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Toward Zero Prescribed Opioids for Outpatient General Surgery Procedures: A Prospective Cohort Trial

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Short Title: Zero Opioid General Surgery

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ABSTRACT

Background: Achieving satisfactory post-operative pain control for common elective general surgical procedures, while minimizing opioid utilization, remains challenging. Utilizing pre-operative educational strategies, as well as multimodal analgesia, we sought to reduce the post-operative opioid use in elective general surgery cases.

Methods: Between November 2019 and July 2021, patients undergoing elective inguinal hernia repair (IHR) or cholecystectomy were enrolled in the study. Patients were divided into three cohorts: Control, opioid sparing (OS), or zero-opioid (ZO). Control patients did not have any intervention; OS patients had an opioid reduction intervention protocol applied (patient education and perioperative multimodal analgesia) and were provided an opioid prescription at discharge; the ZO had the same protocol, however patients were not provided opioid prescriptions at discharge. Two weeks after discharge patients were interviewed to record opioid consumption, pain scores, and level of satisfaction since discharge.

Results: 129 patients were recruited for the study. 88 patients underwent inguinal hernia repair and 41 patients underwent cholecystectomy. Median post-operative morphine equivalents consumed in the Control cohort (n=58); 46 (37.5-75) were significantly reduced when the OS protocol was enacted (n=42); 15 (11-22.5) and further reduced to zero for every patient in the ZO cohort (n=29) (*p=0.0001*). There were no differences in patient-reported average pain scores after discharge (*p=0.08*) or satisfaction levels with experience (*p=0.8302*).

Conclusions: Our study demonstrates that patient education and preoperative interventions can result in zero opioids prescribed after common general surgery procedures with equivalent patient satisfaction and pain scores.

Keywords: Postoperative Pain Control; Opioid Reduction; General Surgery

INTRODUCTION

In 2021, the Center for Disease Control (CDC) reported an estimated 100,306 overdose deaths from opioids in the United States (US).[1] Since 2015, opioid overdose has been the leading cause of injury-related deaths in the US, with 6% of the US population reportedly abusing opioids compared to <1% in most other countries.[2, 3] Medical prescribers represent the only legal source contributing to available opioids, with a substantial portion coming from procedure-based specialists. One Veterans Affairs (VA) study measured the number of outpatient opioid prescriptions at 10,256,706 over three years from proceduralists.[4] The percentage of these pills that go unused ranges from 54-86%.[5-7] For general surgeons specifically, the number has been reported at 71% of prescribed pills.[8]

Each year in the United states, approximately 800,000 inguinal hernia repairs and 300,000 cholecystectomies are performed.[9] Previous reports noted that, on average, physicians prescribed around 33 opioid pills for inguinal hernia repairs and 35 for cholecystectomies.[8] These patterns would result in approximately 26.4 million opioids being prescribed for inguinal hernia repairs and 10.5 million for cholecystectomy; factoring in the estimated 71%, there could be up to 18.8 million of these opioid pills possibly available to enter the community.[8]

In response to the opioid crisis, professional medical societies, organizations, and state medical boards have been working diligently to contain the number of opioids prescribed and educate physicians on appropriate prescribing patterns (*i.e.*, American College of Surgeons (ACS) Safe and Effective Pain Control After Surgery).[10] Despite these efforts, there is an opportunity for physician and patient-level interventions targeting both increased education and non-opioid pain control in common outpatient general surgery procedures.

Our study sought to evaluate the impact of an opioid reduction protocol (which combined multiple strategies: patient-education, non-opioid perioperative pain management, and safe opioid prescribing practices) on postoperative opioid utilization. We hypothesized that a

standardized protocol for common outpatient general surgery procedures, could decrease opioids utilization at our institution without compromising pain control or patient satisfaction.

METHODS

Study design: This was a prospective cohort study and was approved by the Institutional Review Board (IRB) of Thomas Jefferson University on October 2019 prior to patient enrollment (Control #19D.688) and registered on clinicaltrials.gov (NCT05327777). This study was exempt from requiring informed consent.

