Significant reduction of postoperative pain and opioid analgesics requirement with an Enhanced Recovery After Thoracic Surgery protocol

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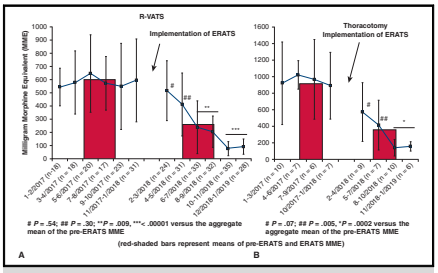
ABSTRACT

Objective: To evaluate differences in postoperative pain control and opioids requirement in thoracic surgical patients following implementation of an Enhanced Recovery after Thoracic Surgery protocol with a comprehensive postoperative pain management strategy.

Material and Methods: A retrospective analysis of a prospectively maintained database of patients undergoing pulmonary resections by robotic thoracoscopy or thoracotomy from January 1, 2017, to January 31, 2019, was conducted. Multimodal pain management strategy (opioid-sparing analgesics, infiltration of liposomal bupivacaine to intercostal spaces and surgical sites, and elimination of thoracic epidural analgesia use in thoracotomy patients) was implemented as part of Enhanced Recovery after Thoracic Surgery on February 1, 2018. Outcome metrics including patient-reported pain levels, in-hospital and postdischarge opioids use, postoperative complications, and length of stay were compared before and after protocol implementation.

Results: In total, 310 robotic thoracoscopy and 62 thoracotomy patients met the inclusion criteria. This pain management strategy was associated with significant reduction of postoperative pain in both groups with an overall reduction of postoperative opioids requirement. Median in-hospital opioids use (morphine milligram equivalent per day) was reduced from 30 to 18.36 ($P = .009$) for the robotic thoracoscopy group and slightly increased from 15.48 to 21.0 ($P = .27$) in the thoracotomy group. More importantly, median postdischarge opioids prescribed (total morphine milligram equivalent) was significantly reduced from 480.0 to 150.0 ($P < .001$) and 887.5 to 150.0 ($P < .001$) for the thoracoscopy and thoracotomy groups, respectively. Similar short-term perioperative outcomes were observed in both groups before and following protocol implementation.

Conclusions: Implementation of Enhanced Recovery after Thoracic Surgery allows safe elimination of epidural use, better pain control, and less postoperative opioids use, especially a drastic reduction of postdischarge opioid need, without adversely affecting outcomes. (J Thorac Cardiovasc Surg 2021;161:1689-701)



Step-wise reduction in postdischarge opioid prescriptions with Enhanced Recovery after Thoracic Surgery.

CENTRAL MESSAGE

Multimodal nonopioid analgesics and liposomal bupivacaine intercostal nerve blocks as part of Enhanced Recovery after Thoracic Surgery diminish postoperative pain and in-hospital and postdischarge opioid requirement.

PERSPECTIVE

Implementation of Enhanced Recovery after Thoracic Surgery is associated with significantly improved postoperative pain control and an overall reduction of opioid requirement without adversely affecting clinical outcomes. Minimizing postdischarge narcotic dispensing and reducing its availability to the public contributes to the fight against the opioid abuse epidemic.

See Commentaries on pages 1702 and 1703.

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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
R-VATS = robotic video-assisted thoracoscopic surgery
TEA = thoracic epidural analgesia

Thoracic surgical procedures, especially those requiring thoracotomy, have historically been associated with significant pain and discomfort. Many patients undergoing thoracic surgical procedures have serious cardiopulmonary comorbidities that can be exacerbated by inadequate pain control. Neuropathic pain is also a common, well-recognized component of postoperative pain that persists long after the resolution of incisional pain. For these reasons, effective and safe pain management is of utmost importance in the management of thoracic surgical patients. An increasing body of recent literature supports the implementation of Enhanced Recovery After Thoracic Surgery (ERATS) protocol for patients undergoing thoracic procedures, particularly pulmonary resections.[1-3] Common goals of such care pathways are to ensure safe and rapid recovery, to optimize outcomes, and to provide cost-effective care with high patient satisfaction scores.[1-6] Elements of these protocols are implemented throughout the course of patient management starting with preoperative consultations continuing through intra-, peri-, and postoperative care and concluding with postoperative clinic visits. Historically, the main component of acute postoperative pain control is systemic opioids given either orally, intravenously, or by thoracic epidural analgesia (TEA). Opioids afford excellent pain control yet are associated with significant side effects that negatively impact rapid recovery. ERATS contains all the essential components of standard Enhanced Recovery After Surgery (ERAS) protocols but is adapted to address specific needs of thoracic patients.[1-6] It is well demonstrated that all components of ERATS act in synergy to produce satisfactory outcomes. Successful development and implementation of ERATS require a close collaboration of all health care providers, a high level of compliance, and ongoing adjustment for protocol optimization.

We initiated an ERATS program tailored by evidence-based guidelines[1-6] to unify the care for and to optimize the pain management of thoracic surgical patients. One year following ERATS protocol implementation, a "before-and-after" analysis was performed to evaluate the impact of this quality improvement protocol. We hypothesized that the implementation of our ERATS protocol with emphasis on multimodality pain management strategy would result in less postoperative pain, reduced need for opioid analgesics, and possible improvement of clinical outcomes and shortened hospital length of stay (LOS).

PATIENTS AND METHODS

Patient Population

Following approval from the institutional review board (2018082; date of approval: October 31, 2018), a retrospective analysis was performed on data extracted from our thoracic surgery database and the medical record of patients undergoing thoracic surgical procedures at the University of Miami Hospital from January 1, 2017, to January 31, 2019. All adult patients (>18 years old) undergoing elective robotic video-assisted thoracoscopy (R-VATS) or thoracotomy in the lateral decubitus position for pulmonary resections or resection of pleural or mediastinal tumors, where safe and complete access to posterior intercostal spaces obtained for intrathoracic intercostal nerve blocks, were included in this study. The following patients were excluded from the analysis: sternotomy (n = 2), hemi-clamshell/incision (n = 1), chest wall resections (n = 4), radical pleurectomy (n = 2), R-VATS esophageal procedures (n = 7), those in whom accurate assessment of postoperative pain and narcotic use was not feasible (postoperative endotracheal intubation, n = 3), and those on long-term opioids use for chronic pain (determined by clinical history of taking scheduled opioid analgesics for at least 2 months immediately preceding thoracic procedures; n = 3). The cohort was split into 2 groups for comparison, patients before and patients after February 1, 2018, the date of full ERATS implementation. Patients were further stratified into R-VATS and thoracotomy cohorts.

Surgical Approach

The vast majority of R-VATS pulmonary resection for malignancy comprises early stages (stages I A/B and II) primary lung cancer or pulmonary metastasectomy. Thoracotomy (latissimus dorsi muscle-sparing posterior/lateral thoracotomy with harvesting of the fifth intercostal muscle flap for buttressing of bronchial stumps or anastomosis) is used for complex pulmonary procedures such as sleeve resection, pneumonectomy, and intrapleural/mediastinal tumors requiring concomitant pericardial and/or lung resection; patients undergoing R-VATS converted to thoracotomy were also included in the thoracotomy group.

