the exception of moderate pain being reported in equal numbers across all time points.

Conclusions

Despite lacking statistical significance, our data suggest an overall reduction in reported symptoms associated with the ERAS protocol at hospital discharge, compared to ICU transfer (**Table 3** ; 10/16 ORs < 1). Conversely, the data also suggest an overall increase in symptom reporting associated with the ERAS protocol at the 2-week outpatient visit, compared to hospital discharge (**Table 3** ; 14/16 ORs >1). The notable exception to this was the odds of reporting severe pain at the 2 weeks follow up vs. hospital discharge (p=0.075). However, this relationship can be partially explained by the very low reporting of severe pain at hospital discharge for the ERAS group. In our sample, patients rarely reported any outcome with frequency beyond "some of the time".

Surgeons have proven to be high opioid prescribers, and previously there was limited evidence to support discrete recommendations [11-13]. In general however, surgeons have been found to be over-prescribers of opioid pain medications [11]. This has prompted the proliferation and study of protocols which minimize narcotic pain medications. Few studies in the cardiothoracic literature have specifically addressed the influence of pain medication regimens, and adequacy of pain control on patient satisfaction with an ERAS protocol. Wagner et al performed a multicenter retrospective analysis on patient undergoing CABG and identified that in their study 28% of opioid naïve patients could be discharged without an opioid prescription and the vast majority of these never required an opioid prescription at follow-up [14]. Pan et al evaluated

patients' satisfaction after elective cesarean section.[15] The study noted that patients who were treated with an ERAS protocol reported a decreased incidence of intraoperative nausea, decreased pain scores during the first 24 hours at rest, and during motion in the first 24 hours and 48 hours after surgery. They also reported that patient satisfaction was higher in the ERAS group. Li et al published a review article on the use of ERAS protocols in colorectal surgery.[16] Four of the 15 publications discussed patient satisfaction with the use of an ERAS protocol. There was no difference in patient satisfaction in 2 of these studies. Just one study noted an improvement in overall patient satisfaction scores. Li et al concluded that patient satisfaction was not worse with an ERAS protocol, which is similar to the results of our study. Debono et al noted the use of an ERAS protocol in spine surgery, specifically spine fusion surgery.[17] The study noted, based on a 5-point Likert scale, that 86.5% of patients were satisfied or very satisfied with overall care. Rege et al also noted improved pain scores with an ERAS protocol in laparoscopic donor nephrectomy.[18] Echeverria-Villabolos et al conducted a study to evaluate ERAS protocol to reduce postoperative opioid use.[19] The study noted that an effective multi-modality pain regimen that was narcotic-free, including medications such as nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, gabapentin, regional anesthetic medications, etc, was associated with decreased narcotic use in the postoperative setting.

Limited studies exist that evaluate patient satisfaction in the postoperative environment with regard to pain control in all of the surgical literature. This study evaluates the use of a multi-modality minimal narcotic pain regimen for cardiac surgery patients. When compared to a more traditional narcotic based pain regimen, patients' satisfaction demonstrated no difference. This study emphasizes in addition to other ERAS studies in cardiac surgery, that patients' recovery quality can be maintained and potentially benefit from a minimal narcotic regimen.

There are some limitations in our study to consider. The analysis sample was recruited via mutually exclusive pre-defined recruitment windows for each treatment group, potentially contributing to some degree of bias among the study characteristics between the treatment groups. The limited time window for data collection paired with the patient throughput restricted the sample further than desired leaving some potentially clinically meaningfully differences undetected.

Future studies would benefit from additional assessment for pain intensity, such as the visual analogue scale (VAS) or the numeric rating scale (NRS). Subgroup analyses for surgical approach would uncover potential confounders to the performative evaluation of the ERAS protocol.

In conclusion, we have demonstrated the potential for the ERAS protocol to provide equivalent pain and psychological outcomes compared to PRN opioids for cardiac surgery patients. These results need to be confirmed with rigorously designed randomized clinical trials, including multiple sites and increased patient recruitment. With the potential to drastically reduce the amount of opioids in the community, this research should be a high priority.

