



Enhanced recovery protocol improves postoperative outcomes and minimizes narcotic use following resection for colon and rectal cancer[☆]



Alexander R. Cortez, Al-Faraaz Kassam, Nick C. Levinsky, Andrew D. Jung, Meghan C. Daly, Shimul A. Shah, Janice F. Rafferty, Ian M. Paquette^{*}

Cincinnati Research in Outcomes and Safety in Surgery (CROSS), Department of Surgery, University of Cincinnati, Cincinnati, OH

ARTICLE INFO

Article history:

Received 23 April 2019

Received in revised form 20 May 2019

Accepted 22 May 2019

Available online 2 July 2019

ABSTRACT

Background: Enhanced recovery protocols are associated with improved recovery. However, data on outcomes following the implementation of an enhanced recovery protocol in colorectal cancer are limited. We set out to study the postoperative outcomes, opioid use patterns, and cost impact for patients undergoing colon or rectal resection for cancer.

Methods: A retrospective review of all elective colorectal cancer resections from January 2015 to June 2018 at a single institution was performed. Patient demographics, operative details, and postoperative outcomes were collected. Colon and rectal patients were studied separately, with comparison of patients before and after the implementation of an enhanced recovery protocol.

Results: One hundred ninety-two patients underwent elective colorectal resection for cancer. In January 2016, an enhanced recovery protocol was implemented for all elective resections – 71 patients (33 colon and 38 rectal) underwent surgery before implementation and 121 patients (56 colon and 65 rectal) underwent surgery after implementation of the enhanced recovery protocol. There were no differences with regard to age, gender, or body mass index before or after implementation (all $P > .05$). For both colon and rectal cancer patients, the enhanced recovery protocol reduced time to regular diet (both $P < .05$) and length of stay (colon: 3 vs 4 days; rectal: 4 vs 6 days; both $P < .01$). Enhanced recovery protocol patients also consumed fewer total narcotics (colon: 44 vs 184 morphine milligram equivalents, $P < .01$; rectal: 121 vs 393 morphine milligram equivalents, $P < .01$).

Conclusions: Enhanced recovery protocol use reduced length of stay and narcotic use with similar total costs and no difference in 30-day complications for both colon and rectal cancer resections.

© 2019 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

INTRODUCTION

Over the past decade, enhanced recovery protocols (ERP) have emerged widely and been shown to improve outcomes following a variety of procedures, including colectomy [1]. There has been a large influx of work studying the impact of ERP on colectomy outcomes, and ERP are now recommended by multiple surgical societies [2,3]. However, the majority of studies involve heterogeneous patient groups with varying indications for colorectal resection. Dedicated studies among colorectal cancer patients are important in order to optimize oncologic outcomes, as postoperative complications following colorectal surgery for colorectal cancer (CRC) have been associated with delayed or omitted adjuvant chemotherapy [4,5], as well as increased local recurrence and decreased cancer-specific survival [6,7]. In addition,

given differences in treatment approaches to colon versus rectal cancer, namely resection types and neoadjuvant/adjuvant treatment strategies, independent analyses of ERP safety and efficacy for colon and rectal resections are warranted.

While there is data among CRC patients exploring outcomes within the context of existing ERP, specific analyses on the implementation of ERP among colorectal cancer patients is limited. Moreover, minimal work has stratified outcomes by cancer types of colon versus rectal cancer. Finally, the predominant outcomes studied among ERP literature is length of stay and surgical complications, but limited data exists on the impact to cost and narcotic use.

As such, we set out to examine outcomes following elective colorectal resection for CRC at our institution, stratifying outcomes by cancer type of colon and rectal cancer. The primary outcomes were length of stay and 30-day readmissions, and secondary outcomes were cost and narcotic use (both in patient and post-discharge). We hypothesized that institution of an ERP in patients undergoing resection for both colon and rectal cancer leads to improved clinical outcomes and lower narcotic utilization without increasing cost.

[☆] Presented at the 2018 SSO Annual Cancer Symposium, Chicago, IL, March 21–24, 2018.

^{*} Corresponding author at: Department of Surgery, University of Cincinnati College of Medicine, 2123 Auburn Ave #524, Cincinnati, OH 45219.

E-mail address: ian.paquette@uc.edu (I.M. Paquette).