Pre-ERATS Pain Management

Before the implementation of ERATS, the acute postoperative pain in patients undergoing R-VATS was managed with oral or intravenous narcotics on pro re nata basis with occasional use of patient-controlled analgesia. Other nonopioid analgesics (acetaminophen, tramadol, ketorolac, and ibuprofen) were used sparingly. The exact quantity and formulations of opioids use varied greatly based on the patients' need and the providers' discretion. Thoracic epidural catheter was placed only for thoracotomy patients before the induction of anesthesia and managed by the regional anesthesia team. It was typically removed 1 day after discontinuation of chest tubes. Learning from other reported ERATS studies[2,3] that described a period of "breaking-in" before global implementation of the optimized ERATS protocol, we incrementally adopted multifaceted clinical measures to minimize postoperative cardiopulmonary (atrial fibrillation, atelectasis, postoperative hypoxemia, pneumonia), gastrointestinal and genitourinary (constipation, urinary retention and lower urinary tract infection) complications to facilitate timely discharge.

Development and Implementation of ERATS

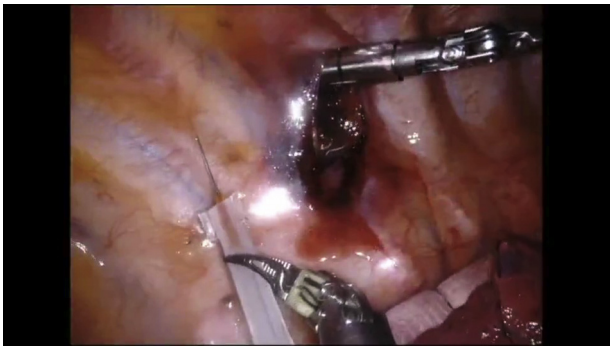
Before formal implementation of ERATS, many of these care components[1-4] were part of our routine practice but not uniform among various

TABLE 1. Components of 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 Two bottles of carbohydrate drinks - 2 h before surgery (Ensure; Abbott, Chicago, Ill)
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, entropy, or bispectral technology to avoid unnecessarily deep anesthetics Intercostal nerve blocks and infiltration of surgical wounds with liposomal bupivacaine
Postoperative care	Analgesics Acetaminophen 1000 mg PO Q8h Tramadol 50 mg PO Q6h Ketorolac 15 mg Q6h IV PRN, for 2 d (if no medical contraindications) Gabapentin 100 mg PO Q8h Oxycodone 5 mg PO Q6h PRN Morphine 2-4 mg IV Q6h PRN or hydromorphone 0.5-2.0 mg IV Q6h PRN for breakthrough pain Heparin 5000 U subcutaneous Q8h Metoprolol 12.5 mg Q 12h (cardiac arrhythmia prophylaxis) Tamsulosin 0.4 mg QD (men >50 years old) Bowel regimen (Colace & Dulcolax scheduled; Miralax & Milk of magnesia PRN) Incentive spirometer and ambulation on POD 0 Regular diet on POD 0/1 Assessment for home oxygen requirement (to prevent discharge delays) Chest tube removal (POD 1-2, when volume <1.5 mL/kg/8h shift) Foley catheter removal (POD 1 for wedges and POD 2 for lobectomy/segmentectomy) Intravenous fluid 1 cc/kg until voiding
Discharge plan	Verbal and printed discharge instructions Postdischarge analgesics Acetaminophen 1000 mg PO Q8h for 10 d Tramadol 50 mg PO Q6h for 3 d (12 tablets) Gabapentin 100 mg PO Q8h for 30 d Ibuprofen 600 mg PO Q8h PRN for 10 d Oxycodone 5 mg PO Q6h PRN for 3 d (12 tablets) Pantoprazole 40 mL PO daily for 10 d

PO, Per os; *Q8h*, every 8 hours; *IV*, intravenous; *Q6h*, every 6 hours; *PRN*, pro re nata; *QD*, quaque die; *POD*, postoperative day.

providers. Extensive discussions among all the stakeholders (surgeons, anesthesiologists, nursing staff, pharmacy, and therapeutic committee) were carried out before clinical implementation. Institutional approval for off-label use of liposomal bupivacaine (LipoB [EXPAREL]; Pacira Pharmaceuticals, Inc, Parsippany, NJ) for intercostal nerve block and surgical wound infiltration was secured. Nursing staff in the preoperative clinic, post-anesthesia care unit, and the floor, as well as the operating room anesthesia staff, all received proper in-service ERATS training before implementation. The floor nursing staff were provided extensive in-service training on a continued basis regarding all components of postoperative care (accurate pain assessment using the visual analog pain scale and assigning pain levels with numerical scores, postoperative ambulation, chest physiotherapy, monitoring for timely resumption of gastrointestinal and genitourinary function, prophylaxis of cardiac arrhythmia for anatomic lung resections and deep vein thrombosis prophylaxis). All components of the ERATS protocol are outlined in Table 1. There was no change in the technical aspects of surgical procedures. One of the key changes adopted after protocol implementation was intercostal nerve block and surgical wound infiltration with LipoB for all patients. For R-VATS, we used a "butterfly" 25-G needle controlled by the anterior robotic arm and we infiltrated 9 intercostal spaces (2nd to 10th) with 1.5 mL of undiluted LipoB to the subpleural space (as shown in Video 1) under direct vision. The remaining 5 to 6 mL was used to infiltrate the incisions at the end of the procedure. For patients undergoing thoracotomy, LipoB was 1:1 diluted with 20 mL of injectable saline and 20 mL was used to infiltrate 9 intercostal spaces as well as the soft tissue at the posterior thoracotomy site above and below



VIDEO 1. Undiluted liposomal bupivacaine was infiltrated in second to tenth interspace during robotic-assisted thoracoscopy. Video available at: https://www.jtcvs.org/article/S0022-5223(20)30739-X/fulltext.

the incision, similar to the technique described by Mehran and colleagues under direct vision using a 21-G spinal needle.[7,8] The remaining 20 mL was used to infiltrate the subdermis of the entire thoracotomy skin edges. The nursing staff performed routinely scheduled objective pain assessment using the visual analog pain scale and administered rescue opioid analgesics (as prescribed) at their discretion. During the initial 3-month of ERATS implementation, clinical compliance by all health care providers was closely monitored and enforced. We routinely evaluated the in-hospital pain levels and the opioids requirement by the patients and tailored our postdischarge opioids prescription practices over time.

