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Impact of adherence to care pathway interventions on recovery following bowel resection within an established enhanced recovery program

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Abstract

Introduction Guidelines recommend incorporation of more than 20 perioperative interventions within an enhanced recovery program (ERP). However, the impact of overall adherence to the pathway and the relative contribution of each intervention are unclear. The aim of this study was to estimate the extent to which adherence to ERP elements is associated with outcomes and identify key ERP elements predicting successful recovery following bowel resection.

Methods Prospectively collected data entered in a registry specifically designed for ERPs were reviewed. Patients undergoing elective bowel resection between 2012 and 2014 were treated within an ERP comprising 23 care elements. Primary outcome was successful recovery defined as the absence of complications, discharge by postoperative day 4 and no readmission. Secondary outcomes were length of hospital stay (LOS), 30-day morbidity, and severity (Comprehensive complication index, CCI, 0–100). Regression analyses were adjusted for potential confounders.

Results A total of 347 patients were included in the study. Median primary LOS was 4 days (IQR 3–7). Patients were adherent to median 18 (IQR 16–20) elements. A total of 156 (45 %) patients had successful recovery. Morbidity occurred in 175 (50 %) patients with median CCI 8.6 (IQR 0–22.6). There was a positive association between adherence and successful recovery (OR 1.39 for every additional element, $p < 0.001$), LOS (11 % reduction for every additional element, $p < 0.001$), 30-day postoperative morbidity (OR 0.78, $p < 0.001$), and the CCI (17 % reduction, $p < 0.001$). Laparoscopy (OR 4.32, $p < 0.001$), early mobilization out of bed (OR 2.25, $p = 0.021$), and early termination of IV fluid infusion (OR 2.00, $p = 0.013$) significantly predicted successful recovery. These factors were also associated with reduced morbidity and complication severity.

Conclusions Increased adherence to ERP interventions was associated with successful early recovery and a reduction in postoperative morbidity and complication severity. In an established ERP where overall adherence was high, laparoscopic approach, perioperative fluid management, and patient mobilization remain key elements associated with improved outcomes.

Keywords Postoperative recovery · Postoperative complications · Length of stay · Outcome and process assessment (health care) · Colorectal surgery · Laparoscopy

Enhanced recovery programs (ERPs) incorporate multiple evidence-based interventions aiming to reduce the metabolic stress occurring during surgery, but also to organize care for patients undergoing a particular procedure by

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limiting unwanted variability in care processes [1]. Guidelines from the ERAS® society recommend the implementation of more than 20 perioperative care components for patients undergoing colorectal surgery [2]. However, compared to traditional care, ERPs have been shown to consistently improve postoperative outcomes regardless of the number, the type, the combination, or the level of evidence of the elements used [3]. Furthermore, each intervention adds complexity to the pathway and may require additional resources.

Monitoring care process to evaluate the quality of perioperative care may be especially relevant for procedures in which serious postoperative events such as reoperation or mortality are rare, as in case for colectomy [4]. In the context of enhanced recovery, the impact of overall adherence to care processes, namely ERP elements, and the relative contribution of each intervention to patient recovery are still questioned. To date, there is preliminary evidence that adherence to care processes is associated with improved patient recovery [5–9]. However, existing reports mainly dealt with early phases of protocol implementation in which overall adherence was low [7], or failed to take into account important confounding factors such as postoperative morbidity [9]. The McGill University Health Centre first implemented an ERP for colorectal patients in 2006 [10] and is currently running a well-established care pathway incorporating a large number of perioperative interventions, which reduces hospital stay and societal costs compared to usual care [11].

The objective of this study was to estimate, in patients enrolled in an established ERP, to what extent the degree of adherence with ERP interventions impacts on recovery after surgery, and to identify which elements are associated with postoperative outcomes.

Methods

This study was designed and reported following the STROBE guidelines for the conducting and reporting of observational cohort studies [12].

