

Optimization of an Enhanced Recovery After Surgery protocol for opioid-free pain management following robotic thoracic surgery



Karishma Kodia, MD, Ahmed Alnajjar, MD, Joanne Szewczyk, MD, Joy Stephens-McDonnough, MsN, Nestor R. Villamizar, MD, and Dao M. Nguyen, MD, MSc, FRCSC, FACS

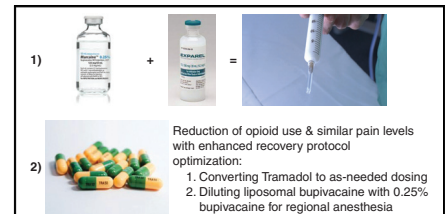
ABSTRACT

Objectives: Our Enhanced Recovery After Thoracic Surgery protocol was implemented on February 1, 2018, and firmly established 7 months later. We instituted protocol modifications on January 1, 2020, aiming to further reduce postoperative opioid consumption. We sought to evaluate the influence of such efforts on clinical outcomes and the use of both schedule II and schedule IV opioids following robotic thoracoscopic procedures.

Methods: A retrospective study of patients undergoing elective robotic procedures between September 1, 2018, and December 31, 2020, was conducted. Essential components of pain management in the original protocol included nonopioid analgesics, intercostal nerve blocks with long-acting liposomal bupivacaine diluted with normal saline, and opioids (ie, scheduled tramadol administration and as-needed schedule II narcotics). Protocol optimization included replacing saline diluent with 0.25% bupivacaine and switching tramadol to as needed, keeping other aspects unchanged. Demographic characteristics, type of robotic procedures, postoperative outcomes, and in-hospital and postdischarge opioids prescribed (ie, milligrams of morphine equivalent [MME]) were extracted from electronic medical records.

Results: Three hundred twenty-four patients met the inclusion criteria (159 in the original and 183 in the optimized protocol). There was no difference in postoperative outcomes or acute postoperative pain; there was a significant reduction of in-hospital and postdischarge opioid requirements in the optimized cohort. For anatomic resections: mean, 60.0 MME (range, 0-60.0 MME) versus mean, 105.0 MME (range, 60.0-150.0 MME), and other procedures: mean, 0 MME (range, 0-60 MME) versus mean, 140.0 (range, 60.0-150.0 MME) ($P < .00001$) with median schedule II opioids prescribed = 0.

Conclusions: Small modifications to our protocol for pain management strategies are safe and associated with significant decrease of opioid requirements, particularly schedule II narcotics, during the postoperative period without influencing acute pain levels. (JTCVS Open 2022;9:317-28)



Drastic reduction of postoperative opioid use following Enhanced Recovery optimization.

CENTRAL MESSAGE

Excellent pain control with minimal (schedule II-free) opioid use after robotic thoracoscopic procedures is achieved by fine-tuning an established Enhanced Recovery After Thoracic Surgery protocol.

PERSPECTIVES

Optimization of an established Enhanced Recovery After Thoracic Surgery protocol to drastically decrease schedule II opioid prescription at discharge following robotic thoracoscopic surgery highlights the role of thoracic surgeons in combating the opioid epidemic.

See Commentaries on pages 329 and 331.

From the Section of Thoracic Surgery, Division of Cardiothoracic Surgery, The DeWitt Daughtry Department of Surgery, University of Miami, Miami, Fla.

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 24, 2021; accepted for publication Sept 24, 2021; available ahead of print Feb 26, 2022.

Address for reprints: Dao M. Nguyen, MD, MSc, FRCSC, FACS, Section of Thoracic Surgery, Division of Cardiothoracic Surgery, The DeWitt Daughtry Department of Surgery, University of Miami, 1295 NW 14th St, Suite J, Miami, FL 33136 (E-mail: DNguyen4@med.miami.edu).

2666-2736

Copyright © 2022 The Author(s). Published by Elsevier Inc. on behalf of The American Association for Thoracic Surgery. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jtc.2021.09.051>

▶ Video clip is available online.

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

Abbreviations and Acronyms

ERAS	= Enhanced Recovery After Surgery
ERATS	= Enhanced Recovery After Thoracic Surgery
LipoB	= liposomal bupivacaine
LOS	= length of stay
MME	= morphine milligram equivalent
PACU	= postanesthesia care unit
R-VATS	= robotic video-assisted thoracoscopic surgery

The Enhanced Recovery After Surgery (ERAS) concept, developed in early 2000s by clinicians in Europe as a care protocol, addresses pre-, peri-, and postoperative components of surgical patients, with an overarching goal to achieve optimal postoperative outcomes, safe discharge, and cost-efficiency.¹ It has subsequently been adopted by many surgical subspecialties, including thoracic surgery. Enhanced Recovery After Thoracic Surgery (ERATS) protocols maintain the initial and evolving components of ERAS¹ and incorporate the nuances associated with care for patients undergoing intrathoracic procedures, either by thoracotomy or by minimally invasive thoracoscopic surgery (eg, video-assisted or robotic thoracoscopy).^{2,3} Such comprehensive care protocols have gained significant traction during the past 5 years and have become standard of care at many institutions, including our own.⁴⁻¹¹ Postoperative pain is intrinsic to thoracic surgical procedures; pulmonary impairment following lung resections and underlying comorbidities have a strong influence on postoperative outcomes. Although all components of ERATS work synergistically to provide optimal outcomes, effective thoracic pain control with an opioid-sparing strategy coupled with posterior intercostal nerve blocks^{12,13} and surgical wound infiltration with the long-acting local anesthetic preparation liposomal bupivacaine (LipoB) (Exparel; Pacira Pharmaceuticals Inc) appears to play an essential role.

We noticed that many patients had significant pain and would require intravenous hydromorphone in the postanesthesia recovery unit (PACU). We wondered if diluting LipoB with 0.25% bupivacaine,¹⁴ instead of normal saline could provide a more rapid onset of intercostal nerve blocks and mitigate acute pain in the immediate postoperative period and the need for intravenous hydromorphone in the PACU. Moreover, as per our original ERATS protocol, we prescribed the schedule IV synthetic opioid tramadol as scheduled administration (every 6 hours) to minimize the use of potent, addiction-prone schedule II opioids such as oxycodone or hydromorphone. However, frequent tramadol use, although not associated with addiction and dependence, is not without significant side effects.¹⁵⁻¹⁷ We

questioned whether or not scheduled administration of tramadol was essential to achieve superior pain control in our original ERATS patients compared with a pre-ERATS cohort, as previously reported.⁹

We hypothesized that scheduled administration of tramadol is not necessary and switching to an as-needed dosing would reduce opioid utilization. We further hypothesized that replacing saline with a short-acting local anesthetic agent like bupivacaine would potentiate the analgesic effect of the intercostal nerve block by LipoB during the immediate postoperative period. We therefore modified our established ERATS protocol by switching tramadol to as-needed instead of every 6 hours dosing and replacing 30 mL saline with 30 mL 0.25% bupivacaine (75 mg bupivacaine mixed with 226 mg liposomal bupivacaine, within 1:2 w/w ratio stipulated by the manufacturer¹⁸ while keeping all other components unchanged and blind to all other health care providers). This retrospective comparative study was performed to evaluate the influence of such optimization on postoperative pain levels and both in-hospital and after discharge opioid requirements for acute pain management in addition to postoperative outcomes in patients undergoing elective robotic thoracoscopic procedures.