Methods

Patient Selection. A retrospective review of all patients from January 2015 to June 2018 undergoing elective colorectal resection for biopsy-proven colorectal cancer at a single institution was performed. Patient demographics, operative details, and postoperative outcomes were collected. Patients who underwent emergent/urgent operations, procedures without a bowel resection, or enterostomy closures were excluded. All operations were performed by the same 3 board-certified colon and rectal surgeons.

Implementation of Enhanced Recovery Pathway. Prior to 2016, patients received a preoperative bowel preparation consisting of a mechanical and oral antibiotic regimen [8]. A clear liquid diet was initiated upon the presence of flatus following surgery and thereafter advanced as tolerated. Postoperative management of urinary catheters was variable among surgeons, typically removed within 2 to 4 days after surgery. Postoperative analgesia was provider dependent. The majority received a transversus abdominis plane (TAP) block and were started on intravenous narcotics with transition to oral narcotics once tolerating an oral diet.

In January 2016, an ERP was implemented at our institution for all elective colorectal resections. Prior to implementation, a multidisciplinary approach in developing our institution's protocol took place, which included our surgeon team, anesthesia, and nursing leadership. Residents were educated on the components of the protocol and an order set was created. These efforts promoted buy in and facilitated universal implementation for colorectal surgery patients without a transition period. The details of our ERP have been previously reported [9] and are consistent with guidelines established by American Society of Colon and Rectal Surgeons [3]. In brief, patients were given oral gabapentin pre- and postoperatively. A mechanical bowel preparation with oral neomycin and metronidazole was given 1 day before surgery. Two Glycemic Endothelial Drinks (SOF Health, Holland, MI) were consumed at that time, along with an additional drink on the morning of surgery. Oral alvimopan was given 2 hours before surgery and continued twice daily until return of bowel function (to a maximum of 7 days). All patients were started on a clear liquid diet immediately after surgery, and a regular diet was initiated on postoperative day one.

Regarding analgesia, a TAP block was performed by the anesthesiologist at the completion of the operation. Patients received scheduled intravenous ketorolac and acetaminophen for 24 hours, followed by transition to scheduled oral ibuprofen and acetaminophen, with oxycodone as needed for breakthrough pain. Patients were given a patient-controlled analgesia (PCA) pump postoperatively which was discontinued on postoperative day 1 for laparoscopic surgery and postoperative day 2 for open surgery. Patients were discharged from the hospital when they were tolerating a regular diet, demonstrated evidence of bowel function (both flatus and bowel movement), and had pain control with oral medications only.

Definitions. The type of resection was categorized as right colectomy, left colectomy, proctectomy (low anterior resection (LAR) or abdominoperineal resection (APR)), or total abdominal colectomy. Surgical site infections included any superficial incisional, deep incisional, or organ space infections. All anastomotic leaks were defined as the presence of air or contrast outside of the colorectal anastomosis. Ileus was defined as lack of bowel function (inability to tolerate a diet or need for nasogastric tube placement) by postoperative day 2. Patient cost data were provided by the hospital billing department and reported as total direct and total pharmacy costs. Daily costs were calculated as total cost divided by length of stay.

Total narcotic dosage was measured in morphine milligram equivalents (MME) and daily narcotic dosage calculated as total MME divided by length of stay. Pre- and post-operative opioid use and refill patterns were assessed using the Ohio Automated Rx Reporting System (OARRS)

(www.ohiopmp.gov). OARRS is a reporting system managed by the State of Ohio Board of Pharmacy that collects information on all outpatient prescriptions for controlled substances. Given the location of our institution and local referral patterns, each patient's OARRS report queried prescriptions filled in Ohio, Kentucky, and Indiana. Preoperative opioid use was defined as having filled a narcotic prescription within 60 days prior to surgery.

Statistical Analysis. Continuous data are reported as median and interquartile range (IQR) and compared using Wilcoxon rank-sum test. Categorical data are reported as total (n) and percentage (%) and compared using Pearson's Chi-square test (or Fischer's exact test for rare occurrences). Statistical significance was set at $P < .05$. All statistical analyses were performed using JMP Pro Version 14.0 (SAS Institute, Cary, NC). This study was approved by our hospital's Institutional Review Board.