Tables

Table 1. Patient Characteristics at Enrollment **Table 1. Patient Characteristics at Enrollment**

Characteristics		**Overall**
(n = 83)	**PRN**	
(n = 49)	**ERAS**	
(n = 34)	**p-value**	
Age (years)		53.30 (14.0
Ethnicity	Hispanic or Latino	3 (4%)
	Not Hispanic or Latino	77 (93%)
	Unknown / Not Reported	3 (4%)
Race	American Indian/Alaska Native	2 (2%)
	Asian	0 (0%)
	Native Hawaiian or Pacific Islander	0 (0%)
	Black or African American	40 (48%)

Table 1. Patient Characteristics at Enrollment	**Table 1. Patient Characteristics at Enrollment**	
	White	38 (46%)
	More Than One Race	1 (1%)
	Unknown / Not Reported	2 (2%)
Male (Y/N)		55 (66%)
Height (cm)		173.88 (9.3
Weight (kg)		89.22 (20.8
BMI (kg/m^2)		29.45 (6.33
History of IV Drug Use (Y/N)	History of IV Drug Use (Y/N)	6 (7%)
Prescription Pain Medication at Home (Y/N)	Prescription Pain Medication at Home (Y/N)	21 (25%)
Cells represent: mean (SD) or n (%)	Cells represent: mean (SD) or n (%)	

BMI, body-mass index; IV, intravenous

Table 2. Surgical characteristics
Characteristics
(n = 83)
(n = 83)
(n = 49)
(n = 34)
(n = 34)
In-hospital mortality (Y/N)
In-hospital stroke (Y/N)
Postoperative atrial fibrillation (Y/N)
Hospital length of stay (days)
ICU length of stay (days)
Ventilator time (days)
30-day mortality (Y/N)
30-day wound infection (Y/N)
30-day readmission (Y/N)
Operative cardiopulmonary bypass time (minutes)
Operative aortic cross-clamp time (minutes)
Follow-up reoperation (Y/N)
Cells represent: mean (SD) or n (%) ICU, intensive care unit.

Table 3. Effect modification of ERAS protocol for various symptoms across study window
Have you had any of the following in the last 24 hours?
vs 48-hrs Post-Extubation
vs 48-hrs Post-Extubation
vs ICU Transfer
vs ICU Transfer
vs ICU Transfer
vs Hospital Discharge
vs Hospital Discharge
Physical comfort
Nausea
Feeling restless
Shaking or twitching
Shivering
Feeling too cold
Feeling dizzy

Table 2. Surgical characteristics

Emotion State
Feeling anxious
Feeling angry
Feeling depressed
Feeling alone
Had difficulty falling asleep
Pain
Moderate pain
Severe pain
Headache
Muscle pains
Backache
Cells represent: adjusted OR (95% CI OR) p-value
Example interpretation: When returning for a 2-week outpatient surgical follow-up visit, there was an associated 12% increa
ICU, intensive care unit.

Figure Legends

Figure 1. Details of the ERAS protocol, Pre-Op

Figure 2. Details of the ERAS protocol, Post-Op

Figure 3. Adjusted symptom probabilities (with 95% CIs) of participants reporting none or some headaches under each protocol across peri-surgical period

Figure 4. Adjusted symptom probabilities (with 95% CIs) of participants reporting none or some pain-related symptoms under each protocol across peri-surgical period.

Figure 5. Adjusted symptom probabilities (with 95% Cis) of participants reporting none or some quality of life-related symptoms under each protocol across peri-surgical period

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Figure 5. Adjusted symptom probabilities of participants reporting none or some quality of life-related symptoms under each protocol across peri-surgical period