Outcome Measures

The thoracic surgery database includes a host of relevant clinical information including demographics, operative details, and pathologic diagnoses including tumor–node–metastasis staging for primary lung cancer, postoperative complications, and hospital LOS in days. The database is maintained by a nurse practitioner and regularly audited for accuracy by the surgical faculty. The following parameters were extracted from our database and hospital electronic medical records: postoperative complications (Clavien–Dindo classification),[9] daily pain scores calculated as averages of multiple readings over a 24-hour period and recorded up to 5 postoperative days), LOS, in-hospital analgesics dispensed (*opioids:* oxycodone, hydromorphone, morphine, fentanyl, meperidine, tramadol and *nonopioids:* acetaminophen, gabapentin, ketorolac, ibuprofen, celecoxib, bupivacaine, lidocaine, liposomal bupivacaine), and pharmacy costs of analgesics including cost of the thoracic epidural set but not the professional fees associated with catheter placement and care. The exact amounts of opioids dispensed to patients after hospital discharge as well as the incidences of postdischarge initial opioids prescriptions filled and any subsequent refills (either by the attending surgeons at postoperative clinic visits or by patients' primary care physicians after hospital discharges) for the entire patient cohort within 90 days postdischarge were obtained from Electronic-Florida Online Reporting of Controlled Substance Evaluation Program. This statewide database is part of The Florida Prescription Drug Monitoring Program containing 2-year data of all controlled substances dispensed to individuals by the Florida-registered pharmacies. Health care providers are required to review the history of controlled substance use for each patient via the Electronic-Florida Online Reporting of Controlled Substance Evaluation Program at the time of writing opioids prescriptions. The quantities of opioids dispensed are expressed as morphine milligram equivalent (MME). Postdischarge readmissions, either to our hospital (via query of our electronic medical record) or to another health care facility (via follow-up telephone call by our nurse practitioner or history taken at clinic visits by the attending surgeons) were recorded.

Statistical Analysis

Statistical analysis was performed with SPSS Statistical software, version 21 (IBM SPSS Statistics for Mac, Version 21.0; IBM Corp, Armonk, NY). Categorical variables were analyzed using χ^2 or Fisher exact tests as indicated, and Wilcoxon rank sum test was used for nonparametric continuous variables. *t* tests were used to compare the pain scores on the respective postoperative days between pre-ERATS and ERATS group in both cohorts (R-VATS and thoracotomy), and Bonferroni correction was applied to control for type 1 error under multiple testing assumption. Alpha level was set at 0.01 and 0.0083 for pain scores in R-VATS and thoracotomy cohorts, respectively.

RESULTS

A total of 372 patients met inclusion criteria and were included in this study. The patient demographics and operative details are summarized in Table 2. There were 310 patients undergoing R-VATS (126 pre-ERATS and 184 ERATS) and 62 patients undergoing thoracotomy (30 pre-ERATS and 32 ERATS). The patient cohorts were very similar with the R-VATS group subdivided into anatomic resections (segmentectomy, lobectomy, bilobectomy) and nonanatomic wedge resections. Clinical outcomes are shown in Table 3. There were no differences in the rate of complications, LOS, or readmission rates in all R-VATS subgroups before and after ERATS. For the thoracotomy group, overall complications were similar between the pre-ERATS and ERATS groups ($P = .383$); however, there was an overall reduction of cardiopulmonary complications, ie, 7 patients (21.8%) in the pre-ERATS group versus 3 patients (10%) in the ERATS group ($P = .04$). In the thoracotomy cohort, median LOS decreased by 1 day (median [interquartile range] 4 [3.5-4.5] vs 3 [2.25-3.25]), $P = .10$, not reaching statistical significance likely due to small sample sizes. There was no increase in the readmission rates in thoracotomy group after implementation of ERATS (Table 3).

A significant reduction of postoperative daily pain scores in patients undergoing R-VATS (Figure 1, *A*) coupled with a modest but statistically significant 38% reduction of in-hospital opioids use was seen in the ERATS group, pre-ERATS median MME: 30 versus ERATS median MME: 18.36, $P < .009$ (Figure 2, *A*; R-VATS). We observed a similar statistically significant decrease in postoperative daily pain scores in the thoracotomy group (Figure 1, *B*), without any discernable increase in the need for rescue opioids analgesics, even with complete elimination of TEA, pre-ERATS median MME: 15.48 versus ERATS median MME: 21, $P = .27$ (Figure 2, *B*; thoracotomy). More importantly, analysis of postdischarge opioids prescriptions filled at outside pharmacies demonstrated a profound (∼65%) drop of postdischarge opioids dispensed in both patients undergoing R-VATS (pre-ERATS Median MME: 480 vs ERATS Median MME: 150, $P < .001$) and patients undergoing thoracotomy (pre-ERATS median MME: 887.5 vs ERATS median MME: 150, $P < .001$) as seen in

TABLE 2. Demographics and operative details of all patients

	Pre-ERATS	ERATS	*P* value
R-VATS	n = 126	n = 184	
Anatomic resections	n = 66	n = 89	
Age, y	66.7 ± 9.2	67.5 ± 11.4	.51
Sex, male/female	30/36	49/50	.87
ASA, median/IQR	3.0/0.5	3.0/0.0	**.032**
Malignant/benign	65/1	87/2	.98
Primary lung cancer	n = 58	n = 82	.84
Stage I A/B	48 (82.7%)	72 (87.8%)	
Stage II-IV	10 (17.2%)	10 (12.2%)	
Secondary lung cancer (other neoplasms)	n = 7	n = 5	
EBL, mL	70.6 ± 68.3	72.1 ± 53.4	.82
Operating time, min	214.5 ± 91.5	214.2 ± 90.4	.97
Wedge resections	n = 60	n = 95	
Age, y	62.7 ± 13.2	61.5 ± 14.8	.60
Sex, male/female	29/31	47/48	.74
ASA, median/IQR	3.0/0.0	3.0/0.0	.6
Malignant/benign	42/18	61/34	.19
Primary lung cancer	n = 13	n = 23	.27
Stage I A/B	7 (53.8%)	16 (69.5%)	
Stage II-IV	6 (46.1%)	7 (30.4%)	
Secondary lung cancer (other neoplasms)	n = 29	n = 38	
EBL, mL	41.5 ± 34.3	35.2 ± 25.4	.19
Operating time, min	135.9 ± 56.5	129 ± 54.8	.45
Thoracotomy	n = 30	n = 32	
Age, y	61.2 ± 13.9	62.1 ± 14.7	.80
Sex, male/female	15/15	18/14	.61
ASA, median/IQR	3.0/0.0	3.0/0.0	.39
Malignant/benign	24/6	29/3	.45
Primary lung cancer	16	18	.091
Stage I A/B	3 (18.7%)	6 (33.3%)	
Stage II-IV	13 (81.3%)	12 (66.7%)	
Secondary lung cancer (other neoplasms)	n = 8	n = 11	
EBL, mL	198.6 ± 195.4	175.3 ± 138.4	.58
Operating time, min	286.5 ± 103.0	255.2 ± 113.5	.26
Extent of resection			.78
Anatomic resections	24	22	
Wedge resections	2	5	
Mediastinal tumors	4	5	

Statistically significant *P* values are in bold. *ERATS*, Enhanced Recovery After Thoracic Surgery; *R-VATS*, robotic video-assisted thoracoscopic surgery; *ASA*, acetylsalicylic acid; *IQR*, interquartile range; *EBL*, estimated blood loss.

Figure 2, *B*. Time–course analysis of the quantities of postdischarge opioids dispensed for the entire R-VATS and thoracotomy cohorts is shown in Figure 3. This analysis demonstrated a dynamic process of system-wide implementation of our ERATS protocol. While a gradual reduction of postdischarge opioids prescription practices occurred over time, more profound decrease was observed only after the first 60 R-VATS cases over a 5-month period (Figure 3, *A*). This trend was more rapid in the smaller thoracotomy group with cases performed throughout the study period and likely reflecting more comfort with prescribing less narcotics in the latter part of the program implementation (Figure 3, *B*).