METHODS**Patient Population**

A retrospective analysis of data extracted from our prospectively maintained thoracic surgery database and the electronic medical record Epic (Epic Systems Corp) of patients at University of Miami Hospital was performed following institutional review board approval with a waiver of patient consent requirement (No. 20180827; date of approval: October 31, 2018). Patients undergoing robotic thoracic surgical procedures from July 1, 2018, to December 31, 2020, were reviewed. All adult patients older than age 18 years) undergoing robotic video-assisted thoracoscopic surgery (R-VATS) for pulmonary resections (nonanatomic wedge resections and anatomic resections: segmentectomy, lobectomy, and bi-lobectomy with intrathoracic lymphadenectomy for pulmonary malignancy) or mediastinal-pleural procedures (eg, thymectomy, resection of thymoma or posterior mediastinal tumors/cysts, pleurectomy for pneumothorax) in whom safe and complete access to the posterior intercostal spaces for intercostal nerve block using LipoB could be achieved and who were opioid-naïve¹⁹ were included. Based on the surgical procedure, patients were stratified into an anatomic lung resections (eg, segmentectomy, lobectomy, and bilobectomy) subgroup and a wedge lung resections/mediastinal-pleural procedures subgroup to minimize heterogeneity. Patients in whom accurate assessment of postoperative pain and narcotic use was not feasible, such as those remaining on endotracheal intubation/mechanical ventilation following R-VATS, those who had a conversion to open thoracotomy and those on long-term opioids use for chronic pain as previously defined (determined by clinical history of use of scheduled opioid analgesics for at least 2 months immediately preceding thoracic procedures) were excluded. Eligible patients undergoing R-VATS procedures between September 1, 2018, and December 31, 2019, received postoperative care with the original ERATS protocol (ERATS group) and served as the historical control group and those having R-VATS between January 1, 2020, and December 31, 2020, received care with the modified protocol (optimized ERATS group). The study was conducted and reported in concordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.²⁰

ERATS

We implemented our original ERATS protocol (Table E1) on February 1, 2018, for all thoracic surgical patients. Detailed description protocol development, implementation, and clinical results of this ERATS protocol for R-VATS patients has been previously reported.⁹ After a 7-month transition period, it became established care pathway for all thoracic surgical patients. Two optimization modifications were made to the original ERATS protocol: switching tramadol from regular dosing to as-needed and replacing saline diluent with an equal volume of 30 mL 0.25% bupivacaine while keeping all other components of the protocol unchanged. Our technique of posterior intercostal nerve blocks has always been an intrathoracic injection of the LipoB solution into the subpleural space of second to 10th intercostal nerves (3 mL/space) under direct vision immediately upon entrance to the hemithorax using a 22G butterfly needle (as depicted in Figure 1) to provide adequate time for LipoB to take effect at the end of the procedure. Cutaneous analgesia was achieved with infiltration of skin and cutaneous tissue with LipoB solution before skin incision. The care providers of the PACU and the thoracic surgery nursing unit were not informed of the modification of the nerve block solution to minimize bias in patients' pain management. The nursing staff performed pain assessments with the visual analog pain scale and administered opioid analgesics per the ERATS protocol. We provided postdischarge prescriptions with the amount and the type of opioids (schedule II oxycodone and/or schedule IV tramadol) based on in-hospital pain levels and opioid requirement on the day of hospital discharge.

Data Source and Attributes

The thoracic surgery database prospectively collects detailed clinical parameters, including but not limiting to patient demographic characteristics, operative details, pathologic diagnoses, tumor-node-metastasis staging for primary lung cancer, 90-day postoperative complications (Clavien-Dindo classification),²¹ hospital length of stay (LOS), and readmission. The database is maintained by our nurse practitioner (J.S.-M.) and regularly audited for accuracy by the surgical faculty (D.M.N.). Additionally, the following measurements were extracted from hospital electronic medical records: daily pain scores (patient-reported pain levels were recorded using the visual analog pain numeric scores by nursing staff multiple times per day because they frequently assessed pain levels to administer as-needed analgesics, as per ERATS protocol; daily pain scores were calculated as averages of multiple readings over a 24-hour period for up to 4 postoperative days), in-hospital analgesics dispensed (schedule II opioids oxycodone, hydromorphone, morphine, fentanyl, and schedule IV opioid tramadol; nonopioid analgesics: acetaminophen, gabapentin, ketorolac, and ibuprofen). The quantities of opioids dispensed are expressed as by-mouth morphine milligram equivalent (MME). Information regarding postdischarge readmissions, either to our hospital or to another health care facility, were obtained from EPIC and via postdischarge telephone follow-ups and clinic visits. Postdischarge analgesics, including types and dosage of opioids prescribed were collected from the discharge summary. The filling and refilling (within 30 days after discharge) of all types of opioids were monitored by reviewing EPIC and by routine surveying of our patients during telephone follow-ups by our advanced practice registered nurse and by the attending surgeons at postoperative clinic visits. Such independently obtained information was frequently cross-referenced for accuracy. Access to the State of Florida's prescription drug monitoring program, E-FORCSE, was occasionally required for verification and cross-reference of ambiguous patient-reported opioid use. We became less dependent on this database as our ERATS protocol matured over time. With reliable monitoring of filling/refilling of opioid prescriptions via postdischarge telephone follow-up and postoperative clinic visits, we have noticed that there is a very tight correlation between E-FORCSE and our records of patients' postdischarge opioid fill requirements.

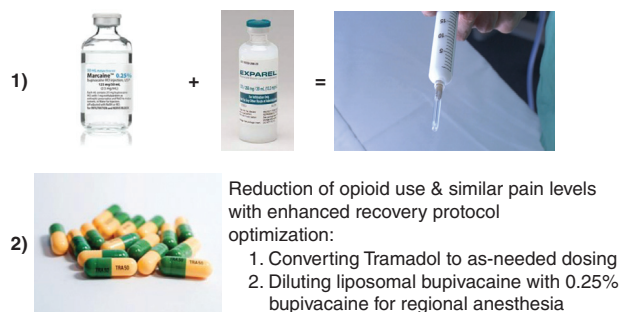


FIGURE 1. Drastic reduction of opioid use following enhanced recovery protocol optimization.

Outcomes

Primary outcomes of this study were postoperative in-hospital and post-discharge total and schedule II or IV opioid utilization in each stratum; patients were grouped into anatomic lung resections and wedge lung resections/mediastinal-pleural procedures subgroups. Secondary outcomes included postoperative patient-reported subjective pain, postoperative complications, and hospital LOS.

Statistical Analysis

Optimized ERATS and control ERATS patients' demographic characteristics, perioperative, schedule II or IV opioid use, and clinical outcomes were summarized (frequencies, percentages, medians, and interquartile range [IQR] [Q1-Q3]) and compared using χ^2 and Fisher exact for categorical variables, Wilcoxon rank sum test, and Mann-Whitney *U* test for nonparametric continuous variables where appropriate. For postoperative pain, mixed linear model test was used to analyze the pain scores up to day 3 postoperatively. We assumed linear time trends, giving rise to the intercept (initial pain at day 0) and the slope (rate of change in pain per day on study) estimates. Statistical analysis was performed with SAS software, version 9.4 (SAS Institute Inc).

