

Achieving Opioid-Free Major Colorectal Surgery: Is It Possible?

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Keywords

Opioid-free surgery · Perioperative outcomes · Colorectal surgery · Enhanced recovery after surgery

Abstract

Introduction: Opioid analgesia remains the mainstay of postoperative pain management strategies despite being associated with many adverse effects. A specific opioid-free protocol was designed to limit opioid usage. **Objective:** The aim of the study was to audit the opioid-free rate within this protocol and to identify factors that might contribute to opioid-free surgery. **Methods:** A retrospective study of all elective patients receiving abdominal colorectal surgery at the Center for Colon and Rectal Surgery at AdventHealth over 6 months was performed. Data on demographics, indications, perioperative management, outcomes, and inpatient and outpatient analgesic requirements were collected with subsequent analysis. **Results:** A total of 303 consecutive patient records were analyzed. Approximately two-thirds (67.7%) of patients did not receive narcotics once they left the postanesthesia care unit as an inpatient. One-third of patients (32.0%) did not receive narcotic analgesia within 30 days of surgery as an outpatient. Patients in the

opioid-free cohort were significantly older and had a malignant indication, less perioperative morbidity, and a shorter length of stay. **Conclusions:** Our study demonstrates that opioid-free analgesia is indeed possible in major colorectal surgery. Study limitations include its retrospective nature and that it is from a single institution. Despite these limitations, this study provides proof of concept that opioid-free colorectal surgery is possible within a specific protocol.

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Introduction

Despite advances in surgical techniques, control of postoperative pain remains dependent largely on opioid-based analgesia. Rates of opioid usage have increased as they have formed the foundation of postoperative analgesia. However, opioids have often been given as monotherapy [1], as demonstrated by a review of a national database of over 1.6 million patients showing that 72% of inpatients treated with IV analgesia received opioid monotherapy [2]. Some of this may be accounted for by the fact that patient satisfaction is linked to reimbursement, with postoperative pain being a major factor. This

is reflected in the national usage of opioids, with the United States now accounting for 80% of the world's opioid consumption [3]. Despite these high rates of narcotic analgesia, pain management remains suboptimal in the inpatient care setting [4, 5].

Opioid analgesia has many adverse effects for patients, including nausea and vomiting, respiratory depression, higher rates of ileus, constipation and urinary retention, increased risk of falls, and the pitfalls associated with excessive sedation. Elderly patients suffer additional problems, including risks of delirium and concerns about cognitive impairment [6]. Apart from these short-term effects, the long-term specter of dependence and potential addiction has increasingly become more important to patients and physicians, with devastating effects. In the United States, a death occurs every 36 min which is attributable to opioid usage. These rising rates of opioid overdose deaths in the United States and internationally have raised further apprehensions about the rate of opioid usage in the community [6, 7]. Many of those patients with opioid dependence can link their first use of opioids to surgery [8]. States including Florida have enforced drug monitoring programs and more restrictive prescribing patterns to curb this growing problem [9, 10]. However, with opioid-related deaths still rising, more emphasis needs to be placed on prevention and education [11].

With increasing adoption of enhanced recovery after surgery (ERAS) protocols for colorectal surgery, the use of multimodal and opioid-sparing techniques has come to the fore due to the adverse effects that opioids have on patient recovery [12, 13]. Nonetheless, most patients are still receiving some form of opioids during their postoperative period, in the form of intravenous, oral, or patient-controlled analgesia [14]. The Center for Colon and Rectal Surgery at AdventHealth Orlando has recently introduced an opioid-sparing ERAS protocol. The primary aim of this study was to audit our perioperative opioid usage with an opioid-sparing enhanced recovery protocol, and the secondary aim was to identify factors that might contribute to opioid-free surgery.