Inclusion and Exclusion Criteria. The study took place between November 2019 and July 2021 at a single academic medical center. Inclusion criteria included: opioid naïve patients, age > 18, being scheduled for an outpatient, elective inguinal hernia repair or cholecystectomy with one of three general surgeons. Exclusion criteria included: urgent/emergent status, and/or previous cholecystostomy tube placement.

Opioid reduction Intervention Protocol: The protocol (**Table 1**) included: a) an educational component provided at the outpatient visit with the surgeon with instructions tailored to the specific procedure, as well as the American College of Surgeon's (ACS) Safe and Effective Pain Control After Surgery patient tool[10] (**Figure 1**); b) preoperative multimodal analgesia provided 1 hour prior to operation (800 milligrams (mg) of ibuprofen, 1,000 mg of acetaminophen, and 75 mg of pregabalin for patients <70 years old); c) goal-directed fluid management, limited intraoperative opioid administration at the discretion of the anesthesiologist, and local anesthetic administered at incision sites; d) postoperative elements of the protocol included limited PACU administration of opioids based on pain scores (opioids only allowed for pain visual analog score (VAS) > 6), discharge counseling regarding limited opioid use at home, and instructions to alternate between acetaminophen and ibuprofen every 3 hours at home for pain.

Prior to the launch of the study, the senior author held two consecutive educational sessions on the protocol and its implementation with the perioperative nursing, anesthesia, and surgical staff.

Phases of Study and Chronology of Interventions. The study was designed to have an assessment phase (referred to as the "Control" cohort) and two intervention phases (**Figure 2**).

In the assessment phase of the study (November 2019 - February 2020), in order to establish a reference control cohort, patients were monitored for their opioid utilization per routine, established practice, prior to any intervention. In the intervention phases, data were collected after the opioid reduction intervention protocol was initiated (**Table 1**).

In the intervention phases, two chronologically consecutive intervention cohorts were created. In the first one ("Opioid Sparing" (OS); March 2020 - October 2020), patients were discharged with instructions to alternate between acetaminophen and ibuprofen and to use the opioids only for breakthrough pain (prescription for 10 pills of 5 milligram oxycodone or 50 milligram tramadol every 4-6 hours was provided at discharge); in the second cohort ("Zero Opioid" (ZO); November 2020 - July 2021), patients were discharged without a prescription for opioids, but rather instructed to contact the provider should pain control not be adequate with acetaminophen and ibuprofen alone. Importantly, it is worth noting that at our institution elective cases were cancelled due to the COVID-19 pandemic during the intervention phases which impacted the sample size, as well as decision of when to move on to the ZO stage of the protocol.

Data Collection. Demographic, clinical, and perioperative variables were collected by retrospective review of the electronic medical record and included age, sex, race/ethnicity, BMI, American Society of Anesthesiologists (ASA) class, smoking status, history of substance abuse, procedure, technique (open, laparoscopic, or robotic), whether the minimally invasive inguinal

repair was trans-abdominal pre-peritoneal (TAPP) or totally extra-peritoneal (TEP), length of procedure, estimated blood loss, total intravenous fluid given during the procedure, total local anesthetic given during the procedure, total intraoperative morphine milliequivalents administered, length of stay after procedure, and patient-reported pain scores at 1 hour after the procedure and at discharge.

Outcomes. Outcome variables were obtained by the electronic medical record and/or by utilization of a brief telephone survey (intended for internal use only) which was administered by members of the study team who contacted the patients 14 days after discharge (**Figure S1**). Outcomes of interest included: total morphine milligram equivalents (MMEs) in the post-anesthesia care unit (PACU), patient-reported total MMEs after discharge, and patient-reported pain scores and satisfaction scores after discharge. Satisfaction scores were on a scale of 1 to 10 with 1 being extremely dissatisfied and 10 being extremely satisfied. Additionally, number of calls to the surgeon's office with a complaint of pain and number of pain medication refills prescribed were recorded for 30 days following the procedure. For MME calculations, patients were asked how many pills of each pain medication they had taken after discharge and based on their responses these were converted and recorded by the research team.

Statistical Analysis. Chi-square test was used to compare categorical variables. For continuous variables, Shapiro-Wilk test was performed to determine if data were normally distributed. For normally distributed data, analysis of variance (ANOVA) test was performed, and results were reported as means with standard deviations. For variables that were not normally distributed, Kruskal-Wallis's test was performed, and results were reported as medians with interquartile ranges (IQR). For all comparisons two-sided statistical significance was set a priori at $p<0.05$. All statistical analyses were performed using Stata/MP 17.1 (Statacorp, College Station, TX).

