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The impact of preoperative opioid use on outcomes after elective colorectal surgery: A propensity-matched comparison study

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ABSTRACT

Background: The impact of recent preoperative opioid exposure on outcomes of colorectal surgery is unclear. Our aim was to evaluate the impact of preoperative opioid use on outcomes and opioid prescribing patterns after colorectal surgery.

Methods: We performed a retrospective review of all patients undergoing elective resection at a single institution from 2015 to 2017. Primary outcomes included in-hospital narcotic use and cost. Secondary outcomes included postoperative surgical outcomes and discharge prescribing patterns.

Results: A total of 390 patients underwent elective colorectal surgery, of whom 63 (16%) had a recent history of preoperative opioid use. Opioid users had similar age, sex, American Society of Anesthesiologists score, and operative indication compared with opioid-naïve patients ($P > .05$ for each). Postoperatively, the 30-day readmission rate was greater among opioid users (18% vs 9%, $P = .03$). Opioid users had greater total narcotic use (218 morphine milligram equivalents vs 111 morphine milligram equivalents, $P = .04$) and direct costs ($11,165 vs $8,911, $P < .01$). These patients were also more likely to require an opioid prescription on discharge (90% vs 68%, $P < .01$) and an opioid refill within 30 days (54% vs 21%, $P < .01$).

Conclusion: Recent preoperative opioid exposure among colorectal surgery patients was associated with increased opioid consumption and costs. Moreover, unadjusted analysis was pertinent for more readmissions after surgery among preoperative opioid users. This work underscores the negative impact of preoperative, chronic opioid use on surgical outcomes and highlights the need for developing protocols to minimize perioperative narcotics.

Introduction

Opioid prescribing has increased dramatically during the past 3 decades. Concurrently, opioid abuse has become a major public health crisis. In 2015, the Centers for Disease Control estimated 52,000 opioid-related deaths and an annual cost of total health care of $501 billion.[1] Despite this, opioids continue to be the predominant medication used for the management of postoperative pain, primarily because of the perceived lack of suitable alternatives. This misunderstanding has stark implications, however, because perioperatively prescribed opioids can result in chronic opioid use in up to 6% of opioid-naïve patients.[2–4] More recently, however, emerging experiences with narcotic-free postoperative care have begun to challenge these practices.[5,6]

As surgeons have become increasingly aware of the opioid epidemic and the role they play in prescribing narcotics, many efforts to minimize opioid prescribing in the postoperative period have emerged.[7,8] Nonetheless, given the widespread use of opioids across all medical specialties, many patients have already been prescribed opioids at the time of their initial surgical evaluation. Understanding the impact of preoperative opioid exposure on postoperative outcomes is therefore, important. Existing literature in a variety of fields of surgery has demonstrated the negative impact of preoperative opioid use;[9–12] however, the effects of opioid use in colorectal patients have not been well defined. In addition, although enhanced recovery protocols (ERPs) in colorectal surgery have been shown to improve outcomes and decrease

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in-hospital consumption of opiods, whether opioid users benefit to the same degree has not been studied.[13]

The primary aim of this study was to evaluate the impact of recent preoperative opioid use on postoperative outcomes and opioid prescribing patterns among patients undergoing elective colorectal resection. Primary outcomes included in-hospital narcotic use and cost, and secondary outcomes included postoperative surgical outcomes and postdischarge prescribing patterns. The secondary aim of this study was to evaluate how the implementation of an ERP affected outcomes in patients with preoperative opioid use. We hypothesized that patients with preoperative opioid exposure would incur greater utilization of health care resources but benefit from ERP to a similar degree as opioid-naïve patients.

