

Factors associated with home opioid use after thoracic surgery



Jeffrey D. Hodges, MD, MS,^a Duc T. Nguyen, MD, PhD,^b Jane Doan, MPA,^a Leonora M. Meisenbach, DNP, RN, ACNP-BC,^a Ray Chihara, MD, PhD,^{a,c} Edward Y. Chan, MD, FACS,^{a,c} Edward A. Graviss, PhD, MPH, FIDSA,^b and Min P. Kim, MD, FACS^{a,c}

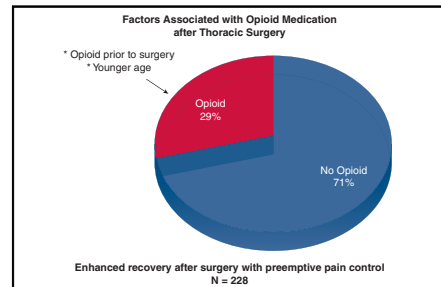
ABSTRACT

Objective: Enhanced recovery after surgery (ERAS) with a pre-emptive pain management program has been shown to decrease opioid prescriptions after thoracic surgery. We sought to determine which patient or procedural factors were associated with the need for prescription opioid medications after thoracic surgical procedures.

Methods: We performed a retrospective analysis of a postoperative pain survey at the time of follow-up in combination with procedural and patient characteristic data. We then performed univariate and multivariate logistic regression to determine factors associated with prescription opioids use.

Results: Two hundred twenty-eight patients completed questionnaires at a median of 37 days after surgery. Most patients received minimally invasive surgery (n = 213, 93%) with the 2 most common types of operations being foregut (n = 92, 40%) and pulmonary resection (n = 80, 35%). Thirty-nine percent of patients (n = 89) were taking chronic pain medications preoperatively, with 15% on chronic opioids medication (n = 33). After surgery, 166 patients (72%) did not take opioids at home. Multivariate analysis showed any chronic opioid medications before surgery (odds ratio, 28.8; 95% confidence interval, 9.13-90.8, P < .001) were associated with opioid use postoperatively. In contrast, increase in age was associated with a decrease in opioid use (odds ratio, 0.96; 95% confidence interval, 0.93-0.99, P = .01).

Conclusions: ERAS with pre-emptive pain management was associated with patients avoiding opioid prescriptions during recovery. The patient factor of preoperative opioid pain medication(s) and younger age is a significant factor for the patient needing opioids at home after surgery instead of procedural factors. Patient characteristics should be considered when tailoring the patient’s pain management after thoracic surgical procedures. (JTCVS Open 2021;5:173-86)



Opioid use before surgery and younger age were associated with opioid use after surgery.

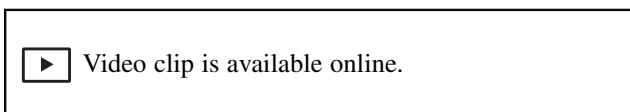
CENTRAL MESSAGE

Taking pain medication before a thoracic operation is the main risk factor for requiring opioid medication after surgery.

PERSPECTIVE

An ERAS program with an emphasis on pre-emptive pain control was associated with most of the patients recovering from the thoracic operation without a need for opioid prescriptions. The main risk factor requiring opioid pain medication after surgery is chronic pain medication before surgery.

See Commentaries on pages 187 and 189.



From the ^aDivision of Thoracic Surgery, Department of Surgery, ^cDepartment of Surgery and Cardiothoracic Surgery, Weill Cornell Medical College, and ^bDepartment of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Tex. Accepted for the 100th Annual Meeting of The American Association for Thoracic Surgery.

Received for publication Nov 23, 2020; accepted for publication Nov 24, 2020; available ahead of print Jan 15, 2021.

Address for reprints: Min P. Kim, MD, FACS, 6550 Fannin St, Suite 1661, Houston, TX 77030 (E-mail: mpkim@houstonmethodist.org).

2666-2736

Copyright © 2020 The Authors. 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.jxon.2020.11.010>

Enhanced Recovery After Surgery (ERAS) with pre-emptive pain management, opioid-sparing protocols has been shown to decrease postoperative opioid requirements in thoracic surgery.¹⁻³ Moreover, enhanced recovery programs in thoracic surgery have been shown to reduce the length of stay, total fluid balance, and mean inflation-adjusted hospital costs.⁴ Consequently, most institutions have implemented these protocols to curb the opioid epidemic and decrease hospital costs.⁵ Still, some patients require opioid medications in the perioperative period for adequate pain management following thoracic surgical procedures. In the era of ERAS, it is unclear which patient or procedural factors are associated with being able to manage without opioid pain medications at home after thoracic surgery. Moreover, studies have shown that patient-derived

Abbreviations and Acronyms

- ASA = American Society of Anesthesiologists
- CI = confidence interval
- ERAS = Enhanced Recovery After Surgery
- IQR = interquartile range
- OR = odds ratio

outcomes data can provide a unique insight into patient pain medication use and overall pain control.^{6,7} Using patient-derived outcomes, we sought to determine which factors were associated with the need for prescription opioid medications after thoracic surgical procedures.

METHODS

The institutional review board at Houston Methodist Research Institute approved the study (Pro00013680), and patients consented. We performed a retrospective cohort analysis of patients who underwent thoracic surgery procedures from 2018 to 2019 who completed our postoperative pain survey. Before the study period, we had implemented an ERAS program (Table 1)^{1,8} with pre-emptive pain control (Table 2).² To summarize, all study patients went through the ERAS program that emphasized improvements in the preoperative, operative, and postoperative phases of care (Table 1). One of the most important aspects of the operative phase of care was performing minimally invasive surgery and thoracic nerve block with liposomal bupivacaine (Video 1) for chest cases and injection of liposomal bupivacaine around transversus abdominis plane in abdominal cases. The pre-emptive pain control program emphasizes the use of nonopioid scheduled pain medication as the primary mode of pain control at home, along with patient education about the program (Table 2). Patients were discharged by a physician assistant or resident. Most patients were given pain medication based on the standard protocol (Table 2). If the patients' pain was not well controlled at the time of discharge on a standard protocol, patients were prescribed opioids. For patients with chest surgery, pain assessment was made after the removal of the chest tube. The evaluation was made based on the probability that the standard pain medication protocol would be successful in managing pain. We set the patient expectation

by explaining to the patient that the goal is to manage the pain instead of having no pain. If the standard nonopioid pain medication is providing excellent pain relief, there is a high likelihood that the patient's pain will be successfully managed without opioid pain medication, and they will be discharged home on standard medication. If the standard nonopioid pain medications do not provide any relief, the patient will be discharged home on opioids. If patients called within 5 days of surgery due to pain, the provider who discharged the patient received the call to manage patient's pain. This improved the ability of the provider to assess and predict the pain medication need of the patient. We obtained institutional data collected for the Society of Thoracic Surgeons database, as well as data from electronic health records on patient and procedural characteristics. We recorded patient features such as demographics, comorbidities, surgical history, social history, and American Society of Anesthesiologists (ASA) classification. Surgical factors were categorized as anatomy, open versus minimally invasive, type of minimally invasive procedure (robot-assisted, video-assisted thoracoscopic surgery, or laparoscopic), surgery through the abdominal or thoracic cavity, time in the operating room, and primary surgeon who operated. The postoperative pain survey was given at the time of follow-up visit in the office. The survey inquired which, if any, pain medications patients took before surgery and after surgery, as well as the pain level (1-10 scale) at the time of follow-up (3-8 weeks after surgery) (Figure 1).