RESULTS

Demographic and Clinical Characteristics. One hundred and forty-eight patients met inclusion criteria, however only 129 had complete follow-up and were enrolled in the study: 58 patients in the Control cohort, 42 in the Opioid Sparing cohort (OS), and 29 in the Zero-Opioid cohort (ZO). Demographic and clinical characteristics were statistically equivalent between cohorts, except for significantly fewer female patients being present in the ZO cohort (6.9%) compared to the Control (32.8%) and OS (23.8%) cohorts (*p=0.029*) and (**Table 2**).

Perioperative Characteristics. Between cohorts, more inguinal hernias were done in the ZO and OS cohorts than the Control (ZO: 25/29 (86.2%) v OS: 31/42 (73.8%) v Control: 32/58 (55.2%), *p=0.009*). More open procedures were performed in the ZO and OS cohorts as well (ZO: 37.9% v OS: 35.7% v Control: 18.2%, *p=0.017*) compared to minimally invasive or robotic. Length of stay after the procedure was significantly longer in the ZO and OS groups (ZO: 5.1 hours v OS: 4.7 hours v Control: 2.7 hours, *p=0.0001*) (**Table 3**). Estimated blood loss, total intravenous fluid given, and total intraoperative MME were statistically, but not clinically, different. The rest of the perioperative characteristics studied were statistically equivalent.

Postoperative Outcomes. Total MMEs after discharge were significantly reduced from Control (46 (37.5-75)) to (15 (11-22.5) in the OS cohort and further reduced to zero in the ZO cohort (*p=0.0001*). No significant differences were seen in the patient-reported pain ((*p=0.08*) or satisfaction scores (*p=0.8302*) after discharge. The number of calls to the surgeon's office with complaints of pain as well as number of pain medication refills prescribed within 30 days of operation were both zero in the ZO cohort (**Table 4**). Additionally, no patients in any cohort presented to the emergency room after their operation with a complaint of pain or request for pain medications in our study.

DISCUSSION

In the United States 1.1 million elective inguinal hernia repairs and cholecystectomies are performed each year, with 26.4 million opioid pills being prescribed to treat postoperative pain, with more than two-thirds of those pills at risk of being unused and available to circulate in the community.[8, 9] We believe that despite previous successful interventions implemented, elective general surgery procedures represent a significant opportunity to critically reduce the total amount of opioids prescribed by surgeons.

Our study utilized a perioperative opioid reduction intervention protocol to first significantly reduce the number of opioids used by patients after discharge from common elective general surgery and then, subsequently, drive that number down to zero by not providing an opioid prescription at discharge. During this study period, there was no significant difference in pain or satisfaction scores, suggesting patient experience and care were not compromised. Finally, we saw a reduction in office calls and pain medication refills prescribed to zero. We attributed this change to the increased efforts towards patient education both pre- and post-operatively. Our results provide a framework to reduce opioid overuse, by directly intervening on patients undergoing common surgical interventions and increasing awareness on postoperative pain management and proper disposition of unused pills.

Strategies to successfully reduce opioid use across various procedural fields including colorectal surgery[11], neurosurgery[12], and general surgery[13] have been proven in previous studies. For example, Hartford *et al* were able to decrease the total morphine milligram equivalents (MMEs) in postoperative cholecystectomy and open hernia repair patients from 100 to 50 utilizing multi-modal, non-narcotic, intra-and postoperative analgesia bundles and showed non-inferior pain scores after application between control and intervention patient cohorts.[14] Others, like Angelo *et al,* using solely patient-education based infographics, successfully

reduced the number of opioid pills prescribed in half from 30 to 15.[15] Our study combined these approaches to create a multifaceted protocol to reduce opioid utilization.