RESULTS

A total of 342 patients met the inclusion criteria (159 underwent the original ERATS protocol and 183 underwent the optimized protocol). The study populations were stratified into anatomic lung resections (segmentectomy, lobectomy, or bilobectomy) as 1 subgroup and wedge lung resections/mediastinal-pleural procedures as the other subgroup. Patient demographic characteristics and clinical characteristics of each subgroup of ERATS and optimized ERATS cohorts were comparable (Table 1).

In both subgroups of the optimized ERATS and the original ERATS protocols the following outcomes were achieved:

First, patients of the optimized ERATS group required slightly less intravenous schedule II opioid (mainly hydromorphone) in PACU than patients of the original ERATS group (median, 1.5 MME [IQR, 0-3.0 MME] vs median, 3.0 MME [IQR, 0-6.0 MME]; $P < .00001$). Second, there was a clear reduction of in-hospital and postdischarge opioid utilization in both the anatomic lung resection and wedge lung resection/mediastinal-pleural procedures subgroups

TABLE 1. Demographic and clinical characteristics of all patients

Characteristic	ERATS (n = 159)	Optimized ERATS (n = 183)	P value
Anatomic resections	78	89	
Age	70.0 (63.0-75.0)	66.0 (61.0-73.0)	.26
Sex			
Male	36	43	
Female	42	46	
ASA	3 (3-3)	3 (3-3)	
BMI	26.6 (23.2-31.1)	27.5 (23.8-32.2)	.49
FEV1 (% normal)	88.0 (77.0-99.0)	91.0 (80.5-101.0)	.48
DLCO (% normal)	81.0 (69.0-95.0)	81.0 (71.0-95.8)	.15
Malignant	78	85	.8
Benign	0	4	
Primary lung cancer	72/78 (92.3)	81/85 (95.3)	
Stage I A/B	61/72 (84.7)	56/81 (69.1)	.0349
Stage II-IV	11/72 (15.3)	25/81 (30.8)	
Secondary lung cancer/other neoplasms	6/78 (7.7)	4/85 (4.7)	
Wedge resections and mediastinal-pleural procedures	81	94	
Age (y)	63.0 (55.0-72.0)	62.0 (49.7-70.2)	.14
Sex			
Male	42	38	
Female	39	56	
ASA	3 (3-3)	3 (3-3)	
BMI	27.7 (24.4-31.3)	27.6 (23.9-32.7)	.39
FEV1 (% normal)	89.5 (77.6-96.0)	87.0 (76.0-95.0)	.49
DLCO (% normal)	85.0 (70.0-96.2)	78.0 (69.0-86.0)	.96
Malignant	53	54	.35
Benign	28	40	
Primary lung cancer	13/53 (24.5)	16/54 (29.6)	
Stage I A/B	9/13 (69.2)	10/16 (62.5)	1
Stage II-IV	4/13 (30.8)	6/16 (37.5)	
Secondary lung cancer/other neoplasms	40/53 (75.4)	38/54 (70.4)	

Values are presented as n, n (%), or median (interquartile range). ERATS, Enhanced Recovery After Surgery; ASA, American Society of Anesthesiologists physical classification score; BMI, body mass index; FEV1, forced expiratory volume at the end of 1 second; DLCO, diffusing capacity for carbon monoxide.

(Table 2). In the anatomic lung resection cohort, there was a 1.5- to 2-fold reduction of postoperative opioid requirements in the optimized ERATS groups (in-hospital MME: median, 20.0 MME [IQR, 7.5-46.5 MME] vs median, 47.5 MME [IQR, 22.5-86.4 MME] and postdischarge MME: median, 60.0 MME [IQR, 0-60.0 MME] vs median, 105 MME [IQR, 60.0-150.0 MME]; both P values $< .00001$). Slightly lower percentages of patients in the optimized ERATS cohorts used opioids while in the hospital (90% vs 98.7% of the control cohort; $P = .0204$). Furthermore, only 54% of patients in the optimized ERATS group, versus 86% of the control group ($P < .00001$), needed any opioid upon discharge. Only 8% of patients in the optimized ERATS versus 65% of the control group used schedule II opioids ($P < .00001$). In the wedge resection/mediastinal-pleural procedures cohort, patients of the optimized ERATS group similarly required fewer opioids, particularly after discharge (in-hospital MME: median, 14.2 MME [IQR, 3.0-28.0 MME] vs median, 27.4 [IQR, 20.0-41.5 MME] and postdischarge MME: median, 0 MME [IQR, 0-60.0 MME] vs median, 140.0 MME [IQR, 60.0-150.0 MME]; $P < .00001$).

Similarly, fewer patients in the optimized ERATS group required opioids in the postoperative period (Table 2). Specifically, in the optimized ERATS group only 30.8% used any opioid and only 10.6% required schedule II oxycodone at discharge compared with 80.2% and 66.7% of the control group ($P < .00001$). Finally, there was a very low incidence of opioid refills after discharge in both ERATS groups, an indication of satisfactory pain control even with significantly reduced amounts of opioids prescribed.

Figures 2, A, and 3, A, provided granular analysis of the types of opioid used in-hospital by the 2 ERATS groups following anatomic resection (Figure 2, A,) or wedge resection/mediastinal-pleural procedures (Figure 3, A,). The significantly decreased total opioid use by optimized ERATS patients was attributable to lower tramadol use secondary to switching to as-needed dosing while schedule II opioid consumption were similar between groups. More importantly, minimal schedule II opioids (median, 0; percentage of patients requiring schedule II opioids ranged from 8% to 11%) were prescribed at discharge for the optimized ERATS patients, with the total amounts of opioids

TABLE 2. Primary outcomes

Outcome	ERATS (n = 159)	Optimized ERATS (n = 183)	P value
Anatomic resections	78	89	
In-hospital opioid use (MME)	47.5 (22.5-86.4)	20.0 (7.5-46.5)	<.00001
n (%)	77 (98.7)	80 (89.9)	.0204
Discharge opioid use (MME)	105.0 (60.0-150.0)	60.0 (0-60.0)	<.00001
Opioid filled	67 (85.9)	48 (53.9)	<.00001
Opioid refilled	11 (14.1)	7 (7.8)	.2191
Schedule II filled/refilled	51 (65.4)	7 (7.8)	<.00001
Wedge resections/mediastinal-pleural procedures	81	94	
In-hospital opioid use (MME)	27.4 (20.0-41.5)	14.2 (3.0-28.0)	<.00001
n (%)	80 (98.8)	78 (82.9)	.0005
Discharge opioid use (MME)	140.0 (60.0-150.0)	0 (0-60.0)	<.00001
Opioid filled	65 (80.2)	29 (30.8)	<.00001
Opioid refilled	9 (11.5)	3 (3.2)	.0681
Schedule II filled/refilled	54 (66.7)	10 (10.6)	<.00001

Values are presented as n, n (%), or median (interquartile range). ERATS, Enhanced Recovery After Surgery; MME, morphine milligram equivalent.

given were all attributed to tramadol (Figure 2, B, and Figure 3, B).