Methods

After approval by The Christ Hospital (Cincinnati, OH) Institutional Review Board a retrospective review was performed of all patients who underwent elective colorectal resection from 2015 to 2017 at a single institution. Patient demographics, operative details, postoperative outcomes, and postdischarge prescribing patterns were examined. In January 2016, our institution initiated an ERP for all patients undergoing elective resection in part to attempt to decrease the need for opioids in postoperative pain management. Elsewhere, we have reported the components of our ERP which follow guidelines set forth by the American Society of Colon and Rectal Surgeons.[13,14]

In brief, our ERP included preoperative patient education, multimodal pain control, early enteral feeding, regular postoperative ambulation, and judicious intravenous fluid use. A mechanical bowel preparation with oral neomycin and metronidazole was given one day before surgery. All patients were received gabapentin (300mg PO TID) three days before surgery, which was continued until discharge. Two Glycemic Endothelial Drinks (SOF Health, Holland, MI) were consumed the day before surgery and one the morning of surgery. Alvimopan (12mg PO BID) was started on the day of surgery and continued postoperatively until return of bowel function (for a maximum of seven days). All patients received a transverse abdominis plane (TAP) block placed by the anesthesiologist in the operating room under ultrasound guidance. A patient-controlled analgesia (PCA) pump was provided for the first night following surgery. Patients also received scheduled intravenous ketorolac and acetaminophen for 24 hours, which was transitioned to scheduled oral ibuprofen and acetaminophen thereafter. No additional intravenous narcotics were given and oral oxycodone was used on an as needed basis for breakthrough pain. Patients were started on a clear liquid diet immediately after surgery, and a regular diet was initiated on postoperative day one. Indwelling urinary catheters were removed on postoperative day one for laparoscopic procedures and postoperative day two for open procedures.

Colorectal resections included right colectomy, left colectomy, proctectomy, and total abdominal colectomy. Exclusions included urgent or emergent operations and procedures without a bowel resection. Any infection of the superficial, deep incisional, or organ spaces were considered a surgical site infection. A clinical diagnosis of ileus was based on the absence of bowel function by the third postoperative day, and all anastomotic leaks were confirmed by radiographic imaging or in the operating room at the time of reoperation. Direct cost and pharmacy costs were obtained from our hospital's billing department and are reported as total and daily costs.

The Ohio Automated Rx Reporting System ([OARRS] www.ohiopmp.gov) is a monitoring system run by the Board of Pharmacy of the State of Ohio, which tracks all outpatient prescriptions filled for controlled substances and was used to assess preoperative opioid use and postoperative opioid prescribing patterns. Patient reports were queried for Ohio, Kentucky, and Indiana given the demographics of our patient population. Preoperative opioid use was defined as having filled a narcotic prescription within 60 days before the date of the colorectal operation. The first narcotic prescription filled postoperatively was considered the discharge prescription, and additional narcotic prescriptions filled thereafter, but within 30 day of discharge, were considered refills. The OARRS system does not capture narcotics provided within medical facilities, and therefore patients discharged to a skilled nursing facility were excluded from the analyses on postdischarge prescribing patterns. Narcotic use is reported as total and daily amounts and is reported as morphine milligram equivalents (MME).

Continuous data are reported as median and interquartile range (IQR) and compared using the Wilcoxon rank-sum test. Categorical data are reported as total (n) and percentage (%) and compared using the Pearson's χ^2 test (or the Fischer exact test for rare occurrences). Multivariate logistic regression analyses were performed to identify predictors of requiring an opioid prescription at discharge and requiring a refill within 30 days of discharge. Covariates include preoperative narcotic use, age, sex, body mass index (BMI), tobacco use, American Society of Anesthesiologists (ASA) score, operative indication, and total inpatient narcotic usage.

To control for differences in patient demographics, a 1:1 propensity-score match using logistic regression was performed. Patients were matched for age, ASA score, preoperative risk factors and comorbidities, operative indication, and operation type, yielding 62 opioid-naïve patients and 62 opioid users. The predicted probabilities from this model served as propensity scores, which were then used in a SAS macro to form matched pairs between the groups. The balance in the baseline characteristics between the 2 groups was assessed by testing for within-pair differences in baseline covariates. The McNemar's test was used to assess within-pair differences for categorical outcomes, and the Wilcoxon signed-rank test was used for continuous outcomes. All data were analyzed using the statistical package SAS 9.4 and JMP Pro 14 (SAS Institute, Cary, NC).