Many state, society, and institution-level interventions have been implemented to reduce the opioid prescribing rate. On the state level, legislative restrictions have been implemented on the number of opioids allowed to be prescribed for certain procedures.[16] Additionally, as mentioned earlier, the ACS has published multiple educational materials for providers on appropriate prescribing practices and for patients on appropriate indications for opioid consumption for common surgical procedures.[10] Finally, at the institution level, specific education materials have been published to target at-risk patient populations.[17] In addition, pathways which work towards reducing perioperative opioid use, namely the enhanced recovery after surgery (ERAS) protocols, have been implemented for select procedures.[18] All of these interventions have had success on lowering the amount of opioid consumption and prescribing however, few specifically target elective outpatient procedures.

On top of these efforts, recent calls to arms have highlighted the need to eliminate prescriptions completely. This is obviously not realistic for all procedures, but is a strategy advocated for and utilized by some routine minimally invasive teams. One example is the robotics urology team at the University of Pittsburgh that, anecdotally, describes how they stopped prescribing opioids for their robotic prostatectomy and nephrectomy patients postoperatively, without an observed increase in emergency room visits for pain or outpatient phone calls.[19] These authors advocate “anchoring to zero exposure” by simply not prescribing patients opioids after their surgery and educating them on the use of non-narcotic pain control at home. While our ZO cohort was 100% successful in this study, that level of success will likely vary from institution to institution and procedure to procedure, considering the majority of cases in our study was performed by a small group of surgeons with one contributing a majority of the cases.

We believe a key to our success in driving opioid utilization toward zero in our study, was the requirement to call the office should the patient need an opioid prescription, instead of providing one on discharge. In our study, patients went from taking 46 MMEs after discharge in the control cohort to 15 in the OS and 0 in the ZO group. This equates to around six 5mg oxycodone pills taken in the Control group and one to two pills in the OS group. Within the OS group, when asked why they had taken the 1-2 pills over the two-week period, many patients reported using the opioids as first line pain control, to aid in sleep, and/or simply because they thought they were supposed to since their surgeon had prescribed them. Once the prescription was removed from the routine discharge materials, patients easily adjusted to the recommendations, few calls occurred, and no additional opioids were requested. These findings were not combined with any significant increase in reported pain from our cohort. We believe that in correctly selected procedures, opioid prescriptions should no longer be routinely provided. A critically important component of the study's protocol was early education and engagement of the entire perioperative nursing, anesthesia, and surgery staff with the elements of the intervention.

An important point to consider in implementing opioid reduction protocols is cost. As we reported, patients in both intervention arms spent longer in the hospital and received additional medications preoperatively which, while challenging to assign a true expense to, likely drove the hospital costs higher. Some previous studies have shown that these types of pathways are cost-effective when considering reduced re-admissions and post-operative complications[20-22], however some showed no difference.[23, 24] No studies we identified showed an overall increase in cost after implementation. In our experience, while costs may be higher in the index admission, these types of pathways are ultimately cost-effective in their ability to reduce subsequent healthcare resource utilization and physician-contribution to the opioid epidemic.

That being said, formal cost-effectiveness analysis would need to be performed to truly capture the full economic impact of implementing these types of protocols.

An additional, and certainly significant, benefit of these efforts aimed at reducing the number of available opioids was education in appropriately discarding unused pills. We believe this information should be included in all pre- and post-operative patient education with the same emphasis we place on keeping wounds clean and notifying a physician should any complications arise. In our study, instructions on how to discard opioids properly were included in our patient education handout (**Figure 1**). Porter *et al* utilized strong patient education and a "convenient drop-box" in their hospital's pharmacy, with directions to its location provided to the patient, to achieve a rate of 83% FDA-compliant disposal of excess pills in their cohort.[25] We believe FDA-compliant drop-boxes should be located in all hospital pharmacies. We also suggest the implementation of programs where patients can appropriately dispose their unused opioids at their postoperative appointments to increase convenience, but more importantly compliance.