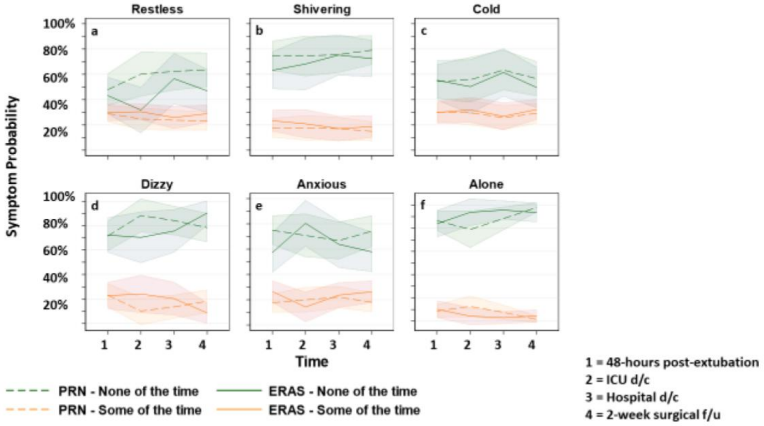
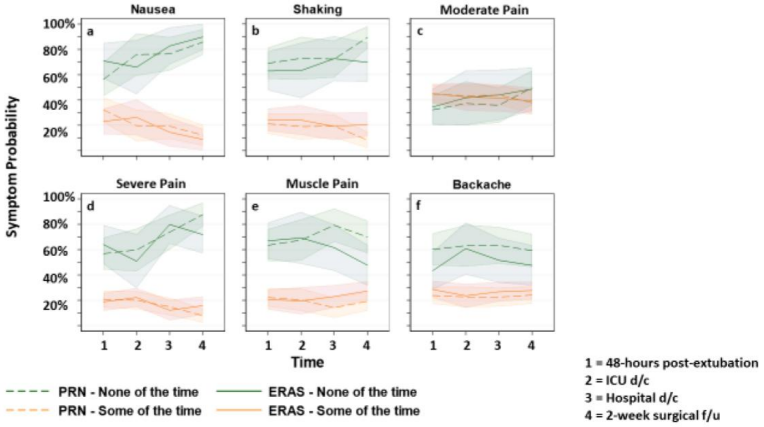


Figure 4. Adjusted symptom probabilities of participants reporting none or some pain-related symptoms under each protocol across peri-surgical period



ERAS Protocol

ERAS protocol for Cardiac Surgery (version 6)

NOTE: Only for those deemed appropriate for fast track extubation

Pre-Op

Carbohydrate drink (non-diabetic) or Carbohydrate-free drink (diabetic) up to 6 hours preop and pre-op meds given to patient to take prior to arrival on day of surgery.

Order Meds: ***Pain Options***
APAP - Acetaminophen 1000 mg PO x 1 (omit for T Bili >1.5)
Gabapentin x 1 dose (@ least 2 hrs prior to surgery)
- CrCl ≥60 : 600 mg
- CrCl 16-59 : 300 mg
- CrCl ≤15 : 100 mg

Additional Options
Antibiotics on call to OR

PONV Prevention Options *(to be given immediately after reversal)*
Zofran 4mg IV
Promethazine 12.5 mg IV or rectally

Post-Op

Order Meds: ***Pain Options*** (after extubation and consider for duration of 48 hours)
Tylenol 650 mg PO q6h (omit for T Bili >1.5)
**alternating doses with NSAID
Ketorolac 15 mg IV or Ibuprofen 600 mg PO q6h
(**Exclude if Age >65yo and/or CABG)
(may be used if CrCl >60 mL/min or ESRD long term iHD pts)
(NSAIDS – if on Aspirin, no NSAID needed)
Gabapentin - dictated by renal function
- CrCl ≥60 : 300 mg po TID
- CrCl 30-59: 300 mg po BID
- CrCl 15-29: 200 mg po BID
- CrCl <15: 100 mg po HS

Lidocaine 5% patch daily
- on for 12 hrs/off for 12 hrs

Tramadol 50 mg po
- q6h scheduled for first 24 hrs
- Will develop a weaning protocol/taper to minimize need for usage post discharge

Afib Prevention
Will consider an agent if/when eligible per hemodynamics

PONV Prevention Options (duration of 48 hrs post-op)
Zofran 4mg IV Q6 PRN nausea
Promethazine 12.5 mg IV or rectally Q6 PRN

Bowel regimen:
Pericolace 2 tab po daily
or
Colace 100mg po BID
or
Lactulose 10g po BID
or
Miralax 17g po BID

May also consider Psyllium (Metamucil) – 1 packet daily
Additional considerations - Melatonin 10 mg PO QHS