Methods

A retrospective analysis of all patients receiving abdominal colorectal surgery within the Center for Colon and Rectal Surgery at AdventHealth Orlando from October 2017 to March 2018 was performed. AdventHealth is a tertiary level, single-institution, multicenter hospital system, and this study encompassed four of those centers. All nonurgent patients having abdominal colorectal surgery were included; the only exclusion criterion was whether

Table 1. Patient demographic and outcome data

Total patients	303
Median age (range), years	59 (15–92)
Approach	
Open	97 (32%)
Laparoscopic	159 (52.5%)
Hybrid	30 (9.9%)
Robotic	17 (5.6%)
Type of operation	
Right hemicolectomy	53 (17.5%)
Sigmoid colectomy	20 (6.6%)
Low anterior resection	119 (39.3%)
Abdominoperineal resection	5 (1.6%)
Total colectomy	12 (4.0%)
Total proctocolectomy	3 (1.0%)
Pouch procedures	16 (5.3%)
Loop ileostomy closure	31 (10.2%)
Closure end ostomy	26 (8.6%)
Other	18 (5.9%)
Indication	
Cancer	99 (32.7%)
Inflammatory bowel disease	49 (16.2%)
Benign	101 (33.3%)
Ostomy closure	57 (18.8%)
Average LOS (range), days	4.7 (0–58)
Received preoperative analgesia	
Received all	215 (71%)
Received part	22 (7.3%)
Received none	66 (21.7%)
Postoperative narcotic use	
Received no narcotic	93 (30.7%)
Received narcotic in PACU	109 (36%)
Received narcotic in ward	39 (12.8%)
Received narcotic in both	62 (20.5%)
Complications	50 (16.5%)
30-day readmission	50 (16.5%)

LOS, length of stay; PACU, postanesthesia care unit.

patients had emergency surgery. Data on patient demographics, surgical approach, indications, preoperative medications, anesthetic medications, and postoperative analgesia, length of stay (LOS), complications, and readmissions were collected. Outpatient script data were collected via E-FORCSE, the Florida Prescription Drug Monitoring Program, and deemed to be related to the surgery if collected within 30 days of the operation. Data were analyzed with one-way ANOVA and χ^2 test (Minitab 18, PA, USA). A *p* value of <0.05 was considered statistically significant. Ethics approval for this study was granted by the Institutional Review Board as a quality improvement study (Number: 1320286-1).

Our ERAS protocol, as specifically related to perioperative analgesia, is listed in the Appendix. We use many opioid-sparing medications, including intravenous acetaminophen, nonsteroidal inflammatory drugs (NSAIDs), and neuropathic agents such as gabapentin. In addition, a bupivacaine liposome injectable suspension (Exparel, Pacira Pharmaceuticals, CA, USA) was used for lo-

Table 2. Detailed breakdown of analgesic data

	No narcotic	PACU	Ward	<i>p</i> value
Total patients	93	109	101	
Median age (range), years	66 (15–92)	55 (19–84)	57 (19–85)	0.001
Gender, male	41 (44.1%)	57 (52.3%)	39 (38.6%)	0.13
Approach				
Open	20 (21.5%)	34 (31.2%)	43 (42.6%)	0.076
Lap	57 (61.3%)	55 (50.5%)	47 (46.5%)	
Hybrid	10 (10.8%)	12 (11.0%)	8 (7.9%)	
Robotic	6 (6.5%)	8 (7.1%)	3 (3%)	
Indication				
Malignancy	41 (44.1%)	32 (29.4%)	26 (25.7%)	0.002
Inflammatory bowel disease	7 (7.5%)	14 (12.8%)	28 (27.7%)	
Benign	28 (30.1%)	39 (35.8%)	34 (33.7%)	
Ostomy	17 (18.3%)	24 (22.0%)	16 (15.8%)	
Average LOS (range), days	3.2 (1–13)	3.3 (3–13)	7.6 (1–58)	<0.0001
Preoperative analgesia				
All	68 (73.1%)	76 (69.7%)	71 (70.3%)	0.76
Partial	4 (4.3%)	10 (9.2%)	8 (7.9%)	
None	21 (22.6%)	23 (22.5%)	22 (21.8%)	
ASA score				
1	2 (2.1%)	10 (9.2%)	4 (4%)	0.092
2	65 (69.9%)	68 (62.4%)	64 (63.3%)	
3	26 (28.0%)	30 (27.5%)	29 (28.7%)	
4	0	1 (0.9%)	4 (4%)	
Postoperative analgesia				
Meperidine	0	10 (9.2%)	13 (12.9%)	
Hydromorphone, IV	0	98 (89.9%)	87 (8.6%)	
Hydromorphone, PCA	0	0	9 (8.9%)	
Hydromorphone, oral	0	0	2 (2.0%)	
Morphine	0	0	13 (15.8%)	
Fentanyl	0	4 (3.7%)	7 (6.9%)	
Oxycodone	0	0	81 (80.2%)	
Exparel usage	92 (98.9%)	109 (100%)	101 (100%)	
Tramadol usage	32 (34.4%)	51 (46.8%)	48 (47.5%)	
Complications	9 (9.7%)	12 (11.0%)	29 (28.7%)	<0.001
30-day readmission	13 (14.0%)	17 (15.6%)	20 (19.8%)	0.52