RESULTS

Patient Cohort. From 2015 to 2018, 436 patients underwent elective colorectal resection at our institution, of which 192 (44.0%) were cancer operations and included in this study. A total of 71 patients underwent surgery in the pre-ERP period and the remaining 121 consecutive cases occurred in the post-ERP period. Between the pre-ERP and post-ERP periods, there was an even distribution of colon cancer ($n = 33, 46.5\%$ vs $n = 56, 46.3\%$) and rectal cancer ($n = 38, 53.5\%$ vs $n = 65, 53.7\%$, $P = .98$) among the cohort.

Demographics and Operative Details. Overall, 89 patients had colon cancer and 103 had rectal cancer. Patient demographics for each cohort are depicted in Table 1. Among colon and rectal cancer patients there were no differences in age, gender, body mass index (BMI) or preoperative comorbidities in the pre-ERP era compared to post-ERP era (all $P > .05$), except for a slightly higher proportion of rectal cancer patients having had a prior abdominal operation in the post-ERP period (39.5% vs 67.7%, <0.01). The use of neoadjuvant chemoradiation for rectal cancer was also similar before and after ERP implementation (71.1% vs 67.6%, $P = .72$).

Table 2 illustrates the operative details for colon and rectal cancer patients. Operative details were similar in the pre- versus post-ERP era for both the colon and rectal cancer subgroups. Among rectal cancer patients, however, there were lower rates of ostomy creations (89.5% vs 73.9%) and slightly shorter operative times (261 vs 237 minutes) with ERP, though these did not reach statistical significance ($P = .06$ for each).

Postoperative outcomes. Given differences in resection type and use of neoadjuvant chemoradiation for colon versus rectal cancer, postoperative outcomes were examined by cancer type and are reported in Table 3. Among patients with colon cancer, ERP decreased time with a urinary catheter (1 vs 2 days, $P = .01$), time to initiation of a regular diet (2 vs 3 days, $P < .01$), and total length of stay (3 vs 4 days, $P < .01$). Moreover, ERP patients had shorter durations of PCA use (2 vs 3 days, $P < .01$), consumed significantly fewer total inpatient narcotics (44 vs 184 MME, $P < .01$), and required fewer opioid refills within 30 days of discharge (20.5% vs 47.1%, $P = .04$).

Similarly, rectal cancer patients who received ERP had decreased time with a urinary catheter (2 vs 3 days, $P < .01$), time to initiation of a regular diet (2 vs 4 days, $P < .01$), and total length of stay (4 vs 6 days, $P < .01$). ERP in the rectal cancer group was also associated with significantly lower rates of postoperative ileus (13.9% vs 39.5%, $P < .01$). The rectal cancer cohort saw similar improvements for inpatient narcotic use with ERP, as evidenced by shorter durations of PCA use (2 vs 3 days, $P < .01$) and fewer total inpatient narcotics (121 vs 393 MME, $P < .01$). Finally, ERP in both the colon and rectal cancer cohorts was not associated with increased total direct costs or total pharmacy costs ($P > .05$ for each).

Table 1
Demographics of patients undergoing elective resection for colorectal cancer