Statistical Analysis

Multiple logistic regression modeling (with the clustered variance estimator option for surgeon level) was performed to determine statistical association with the opioid prescription at discharge after thoracic surgery. Variables for multiple logistic regression models were selected based on the clinical significance and also by the Stata's Lasso technique with the cross-validation selection option.^{9,10} To summarize, all variables used in the univariable analysis were assessed by the Lasso. The program suggested models that included the variables with the greatest probability of being a risk factor. The likelihood ratio test further reduced model subsets. During the modeling process, the potential risk factors were discussed with the senior clinicians who have extensive clinical experience in the field to ensure the biological plausibility of the selected covariates. Logistic regression analysis was also repeated in the cohort of patients who were opioid-naïve to identify additional factors associated with an opioid prescription at discharge after thoracic surgery. Missing data were assessed for missing

TABLE 1. Enhanced recovery after surgery protocol with pre-emptive pain control

	Preoperative	Intraoperative	Postoperative
Patient	Walk 1 mile a day Practice incentive spirometer Quit smoking 4 wk before surgery Stop drinking alcohol 2 wk before surgery Evaluation of steroids and blood thinners		Ambulate 3 × a day Sit in a chair for total of 6 h Incentive spirometer 10 × every hour Take around-the-clock pain medication
Nurse	Give pain medication Inject enoxaparin		Give pain medication Inject enoxaparin
Surgeon		Minimally invasive surgery Inject liposomal bupivacaine	
Anesthesiologist		Total intravenous anesthetic Less CVL, Foley, and a-line IV antibiotics before incision Maintain normothermia Control postoperative nausea and vomiting Maintain euolemia Give pain medication	

CVL, Central venous line; a-line, arterial line; IV, intravenous.

TABLE 2. Standard and breakthrough pain medication for pre-emptive pain control

	Preoperative	Intraoperative	Postoperative inpatient	Postoperative outpatient
Standard	Tramadol Gabapentin	Acetaminophen Ketorolac*	Acetaminophen Ketorolac* Gabapentin Methocarbamol Lidoderm patch Tramadol as needed	Acetaminophen 1 g PO 3 × a day for 5 d Naproxen 220 mg PO 2 × a day for 3 d* Gabapentin 300 mg PO 3 × a day for 7 d† Methocarbamol as needed† Lidoderm patch as needed†
Breakthrough			Dilaudid IV × 2 Dilaudid PCA Convert to PO opioid	Tramadol Acetaminophen with codeine #3 Acetaminophen with hydrocodone

PO, Per os; IV, intravenous; PCA, patient-controlled analgesia. *Ketorolac and Naproxen was given for patients <75 years old with Cr < 1 and approval by surgeon. †For chest surgery.

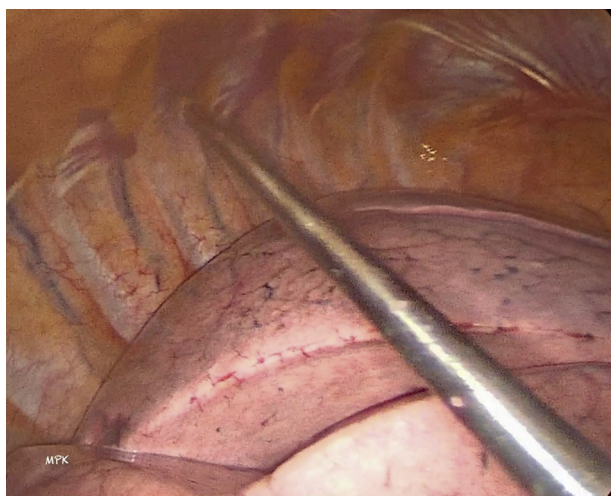
completely at random using the Little's χ^2 test.¹¹ All the analyses were performed on Stata, version 16.1 (StataCorp LLC, College Station, Tex).⁹

RESULTS

Two hundred twenty-eight patients met the inclusion and exclusion criteria and all patients consented to be part of the study. The median age of the cohort was 63 years old; patients were mostly female (58%), and white (90%, Table 3). The 3 most common comorbidities were hypertension (56%), coronary artery disease (17%), and diabetes (13%). There were 94 patients (41.2%) who were current or former smokers, 17 patients (8%) had a clinical diagnosis of opioid dependence, and 19 patients (8%) had a diagnosis of alcohol dependence (Table 3). In the survey, there were 33 patients (15%) who were taking opioids

chronically before surgery, and there were 89 patients (39%) who were taking either opioids or nonopioid pain medication to treat chronic pain. There were 63 patients (29%) who took opioids after surgery (Table 4). The 2 most common operations for the patients in the cohort were foregut (n = 92, 40%) and pulmonary resection (n = 80, 35%, Table 4). Most patients underwent minimally invasive surgery (n = 212, 93%) with the 2 most common minimally invasive approaches being robot-assisted thoracoscopic surgery (n = 93, 41%) and robot-assisted laparoscopic surgery (n = 94, 41%). Most patients underwent a transthoracic surgical procedure (n = 131, 58%) with median time for the operation of 2.9 hours. Most of the cases were performed by one surgeon (n = 145, 83%). The median time between surgery and the questionnaire was 37 days. There was no significant difference in the time between surgery and opioid users versus nonusers filling out the survey ($P = .14$, Table 4). The median postoperative length of stay of the entire cohort was 1 day (interquartile range [IQR], 1, 3) (Table E1).