Study design

This is a retrospective review of a prospectively collected database including patients undergoing elective bowel surgery treated within an ERP in a university-affiliated tertiary teaching institution. Study approval was granted by the institutional review board (14-170-SDR). Patients who underwent scheduled bowel resection between September 2012 and December 2014 were identified from the institutional operating room database and cross-checked with a prospective database specifically designed to capture adherence to ERP care processes and postoperative outcomes. Patients not followed prospectively by a clinical auditor were excluded from the study.

Enhanced recovery program

In 2006, an ERP for selected patients undergoing laparoscopic colorectal resection was first introduced in our institution [10]. In August 2010, this ERP was modified to include a total of 23 perioperative care components (Table 1) and was extended to all patients undergoing elective bowel resection [13].

Patients were admitted to hospital on the day of surgery. All cases were performed by one of three fellowship-trained colorectal surgeons (BS, ASL, PC). Discharge was planned for postoperative day (POD) 3 or earlier if patients achieved the following discharge criteria: tolerance of oral intake, recovery of gastrointestinal function (i.e., passage of flatus), adequate pain control with oral analgesia, ability to mobilize and self-care, and no evidence of complication or untreated medical problems. Final decision on discharge remained at the individual surgeon's discretion.

Data collection

From September 2012 a dedicated, trained clinical auditor prospectively collected patient data up until 30 days after surgery. Data were entered into the ERAS Interactive Audit System (http://www.erassociety.org, ENCARE, Kista, Sweden), an international web-based registry that was specifically designed for interactive audit and research. Each patient data field contained approximately 140 different variables including preoperative patient characteristics, operative data, adherence to perioperative care processes, and postoperative outcomes. Every 3–4 months, the auditor reviewed adherence and outcome data with the ERP team and discussed any new trend or issue arising from the latest time period. A clinical researcher unaware of patient's adherence to ERP components verified postoperative outcome data for each patient by reviewing medical charts and the electronic medical record. Additional information was retrieved from medical records to compute Charlson comorbidity index [14], CR-POSSUM score [15], Apfel postoperative nausea and vomit (PONV) risk score [16], and the comprehensive complication index (CCI) [17], which were not originally included in the ERAS audit system.

Adherence and outcome measures

Adherence to each ERP component was defined as the successful completion of a planned intervention (e.g., a patient planned to have regular food on POD 1 actually

Table 1 Perioperative care ERP interventions and definition of adherence

ERP intervention	Definition of adherence
Preoperative	
Preadmission education	Patient received preoperative counseling from a nurse and a physician, and a dedicated booklet including information on recovery goals and expectation about hospital stay
Selective MBP	No MBP used for colonic resection. MBP used for patients with a planned stoma formation during rectal resection
Carbohydrate loading	Intake of a preoperative carbohydrate drink up until 2 h before anesthesia with at least 50 g carbohydrate in at least 400 mL fluid
No long-acting sedation	No long-acting sedating medication used before surgery (e.g., opioids, antihistamines, benzodiazepines)
Intraoperative	
Antibiotic prophylaxis	Antibiotic prophylaxis completed prior to surgical incision
Epidural anesthesia	Thoracic epidural analgesia started before surgical incision
Laparoscopic approach	Successfully completed laparoscopic resection
Balanced intravenous fluids	Intraoperative maintenance fluids excluding replacement of blood loss: for laparoscopy <3 ml/kg/h; for open < 5 ml/kg/h
	If bowel preparation is used an extra 1000 ml of fluid is administered to cover losses
PONV prophylaxis	Multimodal prophylaxis administered according to Apfel score [16]
No abdominal or pelvic drainage	No resection-site drainage used
Normothermia	Body temperature measured at the end of surgery ≥36.0 °C
TED prophylaxis	TED prophylaxis with low molecular weight heparin
Avoidance of nasogastric tube	Nasogastric tube removed at the end of general anesthesia
Postoperative	
Opioid-sparing multimodal analgesia	Use of opioid-sparing strategies including thoracic epidural analgesia, abdominal trunk blocks, acetaminophen, NSAIDs
Oral liquids on POD 0	Patient received clear liquids on the day of surgery postoperatively
Oral nutritional supplements on POD 0	Patient received one or more nutritional drinks on the day of surgery postoperatively
Early mobilization out of bed	Patient mobilized out of bed within the first 24 h after surgery
Early termination of IV fluid infusion	Termination of intravenous fluid infusion by the morning of POD 1
Early termination of urinary drainage	Removal of urinary catheter by POD 1
Free diet on POD 1	Patient received at least one meal with regular food by POD 1
Chewing gum	Patient chewing gum at least three times a day for 30 min starting by POD 1
Laxative	Laxative medication (e.g., magnesium hydroxide) started by POD 1
Transition to oral analgesia by POD 2	Successful termination of thoracic epidural analgesia or PCA and transition to oral analgesics by POD 2