Results

Study population

A total of 390 patients underwent elective colorectal surgery during the 3-year study period. Preoperative opioid use was present among 63 patients (16.2%), and the remaining 327 patients (83.8%) were opioid naïve. Patient demographics for these groups are reported in Table I. The 2 groups were similar with regard to age, sex, BMI, ASA score, and preoperative comorbidities (all $P > .05$). The distribution of operative indications was similar, and a predominant use of laparoscopy was utilized among both cohorts. Of note, preoperative steroids (19% vs 7.3%; $P < .01$) and use of biologics (14% vs 5.2%; $P = .01$) were greater in the narcotic group compared with the opioid-naïve group.

Preoperative opioid use impacts postoperative outcomes

Postoperatively, patients had similar incidences of ileus, anastomotic leak, and surgical site infection (Table II). Compared with opioid-naïve patients, opioid users were more likely to have a readmission within 30 days (9% vs 17.5%; $P = .03$). There were a variety of indications for readmission among the groups. Among the opioid group, readmission occurred more frequently for infectious complications, whereas readmission among opioid-naïve patients was more frequently for episodes of ileus, nausea and vomiting, and dehydration. During the index admission, opioid users maintained use of their PCA for a greater time than opioid-

Table I
Demographics of opioid-naïve patients versus opioid users undergoing colorectal surgery

	Preoperative opioid-naïve ($n = 327$)	Preoperative opioid use ($n = 63$)	P
	n (%) or median (IQR)	n (%) or median (IQR)	
Age, y	59 (49–70)	55 (42–67)	.06
Sex, male	149 (45.6%)	32 (501%)	.45
BMI, kg/m^2	27 (24–32)	29 (24–34)	.11
ASA classification			.09
Class I–II	193 (59.0%)	30 (48%)	
Class III–IV	134 (41.0%)	33 (52%)	
Patient comorbidities			
DM	65 (19.9%)	11 (18%)	.66
CKD	20 (6.1%)	6 (10%)	.32
CAD	50 (15.3%)	10 (16%)	.91
CVD	13 (4.0%)	4 (6%)	.40
Preoperative risk factors			
Tobacco use	95 (29.1%)	24 (38%)	.15
Prior abdominal surgery	190 (58.1%)	37 (59%)	.93
Radiation	60 (18.4%)	12 (19%)	.90
Steroids use	24 (7.3%)	12 (19%)	< .01*
Immunomodulator use	22 (6.7%)	7 (11%)	.23
Use of biologics	17 (5.2%)	9 (14%)	.01*
Operative indication			.18
Cancer	149 (45.6%)	26 (41%)	
Diverticulitis	57 (17.4%)	17 (27%)	
IBD	43 (13.2%)	11 (18%)	
Polyp	56 (17.1%)	5 (8%)	
Other	22 (6.7%)	4 (6%)	
Operative approach			.22
Laparoscopic	252 (77.1%)	44 (70%)	
Open	75 (22.9%)	19 (30%)	
Operation			.37
Left colectomy	94 (28.8%)	22 (35%)	
Right colectomy	107 (32.7%)	14 (22%)	
Total abdominal colectomy	18 (5.5%)	5 (8%)	
Proctectomy	108 (33.0%)	108 (35%)	
Ostomy creation	103 (31.5%)	25 (40%)	.24

BMI, body mass index; *ASA*, American Society of Anesthesiologists; *DM*, diabetes mellitus; *CKD*, chronic kidney disease; *CAD*, coronary artery disease; *CVD*, cerebrovascular disease; *IBD*, inflammatory bowel diseases.
* $P < .05$.