Secondary outcomes included postoperative patient-reported subjective pain scores, which were no different between the 2 subgroups in either strata, anatomic resection subgroup (0.4303; 95% CI, -0.3675-1.2282; P = .2887) or wedge resection/mediastinal-pleural procedure subgroup (0.01083; 95% CI, -0.6706-0.6490; P = .9742) (Figure 4, A and B). There were also no differences in the incidence or severity of postoperative complications, or readmissions between stratified ERATS and optimized ERATS subgroups. There was a slight but statistically significant reduction in length of stay in the optimized ERATS cohort (average 2.6 days) compared with the original

ERATS group (3.2 days) although the median (2.0 days; IQR, 2.0-3.0 days) was the same between groups (P = .0117) (Mann-Whitney U test) (Table 3).

DISCUSSION

A hypothesis-driven modification of an established ERATS protocol such as our own resulted in a significant reduction of opioid requirements during the postoperative period (in PACU, in the hospital, and after discharge) without an adverse effect on patient-reported subjective pain levels or operative complications. More importantly, such efforts almost eliminated the dependence on schedule II opioids after discharge without inadvertently denying patients access to potent opioid analgesics for

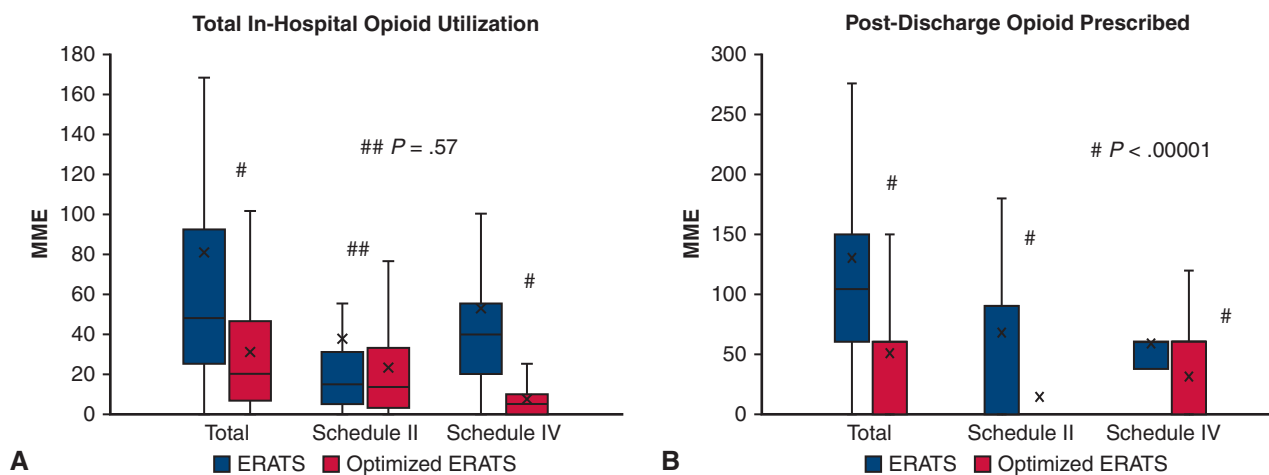


FIGURE 2. Total opioid utilization (in-hospital [A]) or prescribed (postdischarge [B]) expressed as milligram morphine equivalents (MME) following anatomic lung resections (blue indicates original Enhanced Recovery After Thoracic Surgery [ERATS] protocol [red indicates optimized ERATS protocol). Data are expressed using box-whisker plots (horizontal lines are minimal and maximal values). The reduction of in-hospital MME was attributable to the decrease of tramadol use in the optimized ERATS group with as-needed dosing. Postdischarge drastic reduction of prescribed MME was due to both decreased use of tramadol and elimination of oxycodone.

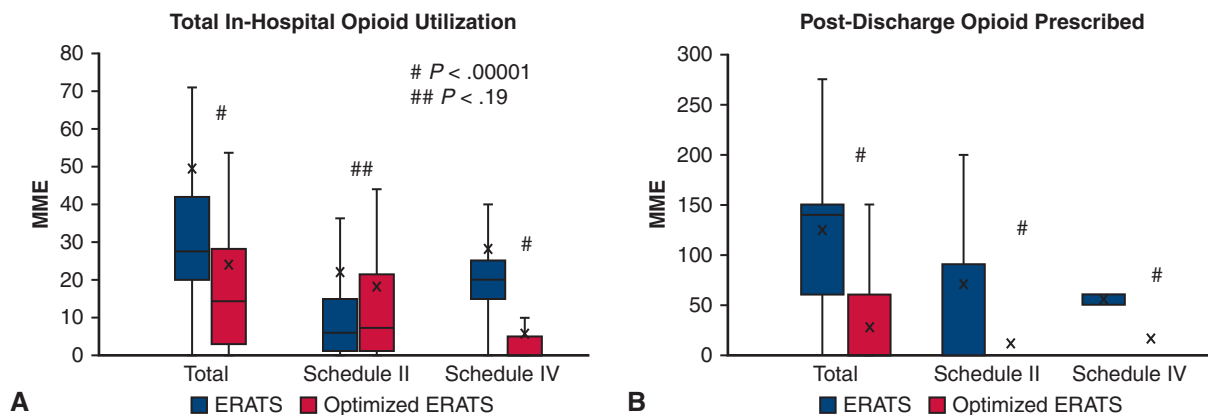


FIGURE 3. Total opioid utilization (in-hospital [A]) or prescribed (postdischarge [B]) expressed as milligram morphine equivalents (MME) following wedge lung resection and mediastinal-pleural procedures (blue indicates original Enhanced Recovery After Thoracic Surgery [ERATS] protocol; red indicates optimized ERATS protocol). Data are expressed using box-whisker plots (horizontal lines are minimal and maximal values). The reduction of in-hospital MME was totally attributable to the decrease of tramadol use in the optimized ERATS group due to as-needed dosing. Postdischarge profound reduction of prescribed MME was accounted for by elimination of both tramadol and oxycodone.

effective pain control, as was evidenced by a very low rate of opioid refills.

Implementations of ERATS protocols has gained significant traction and yielded concrete salutary results for thoracic surgical patients.⁴⁻¹¹ For patients undergoing minimally invasive thoracoscopic surgery in whom hospital LOS and postoperative complications are sufficiently low, ERATS may not further impact these outcome metrics.^{5,8,9} The main benefit of ERATS for this patient population is reduced postoperative pain and dependence on opioids for pain management. A drastic reduction of in-hospital and postdischarge opioid requirements after ERATS implementation has been previously reported.^{1,9,11,22} Our group quantified the influence of ERATS on postoperative opioid consumption by showing a 3- to 5-fold reduction of postdischarge total opioid requirements following robotic thoracoscopy and thoracotomy, respectively.⁹ The detrimental effects of overprescribing potent addicting schedule II opioids have been well documented.²³⁻²⁵ Not only is there an increased risk for persistent opioid use in patients undergoing surgery, but there is also a notable overdispensing and underutilization of the prescribed opioids, predisposing to diversion and abuse by other than the intended recipients.^{23,24} In a systemic review of opioid utilization in patients undergoing thoracic, orthopedic, obstetrics, and general surgical procedures, Bicket and colleagues²³ reported that of all the opioid tablets obtained by patients, 42% to 71% went unused, largely due to adequate pain control and/or concerns for side effects. Furthermore, the authors state that 73% to 77% of patients reported that their unused opioids were not stored properly in locked containers, increasing the risk for misuse. ERATS provides a very suitable platform to institute modifications to further reduce opioid utilization as 1 important built-in feature of ERAS is the periodic auditing of results and