Limitations

There were a few limitations in our study worth noting. For one, this study was performed on only general surgery, opioid naïve, elective patients and, thus, it is likely not generalizable to patients outside of this inclusion criteria. However, other studies have shown success with similar programs in higher acuity and chronic pain patient populations.[26] Moreover, some clinically significant demographic and perioperative characteristics were statistically different between our cohorts. For one, there were significantly less females and more open procedures in the zero-opioid (ZO) cohort and opioid sparing (OS) cohort. However, since men have been shown to abuse opioids more frequently, and minimally invasive procedures have been shown to decrease postoperative pain and subsequent opioid use, we believe these two statistical differences actually strengthen the hypothesis that our intervention protocol was

successful since these intervention cohorts also had significantly lower opioid use.[27, 28] Additionally, we performed a sub-analysis of only the inguinal hernia repairs in our study which showed the same direction of trends and significance for all demographic, clinical, and postoperative variables included in our larger study except that the female to male distributions were statistically equivalent. That being said, a larger study which can control for all covariates should be done. We also reported a significantly longer length of stay in the ZO and OS cohorts. The difference was only 2 hours which is either a product of small cohort size and chance, or a real effect which, when weighed against reduction of opioids, is worth it in our opinion. We utilized a survey administered via telephone or at postoperative visit which required patients to recall how many pain pills had been taken after discharge which is subject to recall bias and may skew the results. Also, all the procedures included in our study were performed by three surgeons, with a majority of them being performed by a single surgeon, creating the potential for a selection bias. Similarly, in regards to cohort size, despite our ZO intervention phase spanning the longest amount of time (9 months), it contained the least number of patients (n=29). This was secondary to elective cases being cancelled to the COVID-19 pandemic for a majority of that time period. Despite this, we believe the cohort was adequate in size to display the intended outcome effects.

CONCLUSIONS

With recent emphasis on opioid reduction strategies to combat the opioid dependence and abuse epidemic in the US, our study demonstrated that patient education and perioperative interventions can significantly reduce opioid use in the outpatient elective general surgery patient. Additionally, by requiring the patient to call in to the office to obtain an opioid prescription rather than providing it at discharge, we were able to drive our opioid use rate down to zero while maintaining pain control and satisfaction scores. We hope our protocol can serve as a model for opioid reduction in other outpatient elective surgeries and spur discussion on

strategies to mitigate opioid use in more urgent/emergent or extensive procedures in an effort to reduce the contribution of provider-prescribed opiates to the current epidemic.

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346 **TABLES:**

347 **Table 1.** Opioid Reduction Intervention Protocol

Opioid Reduction Intervention Protocol	
Preoperative/Intraoperative Interventions	**Postoperative Intervention**
1) Preoperative opioid reduction education given to patients in surgeon's office (**Figure 1**)	1) Limited opioid administration in PACU (only for pain visual analog scores > 6)
2) Preoperative multimodal analgesia 1 hour before operation: • Ibuprofen 800 milligrams x 1 • Acetaminophen 1,000 milligrams x 1 • Pregabalin 75 milligrams x 1 (except for patients >70y old)	2) Discharge counseling emphasizing importance of limited opioid use outpatient
3) Intraoperative goal-directed fluid management	3) Instructed to take acetaminophen and ibuprofen alternating every 3 hours for pain
4) Limited intraoperative opioid administration	4) Targeted Discharge Opioid Prescription: a. Opioid sparing (OS) cohort: (10 pills of 5milligram oxycodone or 50 milligram tramadol) b. Zero Opioid (ZO) cohort: no opioid prescription provided at discharge
5) Local anesthetic (bupivacaine 0.5%) administered at incision site	

348 *Abbreviations: PACU = post-anesthesia care unit*

Table 2. Demographic and Clinical Characteristics

	Control (n=58)	Opioid Sparing (n=42)	Zero-Opioid (n = 29)	*P value*
Age (years), Mean ± SD	52.4 ± 1.8	55.3 ± 2.0	58.6 ± 2.9	0.360
Female Sex, N (%)	19 (32.8)	10 (23.8)	2 (6.9)	0.029*
Race/Ethnicity, N (%)				0.233
Black	3 (5.3)	5 (11.9)	7 (24.1)	
White	47 (81.0)	31 (73.8)	22 (75.9)	
Hispanic, Non-Black	5 (8.6)	4 (9.5)	0 (0)	
Asian	2 (3.4)	1 (2.4)	0 (0)	
Other	1 (1.7)	1 (2.4)	0 (0)	
BMI (kg/m2), Median (IQR)	27.8 (25.4-32.1)	27.9 (24.3-31)	25.4 (23.3-28.7)	0.065
ASA Class, N (%)				0.124
≤ 2	46 (79.3)	28 (66.7)	17 (58.6)	
≥ 3	12 (20.7)	12 (28.6)	12 (41.4)	
Smoking Status, N (%)				0.754
Former	16 (27.6)	14 (33.3)	10 (34.5)	
Current	6 (10.3)	7 (16.7)	4 (13.8)	
History of Substance Abuse, N (%)	3 (5.2)	5 (11.9)	4 (13.8)	0.332