| | Colon Cancer | | | Rectal Cancer | | |
|----------------------------|----------------------|----------------------|------|----------------------|----------------------|-------|
| | Pre ERP (n = 33) | Post ERP (n = 56) | P | Pre ERP (n = 38) | Post ERP (n = 65) | P |
| | n (%) / median (IQR) | n (%) / median (IQR) | | n (%) / median (IQR) | n (%) / median (IQR) | |
| Age, y | | | | 55 (48–63) | 61 (50–71) | .08 |
| Gender, male | 13 (39.4%) | 32 (57.1%) | .13 | 24 (63.2%) | 28 (43.1%) | .07 |
| BMI, kg/m ² | | | | 28 (22–32) | 28 (24–33) | .76 |
| ASA classification | | | .27 | | | .07 |
| Class I-II | 16 (48.5%) | 20 (35.7%) | | 20 (52.6%) | 22 (33.9%) | |
| Class III-IV | 17 (51.5%) | 36 (64.3%) | | 18 (47.4%) | 43 (66.1%) | |
| Patient comorbidities | | | | | | |
| DM | 4 (12.1%) | 12 (21.4%) | .39 | 5 (13.2%) | 19 (29.2%) | .09 |
| CKD | 3 (9.1%) | 5 (8.9%) | 1.00 | 3 (7.9%) | 2 (3.1%) | .36 |
| CAD | 9 (27.3%) | 13 (23.2%) | .80 | 7 (18.4%) | 11 (16.9%) | 1.00 |
| CVD | 3 (9.1%) | 3 (5.4%) | .67 | 0 | 3 (4.6%) | .29 |
| Preoperative risk factors | | | | | | |
| Opioid use | 4 (12.1%) | 9 (16.1%) | .76 | 8 (21.1%) | 9 (13.9%) | .41 |
| Tobacco use | 12 (36.4%) | 24 (42.9%) | .66 | 9 (23.7%) | 23 (35.4%) | .27 |
| Prior abdominal surgery | 20 (60.6%) | 35 (62.5%) | 1.00 | 15 (39.5%) | 44 (67.7%) | <.01* |
| Neoadjuvant chemoradiation | 0 | 0 | - | 27 (71.1%) | 44 (67.6%) | .72 |

BMI, body mass index; ASA, American Society of Anesthesiologists; DM, diabetes mellitus; CKD, chronic kidney disease; CAD, coronary artery disease; CVD, cerebrovascular disease.

* $P < .05$.

Rectal cancer analysis by surgery type. Given the difference in high versus low rectal resection, we performed a subset analysis on the impact of ERP among patients with rectal cancer stratified by those who underwent LAR and APR, as demonstrated in Table 4. Patients who underwent LAR and received ERP had decreased time with a urinary catheter, time to diet initiation, overall length of stay, and narcotic use ($P < .05$ for each). Patients who underwent APR and received ERP similarly had decreased total narcotic use ($P = .04$), but length of stay, though decreased, was not statistically significant (5 vs 8 days, $P = .10$).

Discussion

In this study, we found that patients with both colon and rectal cancer had earlier initiation of a regular diet, fewer days with a urinary catheter, and shorter length of stay with the use of ERP. Moreover, both groups had fewer days with a PCA and consumed significantly fewer narcotics. Subset analysis for rectal cancer patients by surgery type as a surrogate for cancer location (i.e. LAR for high rectal and APR for low rectal tumors) also demonstrated a beneficial impact among

Table 2
Operative details for patients undergoing elective resection for colorectal cancer

| | Colon Cancer | | | Rectal Cancer | | |
|---------------------------|----------------------|----------------------|-----|----------------------|----------------------|-------|
| | Pre ERP (n = 33) | Post ERP (n = 56) | P | Pre ERP (n = 38) | Post ERP (n = 65) | P |
| | n (%) / median (IQR) | n (%) / median (IQR) | | n (%) / median (IQR) | n (%) / median (IQR) | |
| Operative approach | | | .68 | | | .33 |
| Laparoscopic | 26 (78.8%) | 42 (75.0%) | | 23 (60.5%) | 46 (70.8%) | .29 |
| Open | 7 (21.2%) | 14 (25.0%) | | 13 (39.5%) | 19 (29.2%) | |
| Operation | | | .48 | | | - |
| Left colectomy | 8 (24.2%) | 20 (35.7%) | | 0 | 0 | |
| Right colectomy | 24 (72.7%) | 31 (55.4%) | | 0 | 0 | |
| Total abdominal colectomy | 1 (3.0) | 3 (5.4%) | | 0 | 0 | |
| Proctectomy | 0 | 2 (3.6%) | | 38 (100.0%) | 65 (100.0%) | |
| Primary anastomosis | 32 (97.0%) | 54 (96.4%) | .89 | 24 (63.2%) | 41 (63.1%) | .99 |
| Ostomy creation | 3 (9.1%) | 5 (8.9%) | .98 | 34 (89.5%) | 48 (73.9%) | .06 |
| Operative time, min | 143 (110–174) | 158 (129–199) | .12 | 261 (219–311) | 237 (188–270) | .06 |
| Intraoperative fluids, L | 1.8 (1.4–2.4) | 1.7 (1.3–2.1) | .80 | 3.0 (2.6–3.6) | 2.3 (1.9–2.9) | <.01* |
| Estimated blood loss, ml | 50 (25–100) | 50 (40–100) | .72 | 225 (100–500) | 200 (100–300) | .16 |

* $P < .05$.