There was no difference in the proportion of initial opioids prescriptions filled (pre-ERATS: 97% vs ERATS: 91%, $P = .88$) and subsequent refills (pre-ERATS: 13.4% vs ERATS: 15.7%, $P = .63$) in the R-VATS anatomic lung resections (Table 2). In contrast, less initial filling (pre-ERATS: 96.7% vs ERATS: 83.1%, $P = .09$) and subsequent refilling of postdischarge opioids prescriptions (pre-ERATS: 20% vs ERATS: 3.1%, $P = .01$) was observed in the R-VATS wedge resection group (Table 2). In the thoracotomy group, there was a statistically significant decrease in the initial filling of postdischarge opioids prescriptions (pre-ERATS: 100% vs ERATS: 87.5%,

TABLE 3. Clinical outcomes for all patients

	Pre-ERATS	ERATS	*P* value
R-VATS	n = 126	n = 184	
Anatomic resections	n = 66	n = 89	
Complications (Clavien–Dindo)			.18
0	49 (74.2%)	65 (73.0%)	
1-2	16 (24.2%)	21 (23.6%)	
3-4	1 (1.5%)	3 (3.4%)	
LOS, d			
Median (IQR)	3.0 (2.0-4.0)	3.0 (2.0-4.0)	.33
Opioid Rx filled, n (%)	64 (96.9%)	81 (91.2%)	.89
Opioid Rx refilled, n (%)	9 (13.4%)	14 (15.7%)	.69
Readmissions	3%	3.4%	.29
Wedge resections	n = 60	n = 95	
Complications (Clavien–Dindo)			.86
0	52 (86.7%)	84 (88.4%)	
1-2	8 (13.3%)	10 (10.5%)	
3-4	0 (0%)	1 (1.0%)	
LOS, d			
Median (IQR)	1.0 (0.5-1.5)	1.0 (0.5-1.5)	.79
Opioid Rx filled, n (%)	58 (96.7%)	79 (83.1%)	.09
Opioid Rx refilled, n (%)	12 (20.0%)	3 (3.1%)	**<.001**
Readmissions	0 (0%)	1 (1.0%)	.62
Thoracotomy	n = 30	n = 32	
Complications (Clavien–Dindo)			.38
0	15 (50%)	22 (68.7%)	
1-2	9 (30%)	6 (18.7%)	
3-4	6 (20%)	4 (12.5%)	
LOS, d			
Median (IQR)	4 (3.5-4.5)	3 (2.25-3.25)	.10
Opioid Rx filled, n (%)	30 (100%)	28 (87.5%)	**.044**
Opioid Rx refilled, n (%)	12 (40%)	6 (18.7%)	**.010**
Readmissions	3 (10%)	4 (12.5%)	.88

Statistically significant *P* values are in bold. *ERATS*, Enhanced Recovery After Thoracic Surgery; *R-VATS*, robotic video-assisted thoracoscopic surgery; *LOS*, length of stay; *IQR*, interquartile range.

$P = .044$). In addition, yet even with the significantly lower total amounts of postdischarge opioids prescribed, only 18.7% of the ERATS patients needed a second or third opioids prescription refills compared with 40% of those in the pre-ERATS group ($P = .01$).

Figure 4, *A* and *B* depict changing landscapes of the different classes of analgesics used for acute in-hospital postoperative pain control. A shift toward more non-opioid analgesics was seen following ERATS implementation without affecting the subjective pain levels (Figure 1). The wide discrepancy of pharmacy costs in patients undergoing R-VATS is entirely attributable to the use of LipoB (Figure 4, *C*). The cost of LipoB in the thoracotomy group is balanced by the cost of the epidural set. Implementation of ERATS offers a slight cost savings of about $60/case ($P = .011$) for the thoracotomy group, but was indeed costly (~$350/case; $P < .0001$) for the R-VATS group to achieve significant reduction of pain and of overall opioids use.

DISCUSSION

Significant reduction of both postoperative pain as well as in-hospital and particularly postdischarge opioid analgesics requirement was observed in patients undergoing R-VATS and thoracotomy following ERATS implementation at our hospital (Figure 5). A novel feature of our study is the ability to track and document postdischarge opioids dispensed by pharmacies both as initial opioids prescriptions filled and subsequent refills in all of our patients. ERATS-mediated reduction of postoperative pain and opioid need in R-VATS is associated with an increase in the pharmacy costs of analgesics that is mainly attributable to the use of LipoB. Finally, complete elimination of TEA and its potential side effects, dependence on acute pain service, and elaborate care in patients undergoing ERATS thoracotomy is cost-neutral while not associated with significant increase in opioid needs. Our study is noteworthy for the following reasons:

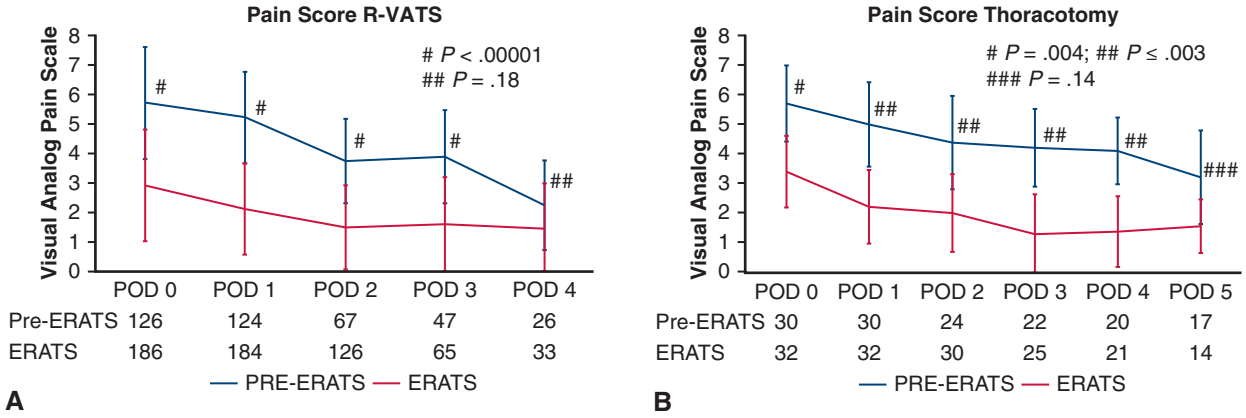


FIGURE 1. The effect of ERATS on postoperative pain. Significantly less postoperative pain as reported by patients using the visual analog pain scale (0: no pain to 10: worse pain possible) in both R-VATS (A) and thoracotomy (B) patients before and after ERATS implementation. Daily pain scores (calculated as averages of multiple readings over a 24-hour period for each patient) are expressed as mean ± standard deviation over multiple PODs for each group; n represents the number of subjects per group for that particular POD. *R-VATS*, Robotic video-assisted thoracoscopic surgery; *ERATS*, Enhanced Recovery After Thoracic Surgery; *POD*, postoperative day.