LOS, length of stay; ASA, American Society of Anaesthesiologists; IV, intravenous; PCA, patient-controlled analgesia; PACU, postanesthesia care unit.

cal anesthesia, to provide a longer lasting analgesic blockade. Other elements of ERAS deployed included preoperative patient education, informing patient expectations, education of the medical and ward nursing staff, and insistence on early mobilization, early removal of Foley catheters, and timely advancement of diet.

Results

A total of 303 consecutive patient records were analyzed during the study period. A summary of the overall demographic and outcome data is outlined in Table 1. Of

note, the majority of patients (206, 68%) received minimally invasive surgery, and the indications ranged from malignancy, inflammatory bowel disease, and reversal of ostomies. Ileostomy closures were considered open procedures for the purposes of this study. The median LOS was 4.7 days. In all, 93 (30.7%) patients did not receive any narcotics in the postoperative period. A further 109 (36%) patients did not receive narcotics once they left the postanesthesia care unit (PACU). It must be noted that the clear majority did get narcotics on induction, including 78 of the 93 patients in the nonnarcotic group which received fentanyl on induction.

Table 3. After discharge opioid use

Analgesic	Patients, <i>n</i>
Nonopioid analgesia	233 (76.9%)
Opioid analgesia	70 (23.1%)
Total patients with tramadol scripts	125 (41.3%)
Scripts filled	109 (36.0%)
Total patients with opioid scripts	87 (28.7%)
Scripts filled	71 (23.4%)
Codeine only	1 (0.3%)
Tramadol only	103 (34.0%)
Tramadol and oxycodone	5 (1.7%)
Tramadol and hydrocodone	1 (0.3%)
Oxycodone only	48 (16.0%)
Hydrocodone only	13 (4.2%)
Oxycodone and hydrocodone	2 (0.6%)
Oral morphine only	1 (0.3%)

Table 4. Breakdown of total opioid use

Category of use	Patients, <i>n</i>
Total nonopioid analgesia	97 (32.0%)
Tramadol only (inpatient or outpatient)	49 (16.2%)
Inpatient narcotic use only	98 (32.3%)
Inpatient PACU use only	53 (17.5%)
Inpatient floor use	45 (14.9%)
Outpatient narcotics use only	6 (1.9%)
Both inpatient and outpatient narcotics	112 (37.0%)

PACU, postanesthesia care unit.

Table 2 describes the differences between the different cohorts. There were no significant differences between gender, surgical approach, use of preoperative medications, ASA, and 30-day readmission. There were significant differences between the cohorts for age, indication, LOS, and complication rates. In particular, patients in the nonnarcotic cohort were significantly older, more likely to be operated on for malignancy, and less likely to have a postoperative complication. In addition, patients who received opioid-free surgery had a shorter LOS (3.2 vs. 7.6 days, $p = 0.0001$) and fewer complications (9.7 vs. 28.7%, $p < 0.001$).

Tables 3 and 4 describe the use of narcotics once patients were discharged into the community. Most patients either did not use narcotic analgesia (112, 37%) at all or used only tramadol (103, 34.4%). The remaining patients used either hydrocodone or oxycodone as a mainstay, with a few other narcotic analgesia combinations. Approximately one-third of the patients did not use opioid medication after their discharge from the PACU.