Table 3
Outcomes following elective resection for colorectal cancer

| | Colon Cancer | | | Rectal Cancer | | |
|-----------------------------------|----------------------|----------------------|-----------|-----------------------|----------------------|-------|
| | Pre ERP (n = 33) | Post ERP (n = 56) | P | Pre ERP (n = 38) | Post ERP (n = 65) | P |
| | n (%) / median (IQR) | n (%) / median (IQR) | | n (%) / median (IQR) | n (%) / median (IQR) | |
| Length of stay, d | 4 (4–5) | 3 (2–4) | <.01*†, ‡ | 6 (4–9) | 4 (3–5) | <.01* |
| Postoperative ileus | 3 (9.1%) | 3 (5.4%) | .66 | 15 (39.5%) | 9 (13.9%) | <.01* |
| Surgical site infection | 1 (3.0%) | 2 (3.6%) | 1.00 | 4 (10.5%) | 1 (1.5%) | .06 |
| Anastomotic leak | 1 (3.0%) | 4 (7.1%) | .65 | 1 (2.6%) | 1 (1.5%) | 1.00 |
| Time with urinary catheter, d | 2 (1–3) | 1 (1–2) | .01* | 3 (2–6) | 2 (1–2) | <.01* |
| Day of diet advancement | 3 (2–4) | 2 (1–2) | <.01* | 4 (3–5) | 2 (2–4) | <.01* |
| Discharge to SNF | 6 (18.2%) | 1 (1.8%) | .01* | 4 (10.5%) | 2 (3.1%) | .12 |
| Total inpatient narcotic use, MME | 184 (105–386) | 44 (15–116) | <.01* | 393 (100–1101) | 121 (26–207) | <.01* |
| Daily inpatient narcotic use, MME | 46 (20–106) | 14 (5–43) | <.01* | 75 (18–150) | 23 (8–51) | <.01* |
| PCA duration, d | 3 (2–3) | 2 (1–2) | <.01* | 3 (3–5) | 2 (1–3) | <.01* |
| Opioid discharge prescription† | 17 (63.0%) | 39 (70.9%) | .47 | 19 (55.9%) | 50 (79.4%) | .02* |
| Opioid refill within 30 days‡ | 8 (47.1%) | 8 (20.5%) | .04* | 9 (47.4%) | 14 (28.0%) | .13 |
| 30-day readmission | 0 | 5 (8.9%) | .15 | 3 (7.9%) | 12 (18.5%) | .16 |
| 30-day reoperation | 2 (6.1%) | 6 (10.7%) | .70 | 3 (7.9%) | 4 (6.2%) | .71 |
| 30-day mortality | 0 | 0 | - | 1 (2.6%) | 0 | .37 |
| Total direct cost, \$ | 8313 (7296–0858) | 8983 (7192–10,531) | .82 | 12,682 (10653–15,946) | 11,454 (9609–13,994) | .09 |
| Total pharmacy cost, \$ | 1268 (915–1590) | 1394 (1203–1831) | 0.09 | 1948 (1182–2525) | 1659 (1363–2062) | .30 |

ICU, intensive care unit; SNF, short-term nursing facility; MME, morphine milligram equivalents; PCA, patient-controlled analgesia.

* $P < .05$.

† Excludes patients discharged to a skilled nursing facility.

‡ Refill data reported only among patients discharged to home and who received an opioid at discharge.

these patients undergoing more complex operations. Despite hastened postoperative recovery, there was no increase in morbidity, mortality, or cost with ERP.

Over the past 2 decades, ERP regimens have become an important aspect of surgical care and are now advocated for by many subspecialties. While existing literature on ERP is robust, few studies directly evaluate the implementation of ERP among CRC patients. Rather, a number of studies have explored outcomes within the context of an existing ERP and evaluated the impact of specific components. In 2015, the ERAS Compliance Group published data based on a large international registry of ERP outcomes [10]. They demonstrated on multivariate analysis that among nearly 1500 colon cancer and 900 rectal cancer patients that laparoscopy and compliance with ERP decreased the primary outcomes of length of stay and postoperative complications, whereas patient comorbidities, an open approach, and surgery for rectal cancer worsened these outcomes [10].