POD postoperative day, *MBP* mechanical bowel preparation, *PONV* postoperative nausea and vomiting, *NSAIDs* nonsteroidal anti-inflammatory drugs, *TED* thromboembolic disease, *PCA* patient-controlled analgesia

receives a meal and consumes it). Definitions for each measure of adherence can be found in Table 1. Adherence to intraoperative intravenous infusions followed recent recommendations [18], taking into consideration the patient ideal body weight, use of mechanical bowel preparation (MBP), surgical approach, duration of surgery and blood loss. Cutoffs for adherence were set at <3 ml/kg/h for laparoscopic surgery and <5 ml/kg/h for open surgery. Adherence to PONV prophylaxis considered patients Apfel score in accordance with consensus guidelines [19]. Overall adherence to the ERP was also calculated for each patient.

Primary outcome measure of the study was successful recovery, a composite end point defined as discharge by POD 4, no occurrence of complications or hospital readmission within 30 days of operation. Secondary outcomes of the study included length of primary hospital stay (LOS), 30-day postoperative morbidity, and the

comprehensive complication index (CCI). LOS was defined as the number of nights spent in hospital during the primary stay from the day of admission to the day of discharge. Intraoperative and postoperative complications were defined a priori (Supplementary Material 1). The severity of each complication was graded according to the Dindo–Clavien classification [20], and a CCI was then generated for each patient. This is a validated measure summarizing the complete spectrum of complications occurred and their severity in a single score ranging from 0 to 100 [17].

Statistical analysis

We performed a complete case analysis including patients with data for all ERP adherence variables and outcome measures. Relevant characteristics of the included patients and those excluded from the study were compared using Chi-square test or Fisher's exact test for categorical data, and Student's *t* test or Mann–Whitney *U* test for continuous data, as appropriate.

Univariate analysis (i.e., logistic regression for binary outcomes and linear regression for continuous outcomes) was performed to assess the association of patient or procedure-related variables and ERP interventions with outcomes. To identify ERP elements independently associated with the outcomes of interest, we used binary logistic regression (for the outcomes successful recovery and occurrence of 30-day complications) and linear regression (for log-transformed LOS and log-transformed 30-day CCI). Variables significant at $p < 0.10$ were retained in the final model. Only early postoperative elements (up to POD1) were considered in the analysis because it is difficult to distinguish whether adherence to late care processes are indicators or predictors of poor recovery outcomes. In example, delayed transition to oral analgesia can be a consequence of adverse events leading to poor recovery, and not a cause. In the same way, patient mobilization on late postoperative days represents an outcome rather than indicate the adherence to a care process. In fact, both ability to mobilize and pain control with oral analgesia represent discharge criteria. To evaluate the impact of overall adherence to the pathway (i.e., the overall number of ERP elements to which a patient was adherent) on outcomes, we also ran multivariate analyses adjusted for confounding factors.

All multivariate models were adjusted for relevant prognostic factors known to affect patient adherence and postoperative outcomes such as age, gender, preoperative American Society of Anesthesiologists (ASA) score, pelvic surgery and inflammatory bowel disease [21].