Discussion

Our study demonstrates that a multifactorial, multimodal approach to perioperative analgesia can result in high rates of opioid-free or minimal opioid use in the postoperative care setting. Among our patients, 30.7% did not receive narcotics after induction of anesthesia, and a further 36.7% did not receive any narcotics after their discharge from the PACU. This means that just over two-thirds of our patients over the study period required no narcotics while they were on the floor as an inpatient. Further analysis of patient records after discharge using the E-FORCSE database, which is an 8-statewide database of outpatient schedule of medications, shows that almost half of the patients did not use any narcotic analgesia at any stage of their postoperative recovery.

Unsurprisingly, patients who received opioid-free or minimal opioid surgery had shorter LOS and fewer complications. The obvious conclusion from this is that those patients with a more complicated postoperative course also had increased postoperative analgesic challenges. Older patients were also less likely to use narcotics; this may be due to greater pain tolerance levels among the older population, which is supported in the previous literature [15]. Interestingly, cancer patients were also less likely to use narcotics, which is contrary to published evidence on opioid abuse [16]. We speculate that this may be due to survivor resilience and patient motivation to combat their malignancy, which may be brought to the fore during their pre-procedure education where the importance of minimization of opioid usage was emphasized. Although patients who did receive narcotics on the ward were less likely to have undergone a laparoscopic approach, surprisingly, this difference was not statistically significant. This may point to the effectiveness of this protocol regardless of the surgical approach.

The vast majority of patients received some form of opioid-based induction of anesthesia, despite the literature showing the safety of opioid-free anesthesia (OFA) [17–19]. The usage of narcotics in intravenous anesthesia has a strong historical basis. Its use was first reported in 1926 and then popularized via the term balanced anesthesia, leading to induction with a combination of nitrous oxide and intravenous morphine [20]. From a pain perspective, the main concern within the intraoperative period is the blockade of central sensitization, which occurs with the release of glutamate binding to central receptors such as NMDA [21]. Dampening of this in the

intraoperative period has traditionally been conducted with opioids, but recently, OFA techniques have been more popular. A Cochrane review of OFA versus opioid anesthesia found significant benefits, including the reduction of postoperative ileus [22]. Other studies have shown less postoperative pain, nausea, and vomiting [19, 23]. There are also concerns that intraoperative opioids may lead to opioid-induced hyperalgesia [24, 25]. However, with a large department of anesthesia providers, uniformity in the induction approach is very difficult, especially in an area such as OFA where there is a wide range of opinion.

In one-third of our patients, the only opioid treatment that they received after induction was in the PACU. We speculate that as with the induction of anesthesia, opioids form one of the cornerstone options for postoperative pain relief in the PACU. This is likely due to their quick mechanism of action, the availability of monitoring of their adverse outcomes, and the familiarity that staff have with their use. Nonetheless, a part of our implementation of the ERAS protocols involves continued education of the PACU staff.

Our study shows that an opioid-free approach to major abdominal surgery is possible. With growing concerns from physicians, regulators, and the community about opioid abuse, it is important to emphasize that opioids are not a necessary part of postoperative care for every patient. We acknowledge that it is not simply a multimodal approach to analgesia that has produced this result. Three other important components include the pre-procedure education of the patient, careful management of patient expectations of their postoperative course and pain management strategies, and education of medical and nursing staff of the concept and benefits of opioid-free surgery in conjunction with multimodal analgesia.