Multiple logistic regression analysis of patient and procedural factors associated with requiring home opioid medication demonstrated that opioid use before surgery (odds ratio [OR], 28.80; 95% confidence interval [CI], 9.13-90.80, $P < .001$) was associated with postoperative home opioid use. In contrast, increase in age was associated with a decrease in home opioid use (OR, 0.96; 95% CI, 0.93-0.99, $P = .01$) (Table 5). Since opioid use before surgery is such a strong independent factor associated with home opioid use after surgery, we analyzed the opioid-naïve patients before surgery to determine additional factors associated with home opioid use in this subset of patients. Multiple logistic regression in opioid-naïve individuals (n = 195) showed that tobacco use (OR, 2.51; 95% CI, 1.09-5.78, $P = .03$), increased ASA classification (ASA 3: OR, 4.09; 95% CI, 1.15-14.53, $P = .03$; ASA 4: OR, 5.25; 95% CI, 1.23-22.45, $P = .03$), and any pain



VIDEO 1. Port placement and liposomal bupivacaine nerve block. Video demonstrates the typical port placement and liposomal bupivacaine nerve block during a robot-assisted lobectomy. Video available at: [https://www.jtcvs.org/article/S2666-2736\(20\)30174-1/fulltext](https://www.jtcvs.org/article/S2666-2736(20)30174-1/fulltext).

Postoperative Pain Questionnaire

1. Which pain medication did you take **after surgery at home?** (Please circle all that apply)
 - Acetaminophen (Tylenol)
 - Ibuprofen (Motrin, Advil)
 - Naproxen (Aleve)
 - Gabapentin (Neurontin)
 - Other _____
 - Tramadol (Ultram)
 - Acetaminophen/codeine (Tylenol #3)
 - Oxycodone (Percocet)
 - Hydrocodone (Norco)

2. Which pain medications, if any, were you taking **before surgery?** (Please circle all that apply)
 - Acetaminophen (Tylenol)
 - Ibuprofen (Motrin, Advil)
 - Naproxen (Aleve)
 - Gabapentin (Neurontin)
 - Other _____
 - Tramadol (Ultram)
 - Acetaminophen/codeine (Tylenol #3)
 - Oxycodone (Percocet)
 - Hydrocodone (Norco)
 - NONE

3. How much pain are you in right now? (0=no pain to 10=worst pain imaginable)

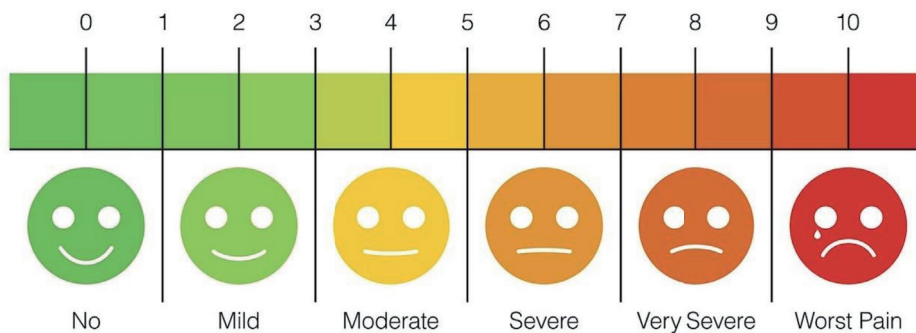


FIGURE 1. Postoperative pain questionnaire asking about specific pain medication patient took after surgery and before surgery as well as patient’s pain at the time of the survey.

medication usage before surgery (OR, 2.78; 95% CI, 1.18-6.53, $P = .02$) were all significantly associated with need for opioid pain management at home after surgery. Moreover, increased age (OR, 0.95; 95% CI, 0.92-0.98, $P = .001$) was associated with a decrease in home opioid use (Table 5). Except for the body mass index, which had 23% of missing data, all the evaluated variables have complete data. Little’s χ^2 test for missing completely at random had a nonsignificant P value (.72), which suggests that the

missing values could be completely random and do not influence the outcome. Of all the variables used in the analysis, only race and body mass index had missing data (26.3% and 23.7%, respectively, Table E2). The descriptive sensitivity analysis indicated that except for time in operation room and postoperative length of stay, the 2 groups of patients had similar level of postoperative outcomes, and specifically no difference in the primary outcome was found (opioids after surgery, $P = .89$, Table 5).

TABLE 3. Patient characteristics and need for opioid prescription after surgery

	Total (N = 228)	Opioids after surgery		P value
		No (n = 165)	Yes (n = 63)	
Age at surgery, y, median (IQR)	63.0 (54.0, 72.0)	65.0 (54.0, 73.0)	60.0 (53.0, 70.0)	.09
Female	132 (57.9)	98 (59.4)	34 (54.0)	.46
White	151 (89.9)	113 (92.6)	38 (82.6)	.08
Height, cm, median (IQR)	170.0 (163.0, 178.0)	169.0 (163.0, 178.0)	170.0 (164.0, 178.0)	.49
Weight, kg, median (IQR)	81.6 (66.5, 94.0)	80.0 (65.6, 94.3)	84.1 (69.4, 93.8)	.31
Body mass index, median (IQR)	27.6 (23.6, 31.5)	27.4 (23.5, 31.5)	28.0 (24.8, 31.4)	.79
Comorbidities				
Hypertension	127 (55.7)	91 (55.2)	36 (57.1)	.79
Congestive heart failure	6 (2.6)	4 (2.4)	2 (3.2)	.67
Coronary artery disease	39 (17.1)	26 (15.8)	13 (20.6)	.38
Myocardial infarction	16 (7.0)	8 (4.8)	8 (12.7)	.046
Atrial fibrillation	9 (3.9)	7 (4.2)	2 (3.2)	1.00
Valvular heart disease	6 (2.6)	4 (2.4)	2 (3.2)	.67
Interstitial lung disease	9 (3.9)	8 (4.8)	1 (1.6)	.45
Major vascular disease	15 (6.6)	11 (6.7)	4 (6.3)	.93
DVT/PE	10 (4.4)	7 (4.2)	3 (4.8)	.86
Cerebrovascular history	16 (7.0)	9 (5.5)	7 (11.1)	.13
Diabetes	29 (12.7)	22 (13.3)	7 (11.1)	.65
Liver dysfunction	4 (1.8)	1 (0.6)	3 (4.8)	.07
On dialysis	2 (0.9)	1 (0.6)	1 (1.6)	.48
Coexisting cancer	21 (9.2)	12 (7.3)	9 (14.3)	.10
Preoperative history of home oxygen	6 (2.6)	3 (1.8)	3 (4.8)	.35
Dementia or neurocognitive dysfunction	3 (1.3)	2 (1.2)	1 (1.6)	1.00
Major psychiatric disorder	64 (28.1)	46 (27.9)	18 (28.6)	.92
Previous cardiothoracic surgery	15 (6.6)	10 (6.1)	5 (7.9)	.61
Reoperation	34 (14.9)	26 (15.8)	8 (12.7)	.56
Preoperative chemotherapy	13 (5.7)	10 (6.1)	3 (4.8)	1.00
Preoperative thoracic radiation therapy	5 (2.2)	5 (3.0)	0 (0.0)	.33
Smoking	94 (41.2)	56 (33.9)	38 (60.3)	<.001
Opioid dependency	17 (7.5)	3 (1.8)	14 (22.2)	<.001
Alcohol abuse	19 (8.3)	10 (6.1)	9 (14.3)	.04
Opioids before surgery	33 (14.5)	5 (3.0)	28 (44.4)	<.001
Any pain medication before surgery	89 (39.0)	46 (27.9)	43 (68.3)	<.001
ASA classification				.10
2	65 (28.5)	53 (32.1)	12 (19.0)	
3	122 (53.5)	86 (52.1)	36 (57.1)	
4	41 (18.0)	26 (15.8)	15 (23.8)	

Values in bold are statistical significance at P values $< .05$. *IQR*, Interquartile range; *DVT*, deep vein thrombosis; *PE*, pulmonary emboli; *ASA*, American Society of Anesthesiologists.