implementation of changes to further improve outcomes.^{1,2} By implementing 2 simple modifications, we were able to optimize our established ERATS protocol to achieve a near independence from schedule II opioids for pain control at discharge and thus eliminate the risk of making schedule II opioids available to the public unsupervised. We did not observe any adverse neurologic or cardiac adverse effects with the addition of 30 mL of 0.25% bupivacaine to LipoB. At the time of discharge on postoperative day 2 or 3 following anatomic lung resection or on postoperative day 1 or 2 following other procedures, the median pain levels were <2, which are very mild, and daily opioid use was very low (data not shown). Our observation of hundreds of ERATS patients who noted little incision-related pain and not using all of their prescribed opioids (either schedule II or IV or both) on first postoperative clinic visits, 10 to 14 days after discharge, empowered us to further limit the amount and type (particularly schedule II) of opioid prescribed. Even with very low amounts of opioid given at discharge, only 3% to 8% of patients of the optimized ERATS group required refilling of opioid prescriptions, an indication of appropriate pain control. Such incidence was lower than that of the original ERATS group (11% to 14%, not statistically significant) although patients in this control cohort received more opioids at discharge (Table 2). This highlights, even in an established ERATS protocol, opioid overprescription may still exist and there is room for improvement. Our observation recapitulates previously published results by Kim and colleagues^{10,11} and collectively demonstrates the power of ERATS in minimizing postdischarge opioid prescription while maintaining satisfactory pain control. It is not possible to determine whether or not replacing saline with 0.25% bupivacaine or switching tramadol to as-needed dosing or both was responsible for the overall effect of reducing opioid use,

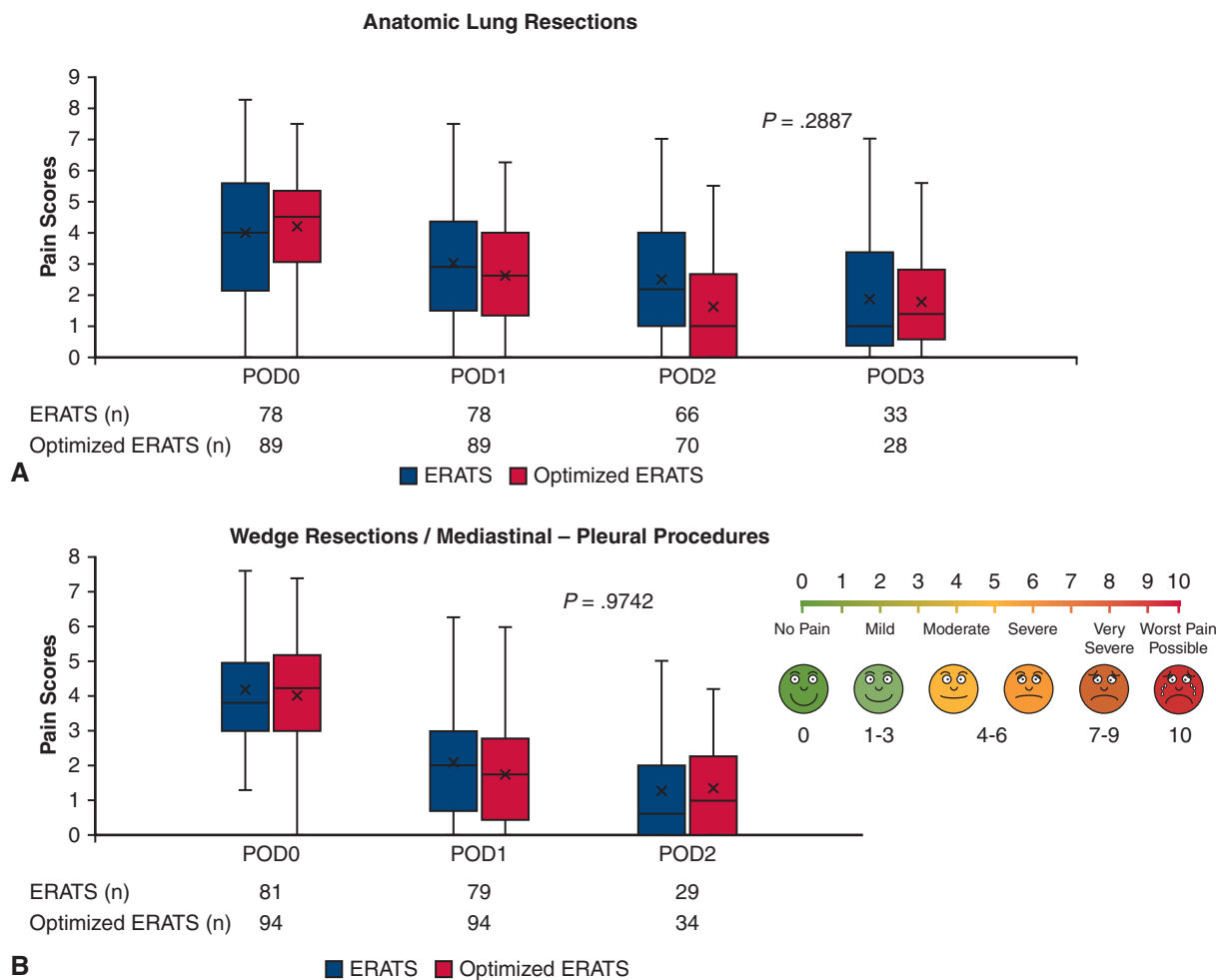


FIGURE 4. Postoperative patient-reported subjective pain levels (visual analog pain scale) of anatomic lung resections cohorts or wedge lung resection and mediastinal-pleural procedures cohorts (blue indicates original Enhanced Recovery After Thoracic Surgery [ERATS] protocol and red indicates optimized ERATS protocol). There was no difference in pain levels following robotic thoracoscopic procedures between the 2 cohorts. Daily pain scores are expressed using the box-whisker plots (horizontal lines are minimal and maximal values) over multiple postoperative days (POD) for each group; n represents the number of subjects per group for that particular POD. Pairwise statistical analysis was performed using mixed linear model.

particularly schedule II opioids, following protocol optimization. Preoperative counseling and creating realistic expectations with patients, effective intercostal nerve blocks with LipoB, meticulous perioperative care by providers who conformed to a protocol emphasizing pain mitigation with scheduled nonopioid analgesics, and early recognition of breakthrough pain requiring opioid titration, all synergize for successful ERATS outcomes. Fine-tuning of our existing ERATS further optimizes one of our primary objectives; that is, maximal pain control with minimal opioid use. Our current challenge is actually to define a strategy to mitigate postoperative neuralgia,²⁶⁻²⁸ which has long-lasting negative influences on patient recovery and satisfaction and in our opinion represents a much more difficult clinical problem to resolve than addressing acute somatic incisional pain.