These studies are important to understand the impact of specific ERP components and optimize protocols. However, work directly comparing the periods before and after ERP implementation is important. Among heterogenous colorectal populations, ERP use has been shown in 2 independent meta-analyses to reduce complication rates and length of stay without increasing readmissions [11,12]. Among colon cancer patients, Ota and colleagues demonstrated quicker initiation of oral diet and shorter length of stay with ERP without increased postoperative complications [13]. Similarly, Khoo et al reported decreased length of stay and complications, but increased postoperative readmissions among CRC patients undergoing resection in a randomized controlled trial of a “multimodal perioperative protocol.” [14] Moreover, their positive results were observed for both the colon and rectal cancer subgroups, though the study was underpowered to detect statistical differences among the rectal cancer patients [14]. Our work further supports these findings of improved outcomes among both CRC patient groups.

Table 4
Outcomes by resection type for patients with rectal cancer

| | LAR (n = 71) | | | APR (n = 32) | | |
|-----------------------------------|----------------------|----------------------|-------|----------------------|----------------------|-------|
| | Pre ERP (n = 27) | Post ERP (n = 44) | P | Pre ERP (n = 11) | Post ERP (n = 21) | P |
| | n (%) / median (IQR) | n (%) / median (IQR) | | n (%) / median (IQR) | n (%) / median (IQR) | |
| Length of stay, d | 6 (4–9) | 4 (2–5) | <.01* | 8 (4–11) | 5 (4–6) | .10 |
| Postoperative ileus | 10 (37.0%) | 4 (9.1%) | .01* | 5 (45.5%) | 5 (23.8%) | .25 |
| Surgical site infection | 1 (3.7%) | 1 (2.3%) | 1.00 | 3 (21.3%) | 0 | .03* |
| Anastomotic leak | 1 (3.7%) | 1 (2.3%) | 1.00 | - | - | - |
| Time with urinary catheter, d | 4 (3–5) | 2 (1–4) | <.01* | 5 (4–5) | 4 (2–5) | .15 |
| Day of diet advancement | 3 (2–7) | 2 (1–2) | <.01* | 2 (1–5) | 2 (2–3) | .63 |
| Total inpatient narcotic use, MME | 581 (95–1200) | 79 (23–188) | <.01* | 340 (138–752) | 149 (70–227) | .04* |
| Daily inpatient narcotic use, MME | 84 (18–178) | 20 (8–45) | <.01* | 32 (17–97) | 34 (19–55) | .40 |
| PCA duration, d | 3 (3–5) | 2 (1–2) | <.01* | 4 (3–7) | 2 (0–3) | <.01* |
| 30-day readmission | 2 (7.4%) | 6 (13.6%) | .70 | 1 (9.1%) | 6 (28.6%) | .37 |
| 30-day reoperation | 2 (7.4%) | 1 (2.3%) | .55 | 1 (9.1%) | 3 (14.3%) | 1.00 |
| 30-day mortality | 1 (3.7%) | 0 | .38 | 0 | 0 | - |

LAR, low anterior resection; APR, abdominoperineal resection; ICU, intensive care unit; MME, morphine milligram equivalent equivalents; PCA, patient-controlled analgesia.

* $P < .05$.

These studies differed in their results on the impact of ERP on postoperative readmissions. Although not statistically significant, our study was associated with a clinically relevant increase in readmissions for both the colon and rectal cohorts. Among patients with colon cancer who received ERP, there were 2 major complications of leak and small bowel obstruction, both of which required an operation. The remaining complications were minor (ileus, melena, and an antibiotic reaction). Among patients with rectal cancer who received ERP, there were 2 major complications of wound dehiscence and small bowel obstruction that required a reoperation and the remainder were minor (urinary tract infection, melena, ileus, nausea/vomiting, C. diff infection, and pelvic hematoma).