Analysis of patients who took opioid medication(s) at home showed that most of the patients who took opioid medications at home required 2 different pain medications (47.6%) to manage pain. In contrast, patients who did not take opioid medications required 1 pain medication (38.8%, $P < .001$, Figure 2). The most common nonopioid pain medication in the opioid group was gabapentin

(55.6%), and the most common opioid medication was tramadol (47.6%) and acetaminophen with hydrocodone (47.6%). In contrast, the most common medication to treat pain after surgery in a group of patients who did not use opioid medication was acetaminophen (82%) (Figure 3). The overall median pain score for the group at follow-up was 0 (IQR, 0.0-2.0). Between patients who

TABLE 4. Procedural characteristics and opioid prescription after surgery

	Total (N = 228)	Opioids after surgery		P value
		No (n = 165)	Yes (n = 63)	
Inpatient	97 (42.5)	64 (38.8)	33 (52.4)	.06
Anatomy				.001
Lungs	80 (35.1)	56 (33.9)	24 (38.1)	
Esophagus	17 (7.5)	14 (8.5)	3 (4.8)	
Chest wall	8 (3.5)	2 (1.2)	6 (9.5)	
Pleura	12 (5.3)	7 (4.2)	5 (7.9)	
Mediastinum	15 (6.6)	9 (5.5)	6 (9.5)	
Diaphragm	4 (1.8)	1 (0.6)	3 (4.8)	
Foregut	92 (40.4)	76 (46.1)	16 (25.4)	
Approach				.04
Minimally invasive	212 (93.0)	157 (95.2)	55 (87.3)	
Open	16 (7.0)	8 (4.8)	8 (12.7)	
Procedure type				.004
Open	16 (7.0)	8 (4.8)	8 (12.7)	
Robot-assisted thoracoscopic	93 (40.8)	60 (36.4)	33 (52.4)	
Robot-assisted laparoscopic	94 (41.2)	78 (47.3)	16 (25.4)	
VATS	24 (10.5)	19 (11.5)	5 (7.9)	
Laparoscopic	1 (0.4)	0 (0.0)	1 (1.6)	
Thoracic versus abdominal cavity				.003
Abdominal cavity	97 (42.5)	80 (48.5)	17 (27.0)	
Thoracic cavity	131 (57.5)	85 (51.5)	46 (73.0)	
Time in OR, h, median (IQR)	2.9 (1.9, 3.9)	2.7 (1.8, 3.8)	3.3 (2.4, 4.5)	.01
Surgeon				.02
Surgeon 1	145 (83.3)	111 (88.1)	34 (70.8)	
Surgeon 2	22 (12.6)	12 (9.5)	10 (20.8)	
Surgeon 3	7 (4.0)	3 (2.4)	4 (8.3)	
Time between surgery and survey, d, median (IQR)	37.0 (34.0, 40.0)	39.0 (35.0, 40.0)	36.0 (33.0, 40.0)	.14

Values are in frequency and % unless otherwise specified. Foregut–hiatal hernia repair with Nissen, Toupet, or LINX and Heller myotomy with Dor fundoplication. Values in bold are statistical significance at P values < .05. VATS, Video-assisted thoracoscopic surgery; OR, operating room; IQR, interquartile range.

had opioids at home versus no opioids, patients who were on opioids at home after surgery had a significantly greater median pain score of 2 (IQR, 0.0, 4.0, pain scale 1-10) compared with the patients who were taking no opioids at home after surgery, with a median pain score of 0 (IQR, 0, 1; $P < .001$) at follow-up. The use of different pain medications after a specific type of surgery is presented in the [Tables 6](#) and [E3](#).

DISCUSSION

Our previous studies showed that an ERAS program with an emphasis on pre-emptive pain control in thoracic surgery shows the ability to manage a patient's pain after a thoracic surgical procedure at home without opioids.² A majority of patients in our cohort did not require opioid pain medications at home after surgery, and at follow-up, patients had excellent pain control. Our study shows that in the era before ERAS, thoracic surgeons often prescribed more opioids than patients needed to control their pain adequately. Studies looking at opioid prescriptions and usage after

surgery before the ERAS era show that 7%-14% of patients fill opioid prescriptions without taking any pills dispensed, and up to 21% of the patients do not fill their opioid prescriptions at all.^{12,13} Moreover, Bartels and colleagues¹⁴ found 45% of patients after thoracic surgery took no or very few (5 or less) prescribed opioid pills. Thus, the ERAS program, especially with the emphasis of pre-emptive pain control, can have a significant impact reduction of opioid use after surgery. However, in our study, there was still a group of patients who required opioid pain medication at home.

In our cohort, the 2 most significant factors that contributed to the requirement of opioid pain medication after surgery were the use of opioid medications before surgery and younger age. The prevalence of opioid use before thoracic surgery was in line with observational study at a tertiary care academic medical center that included 34,186 patients.¹⁵ Their research showed that overall, about 23% of patients were taking preoperative opioids before all surgical procedures, with 65% in the orthopedic, 55% in the

TABLE 5. Univariable and multivariable logistic regression of characteristics associated with opioid prescription (n = 228)

	Univariable		Multivariable	
	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Age at surgery, y, median (IQR)	0.98 (0.97-1.00)	.12	0.96 (0.93-0.99)	.01
Smoking	2.96 (1.63-5.38)	<.001	2.16 (0.99-4.72)	.052
Alcohol abuse	2.58 (1.00-6.70)	.051	2.75 (0.86-8.75)	.09
ASA classification				
2	(reference)		(reference)	
3	1.85 (0.88-3.87)	.10	2.43 (0.85-6.92)	.10
4	2.55 (1.04-6.22)	.04	2.84 (0.82-9.89)	.10
Opioids before surgery	25.60 (9.24-70.95)	<.001	28.80 (9.13-90.80)	<.001
Surgical approach				
Minimally invasive	(reference)		(reference)	
Open	2.85 (1.02-7.97)	.045	2.57 (0.67-9.87)	.17
Cavity	(reference)			
Abdominal cavity	2.55 (1.35-4.80)	.004	(reference)	
Thoracic cavity	1.15 (0.98-1.35)	.09	2.17 (0.91-5.18)	.08
Time in operating room, h	0.98 (0.97-1.00)	.12	1.18 (0.97-1.45)	.10