Table II
Postoperative outcomes among opioid-naïve patients versus opioid users after colorectal surgery

	Preoperative opioid-naïve ($n = 327$)	Preoperative opioid use ($n = 63$)	P
	n (%) or median (IQR)	n (%) or median (IQR)	
Postoperative ileus	37 (11%)	10 (16%)	.62
Anastomotic leak	11 (3%)	4 (6%)	.24
Surgical site infection	13 (4%)	3 (5%)	.77
Length of stay, d	3 (3–5)	4 (2–6)	.44
Discharge to SNF	14 (4%)	3 (5%)	.86
PCA duration, d (mean ± SD)	2.1 ± 1.9	2.7 ± 2.2	.02*
Inpatient narcotic use, MME	111 (40–285)	218 (74–1,916)	< .01*
30-d readmission	28 (9%)	11 (18%)	.03*
30-d reoperation	17 (5%)	4 (6%)	.71
30-d mortality	1	0	.66
Total direct cost, US$	8,911 (7,164–11,591)	11,165 (7,717–13,788)	< .01*
Total pharmacy cost, US$	1,369 (1,104–1,874)	1,662 (1,181–2,305)	.01*

PCA, patient-controlled analgesia; *SNF*, short-term nursing facility; *MME*, morphine milligram equivalents.
* $P < .05$.

naïve patients (2.7 days versus 2.1 days; $P = .02$) and consumed considerably greater total amounts of opioids (218 MME versus 111 MME; $P = .04$). These findings ultimately contributed to the greater total direct costs ($11,165 vs $8,911; $P = .04$) and total pharmacy costs ($1,662 vs $1,369, $P = .01$).

Preoperative opioid use impacts the patterns of discharge opioid prescribing

The opioid prescribing patterns after discharge for the 2 cohorts are illustrated in Table III. At discharge, opioid users were more likely to require a narcotic prescription (90% vs 68.4%, $P < .01$). Moreover, opioid users were more likely to receive an opioid refill within 30 days of discharge (54% vs 21.0%; $P < .01$) and had a greater total number of refills (2 vs 1; $P < .01$). These patients were also more likely to obtain an additional refill from a provider other than their surgeon within 30 days of surgery (45% vs 20.0%; $P = .02$%).

On multivariate analysis, preoperative opioid use (OR = 3.66, 95% CI 1.48–9.07; $P < .01$), age (OR = 0.96, 95% CI 0.94–0.98; $P < .01$), and an active smoking status (OR = 2.48, 95% CI 1.38–4.48; $P < .01$) were independently assocaiated with requiring an opioid on discharge. In addition, preoperative opioid use (OR = 3.10, 95% CI

Table III
Postoperative opioid prescribing patterns among opioid-naïve patients versus opioid users after colorectal surgery

	Preoperative opioid-naïve* ($n = 313$)	Preoperative opioid use* ($n = 60$)	P
	n (%) or median (IQR)	n (%) or median (IQR)	
Discharged home with opioid prescription	214 (68.4%)	54 (90%)	< .01†
Total discharge amount, MME	300 (225–450)	300 (225–450)	.43
Opioid refill within 30 d‡	45 (21.0%)	29 (54%)	< .01†
Days to first refill	11 (8–17)	8 (5–18)	.27
Total refill amount, MME	300 (225–450)	450 (225–600)	.11
Total refills within 30 d	1 (1–1)	2 (1–3)	< .01†
Refill by non-surgeon	9 (20.0%)	13 (45%)	.03†

MME, morphine milligram equivalents.
* Excludes patients discharged to a skilled nursing facility ($n = 14$ versus $n = 3$, respectively).
† $P < .05$.
‡ Refill data reported only among patients discharged to home and having received an opioid at discharge ($n = 214$ versus $n = 54$, respectively).

1.49–6.46; $P < .01$) and age (OR = 0.95, 95% CI 0.92–0.98; $P < .01$), in addition to BMI (OR = 1.07, 95% CI 1.02–1.13; $P < .01$), were independent predictors of requiring an opioid refill within 30 days of discharge.

ERP has a beneficial impact on preoperative opioid users

To study the impact of ERP on preoperative opioid users, we compared patients before and after universal implementation of ERP for all elective colorectal resections that occurred in January 2016 at our institution. The impact of ERP among preoperative opioid users is reported in Table IV. Consistent with our earlier work demonstrating the benefit of ERP,[13] ERP decreased total duration of stay by 2 days (3 days vs 5 days, $P = .03$), time using a PCA (2 days vs 3 days, $P < .01$), and total inpatient narcotic consumption (153 MME vs 300 MME, $P = .04$). Although ERP may have affected the proportion of patients discharged home with an opioid prescription (84.6% vs 100%, $P = .06$), ERP decreased those patients who received an opioid refill within 30 days of discharge (39.4% vs 76.2%, $P = .01$). In addition, there was a trend of a decreased in total direct cost ($10,484 vs $11,835, $P = .07$), though total pharmacy costs remained similar ($1,618 vs $1,882, $P = .20$).