1. We observed reduction of postoperative pain in both patients undergoing R-VATS and thoracotomy whereas other ERATS programs such as the one reported by Martin and colleagues[2] did not. Rice and colleagues[8] and Khalil and colleagues[10] reported reduction of postoperative pain with LipoB intercostal blocks in patients undergoing thoracotomy but not patients undergoing minimally invasive surgery.[8]
2. We achieved reduction of in-hospital opioid needs in patients undergoing ERATS R-VATS and no significant increase of opioid use in patients undergoing ERATS thoracotomy. This is comparable with previous reports

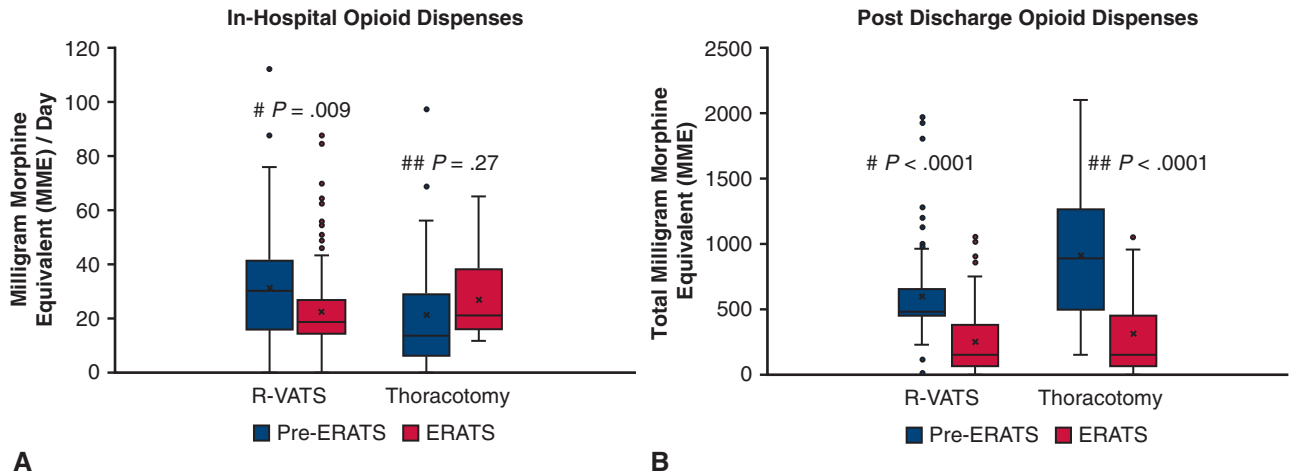


FIGURE 2. The effect of ERATS on postoperative opioid use in patients undergoing R-VATS or thoracotomy. A, Following ERATS implementation, a moderate but statistically significant decrease of in-hospital opioid requirement (median MME per hospital day: pre-ERATS: 30.0 vs ERATS: 18.4, $P = .009$) was noted in patients undergoing R-VATS, whereas it remained essentially unchanged in thoracotomy patients (median MME per hospital day: pre-ERATS: 15.5 vs ERATS: 21.0, $P = .27$ with no thoracic epidural analgesia in ERATS patients); data are expressed as median, interquartile range, and minimum and maximum MME/hospital stay. B, A very profound reduction of postdischarge opioid use (total MME dispensed to patients at outside pharmacies and recorded by the State of Florida database E-FORSCE) in both R-VATS (pre-ERATS median MME: 480.0 vs ERATS median MME: 150.0, $P < .001$) and thoracotomy patients (pre-ERATS median MME: 887.5 vs ERATS median MME: 150.0, $P < .001$) within 90 days after discharge from the hospital following the primary thoracic surgical procedures (capturing initial and any subsequent filling of opioid prescriptions); data are expressed as median, interquartile range, and minimum and maximum total MME. *ERATS*, Enhanced Recovery After Thoracic Surgery; *MME*, morphine milligram equivalent; *R-VATS*, robotic video-assisted thoracoscopic surgery.

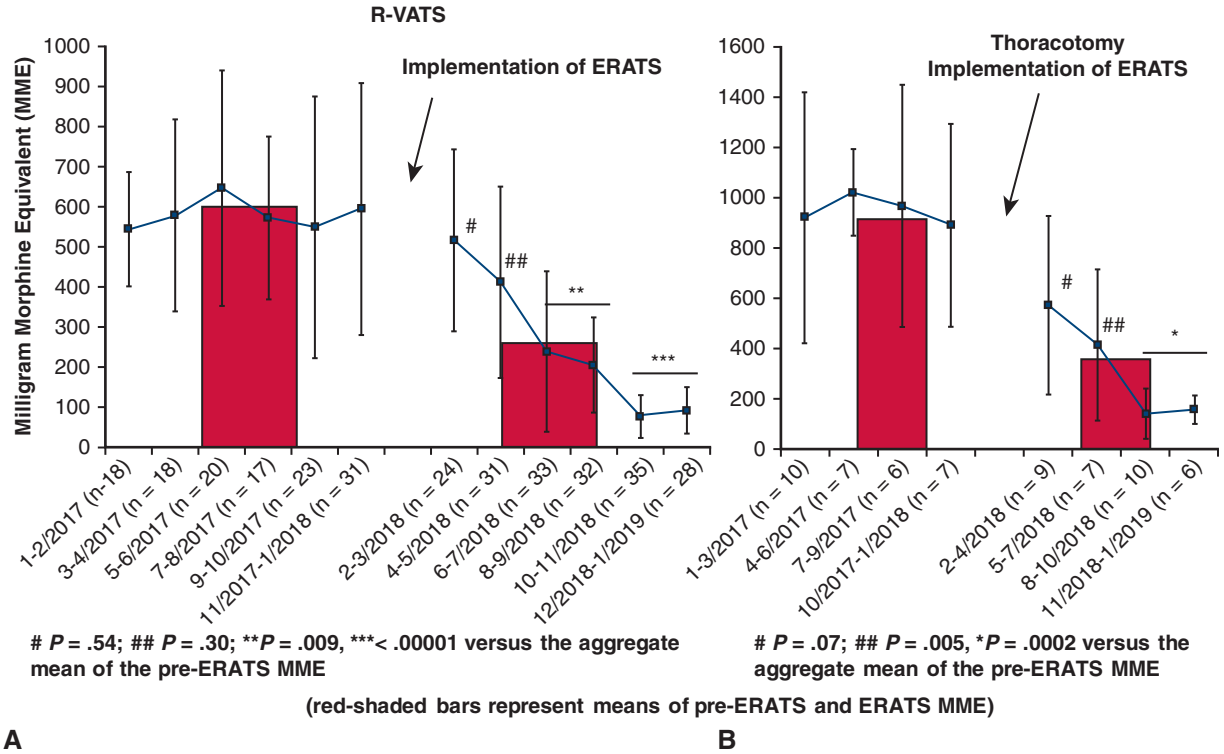


FIGURE 3. Time–course analysis of amounts of post-discharge opioids dispensed (total MME) for patients undergoing R-VATS (n = 310) (A) and thoracotomy (n = 62) (B) before and after implementation of ERATS; Means ± standard deviation of MME per 2-month intervals with n represents the number of patients/time period. The *shaded bar* represents the collective group mean MME of patients undergoing R-VATS and thoracotomy. Subsequent to ERATS implementation, steady reduction of postdischarge MME was observed, an indication of adaptive change to reduce opioid prescribed in response to lower outpatient need and a "steady-state" of postdischarge mean MME of 150 was achieved in the last 90 patients undergoing R-VATS of the ERATS group (A). A similar pattern of changes of postdischarge total MME prescribed/dispensed was observed in patients undergoing thoracotomy (B). *R-VATS*, Robotic video-assisted thoracoscopic surgery; *ERATS*, Enhanced Recovery After Thoracic Surgery; *MME*, morphine milligram equivalent.