Values in bold are statistical significance at P values < .05. OR, Odds ratio; CI, confidence interval; IQR, interquartile range; ASA, American Society of Anesthesiologists.

neurosurgical spine, and 15% in the thoracic surgery group. However, the use of opioids before surgery is not a factor that researchers often look at when they perform analysis of risk factors associated with the need for opioids after surgery. The population-based study of opioid prescriptions across health systems in Michigan in 2392 patients did not show that opioid use before surgery or any pain medication before surgery for chronic pain conditions.¹⁶ The main reason for lack of association between the pain medication before surgery and opioid pain medication after surgery in their study is that they did not use opioid or pain medication before surgery as a factor in their analysis. When this factor is used in the report, the use of opioids before surgery is associated with the need for opioid use after surgery.^{17,18} Moreover, using chronic pain as a patient factor shows an

increase in risk for prolonged postoperative opioid use.¹⁹ Since our study shows a strong association between the pain medication before surgery and the need for opioids at home after surgery, it is essential to consider these factors in tailoring the patient’s pain regimen after surgery. More likely than not, this group of patients will quickly fail the nonopioid pre-emptive pain regimen to manage pain after surgery. Although age was not significantly different in the univariable analysis between groups of no-home opioids and home opioids, this difference is borderline, with a median of 65.0 (IQR, 54.0, 73.0) versus 60.0 (IQR, 53.0, 70.0), respectively, P = .09. After we adjusted for the effect of other covariates in the multivariable analysis, the association between home opioids and age became significant.

In the cohort of patients who were opioid-naïve before surgery, we discovered that any pain medication before surgery, history of tobacco use, greater ASA classification, and younger age were associated with the need for opioid pain medication at home after thoracic surgery. The history of tobacco use is an independent factor for opioid use in other studies.^{16,20} A retrospective analysis of national insurance claims data of 36,177 patients after surgery has shown that smoking is an independent factor associated with persistent opioid use.²⁰ The association between smoking and opioid use is likely due to those patients with a history of smoking may have a different perception of pain after surgery. Retrospective analysis of patient-reported outcomes evaluating pain after major surgery showed that current smokers have high pain intensity after surgery as well as a greater need for opioid pain medication after surgery.²¹ In addition, younger age^{16,19,22,23} as well as a high ASA score¹⁶ has been identified as patient factors for the need for an opioid medication after surgical procedures in other

TABLE 6. Multivariable logistic regression of characteristics associated with opioid prescription in patients naïve with both opioids and nonopioids before surgery (n = 139)

	Adjusted OR (95% CI)	P value
Age at surgery, y	0.95 (0.91-0.99)	.02
Smoking	4.42 (1.45-13.50)	.01
ASA classification		
2	(reference)	
3	3.65 (0.74-18.10)	.11
4	3.97 (0.71-22.13)	.12
Cavity		
Abdominal cavity	(reference)	
Thoracic cavity	3.86 (0.89-16.76)	.07

Area under receiver operating characteristic curve = 0.78. Values in bold are statistical significance at P values < .05. OR, Odds ratio; CI, confidence interval; ASA, American Society of Anesthesiologists.

studies. It is unknown why these factors are associated with more pain after surgery.

In our study, there was no procedural factor that contributed to the need for opioids after surgery. This points to the fact that patient characteristics and their use of pain before surgery play a more critical factor in the need for opioids at home after surgery compared with the procedural factors. This is in contrast to other studies that show that procedure is a factor in the risk of opioid use after major surgery.^{16,24,25} For example, Clarke and colleagues²⁵ performed a retrospective analysis of 39,140 patients who underwent major elective surgery at acute care hospitals found that patients who had the thoracic procedure had significantly prolonged opioid use compared with patients undergoing open radical prostatectomies. One major limitation of such analysis is that there are different groups of surgeons who are proscribing opioids after prostatectomy compared with thoracic procedures. Moreover, each group might have a different protocol in terms of evaluating pain and prescribing opioids. Thus, the major flaw of the study that looks at a large health care system is that it does not control for the prescriber. In contrast, in our cohort, all patients were treated in a similar fashion using a standardized regimen for the treatment of pain. This is one of the reasons for the lack of association of procedure with opioid medication in our study in contrast to the other studies. Another possible reason for the muting effect of the procedural factor may be that most of the patients underwent a minimally invasive approach. Overall, patients have lower pain levels after minimally invasive surgery, leading to less need for opioid medication at the time of discharge.

The pain survey was a very effective patient-reported outcome measure at the time of follow up that provided a quick and more accurate snapshot of the patient's pain medication requirement after surgery, their pain level at the time of the visit and the pain medications patients took before surgery. The survey was a better measure of the medications that patients took compared with the data on the prescribed medication. The analysis of the pain medication that the patient took showed that not all patients received the recommended regimen of pain medication at home. All patients who were going home without opioids were instructed to take acetaminophen; however, only 82% of the patients took the medication. This shows that the medications that were given to patients at discharge are not necessarily what the patient will take at home. Thus, this patient-reported outcome provided a more accurate assessment of the patient's pain level and pain medication needs after surgery.

There were several additional limitations to our study. Our study is a retrospective analysis of data that was collected in a single institution with most of the operations performed by a single surgeon. However, the data were collected from the patient's report of their perception of

pain and use of pain medication before and after surgery at the time of follow-up visit, providing an accurate assessment of pain and the pain medication that was taken after the surgery. Moreover, having a single-institution analysis allowed for an outcome of a mature ERAS program with an emphasis on pre-emptive pain control. Moreover, one of the limitations was a wide range of dates of follow-up between 3 and 8 weeks. However, there was no significant difference in the follow-up time between the patients who required opioids after surgery and who did not require opioids after surgery. Furthermore, since the survey asked for all pain medications patients took after surgery, the range of the dates had a limited impact on the conclusion of the study. Another limitation of the study is that most of the patients underwent a minimally invasive approach; thus, the conclusions may not apply to a program that performs most of the operations in an open manner. The final limitation is that we may not have included all factors that could contribute to pain after surgery. Although we had a comprehensive list of patient and procedural factors, we may have missed other factors that could have contributed to the need for an opioid medication after surgery. Factors such as major complications after surgery were not studied in the analysis since the current cohort was unable to answer the question about the relationship between complications and opioid use.