Propensity-match analysis

Although the two groups were not statistically different, we performed a 1:1 propensity match to adjusting for age, ASA score, preoperative risk factors and comorbidities, operative indication, and operation type to more robustly study select outcomes and adjust for potential confouding. This analysis yielded 62 opioid-naïve patients and 62 preoperative opioid users. Consequently, there were no differences regarding age, BMI, sex, ASA score, preoperative risk factors and comorbidities, operative indication, or operation type (all $P > .05$). In this matched subset, inpatient narcotic use was greater (210 MME vs 135 MME, $P = .046$), total direct cost was $2,277 more expensive ($P = .02$), and total pharmacy cost was $256 more expensive ($P = .01$) for opioid users compared with opioid-naïve patients, but, there was no difference in 30-day readmission (16% vs 10%, $P = .28$).

Discussion

In this study, we examined the effect of preoperative opioid use on postoperative outcomes of narcotic consumption, surgical outcomes, cost, and postdischarge prescribing patterns among patients undergoing elective colorectal resection. The study occurred over a 3-year period during which an ERP was implemented, also allowing us to investigate the impact of ERP on our study population. Our findings demonstrate that preoperative opioid use was associated with increased utilization of health care resources after elective colorectal surgery, as manifested by greater durations of PCA use, increased total narcotic consumption, and greater total costs. It is worth noting that, although these patients had similar hospital stays and rates of discharge to a skilled nursing facility, their costs and 30-day readmissions were greater, demonstrating the heavy toll opioid use places on individuals and the health care system at large. Finally, these patients were more likely to require an opioid prescription at discharge and receive a refill within 30 days, further perpetuating the cycle of opioid dependency.

A growing body of literature across several fields of surgery, including elective abdominal, acute care, orthopedic, urologic, and gynecologic surgery, have demonstrated that preoperative opioid use negatively affects patient outcomes, increases costs, and increases the prescribing of postoperative opioids.[11,15–19] Kim et al[9] reported that preoperative opioid users who underwent emergency general surgery had increased durations of hospital stay, total costs, 30-day readmissions, postdischarge opioid refills, and rates of developing chronic opioid use.[9] However, the negative ramifications of preoperative opioid use have not been well studied in the colorectal literature. To our knowledge, this is the first study to evaluate the impact of preoperative opioid exposure in the colorectal patient population.

The cost of preoperative opioid use can be measured both directly and indirectly. Our study demonstrated that patients who used opioids before colorectal surgery incurred both an increase in total hospital and total pharmacy costs. The increased hospital cost was not associated with a greater hospital stay, thus there was a greater per diem cost in this patient population. The increased pharmacy cost was likely the result of greater durations of PCA usage and overall increased usage of opioid medications while inpatient. Although the impact of a mean difference in 0.5 days can be questioned, this difference in transitioning from a PCA to adequate oral pain control in the morning versus the evening would likely result in an additional night of hospitalization, thereby incurring greater cost. Moreover, what is not captured in our cost analysis is the additional costs associated with more frequent readmissions among patients with preoperative opioid use. These findings are consistent with existing data that, in addition to resource utilization, chronic opioid users incur greater costs of care.[11] Taken together, our data suggest that patients who use opioids before elective colorectal surgery have more complex postoperative courses, although further work is needed to assess whether opioids are simply a surrogate marker for this or in fact contribute to these observations. Given that 30-day readmission was not different on adjusted propensity-match analysis, this

Table IV
Impact of enhanced recovery protocol on preoperative opioid users after colorectal surgery