Given the increased complexity with rectal resections, particularly low-lying tumors, hesitancy for ERP use or consideration of ERP modifications is understandable. While ERP appears to be safe and effective in the setting of surgery for colon cancer, our work suggests that ERP is similarly safe and effective and concern over ERP for rectal surgery is largely unnecessary. It is important to shift the collective mentality away from thinking of ERP as a way to “fast-track” the discharge of patients with simple operations, but rather to enhance the overall recovery process and extend similar benefits to patients with both simple and complex cancer operations. Herein, we found that patients with rectal cancer exhibited similar improvements in postoperative length of stay and reduction in narcotic use without increased complications. Although readmissions for both cohorts were slightly higher in the post-ERP era compared to pre-ERP, our readmission rates were similar to those reported by the ERAS Compliance Group, despite our cohort exhibiting increased patient comorbidities than their patient group. Furthermore, we analyzed outcomes for the rectal cancer by surgery type (LAR and APR), which, to our knowledge, has not been examined previously. While both groups were underpowered to achieve statistical significance, particularly the APR group, the observed outcomes were favorable, with trends toward improved postoperative outcomes. We believe the lack of statistical significance may be a type II error and as such, further studies exploring rectal cancer outcomes following ERP, with particular focus in tumor location, are warranted.

The primary outcome studied in the majority of ERP research has been length of stay. However, it has been argued that this metric may be neither the best nor most relevant outcome by which to evaluate ERP [15]. Furthermore, criticisms have been made that outcomes such as time to first flatus or bowel movement have little clinical relevance and instead outcomes of relevance to analgesia and surgical stress should be studied to achieve “pain and risk free” operations [16]. As a result, we included in our study the impact of ERP on cost and narcotic use. We found that the implementation of ERP for colon and rectal cancer patients was not associated with increased overall cost and believe financial concerns by hospital administration against ERP implementation to be largely unjustified. In fact, while total direct costs for colon cancer patients with ERP was slightly higher (+\$670 USD, $P = .82$), rectal cancer patients with ERP saw a substantial reduction in cost (−\$1228 USD, $P = .09$). Consistent with our data, King et al found that ERP among CRC patients had a positive impact on postoperative outcomes, with slightly decreased, though not statistically significant, costs [17]. These cost analyses support our group's recent publication reporting that among a heterogeneous colorectal patient population, ERP was associated with reduced costs [9].

Finally, our nation's opioid epidemic, and the role surgeons play in addressing this problem, mandate studying methods to achieve narcotic-free pathways [18]. To our knowledge, this is the first study to report substantial decreases in opioid use following ERP implementation. To put these findings into context, the 140 MME and 272 MME reductions in inpatient narcotic consumption observed for colon and rectal cancer patients following ERP translates to approximately 20 and 36 fewer 5 mg oxycodone tablets, respectively, during one's 3 to 4-day hospital stay. In addition, we observed a decreased need for narcotic refills within 30 days of discharge for colectomy patients.

There are several limitations to our study. First, it is retrospective and non-randomized and as such is prone to selection bias. We observed that the ERP cohort was slightly more comorbid with increased ASA, diabetes, and prior abdominal operations. Nonetheless, the post-ERP groups had similar or improved outcomes postoperatively, and thus, differences between groups play only a small role, if any, on our analysis. Second, our study design was an intention-to-treat approach without granular details on adherence to each element of the ERP. Consequently, we are unable to comment on the impact of which element had a positive, negative, or null effect on patient outcomes. Third, financial data reported by the hospital is limited to gross total direct and pharmacy costs. As such, we cannot directly parse out what contributes to cost changes following ERP implementation. Although overall costs were not increased, daily total and pharmacy costs increased as a result of ERP's reduction on patient length of stay. Fourth, we do not have details on the specific chemotherapy regimens used for each patient or timing to receipt of adjuvant therapy following surgery and cannot draw conclusions on the impact of ERP with regard to oncologic outcomes. However, all patients were treated by the same medical oncologists without changes in practice patterns before and after implementation of our ERP.

In conclusion, in this study, we found that the implementation of an ERP is safe and effective for patients with colorectal cancer undergoing elective resection at our institution. For both colon and rectal cancer patients, ERP was associated with reduced length of stay and decreased narcotic use, without an increase in postoperative complications. Moreover, total direct and pharmacy costs associated with ERP were not increased, suggesting that ERP in CRC patients should be considered for maximal patient benefit.