CONCLUSIONS

In a mature ERAS program, with an emphasis on pre-emptive pain control in the thoracic surgery program, a majority of patients were able to be managed without opioid medications at home. Also, procedural factors did not have an impact on the need for opioid medication at home; instead, patient factors contributed to the need for opioid medication after surgery. The most substantial factors that are associated with home opioid medicines after surgery are patients taking an opioid medication before surgery. Thus, in this group of patients, prescribers should have a lower threshold to add opioid pain medication after surgery. In patients who are opioid-naïve before surgery, the use of nonopioid pain medication before surgery, younger age, current or former smokers, and patients with greater ASA scores should be factors to be mindful while managing their postoperative pain. Thus, knowing these personal characteristics provides a way to personalize home pain medication regimen after surgery (Figure 4).

Conflict of Interest Statement

Dr Kim has taught courses for Intuitive Surgical, Veran, and Medtronic. Dr Chan has taught courses for Veran. All other 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 thank Elaine Jordan, Libra Broussard, and Jeanette Corvera for their help with the pain questionnaire.

References

- 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.
- Kim MP, Godoy C, Nguyen DT, Meisenbach LM, Chihara R, Chan EY, et al. Pre-emptive pain-management program is associated with reduction of opioid prescriptions after benign minimally invasive foregut surgery. *J Thorac Cardiovasc Surg*. 2020;159:734-44.e4.
- Thompson C, French DG, Costache I. Pain management within an enhanced recovery program after thoracic surgery. *J Thorac Dis*. 2018;10(Suppl 32):S3773-80.
- 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.
- 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(R)) Society and the European Society of Thoracic Surgeons (ESTS). *Eur J Cardiothorac Surg*. 2019;55:91-115.
- Medbery RL, Fernandez FG, Khullar OV. ERAS and patient reported outcomes in thoracic surgery: a review of current data. *J Thorac Dis*. 2019;11(Suppl 7):S976-86.
- Holmes MM, Lewith G, Newell D, Field J, Bishop FL. The impact of patient-reported outcome measures in clinical practice for pain: a systematic review. *Qual Life Res*. 2017;26:245-57.
- Brown JK, Singh K, Dumitru R, Chan E, Kim MP. The benefits of enhanced recovery after surgery programs and their application in cardiothoracic surgery. *Methodist Debaquey Cardiovasc J*. 2018;14:77-88.
- Stata Base Reference Manual Release 16: A Stata Press publication. College Station, TX: StataCorp; 2019.
- Hastie T, Tibshirani R, Wainwright M. *Statistical Learning with Sparsity: The Lasso and Generalizations*. 1st ed. Boca Raton, FL: CRC Press; 2015.
- Little RJA. A test of missing completely at random for multivariate data with missing values. *J Am Stat Assoc*. 1988;83:1198-202.
- Holst KA, Thiels CA, Ubl DS, Blackmon SH, Cassivi SD, Nichols FC III, et al. Postoperative opioid consumption in thoracic surgery patients: how much is actually used? *Ann Thorac Surg*. 2020;109:1033-9.
- 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.
- Bartels K, Mayes LM, Dingmann C, Bullard KJ, Hopfer CJ, Binswanger IA. Opioid use and storage patterns by patients after hospital discharge following surgery. *PLoS One*. 2016;11:e0147972.
- Hilliard PE, Waljee J, Moser S, Metz L, Mathis M, Goesling J, et al. Prevalence of preoperative opioid use and characteristics associated with opioid use among patients presenting for surgery. *JAMA Surg*. 2018;153:929-37.
- Howard R, Fry B, Gunaseelan V, Lee J, Waljee J, Brummett C, et al. Association of opioid prescribing with opioid consumption after surgery in Michigan. *JAMA Surg*. 2019;154:e184234.
- Hirji SA, Landino S, Cote C, Lee J, Orhurhu V, Shah RM, et al. Chronic opioid use after coronary bypass surgery. *J Card Surg*. 2019;34:67-73.
- Harbaugh CM, Lee JS, Hu HM, McCabe SE, Voepel-Lewis T, Englesbe MJ, et al. Persistent opioid use among pediatric patients after surgery. *Pediatrics*. 2018;141:e20172439.
- Stafford C, Francone T, Roberts PL, Ricciardi R. What factors are associated with increased risk for prolonged postoperative opioid usage after colorectal surgery? *Surg Endosc*. 2018;32:3557-61.
- Brummett CM, Waljee JF, Goesling J, Moser S, Lin P, Englesbe MJ, et al. New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surg*. 2017;152:e170504.
- Montbriand JJ, Weinrib AZ, Azam MA, Ladak SSJ, Shah BR, Jiang J, et al. Smoking, pain intensity, and opioid consumption 1-3 months after major surgery: a retrospective study in a hospital-based transitional pain service. *Nicotine Tob Res*. 2018;20:1144-51.
- Behman R, Cleary S, McHardy P, Kiss A, Sawyer J, Ladak SSJ, et al. Predictors of post-operative pain and opioid consumption in patients undergoing liver surgery. *World J Surg*. 2019;43:2579-86.
- Namba RS, Singh A, Paxton EW, Inacio MCS. Patient factors associated with prolonged postoperative opioid use after total knee arthroplasty. *J Arthroplasty*. 2018;33:2449-54.
- Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. *JAMA Intern Med*. 2016;176:1286-93.
- Clarke H, Soneji N, Ko DT, Yun L, Wijeyesundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ*. 2014;348:g1251.

Key Words: enhanced recovery after surgery, minimally invasive thoracic surgery, postoperative pain control, opioid medication

TABLE E1. Postoperative parameters*

	Total (N = 228)	Complete data (n = 168)	Missing data (n = 60)	P values*
Opioid after surgery	63 (27.6)	46 (27.4)	17 (28.3)	.89
Any pain medication after surgery	215 (94.3)	160 (95.2)	55 (91.7)	.31
Tylenol after surgery	167 (73.2)	128 (76.2)	39 (65.0)	.09
Aleve after surgery	55 (24.1)	40 (23.8)	15 (25.0)	.85
Motrin after surgery	35 (15.4)	24 (14.3)	11 (18.3)	.46
Neurontin after surgery	96 (42.1)	67 (39.9)	29 (48.3)	.25
Flexeril after surgery	2 (0.9)	1 (0.6)	1 (1.7)	.44
Celebrex after surgery	1 (0.4)	0 (0.0)	1 (1.7)	.09
Lidoderm patch after surgery	2 (0.9)	2 (1.2)	0 (0.0)	.40
Lyrica after surgery	1 (0.4)	1 (0.6)	0 (0.0)	.55
Ultram after surgery	30 (13.2)	26 (15.5)	4 (6.7)	.08
Tylenol #3 after surgery	10 (4.4)	7 (4.2)	3 (5.0)	.79
Percocet after surgery	3 (1.3)	2 (1.2)	1 (1.7)	.78
Norco after surgery	28 (12.3)	17 (10.1)	11 (18.3)	.10
Morphine after surgery	3 (1.3)	1 (0.6)	2 (3.3)	.11
Hydrocodone after surgery	1 (0.4)	0 (0.0)	1 (1.7)	.09
Fentanyl after surgery	2 (0.9)	1 (0.6)	1 (1.7)	.44
Oxycodone after surgery	1 (0.4)	1 (0.6)	0 (0.0)	.55
Hydromorphone after surgery	1 (0.4)	1 (0.6)	0 (0.0)	.55
Number of different types of medications after surgery	2.0 (1.0, 3.0)	2.0 (1.0, 2.0)	2.0 (1.0, 3.0)	.90
Narcotics after surgery	63 (27.6)	46 (27.4)	17 (28.3)	.89
Pain level at time of follow-up	0.0 (0.0, 2.0)	0.0 (0.0, 2.0)	0.0 (0.0, 3.0)	.06
Time in OR, h, median (IQR)	2.9 (1.9, 3.9)	3.1 (2.3, 4.1)	1.9 (1.2, 3.0)	<.001
Postoperative length of stay, d, median (IQR)	1.0 (1.0, 3.0)	1.0 (1.0, 2.0)	2.0 (1.0, 3.5)	.02