	Pre-ERP ($n = 23$)	Post-ERP ($n = 40$)	P
	n (%) or median (IQR)*	n (%) or median (IQR)*	
Duration of postoperative hospital stay, d	5 (4–7)	3 (2–4)	.03†
PCA duration, d	3 (2–5)	2 (1–3)	< .01†
Inpatient narcotic use, MME	300 (111–1,090)	153 (62–380)	.04†
Discharge to SNF	2	1	.27
30-day readmission	3 (13%)	8 (20%)	.48
Discharged home with opioid prescription†	21 (100%)	33 (85%)	.06
Total discharge amount, MME	300 (225–413)	375 (225–600)	.56
Opioid refill within 30 d‡	16 (76%)	13 (39%)	.01†
Days to first refill	9 (7–20)	8 (5–11)	.28
Total refill amount, MME	300 (206–563)	600 (300–750)	.18
Total refills within 30 d	2 (2–3)	1 (1–2)	.05
Refill by non-surgeon	9 (56%)	4 (31%)	.17
Total direct cost, US$	11,835 (9,310–14,763)	10,484 (7,440–13,364)	.09
Total pharmacy cost, US$	1,882 (1,180–2,923)	1,618 (1,193–2,219)	.20

PCA, patient-controlled analgesia; *SNF*, short-term nursing facility; *MME*, morphine milligram equivalents.
* Excludes patients discharged to a skilled nursing facility ($n = 2$ versus $n = 1$, respectively).
† $P < .05$.
‡ Refill data reported only among patients discharged to home and received an opioid at discharge ($n = 16$ versus $n = 13$, respectively).

outcome is likely driven by multiple factors rather than just preoperative opioid use.

Prescribing of opiates on discharge represents a potential event in which surgeons have the opportunity to combat the opioid crisis, recognizing that large variations in opioid prescriptions for common general surgery procedures exist, guidelines for discharge opioid prescribing have emerged.[4,7,8] Earlier studies have identified that many prescribed opioids go unused by the individual for whom they were intended.[4] This results in the potential for opioid abuse by individuals for whom the medications were not prescribed. In fact, the majority of illicitly used opioids were first obtained by prescription, and many patients who now abuse heroin began with nonmedical use of opioid medications.[20,21] On multivariate analysis, we were unable to identify inpatient factors that contributed to postdischarge opioid use; however, we found that preoperative opioid users, as well as younger patients, were more likely to require both an opioid prescription at discharge and require a refill within 30 days. Providers should be aware of these risk factors when caring for patients in the postoperative setting.

One such way that colorectal surgeons have contributed to combating the overprescribing of opioids may be through the widespread use of ERP. Among colorectal patients, ERPs have been shown to decrease hospital stay, rates of ileus, costs, and total opioid usage.[13] Whether ERP benefits preoperative narcotic users to the same degree, or if ERP modifications are needed, however, has not been studied. In this work, we demonstrated that, even among opioid users, ERP was associated with substantial benefits, including decreased hospital stays, duration of PCA use, total in-hospital opioid consumption, and need for a postdischarge opioid refill. In fact, ERP was associated with a 58% relative risk reduction in requiring an opioid refill in the postoperative setting. There was also a trend ($P = .06$) toward decreased prescribing of opioids at discharge. Although preoperative opioid use negatively impacts patients and may be a risk factor beyond the surgeon's control, use of ERP serves as an intervention that can be implemented to benefit these patients. Consequently, the impact of ERP on opioid use has immediate benefits not only to the patient, but also to our health care system and society at large.

The results of our study should be considered with several limitations. First, the retrospective nature of this study exposes it to potential reporter-bias. Second, the study uses a statewide monitoring system (OARRS) to determine opioid prescriptions for both initial and refills which were filled and collected by the patient. This is a different value than opioid medications that were in fact consumed by the patient and could result in over-reporting of opioid use. Similarly, we dichotomized preoperative narcotic use and therefore, cannot evaluate the implications of one's duration of use, which may have implications at the patient level. Third, we cannot identify the indication(s) for which the opioid medication was filled—Was it prescribed for symptoms associated with the colorectal pathology or for an unrelated, chronic problem? Nonetheless, these patients present for preoperative evaluation already exposed, and the impact of such reality is important. Fourth, our cost analysis is limited to comparison of total costs. As a result, we cannot determine the specific aspects contributing to the increased cost incurred by preoperative opioid users, although increased narcotics are a contributor. Finally, our findings are limited to concluding that preoperative opioid exposure identifies patients whose postoperative course may be complicated but are unable to assess a causative relationship with these outcomes. Although a propensity-match analysis was performed to adjust for our primary outcomes, the limited sample size restricted our ability to evaluate all outcomes, particularly postdischarge prescribing patterns. Preoperative narcotic users represent a complex patient population, and their worse outcomes are likely impacted by multiple factors. Future work and increased sample sizes through multi-institutional collaborations may allow for examining the impact of preoperative narcotic use on pathology-specific differences in outcomes.