Acute pain in the PACU upon emergence from anesthesia is common in our patients, with 64% to 70% of patients of either ERATS groups requiring intravenous hydromorphone. The main complaint is ipsilateral shoulder pain that is of a visceral and not musculoskeletal nature. Although slightly fewer schedule II opioids were administered in PACU for patients of the optimized ERATS group, substituting saline diluent with 0.25% bupivacaine did not completely mitigate this problem. Unlike other ERATS protocols,^{4,5,10} we do not use preoperative oral celecoxib or intraoperative ketorolac and only administer oral ibuprofen or intravenous ketorolac 4 to 6 hours postoperatively when the chest tube drainage is not high and not frankly sanguineous. Such a practice may reduce our ability to manage this discomfort that is likely due to the chest tube irritating the diaphragm and is not mitigated by intercostal nerve blocks.

TABLE 3. Secondary outcomes

Outcome	ERATS (n = 159)	Optimized ERATS (n = 183)	P value
Anatomic resections	78	89	
Complications: Clavien-Dindo classification			
0	63 (80.8)	81 (91.0)	.7774
1-2	11 (14.1)	4 (4.5)	
3-4	4 (5.1)	4 (4.5)	
5	0	0	
LOS	2.0 (2.0-3.0) 3.1	2.0 (2.0-3.0) 2.6	.01174*
Readmissions	3 (4.5)	4 (4.5)	1.00
Wedge resections/mediastinal-pleural procedures	81	94	
Complications: Clavien- Dindo classification			
0	76 (93.8)	55 (100)	.3658
1-2	4 (4.8)	0	
3-4	1 (1.2)	0	
5	0	0	
LOS	1.0 (1.0-2.0) 2.0	1.0 (1.0-2.0) 1.8	.6924
Readmissions	1 (1.2)	0	.87

Values are presented as n, n (%), or median (interquartile range) average. ERATS, Enhanced Recovery After Surgery; LOS, length of stay. *U test.

Our study has many limitations. This is a retrospective case-controlled comparative analysis to examine the effect of ERATS protocol optimization on postoperative pain and opioid utilization. This is an observational study spanning over 24 months without the ability to correct for inherent biases of time-dependent incremental improvement of patient care unrelated to ERATS. The inclusion of the mediastinal-pleural procedures to the wedge lung resection subgroup reflects the scope of our practice and increases

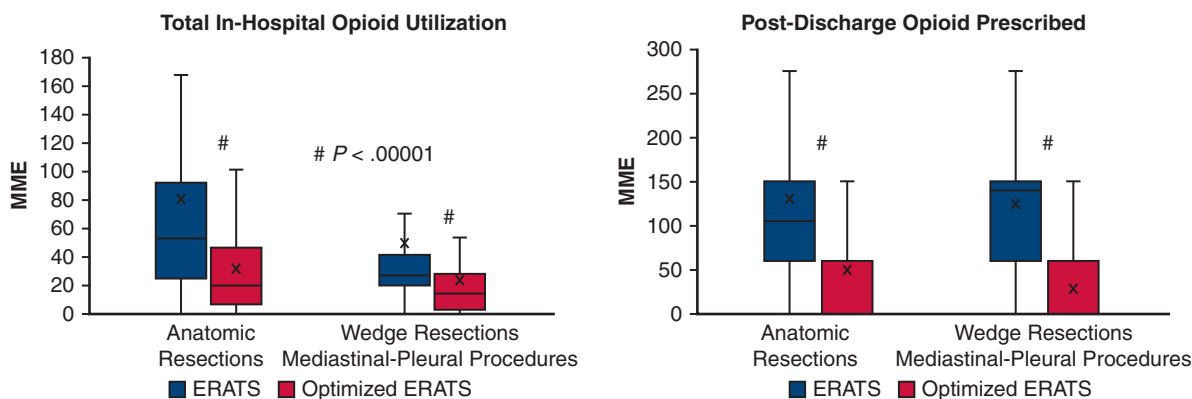
the generality of our observations; however, it may add to the heterogeneity of this cohort. The sample sizes are not large enough for complex statistical analysis such as propensity-score matching. Finally, chronic opioid users (8 patients between the 2 cohorts), were excluded from this study. This number was too small to form a separate subgroup for a meaningful analysis. The finding of this study is not generalizable to this population. A recent publication by Hodges and colleagues²⁹ demonstrated that any

Optimization of an Enhanced Recovery Protocol Following Robotic Thoracic Surgery

Methods: Hypothesis-driven modifications of an established Enhanced Recovery after Thoracic Surgery protocol for robotic thoracic procedures:

1. Switching Tramadol to as-needed
2. Diluting Liposomal bupivacaine with 0.25% bupivacaine for intercostal nerve blocks

Results:



Implications: Significant reduction of postoperative in-hospital and post-discharge opioid needs, with near independence from schedule II narcotics, without impacting subjective pain or complications.

FIGURE 5. Simple modifications of an established Enhanced Recovery After Thoracic Surgery [ERATS] protocol for patients undergoing robotic thoracic procedures were associated with drastic reduction of postoperative opioid use without affecting subjective pain levels and clinical outcomes. MME, Milligram morphine equivalents.

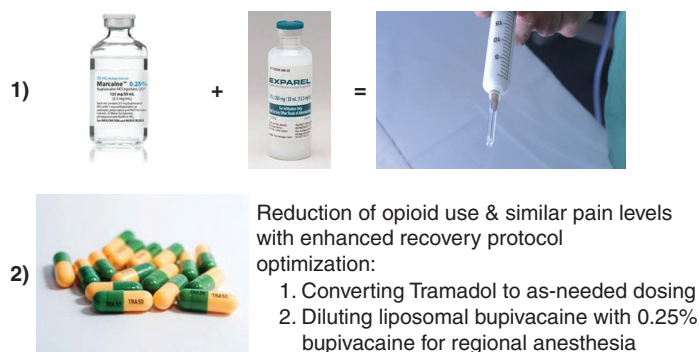


FIGURE 6. Optimization of an established Enhanced Recovery After Thoracic Surgery protocol resulting in drastic reduction of opioid use while maintaining similarly low levels of acute postoperative pain by converting tramadol from scheduled to as-needed dosing or diluting liposomal bupivacaine with 0.25% bupivacaine for regional analgesia (skin incisions and intercostal nerve blocks).

chronic opioid use before operative intervention was strongly associated with postoperative opioid need.

CONCLUSIONS

Hypothesis-driven modifications of an established ERATS protocol for patients undergoing robotic thoracoscopic procedures were found to be associated with significant reduction of in-hospital and postdischarge opioid requirements for acute pain control without affecting patient-reported subjective pain and postoperative outcomes (Figures 5 and 6). We discuss the significance of our findings in Video 1. It is encouraging to see patients in the optimized ERATS cohort who underwent anatomic resections had a slightly shorter hospital stay (Table 3). The most striking outcome by this protocol fine adjustment, in our opinion, is the near-complete elimination of schedule II narcotics for postdischarge pain control. This sets the new standard of perioperative care at our institution for patients undergoing thoracic surgery. Elimination of schedule II opioid overprescription at time of discharge

reduces its availability and misuse by the public and therefore directly contributes to the fight against the epidemic of opioid abuse.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/21%20AM/AM21_P04/AM21_P04_01.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.

We acknowledge the University of Miami for their support of this work, however, no funding was received.