OR, Operating room; IQR, interquartile range. Values are in frequency and % unless otherwise specified. Values in bold are statistical significance at P values $< .05$. *Comparison between patients having complete data versus patients having missing data, using the χ^2 or Fisher exact tests for categorical variables and Wilcoxon rank-sum for continuous variables.

TABLE E2. Missingness of variables used in the analysis

Variable	Total	Missing no.	Percent missing
Age at surgery, y, median (IQR)	228	0	0.0
Sex	228	0	0.0
Race	228	60	26.3
Ethnicity	228	0	0.0
Inpatient	228	0	0.0
Primary payor cat4	228	0	0.0
Body mass index, median (IQR)	228	54	23.7
Hypertension	228	0	0.0
Congestive heart failure	228	0	0.0
Coronary artery disease	228	0	0.0
Myocardial Infarction preop	228	0	0.0
Afib per EKG within last year	228	0	0.0
Valvular heart disease	228	0	0.0
Pulmonary hypertension	228	0	0.0
Interstitial fibrosis or interstitial lung disease	228	0	0.0
Major vascular disease	228	0	0.0
Deep vein thrombosis/pulmonary embolism	228	0	0.0
Cerebrovascular history	228	0	0.0
Diabetes	228	0	0.0
Liver dysfunction	228	0	0.0
On dialysis	228	0	0.0
Coexisting cancer	228	0	0.0
Preoperative chemotherapy or immunotherapy	228	0	0.0
Preoperative thoracic radiation therapy	228	0	0.0
Previous cardiothoracic surgery	228	0	0.0
Preoperative history of home O ₂	228	0	0.0
Smoking	228	0	0.0
Narcotic dependency	228	0	0.0
Alcohol abuse	228	0	0.0
Dementia or neurocognitive dysfunction	228	0	0.0
Major psychiatric disorder	228	0	0.0
ECOG score	228	0	0.0
Reoperation	228	0	0.0
Surgical approach conversion	228	0	0.0
Intraoperative packed RBCs	228	0	0.0

(Continued)

TABLE E2. Continued

Variable	Total	Missing no.	Percent missing
ASA classification	228	0	0.0
Time between surgery and survey, d	228	0	0.0
Surgery type	228	0	0.0
Surgical type	228	0	0.0
Open	228	0	0.0
Minimally invasive type	228	0	0.0
Thoracic versus abdominal cavity	228	0	0.0
Time in OR, h	228	0	0.0
Any pain medication before surgery	228	0	0.0
Any non-narcotic pain medication before surgery	228	0	0.0
Narcotics before surgery	228	0	0.0
Tylenol before surgery	228	0	0.0
Aleve before surgery	228	0	0.0
Motrin before surgery	228	0	0.0
Neurontin before surgery	228	0	0.0
Ultram before surgery	228	0	0.0
T#3 before surgery	228	0	0.0
Percocet before surgery	228	0	0.0
Norco before surgery	228	0	0.0
Fentanyl before surgery	228	0	0.0
Oxycodone before surgery	228	0	0.0
Morphine before surgery	228	0	0.0
Number of different pain medications before surgery	228	0	0.0
Number of different pain medications before surgery	228	0	0.0

IQR, Interquartile range; Afib, atrial fibrillation; EKG, electrocardiogram; ECOG, Eastern Cooperative Oncology Group; RBC, red blood cell; ASA, American Society of Anesthesiologists; OR, operating room.

TABLE E3. Different pain medications used after surgery, stratified by type of surgery

	Type of surgery								P value
	Total N = 228	Lungs N = 80	Esophagus N = 17	Chest wall N = 8	Pleura N = 12	Mediastinum N = 15	Diaphragm N = 4	Foregut N = 92	
No pain medication	13 (5.7)	4 (5.0)	4 (23.5)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	4 (4.3)	.06
Tylenol	167 (73.2)	57 (71.3)	12 (70.6)	4 (50.0)	5 (41.7)	11 (73.3)	1 (25.0)	77 (83.7)	.01
Aleve	55 (24.1)	22 (27.5)	1 (5.9)	1 (12.5)	2 (16.7)	4 (26.7)	0 (0.0)	25 (27.2)	.39
Motrin	35 (15.4)	13 (16.3)	4 (23.5)	1 (12.5)	2 (16.7)	1 (6.7)	2 (50.0)	12 (13.0)	.43
Neurontin	96 (42.1)	57 (71.3)	3 (17.6)	5 (62.5)	8 (66.7)	9 (60.0)	1 (25.0)	13 (14.1)	<.001
Flexeril	2 (0.9)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	.03
Celebrex	1 (0.4)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	<.001
Lidoderm patch	2 (0.9)	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1.00
Lyrica	1 (0.4)	0 (0.0)	1 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	.052
Ultram	30 (13.2)	15 (18.8)	0 (0.0)	1 (12.5)	2 (16.7)	2 (13.3)	2 (50.0)	8 (8.7)	.08
T#3	10 (4.4)	1 (1.3)	0 (0.0)	1 (12.5)	0 (0.0)	4 (26.7)	2 (50.0)	2 (2.2)	<.001
Percocet	3 (1.3)	1 (1.3)	0 (0.0)	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	<.001
Norco	28 (12.3)	11 (13.8)	3 (17.6)	4 (50.0)	2 (16.7)	1 (6.7)	0 (0.0)	7 (7.6)	.03
Morphine	3 (1.3)	0 (0.0)	0 (0.0)	1 (12.5)	1 (8.3)	0 (0.0)	0 (0.0)	1 (1.1)	.03
Hydrocodone	1 (0.4)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	<.001
Fentanyl	2 (0.9)	1 (1.3)	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)	.17
Oxycodone	1 (0.4)	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	.93
Hydromorphone	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	.96
Number of different types of medications									<.001
0	12 (5.3)	4 (5.0)	4 (23.5)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	3 (3.3)	
1	69 (30.3)	13 (16.3)	5 (29.4)	2 (25.0)	4 (33.3)	3 (20.0)	1 (25.0)	41 (44.6)	
2	87 (38.2)	29 (36.3)	6 (35.3)	3 (37.5)	3 (25.0)	7 (46.7)	2 (50.0)	37 (40.2)	
3	49 (21.5)	28 (35.0)	1 (5.9)	0 (0.0)	3 (25.0)	5 (33.3)	1 (25.0)	11 (12.0)	
4	8 (3.5)	5 (6.3)	1 (5.9)	1 (12.5)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)	
5	2 (0.9)	1 (1.3)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
6	1 (0.4)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Narcotics									.001
No	165 (72.4)	56 (70.0)	14 (82.4)	2 (25.0)	7 (58.3)	9 (60.0)	1 (25.0)	76 (82.6)	
Yes	63 (27.6)	24 (30.0)	3 (17.6)	6 (75.0)	5 (41.7)	6 (40.0)	3 (75.0)	16 (17.4)	