by Martin and colleagues.[2] A 75% reduction of median total MME (86 vs 22) was reported, whereas we observed a 33% reduction of total MME (54.7 vs 35.5) or median MME/day (30.0 vs 18.4). Martin and colleagues[2] further reported 59% reduction of total median MME (130 vs 54) in patients undergoing thoracotomy (in the presence of spinal analgesia) whereas we observed slight but nonsignificant greater need for opioid use (median total MME 75 vs 94 or median MME/day 18.3 vs 21.0).

3. We are the first group to report a detailed analysis of postdischarge opioid dispensing and frequency of refills. Kim and colleagues[11] reported a low incidence of patients discharged with potent opioid hydrocodone without quantifying the amount of postdischarge MME.

The application of ERAS to thoracic surgery is not new and they may carry different names (fast-track, care pathway, etc).[12-14] A recent review by Van Haren and Atay[15] of the early work related to thoracic surgery ERAS protocols published in the early 2000s correctly concluded that those studies were of low quality and more work was needed to prove its clinical benefit.[15] Only in the last few years, high-quality publications have shed more light on the positive clinical impacts and reproducibility of well-conceived ERATS programs.[1-3,16,17] A concise collective review provides an objective perspective to this new quality-improvement endeavor.[18,19] It is clear that ERATS has strong clinical benefits for patients undergoing pulmonary resections by thoracotomy,[1-3,17] but similar clinical benefits could not be extrapolated to patients undergoing minimally invasive surgery (either VATS or R-VATS).[20] One has to examine different aspects of clinical outcomes besides complications, LOS, readmission, early ambulation, etc, to learn about the other potential benefits of ERATS protocol. We implemented ERATS at our institution out of the simple desire to unify patient care under one objective enforceable protocol, to streamline perioperative care, and to achieve predictable outcomes. Ongoing feedback evaluation and adaptive changes to patients' need

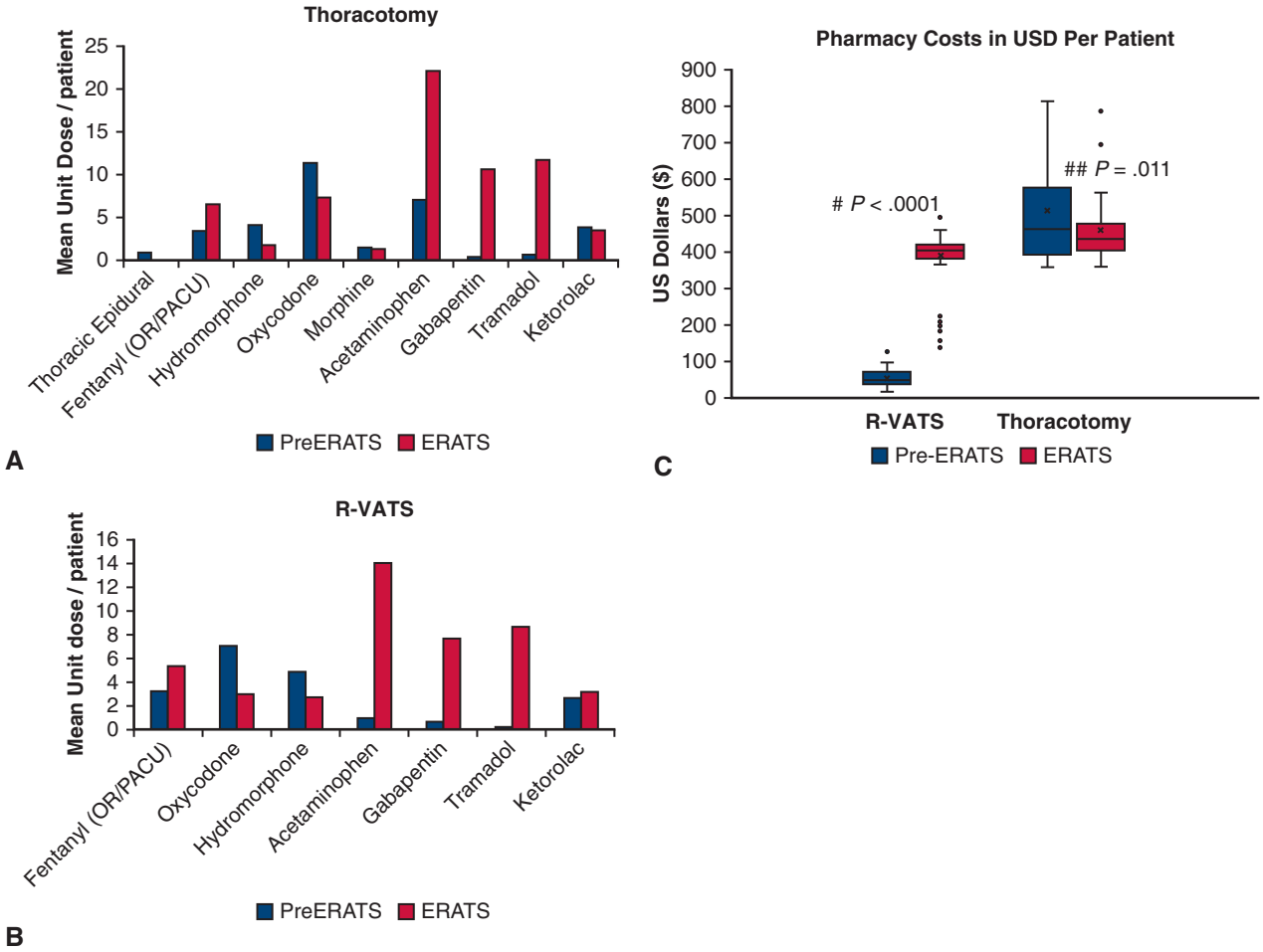


FIGURE 4. The impact of ERATS implementation on the pattern of use of all in-hospital (opioid and nonopioid) analgesics and the total costs of analgesics dispensed. A, Graphic representation of all analgesics dispensed by the hospital pharmacy (means of unit-dose of analgesic/patient; thoracic epidural is considered a unit of pain management strategy) pre-ERATS (*blue*) and ERATS (*red*) for patients undergoing R-VATS (A) and for thoracotomy (B). B, The aggregate pharmacy cost of in-hospital pain management per patient (median, interquartile range, and minimum and maximum pharmacy analgesic costs) following R-VATS or thoracotomy ($P = .0001$ for patients undergoing R-VATS and $P = .011$ for patients undergoing thoracotomy, n = number of patients per group). Implementation of ERATS offers a slight cost savings of about \$60/case ($P = .011$) as the cost of LipoB is offset by the cost of the epidural kit for the thoracotomy group. However, it is costly (~\$350/case, $P < .0001$; entirely attributable to the use of LipoB) for the R-VATS group to achieve significant reduction of postoperative pain and overall opioids use. *ERATS*, Enhanced Recovery After Thoracic Surgery; *R-VATS*, robotic video-assisted thoracoscopic surgery.

and their pain profile in the postoperative period allowed us to comfortably reduce postdischarge opioids prescriptions over time.