References

1. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg.* 2017;152:292-8.
2. 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.
3. Batchelor TJP, Ljungqvist O. A surgical perspective of ERAS guidelines in thoracic surgery. *Curr Opin Anaesthesiol.* 2019;32:17-22.
4. Van Haren RM, Mehran RJ, Mena GE, Correa AM, Antonoff MB, Baker CM, et al. Enhanced recovery decreases pulmonary and cardiac complications after thoracotomy for lung cancer. *Ann Thorac Surg.* 2018;106:272-9.
5. Martin LW, Sarosiek BM, Harrison MA, Hedrick T, Isbell JM, Krupnick AS, et al. Implementing a thoracic enhanced recovery program: lessons learned in the first year. *Ann Thorac Surg.* 2018;105:1597-604.



VIDEO 1. Author discussion of study and clinical relevance in the context of the opioid epidemic. Video available at: [https://www.jtcvs.org/article/S2666-2736\(22\)00004-3/fulltext](https://www.jtcvs.org/article/S2666-2736(22)00004-3/fulltext).

6. Madani A, Fiore JF Jr, Wang Y, Bejjani J, Sivakumaran L, Mata J, et al. An enhanced recovery pathway reduces duration of stay and complications after open pulmonary lobectomy. *Surgery*. 2015;158:899-910.
7. Haro GJ, Sheu B, Marcus SG, Sarin A, Campbell L, Jablons DM, et al. Perioperative lung resection outcomes after implementation of a multidisciplinary, evidence-based thoracic ERAS program. *Ann Surg*. 2021; 274:e1008-13.
8. Brunelli A, Thomas C, Dinesh P, Lumb A. Enhanced recovery pathway versus standard care in patients undergoing video-assisted thoracoscopic lobectomy. *J Thorac Cardiovasc Surg*. 2017;154:2084-90.
9. Razi SS, Stephens-McDonnough JA, Haq S, Fabbro M Jr, Sanchez AN, Epstein RH, et al. Significant reduction of postoperative pain and opioid analgesics requirement with an Enhanced Recovery after Thoracic Surgery protocol. *J Thorac Cardiovasc Surg*. 2021;161:1689-701.
10. Kim MP, Chan EY, Meisenbach LM, Dumitru R, Brown JK, Masud FN. Enhanced recovery after thoracic surgery reduces discharge on highly dependent narcotics. *J Thorac Dis*. 2018;10:984-90.
11. Del Calvo H, Nguyen DT, Meisenbach LM, Chihara R, Chan EY, Graviss EA, et al. Pre-emptive pain management program is associated with reduction of opioid prescription after minimally invasive pulmonary resection. *J Thorac Dis*. 2020;12:1982-90.
12. Mehran RJ, Walsh GL, Zalpour A, Cata JP, Correa AM, Antonoff MB, et al. Intercostal nerve blocks with liposomal bupivacaine: demonstration of safety, and potential benefits. *Semin Thorac Cardiovasc Surg*. 2017;29:531-7.
13. Rice DC, Cata JP, Mena GE, Rodriguez-Restrepo A, Correa AM, Mehran RJ. Posterior intercostal nerve block with liposomal bupivacaine: an alternative to thoracic epidural analgesia. *Ann Thorac Surg*. 2015;99:1953-60.
14. Gadsden J, Long WJ. Time to analgesia onset and pharmacokinetics after separate and combined administration of liposome bupivacaine and bupivacaine HCl: considerations for clinicians. *Open Orthop J*. 2016;10:94-104.
15. Kaye AD. Tramadol, pharmacology, side effects, and serotonin syndrome: a review. *Pain Physician*. 2015;18:395-400.
16. Barakat A. Revisiting tramadol: a multi-modal agent for pain management. *CNS Drugs*. 2019;33:481-501.
17. Jean YK, Gitlin MC, Reynolds J, Candiotti KA. Tramadol-associated hallucinations: a systematic review and narrative synthesis of their pathophysiology, diagnosis, and treatment. *Can J Anesth*. 2020;67:360-8.
18. Exparel prescribing information. Pacira Pharmaceuticals, Inc. Accessed March 1, 2021. http://www.exparel.com/pdf/EXPAREL_Prescribing_Information.pdf
19. Brown LM, Kratz A, Verba S, Tancredi D, Clauw DJ, Palmieri T, et al. Pain and opioid use after thoracic surgery: where we are and where we need to go. *Ann Thorac Surg*. 2020;109:1638-45.
20. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The strengthening the reporting of observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg*. 2014;12:1495-9.
21. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205-13.
22. Rice D, Rodriguez-Restrepo A, Mena G, Cata J, Thall P, Milton D, et al. Matched pairs comparison of an enhanced recovery pathway versus conventional management on opioid exposure and pain control in patients undergoing lung surgery. *Ann Surg*. 2021;274:1099-106.
23. Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription opioid analgesics commonly unused after surgery: a systematic review. *JAMA Surg*. 2017;152:1066-71.
24. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain*. 1996;12:50-5.
25. Hill MV, Stucke RS, McMahon ML, Beeman JL, Barth RJ Jr. An educational intervention decreases opioid prescribing after general surgical operations. *Ann Surg*. 2018;267:468-72.
26. Maguire MF, Ravenscroft A, Beggs D, Duffy JP. A questionnaire study investigating the prevalence of the neuropathic component of chronic pain after thoracic surgery. *Eur J Cardiothorac Surg*. 2006;29:800-5.
27. Finnerup NB, Haroutounian S, Kamerman P, Baron R, Bennett DL, Bouhassira D, et al. Neuropathic pain: an updated grading system for research and clinical practice. *Pain*. 2016;157:1599-606.
28. Guastella V, Mick G, Soriano C, Vallet L, Escande G, Dubray C, et al. A prospective study of neuropathic pain induced by thoracotomy: incidence, clinical description, and diagnosis. *Pain*. 2011;152:74-81.
29. Hodges JD, Nguyen DT, Doan J, Meisenbach LM, Chihara R, Chan EY, et al. Factors associated with home opioid use after thoracic surgery. *J Thorac Cardiovasc Surg Open*. 2021;5:173-86.

Key Words: ERATS, robotic surgery, intercostal nerve block, postoperative pain, postoperative opioid utilization

Discussion

Presenter: Dr Karishma Kodia



Dr Linda W. Martin (Charlottesville, Va). I want to thank the American Association for Thoracic Surgery, Dr Varughese, and Dr Duncan for inviting me to discuss this paper. And I want to congratulate the authors, Dr Kodia and Dr Nguyen, on this excellent paper and thank them for submitting it ahead

of time, and that it got into the top abstracts for this category.

This is an important paper. It looks at a transition in an enhanced recovery program in thoracic surgery from the first 18 months of institution to the most recent calendar year and some changes that were made along the way. I applaud the authors for that continuous process improvement, which is a very key component of any enhanced recovery program. You can't rest on your laurels once you start these programs, you have to keep looking at how to make it better.

I also want to point out that for those of you who don't know, thoracotomy is the most painful incision that we do in all of surgery, but the second most painful incision is minimally invasive thoracic surgery, so video-assisted thoracoscopic surgery and robotic surgery sounds like it's a much lesser evil, but it is right up there. And so, any movement we can make on opioid use is critically important.

And finally, I want to point out how critical this opioid reduction is. Not only for short-term patient outcomes for the risk of addiction in those patients, which has been shown to be as high as 25% in this population as well as the opioid flow into the community, but another area that's less well known is the effect interaction of opioids on cancer progression—something I've been researching myself but there will be a paper in Lung Cancer Three session on Sunday morning that talks about that more.