We recognize that there are limitations to this study. It is retrospective in nature. It is a single-institution multicampus study, which may limit its applicability to the wider community. Nonetheless, the type of surgery and our patient settings do compare favorably with other community settings around the United States. In addition, we have managed to implement this protocol at various sites, with different patient and staff populations. The study only investigated elective patients and, therefore, cannot be immediately applied to the emergent setting. Approximately 20% of our patients did not receive the entire preoperative analgesia package; this was due to the time taken to implement this part of the protocol in all the centers. Our study also highlights pos-

sible factors that may lead to opioid reduction but does not provide the theoretical basis as to why these factors may contribute. We also used scripts filled as surrogate for medication taken, where the rates of actual medication usage may be lower. Earlier in our experience, we gave most of our patients scripts for tramadol and opioids both due to patient expectations and our own concerns regarding patients presenting with pain. This lessened over time as we acknowledged that many of our patients never used the medications that they had filled in.

We also note that many of our patients received tramadol in lieu of an opioid medication, either in the inpatient or outpatient setting. Certainly, at the time of the creation of the protocol, tramadol was identified as a safer drug by the WHO when compared to other opioids [26]. Numerous studies and reviews have studied its abuse potential, and it has been found to be relatively low in the past [27]. A recent study published in the *BMJ* was in contrary to this, suggesting that tramadol has a higher addictive potential [28]. The status of tramadol and its addictive potential, therefore, is in flux. Nonetheless, studies have shown that doses of oral tramadol that we commonly use, such as 50–100 mg, have a smaller addictive potential to tramadol compared to larger doses at the 150- to 200-mg range [29]. Indeed, the abuse potential of tramadol was highlighted to be approximately the same as nonsteroidal medications, which also carry a significant abuse rate, although rarely acknowledged in the literature [30]. For these reasons, we have not included tramadol as an opioid medication within this study. In the broader viewpoint, the authors have been looking at possible alternatives, such as using gabapentin as a discharge medication, changing the mix of NSAIDs, and increasing the dosage of NSAIDs on discharge (commonly, we use over-the-counter dosing levels of ibuprofen).

Conclusion

This study provides proof of concept that opioid-free surgery is possible for a significant proportion of patients within the setting of an ERAS colorectal surgery program. Further work needs to be done to investigate how more patients may be moved to an opioid-free or minimal opioid setting and the factors involved in postoperative analgesic challenges. In addition, the possibility of extending this to other abdominal surgery and other types of surgery needs to be investigated.

Statement of Ethics

Ethics approval for this study was granted by the Institutional Review Board as a quality improvement study (Number: 1320286-1). This study was done in concordance with ethics at Advent-Health.

Disclosure Statement

Justin Kelly is a consultant for Applied Medical.

George Nassif is a consultant for Applied Medical, Mallinckrodt Pharmaceuticals, and Conmed.

Teresa Debeche-Adams is a consultant for Applied Medical and Conmed.

Matthew Albert is a consultant for Applied Medical, Stryker, and Conmed.

John Monson is a consultant for Medtronic and Twistle.

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Author Contributions

Study conception and design: Yap, Nassif, Hwang, Monson.

Acquisition of data: Yap, Nassif, Hwang, Mendez, Erkan, Kelly, Debeche-Adams, Albert, Monson.

Analysis and interpretation of data: Yap, Nassif, Hwang, Mendez, Erkan, Kelly, Debeche-Adams, Albert, Monson.

Drafting of manuscript and critical revision: Yap, Nassif, Hwang, Mendez, Erkan, Kelly, Debeche-Adams, Albert, Monson, Yap, Nassif, Erkan, Kelly, Monson.

Appendix

Perioperative Pain Management Strategy for Colorectal Patients

Pre-Procedure

Patient education and discussion of expectations of the perioperative course.

Arrival at Preoperative Holding Bay

Acetaminophen 1000 mg, oral.

Celecoxib 200 mg, oral.

Gabapentin 600 mg, oral.

Intraoperative

20 cm³ Exparel, diluted appropriately, as a subfascial and subcutaneous block.

Postoperative

Nurse education on the strategy of multimodal analgesia.

Ambulation as soon as safely possible (ideally, day 0)

Acetaminophen 1,000 g q6h IV × 24 h, change to 1,000 g q6h, oral day 1.

Ketorolac 30 mg IV q6h 5 days.

Gabapentin 300 mg q8h × days.

Discharge

Acetaminophen 1000 g q6h, oral. Ibuprofen 400 mg q6h, oral.

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