Values are in number and %.

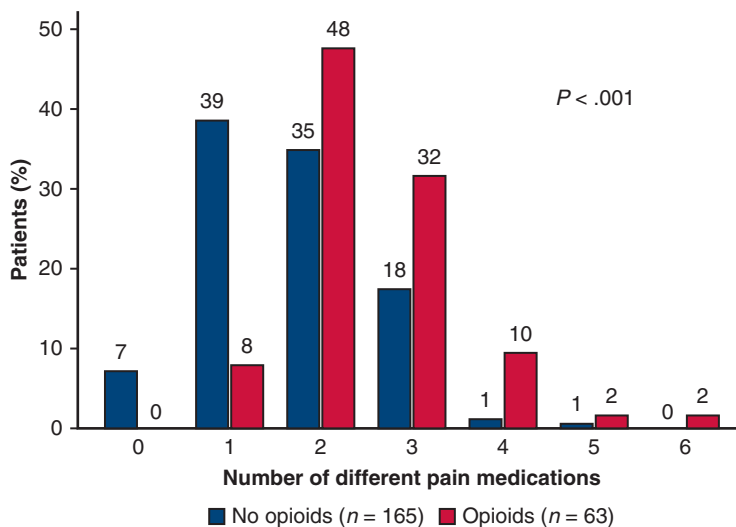


FIGURE 2. The number of different types of pain medications patients took after thoracic surgery. The most predominant proportion (48%) of the patients who took opioids as part of postoperative pain medication (Opioids) took 2 different types of pain medications. In contrast, patients who did not take opioid pain medication after surgery (No opioids) took 1 pain medication (39%, *P* < .001).

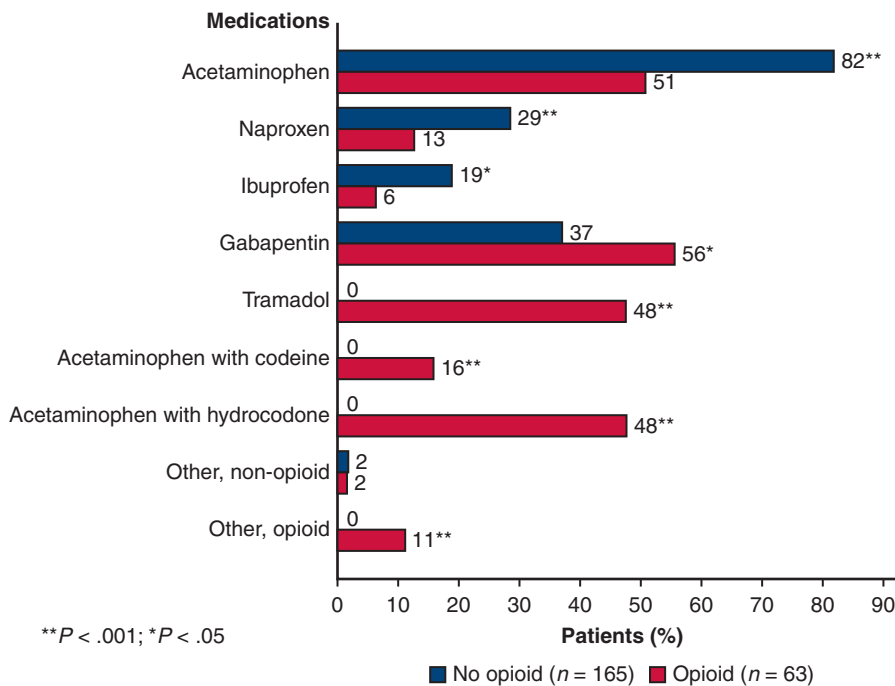


FIGURE 3. Type of pain medication after surgery. The most common nonopioid pain medication in the opioid group was gabapentin (56%), and the most common opioid medication was tramadol (48%) and acetaminophen with hydrocodone (48%). The most common pain medication in patients who did not take opioid pain medication (No opioids) was acetaminophen (82%).

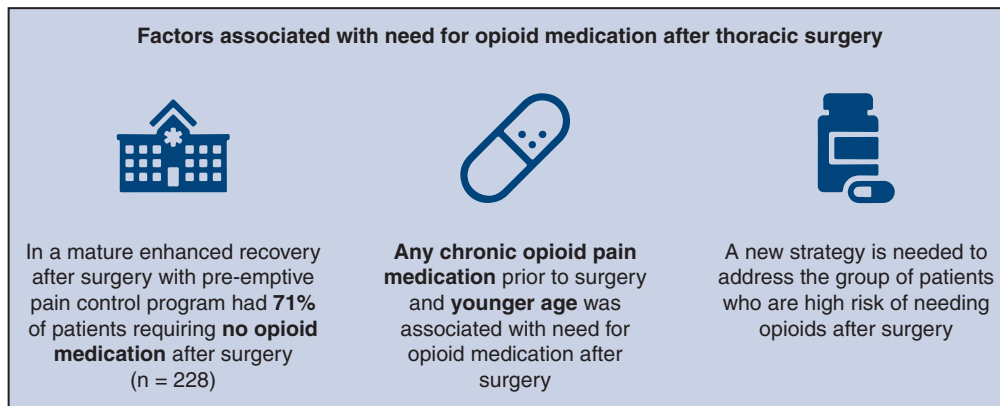


FIGURE 4. In a mature thoracic program with enhanced recovery after surgery with pre-emptive pain control (n = 228), the majority of patients did not require opioid medication after surgery (71%). Any chronic opioid pain medication before surgery and younger age were associated with the need for opioid pain medication after surgery. A different strategy is needed to address this group of patients to maintain pain control after surgery.