In conclusion, this study demonstrates the effect of preoperative opioid use on patient outcomes and postoperative opioid prescribing patterns among patients undergoing elective colorectal surgery. Preoperative opioid use has negative effects on patient outcomes, increases hospital costs, and can predispose patients to developing chronic opioid dependence. In addition, we found that the beneficial effects of ERP extend to preoperative opioid users. Inclusion of patients with preoperative opioid use undergoing elective colorectal operations in ERP can result in improved outcomes and should be viewed by surgeons as an important step in combatting the opioid epidemic.

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Discussion

Dr Mary Otterson (Milwaukee, WI): I want to thank the authors for the opportunity to review their paper and for sending it to me early. It is an interesting observation and combines the timely topics of opioid use as well as ERAS protocols. The manuscript was well written and clear and concise, but I have a few questions.

Opioid use was defined as filling a narcotic prescription within 60 days prior to the surgical procedure. Lomotil is a narcotic and has to be reported in the state of Wisconsin. Did you include Lomotil as a preoperative and postoperative narcotic?

Dr Alexander Cortez: Yes. Thank you for the question. Lomotil is a narcotic but is in fact not captured by the OARRS database. Looking at the OARRS description of data collected, it states they capture all controlled substances plus gabapentin. Having used it, however, they seem to only capture the class II and III opioids, as well as the benzodiazpines, which are a class IV, and then gabapentin. Lomotil is not captured, so we're not able to identify Lomotil use in these patients.

Dr Mary Otterson (Milwaukee, WI): Do you think Lomotil is occupying the opioid receptor that that might influence your data, especially on the preoperative use for patients who are having diarrhea and inflammatory bowel disease?

Dr Alexander Cortez: You are correct that Lomotil may be used a decent amount in IBD patients, though I don't think it has a strong clinical impact. I do not believe that Lomotil has the same potential addictive impact on these patients. Though the diphenoxylate portion of the drug is very addictive, in the United States it's always combined with atropine, which is a drug deterrent. Moreover, Lomotil has a low oral bioavailability, which accounts for its primarily acting on the GI tract. It consequently has low absorption into the bloodstream and across the blood brain barrier. For this reason, the dosages needed to get any CNS effects are really limited by the side effects of atropine at such high doses. Ultimately it is a confounder to be aware of, but I don't think it has a large impact physiologically.

Dr Mary Otterson (Milwaukee, WI): With the current opioid epidemic, do you have any method to capture illegal narcotic use? If you cannot, can you estimate the use in your patient population?

Dr Alexander Cortez: Yes, that is a very important point given the amount of illicit drug use in the United States. We aren't able to comment on that in our data because it is through OARRS, and the medication is written by the provider. That being said, existing literature estimates approximately 5% to 10% of illicit drug use in the surgical population. If you make the assumption that some patients are taking both prescriptions and illicit drugs, then we can estimate an additional 3% to 6% of illicit drug users on top of the 16% of prescription users we identified, which ultimately magnifies our findings more.

Dr Mary Otterson (Milwaukee, WI): Could you specify the measures that were included in your ERAS protocol?

Dr Alexander Cortez: Our ERAS protocol was designed to be consistent with guidelines set forth by a number of societies, including the American Society of Colon and Rectal Surgeons. It addresses the main tenets of ERP, which are preoperative education, multimodal pain control, early ambulation, early enteral feeding, and minimizing fluids.