Author contribution

ARC, AK, and NCL contributed significantly with study design, data collection, data analysis, interpretation of results, and drafting of manuscript; ADJ and MCD contributed to data collection, interpretation of results, and revision of the manuscript; SAS and JFR contributed to interpretation of results and critical revision of the manuscript; IMP contributed to study design, interpretation of results, and drafting and revision of the manuscript.

Conflict of interest

The authors have no conflicts of interest to disclose.

Funding sources

This work received no financial support.

References

- [1] Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. *Ann Surg* Aug 2008;248(2):189–98.
- [2] Gustafsson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: enhanced recovery after surgery (ERAS((R))) society recommendations. *World J Surg* Feb 2013;37(2):259–84.
- [3] Carmichael JC, Keller DS, Baldini G, et al. Clinical practice guidelines for enhanced recovery after Colon and Rectal surgery from the American Society of Colon and Rectal Surgeons and Society of American Gastrointestinal and Endoscopic Surgeons. *Dis Colon Rectum* Aug 2017;60(8):761–84.
- [4] Hendren S, Birkmeyer JD, Yin H, Banerjee M, Sonnenday C, Morris AM. Surgical complications are associated with omission of chemotherapy for stage III colorectal cancer. *Dis Colon rectum* Dec 2010;53(12):1587–93.
- [5] Tevis SE, Kohnhofer BM, Stringfield S, et al. Postoperative complications in patients with rectal cancer are associated with delays in chemotherapy that lead to worse disease-free and overall survival. *Dis Colon rectum* Dec 2013;56(12):1339–48.
- [6] Mirnezami A, Mirnezami R, Chandrakumaran K, Sasapu K, Sagar P, Finan P. Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak: systematic review and meta-analysis. *Ann Surg* May 2011;253(5):890–9.
- [7] Aoyama T, Oba K, Honda M, et al. Impact of postoperative complications on the colorectal cancer survival and recurrence: analyses of pooled individual

- patients' data from three large phase III randomized trials. *Cancer Med* Jul 2017; 6(7):1573–80.
- [8] Midura EF, Jung AD, Hanseman DJ, et al. Combination oral and mechanical bowel preparations decreases complications in both right and left colectomy. *Surgery* Mar 2018;163(3):528–34.
- [9] Jung AD, Dhar VK, Hoehn RS, et al. Enhanced recovery after colorectal surgery: can we afford not to use it? *J Am Coll Surg* Apr 2018;226(4):586–93.
- [10] Group EC. The impact of enhanced recovery protocol compliance on elective colorectal Cancer resection: results from an international registry. *Ann Surg* Jun 2015; 261(6):1153–9.
- [11] Spanjersberg WR, Reurings J, Keus F, van Laarhoven CJ. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database Syst Rev* Feb 16 2011;2:CD007635.
- [12] Adamina M, Kehlet H, Tomlinson GA, Senagore AJ, Delaney CP. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. *Surgery* Jun 2011;149(6):830–40.
- [13] Ota H, Ikenaga M, Hasegawa J, et al. Safety and efficacy of an "enhanced recovery after surgery" protocol for patients undergoing colon cancer surgery: a multi-institutional controlled study. *Surg Today* Jun 2017;47(6):668–75.
- [14] Khoo CK, Vickery CJ, Forsyth N, Vinnall NS, Eyre-Brook IA. A prospective randomized controlled trial of multimodal perioperative management protocol in patients undergoing elective colorectal resection for cancer. *Ann Surg* Jun 2007;245(6):867–72.
- [15] Maessen JM, Dejong CH, Kessels AG, von Meyenfeldt MF. Enhanced recovery after surgery G. length of stay: an inappropriate readout of the success of enhanced recovery programs. *World J Surg* Jun 2008;32(6):971–5.
- [16] Slim K, Kehlet H. Commentary: fast track surgery: the need for improved study design. *Color Dis* Aug 2012;14(8):1013–4.
- [17] King PM, Blazeby JM, Ewings P, et al. The influence of an enhanced recovery programme on clinical outcomes, costs and quality of life after surgery for colorectal cancer. *Colorectal Dis* Jul 2006;8(6):506–13.
- [18] Theisen K, Jacobs B, Macleod L, Davies B. The United States opioid epidemic: a review of the surgeon's contribution to it and health policy initiatives. *BJU Int* Nov 2018;122(5):754–9.