Routine assessment of postoperative pain and analgesics usage was done and documented at the postoperative clinic visits. We conscientiously tailored our prescription strategy and incrementally decreased the number of narcotics prescribed, based on in-hospital opioid requirement. Patients were educated to fill out opioids prescriptions only as needed. Our altruistic goal is to minimize the amounts of potent opioids made available to the public through elimination of unnecessary postdischarge filling of opioids prescriptions by the patients. This is in keeping with ongoing campaign to reduce opioid availability to the public and could potentially contribute to the fight against narcotic abuse/overdose epidemic.[21] Postoperative neurogenic pain, typically appearing around postoperative days 4 to 5 and extend several weeks postdischarge, is a significant source of anxiety for thoracic surgical patients.[22] We observed high incidence of noncompliance to the scheduled gabapentin (300 mg 3 times a day) due to side effects (dizziness, somnolence, hallucinations) during the initial phase of ERATS. Hence, we subsequently reduced the gabapentin dose to 100 mg 3 times a day to ensure compliance. The

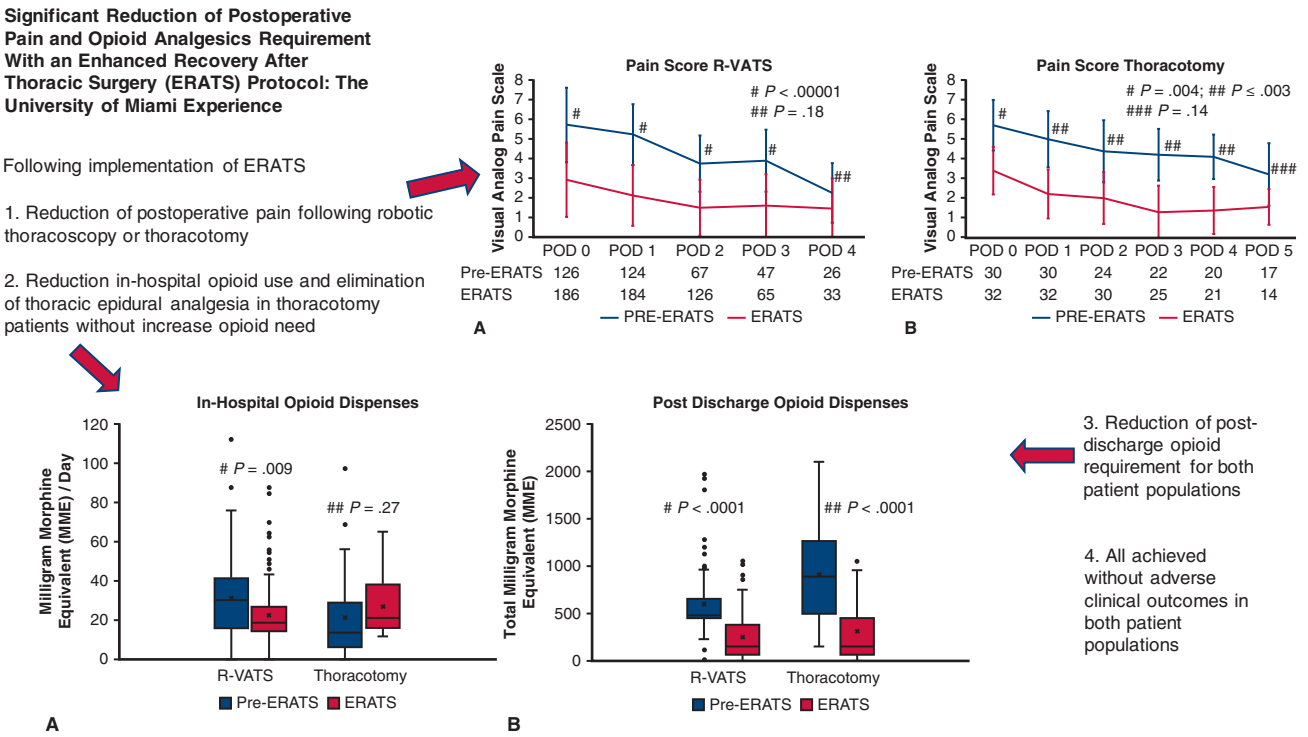


FIGURE 5. Enhanced Recovery after Thoracic Surgery protocol with a comprehensive postoperative pain management strategy was implemented to evaluate differences in postoperative pain control and opioids requirement in thoracic surgical patients. Enhanced Recovery after Thoracic Surgery allow safe elimination of epidural use, better pain control, less postoperative opioids use especially a drastic reduction of post-discharge opioids need without adversely affecting outcomes. *R-VATS*, Robotic video-assisted thoracoscopic surgery; *ERATS*, Enhanced Recovery After Thoracic Surgery; *POD*, postoperative day.

overall LOS is too short for effective titration for optimal gabapentin dosages. A potential avenue for quality improvement is to educate patients about the occurrence of neurogenic pain and various over-the-counter pharmacologic remedies to supplement the postoperative prescription analgesics, including but not limited to, titrating up the gabapentin dose, addition of nonsteroidal anti-inflammatory drugs such as ibuprofen, and over-the-counter xylocaine patches.[23] Finally, the reduction of opioid use, particularly in the postdischarge period, affordable by ERATS is likely attributable to many factors, including patient-driven factors (awareness of opioid abuse epidemic and the desire/willingness to adopt multimodality pain management strategy and open to education) and care-provider factors (effective patient education, strategy maximizing pain control while minimizing use of opioids, providing postdischarge support).

The demographics of our patients, operative techniques, LOS, and complications profile are all compatible with previously published reports.[2,3,24,25] Unchanged clinical outcomes in the presence of robust reduction of postoperative pain and opioid needs following ERATS implementation is an achievement by and of itself. A potential area of quality improvement stemming from the result of our pharmacy cost analysis (Figure 4) is to examine how essential the role of LipoB is, within the multimodal analgesia strategy. Only limited data exist comparing LipoB with bupivacaine in R-VATS.[26,27] Ongoing observational study is currently underway at our institution to answer this question and to determine whether equipoise exists between intercostal nerve blocks with LipoB and bupivacaine with 1:200,000 epinephrine using our current ERATS pain management strategy and outcome metrics.

Our study has obvious limitations. It is a retrospective analysis using a prospectively maintained database to examine clinical outcomes brought on by a dynamic care-improvement process. Our ERATS protocol was implemented without a transition period like the one described by Van Haren and colleagues.[3] Fine adjustments did occur during the study aiming to provide real-time patient care improvement similar to the approach taken by Martin and colleagues.[2] Such strategy may underestimate the ultimate impact of a fully implemented ERATS protocol. This is a before-and-after comparative analysis without the ability to correct for inherent biases and variability. Moreover, the sample sizes are too small for any complex statistical

analysis, such as propensity score matching. Including patients undergoing mediastinal or pleural procedures, might add to the heterogeneity of the patient population.