To address those, all of our patients get specific education by the surgeon and the nursing staff preoperatively on what to expect from surgery, what ERP entails, and their anticipated pain, that they will have some pain and modalities for multimodal pain control. They receive gabapentin preoperatively and scheduled Ibuprofen, Tylenol, gabapentin postoperatively. All patients get a TAP block in the operating room. PCAs are limited to 1day for lap surgery, 2 days for open surgery, and then on those days they are transitioned to oral narcotics for breakthrough pain only. At the same time, the Foley is

removed, and no NG tubes are used. The nursing staff is well educated and does a good job in getting the patient out of bed, in a chair for all meals, ambulating, and we have good success with this protocol.

Dr Mary Otterson (Milwaukee, WI): Do you utilize carbohydrate loading?

Dr Alexander Cortez: Yes, patients get a glycemic drink the day prior to and the morning of surgery.

Dr Mary Otterson (Milwaukee, WI): This is hard to answer based on your data, but do you have any sense of the duration of the effect of narcotic use? So, for example, if the patient ceases narcotics 2 months prior to surgery but had been using them regularly, would you think you will still see the effect?

Dr Alexander Cortez: One of the limitations in defining preoperative use as a prescription within 60 days is getting the granular data as to how many pills one is taking. Obviously, somebody taking pills for 5 days 2 months out is different than the person taking 2 pills every day for 60 days pre-op.

In smoking, we know that if you stop smoking 6 to 8 weeks out, it reduces your pulmonary excretions and such. I don't think we know that data in the opioid field yet. We'll get there. But I think your point is well taken in that there's a difference of the impact depending on how long you're taking it, how much, and that's just the limitation of the definition we use. Thank you.

Dr Margo Shoup (Dansbury, CT): I enjoyed the presentation and look forward to it being published because I think it will add a lot of value to what we do and some of the billing issues that we may have as well as the care issues.

I have two questions for you.

The first one is based on these data showing that the patients who are on chronic or preoperative opioids going in the ERAS protocol have longer length of stay and are overall more difficult to take care of. Should we be excluding them from our actual analysis for ERAS patients for colorectal? Because that really is one of the things we look at is opioid use. I'm not sure if it's fair to include those that have been on it before surgery.

Number two is based on what we heard from the Michigan data quality earlier in this meeting as far as the billing goes, I think this gives us an opportunity to justify putting a 22 modifier on these surgeries when we're doing them, when we actually just explained that these are going to be more difficult patients to manage in the postoperative setting. What are your thoughts on that?

Dr Alexander Cortez: Thank you, President Shoup. Those are great questions. The first one is one that we discussed a lot in analyzing this data, and that's really why we looked at it. Are preoperative opioid users benefiting to the same degree, do they skew our outcomes on enhanced recovery protocol? Probably so, and I think we could look at a lot of the data out there and stratify out the patients who are on narcotics to see how outcomes change, but this hasn't been done before. We didn't include these data but looked at the opioid-naïve patients and their ERP outcomes and compared it to what I showed for the opioid users' outcomes, and they are to a similar degree, but I think a lot of the data out there in ERP are heterogeneous populations that are mixed together. I think looking at that would be very beneficial.

To the point about modifiers, these patients are more complex. We use modifiers for things like complex dissections or high BMI. These patients are difficult to take care of, and I think we all anecdotally say, 'Oh, this patient is going to be difficult.' We kind of know it and anticipate these feelings of a difficult patient, and data are emerging to back this up. Now I think that coding for this would be a step moving forward.

Dr Shawn Safford (Roanoke, VA): You showed a difference in the pre- and post-ERAS differences on the opioid, who had opioid beforehand. Was that impacting the ERAS greater in the naïve or the opioid patients? It would be interesting to look at the variations to see the impact.

Dr Alexander Cortez: Yes. It's not part of our manuscript, but we looked at the opioid-naïve outcomes and they had a similar reduction of 2 days length of stay and a similar decrease in narcotics. We actually saw a decrease in going home with a narcotic in the opioid-use group, but a slight increase in the opioid naïve. So, it seemed these opioid users really were benefiting and to a similar degree.