I'd like to ask a few questions of Dr Kodia and Dr Nguyen. And the first question is, Can you please describe in more detail the time and technique of your injection? I think this is very critical in the success of this approach.



Dr. Karishma Kodia (*Miami, Fla*). Absolutely. Thank you so much for having me. The technique that we use is that we take the anterior robotic arm, and we take a 25-gauge butterfly needle and we inject either Exparel (Exparel; Pacira Pharmaceuticals Inc) or the combination of the bupivacaine

and Exparel into the subpleural space from the second intercostal space to the 10th intercostal space.

Dr Martin has a previous paper that talks about doing a wide injection, which I think is important, so we inject into this subpleural space to hit the perineural fibers and we do it upon entrance into the cavity under direct visualization; before placing our ports we infiltrate the skin wound sites as well.

Dr Martin. Yes. I think that's important to do it at the very beginning and broadly, because when we've tried other techniques it's hard to show that it's an impactful approach. The onset of Exparel is quite slow, as much as an hour or more, and I think the addition of the short-acting bupivacaine was a good move that probably helps overcome that limitation.

And the next question I have is, How did you decide what to discharge patients in terms of narcotics? I see most of your patients leave on day 2 or 3, and I've looked at the pharmacokinetics of this drug, it lasts for 3 to 4 days. You can get sort of duped into thinking that they have no pain. They go home and all of a sudden, they feel it and they start calling because they're feeling it as the Exparel wears off. Could you tell us a little bit about how you calculate your discharge opioids?

Dr Kodia. Yes, we have a protocol in place that essentially looks at, on the day of discharge, the use of narcotics that patients have, and based on what they're using in the hospital we then discharge them accordingly. But I think it's also in line with Enhanced Recovery after Thoracic Surgery where you're still using other medications, like gabapentin and Tylenol (Johnson & Johnson Inc) to also provide pain control that's not just narcotic-based.

Dr Martin. Yes. And again, I think that's an area we're all trying to figure out better, is how best to do the discharge. Another question: I saw that a lot of your nonanatomic resections were wedge resections and most of them were for what sounds like metastatic disease. In my experience those patients are so-called professional patients. They've had usually a laparotomy for liver resection and colon resection. They've sometimes had multiple lung resections for

nodules and they're very sensitized to traumatic experiences and where some patients might need a little medicine, they seem to need more. Have you had to adjust your approach with those patients at all?

Dr Kodia. In some cases. I think it's also important, like in your preoperative counseling, to set up expectations for what patients will experience postoperatively. And with that counseling they do a little bit better, at least in our experience.

Dr Martin. Yes. I think the counseling definitely helps, but I would say with some of those people I've sometimes adjusted the protocol a little bit because they're more sensitized.

I'm wondering if some of the tremendous improvement you've seen from the first cohort to the second cohort might be the greatness of your protocol. We hope. But it might also be that there's a philosophical change going on in society and a greater recognition of the problem of opioids, and patients' acceptance and willingness to try to be opioid sparing might be better. And I'm wondering if you think that's at play here.

Dr Kodia. I think that might be at play. I think that it all ties into the same concept, which is that a lot of patients end up with prescriptions that they don't end up using and then they don't end up storing them appropriately anyway. So, some of that is from the patient end and some of that is from our end, but essentially both forces kind of work synergistically so that at a societal level and individual level we're using fewer narcotics for our patients.

Dr Martin. Great. I've noticed one of the things I find to be most useful with Enhanced Recovery and the protocol that we use, which is similar to yours, is that if you have a need to convert to thoracotomy there's really no change in your pain management protocol. It's a very seamless thing to go from video-assisted thoracoscopic surgery or robotic to open. And we found that our pain scores and our narcotic use are similar between those groups. I was wondering why you chose to exclude your converted patients.

Dr Kodia. I think we parse out a lot of our Estimated Recovery after Thoracic Surgery data into thoracotomy patients only or robotic patients only. So, essentially just inputting these patients into different groups from our data set and then including them in different papers was the reason to do so.

Dr Martin. Okay, great. Congratulations on a great paper.

TABLE E1. Components of Enhanced Recovery After Thoracic Surgery (ERATS) protocol at the University of Miami

Preoperative consultation
Extensive counseling of patients and family members about operative plans
Realistic expectation of postoperative recovery and multimodal pain management
Printed information booklet with instructions
Preoperative clinic visit
Complete review of medical and anesthesia history
Preoperative clearance
Routine preoperative instructions
2 bottles of carbohydrate drinks 2 h before surgery
Perioperative care
Acetaminophen - 1000 mg (1 h before surgery)
Gabapentin - 100 mg (1 h before surgery)
Prophylactic antibiotics (cefazolin 2 g for <120 kg or 3 g > 120 kg; vancomycin 1000 mg for penicillin allergy)
Anesthesia care: Patient-directed fluid management, antiemetics
Intercostal nerve blocks and infiltration of surgical wounds with local anesthetics with diluted liposomal bupivacaine (30 mL 0.9% saline and 20 mL liposomal bupivacaine)
Postoperative care
Analgesics
Acetaminophen 1000 mg orally every 8 h
Tramadol 50 mg orally every 6 h
Ibuprofen 600 mg orally every 8 h postoperatively or toradol 15 mg every 6 h IV as needed for 2 d (if no medical contraindications) timing of first dose at the discretion of the attending surgeon
Gabapentin 100 mg orally every 8 h
Oxycodone 5 mg orally every 6 h as needed (pain scale: 4-6)
Oxycodone 10 mg orally every 6 h as needed (pain scale: 7-10)
Morphine 2 to 4 mg IV every 6 h as needed or hydromorphone 0.5-1.0 mg IV or 2-4 mg orally every 6 h as needed for breakthrough pain
Heparin 5000 U subcutaneous every 8 h
Metoprolol 12.5 mg every 12 h (if not already receiving a beta-blocker following anatomic resection)
Tamsulosin 0.4 mg every d (age >50 y)
Bowel regimen (Colace [Contract Pharamcal Corporation] and Dulcolax [Boehringer Ingelheim Pharmaceuticals Inc.] scheduled; Miralax [Bayer] and milk of magnesia as needed)
Incentive spirometer and ambulation on POD 0
Regular diet on POD 1
Assessment for home oxygen requirement (to prevent discharge delays)
Chest tube removal (POD 1-2, when volume <5 mL/kg/d)
Foley catheter removal (POD 1)
Intravenous fluid 1 mL/kg until voiding following removal of Foley catheter
Discharge plan
Verbal and printed discharge instructions; APRN telephone follow-up POD3 and POD7
Contact ARNP or physician's office for advice and management of excessive neuropathic pain
Postdischarge analgesics
Acetaminophen 1000 mg orally every 8 h for 20 d
Tramadol 50 mg orally every 6 h for 3 d (12 tablets; if used postoperatively in-hospital)
Gabapentin 100 mg orally every 8 h for 60 d (30-d supply refill p1); titrated up to address postdischarge neurogenic pain
Ibuprofen 600 mg orally every 8 h for 20 d
Oxycodone 5 mg orally every 6 h as needed for 3 d (12 tablets; if used postoperatively in-hospital)
Pantoprazole 40 mg orally daily for 20 d

POD, Postoperative day; APRN, advanced practice registered nurse; PO, per os.