In summary, we have demonstrated that a meticulously planned and carefully conceived ERATS protocol implementation with primary focus on multimodal pain management strategy using opioids-sparing analgesics and intercostal nerve blocks with LipoB together with a well-defined care pathway resulted in a significant improvement of pain control, safe elimination of TEA and practice-changing approaches leading to less postdischarge opioids prescriptions while maintaining satisfactory clinical outcomes. This study also enables us to identify novel opportunities that merits our concerted efforts for reducing postoperative pain in a safe and cost-efficient manner.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/19%20AM/Monday_May6/203BD/203BD/S89%20-%20Doing%20the%20right%20thing%20II/S89_6_webcast_052548303.mp4.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: ERATS, postoperative pain management

Discussion

Presenter: Dr Dao M. Nguyen

Dr Gail E. Darling *(Toronto, Ontario, Canada)*. Very nicely presented, Dao. Thank you.

Dr Dao M. Nguyen *(Miami, Fla)*. Thank you, Gail, for your comment. I appreciate it.

Dr Darling. You've really addressed an important topic, which has been highlighted at a number of presentations at this meeting, which is the opioid crisis and where those drugs come from. And of course, we know that a lot of those drugs come from us. So this is a very important measure to actually save lives in this country by reducing the amount of narcotics that we're prescribing to our patients whether they take them or whether their kids take them or somebody picks them out of the garbage. Enhanced Recovery After Surgery (ERAS) also includes preoperative education, and we heard from a previous presentation that preoperative phase is maybe the most important part of ERAS, or Enhanced Recovery After Thoracic Surgery (ERATS). So, my first question is what do you do in terms of your preoperative teaching with regard to a patient's expectations for their pain management or for pain scores, for example?

Dr Nguyen. That's a very good question. I appreciate your bringing it up, Gail. Preoperative preparation as well as setting a realistic expectation of the postoperative course is an essential component of ERAS. We prepared printed booklets that contain pertinent, easy-to-understand information about the preoperative, intraoperative and postoperative cares. We provided these booklets to patients with simple instructions at the time of the preoperative clinic visits. Our preoperative clinic personnel, mainly advanced registered nurse practitioner, also go over the preoperative and perioperative cares with then patients at preanesthesia clinic visits. For instance, we inform our patients that our average postoperative length of stay after a robotic thoracoscopic lobectomy is 3 days, we do our best to achieve that goal. For people who are frail or live alone, we institute postoperative discharge planning on the morning of postoperative day 1.

Dr Darling. Do you do anything specific with regard to pain scores? So for example, what used to happen in our institution, the recovery room nurse would ask the somnolent patient to rate their pain on a scale of zero to 10, 10 being the worst pain, and this patient who is barely rousable would say their pain's at 9, and now we tell them, we expect your pain to be controlled, but it's not going to be necessarily absent. So, if your pain score is 4 or 5, that's okay.

Dr Nguyen. I am glad you brought this issue up for discussion, Gail. The nursing staff use the visual analog pain scale to assess pain levels before the formal institution of our ERATS protocol. They are required to document the level of pain by analog scores in their notes. The pain scores we showed here are means of many recorded pain scores for that particular day.

Dr Darling. I was quite intrigued, because your pain scores postimplementation are lower at the beginning. So that's why I was wondering if they had had some instruction or guidance?

Dr Nguyen. We did not use the pain score recorded in the post-anesthesia care unit (PACU). The scores were those recorded when the patient reached the thoracic surgery unit, usually a few hours after completion of the procedures and the intercostal nerve block by liposomal bupivacaine probably started having good analgesia effect. I skimmed through the slide where I showed the profile of analgesic used. We actually noted that many of our patients, both pre-ERATS and ERATS, were giving intravenous fentanyl or hydromorphone in the PACU, indicative that they all expressed pain when emerging from general anesthesia. Our next quality improvement project is to achieve optimization of pain control immediately after general anesthesia and minimize the need for potent opioids in the PACU.

Dr Darling. So, with regard to that your comment about the cost of the EXPAREL—do you have to use liposomal bupivacaine? Do you have any experience with using nonliposomal bupivacaine?

Dr Nguyen. Yes, EXPAREL is the tradename of liposomal bupivacaine. Interesting you ask about nonliposomal bupivacaine. We realize that the greater pharmacy cost for postoperative analgesics is totally attributable to the cost of liposomal. The hospital administration knows that. They have allowed us to use liposomal bupivacaine as a quality-improvement measure as part of ERATS, but I don't think they would let us do this for so long. We wonder if, within the context of ERATS, replacing the long-acting liposomal bupivacaine with the intermediate-acting preparation Marcaine (0.5%) with epinephrine (1:200,000) would achieve similar pain control effect. So now it is another area of cost-containment project for us to explore.

Dr Darling. We of course are not able to use such expensive things here in Canada, you know, being a third-world country, so we've just been using regular bupivacaine for intercostal blocks and I think that works well.

Dr Nguyen. I agree.

Dr Darling. It gets them over that initial hump. Speaking of tablets, I was interested in your choice of oxycodone as

the discharge narcotic. Do you have any reasons for choosing oxycodone versus hydromorphone?

Dr Nguyen. No, it's just a matter of …

Dr Darling. You still believe the Purdue thing that it's less addictive or …

Dr Nguyen. I don't think so. Just a matter of our own habit of prescribing oxycodone with Tylenol (for example: Percocet).

Dr Darling. One other question I had was do you have any institutional policy or departmental divisional policy about how many tablets are prescribed for a given procedure?

Dr Nguyen. No, there was no restriction until recently—the State of Florida has a policy of restricting the duration of potent opioids to patients. Physicians are obliged by law to check the history of opioid use of patients before prescribing opioid analgesics by accessing the state's Web site Electronic-Florida Online Reporting of Controlled Substance Evaluation Program, and we have to justify the amount and duration of opioid prescribed. There is a nice coincidence of this state requirement and the implementation of our ERATS, as our patients need only a limited amount of opioid after discharge, and this website allows us to track opioid refilled by other physicians not associated with our institution.

Dr Darling. We just implemented a best practice process at the University of Toronto in the department of surgery, and each division developed a guideline with what they felt were appropriate numbers of tablets to be prescribed, for example, VATS versus thoracotomy. And so our patients after VATS are sent home with 15 tablets of hydromorphone 2 mg, and that's it. No refills. So we'll see how that works.

Dr Nguyen. Once our ERATS practice is mature with good in-hospital pain control, our patients are frequently discharged with either 12 5-mg tablets of oxycodone (90 morphine milligram equivalents [MMEs]) or with 12 50-mg tablets of tramadol (60 MMEs) and sometimes both (total MME of 150). We don't use hydromorphone because it is quite powerful.

Dr Darling. I don't know why we chose hydromorphone, but that's what our best practice committee said to use. Thank you very much.

Dr Nguyen. You are welcome. Thank you.

Dr Darling. Thank you very much.