Abbreviations: SD = standard deviation; BMI = body mass index; IQR = interquartile range; ASA = American Society of Anesthesiologists

** denotes statistical significance*

353 **Table 3.** Perioperative Characteristics

	Control (n=58)	**Opioid Sparing (n=42)**	**Zero-Opioid (n=29)**	***P value***
Inguinal Hernia Repair, N (%)	32 (55.2)	31 (73.8)	25 (86.2)	0.009*
Procedure Technique, N (%)				0.017*
Open	10 (17.2)	15 (35.7)	11 (37.9)	
Minimally Invasive (Laparoscopic/Robotic)	48 (82.8)	27 (64.3)	18 (62.1)	
Laparoscopic cholecystectomy, N (%)	26 (54.2)	11 (40.7)	4 (22.2)	
TAPP Inguinal, N (%)	22 (45.8)	11 (40.7)	14 (77.8)	
TEP Inguinal, N (%)	0	5 (18.6)	0	
Length of Procedure (min.), Median (IQR)	101 (80-116)	108 (92-132)	96 (79-126)	0.238
Estimated Blood Loss (mL), Median (IQR)	10 (0-10)	5 (0-20)	0 (0-10)	0.0104*
Total Intravenous Fluid Given (mL), Median (IQR)	1000 (700-1200)	700 (84-1000)	1000 (800-1000)	0.0039*
Total Local Anesthesia Given (mL), Median (IQR)	30 (30-30)	30 (30-30)	30 (30-30)	0.27
Total Intraoperative MME, Median (IQR)	480 (480-720)	420 (240-480)	480 (240-480)	0.0001*
Length of Stay after Procedure (hr), Median (IQR)	2.7 (2.4-3.1)	4.7 (3.8-5.4)	5.1 (4.8-5.7)	0.0001*
Pain Scores 1 hour after Procedure, Median (IQR)	2 (1-5)	3 (1-6)	1 (1-5)	0.061
Pain Scores at Discharge, Median (IQR)	4 (1-6)	2 (1-4)	3 (1-4)	0.062

354 *Abbreviations: TAPP = trans-abdominal pre-peritoneal; TEP = totally extra-peritoneal; min. =*
355 *minutes; IQR = interquartile range; mL = milliliters; MME = morphine milligram equivalents; hr =*
356 *hours*
357 ** denotes statistical significance*

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Table 4. Postoperative Outcomes

	Control (n=58)	Opioid Sparing (n=42)	Zero-Opioid (n=29)	*P value*
Total MME in PACU, Median (IQR)	15 (7.5-22.5)	7.5 (7.5-15)	15 (7.5-15)	0.3368
Total MME after Discharge, Median (IQR)	46 (37.5 – 75)	15 (11 – 22.5)	0 ± 0	0.0001*
Pain Scores after Discharge, Median (IQR)	3 (1-4)	2 (1-3)	4 (3-5)	0.08
Satisfaction Scores after Discharge, Median (IQR)	10 (9-10)	10 (9-10)	10 (8.5-10)	0.8302
Calls to Surgeon's Office with Pain within 30d, N (%)	10 (17.2)	10 (23.8)	0 (0)	0.022*
Pain Medication Refills within 30d, N (%)	3 (5.2)	4 (9.5)	0 (0)	0.218

Abbreviations: MME = morphine milligram equivalents; PACU = post-anesthesia care unit; IQR = interquartile range; d = days ** denotes statistical significance*

FIGURE TITLES and LEGENDS:

Figure 1. *Preoperative Opioid Reduction Patient Education Handout for Inguinal Hernia Repair.* An alternative, but similar handout was created for cholecystectomy.

Figure 2. *Study timeline with assessment and intervention time periods*

Figure S1. *Postoperative Opioid Use, Pain, and Satisfaction Survey* (intended for internal use only)