According to previous research, between 5 and 10 events per independent variable are required to obtain reliable regression coefficients in multivariate logistic regression models [22], and a minimum of 15 subjects per variable are required for linear regression [23]. As ERP elements may be highly correlated with one another, the risk of multicollinearity was assessed by inspecting correlation matrices between independent variables and by computing the variance inflation factor (VIF). VIF values exceeding 10 indicate serious multicollinearity, and values greater than 4 may be a cause for concern [24]. The discriminative power of the logistic model equations was determined by running a receiver operating characteristic (ROC) curve, and by calculating the relative area under the curve (AUC). The goodness-of-fit of the predictive models was assessed through the Hosmer–Lemeshow test.

Because of the confounding effect of intra- and postoperative complications on adherence to ERP components, we also performed a sensitivity analysis excluding patients who experienced intraoperative or early postoperative complications (before POD 2).

Descriptive data are reported as mean (95 % confidence interval, CI), or median (interquartile range, IQR), otherwise specified. Statistical analysis was performed using STATA® version 13.1 software (StataCorp, College Station, TX, USA). All statistical tests were 2-sided, a "*p*" value < 0.05 was considered to indicate statistical significance.

Results

Four hundred and forty patients underwent scheduled bowel resection during the study period. Ninety-three (21 %) patients were excluded from the analysis because they were not followed prospectively through the ERAS interactive audit system. The remaining 347 patients were included in this study. Included and excluded patients had similar demographic and clinical features (Supplementary Material 2).

Table 2 shows baseline characteristics of patients included in the study. One hundred twelve (32 %) patients had a low preoperative physical status as measured by ASA score. Two hundred twenty-eight (66 %) patients were operated for malignancy, 125 of which (55 %) had localized colorectal cancer (TNM stage 0–II).

Table 3 includes patients' operative characteristics. One hundred eighty-two (52 %) patients underwent segmental colonic resection, while 121 (35 %) patients underwent pelvic surgery including low anterior resection, abdominoperineal resection and total proctocolectomy. Two hundred seventy-eight (80 %) patients were approached with laparoscopy, 28 (8 %) required conversion to an open procedure. Intraoperative complications occurred in 25 (7 %) patients.

Table 2 Patient characteristics

Variables	$n = 347$
Age (years), mean (95 % CI)	63.2 (61.6–64.8)
75+ years old	81 (23)
Gender (male/female)	179: 168 (52:48)
BMI (kg/m^2), mean (95 % CI)	26.2 (25.7–26.7)
Obesity (BMI $\geq$ 30)	73 (21)
Medically treated diabetes	46 (13)
Immunosuppressant use within 6 months	18 (5)
Neoadjuvant chemotherapy	42 (12)
Previous radiotherapy to operating field	41 (12)
Previous abdominal surgery	151 (44)
Received multimodal prehabilitation	45 (13)
ASA score	
I–II	235 (68)
III–IV	112 (32)
Apfel PONV risk score	
0–1	149 (43)
2–4	198 (57)
Charlson Comorbidity Index, mean (95 % CI)	2.1 (1.9–2.3)
CR-POSSUM physiologic score, median (IQR)	9 (7–10)
CR-POSSUM operative severity, median (IQR)	8 (7–11)
Diagnosis	
Malignancy	228 (66)
CRC TNM stage 0–II	125 (55)*
CRC TNM stage III	83 (36)*
CRC TNM stage IV	18 (8)*
Other malignancy	2 (1)*
Inflammatory bowel disease	49 (14)
Diverticular disease	28 (8)
Other benign disease	42 (12)

Values are number of patients (%) otherwise noted; *BMI* body mass index, *ASA* American Society of Anesthesiologists, *PONV* postoperative nausea and vomiting, *CRC* colorectal cancer, *TNM* tumor node metastasis

* Percentage relative patients with malignancy only

Table 3 Operative characteristics

Variables	$n = 347$
Procedure performed	
Small bowel resection	9 (3)
Ileocecal resection	9 (3)
Right hemicolectomy	103 (30)
Left hemicolectomy	22 (6)
Rectosigmoidectomy	57 (16)
Subtotal/Total colectomy	15 (4)
Low anterior resection	78 (22)
Abdominoperineal resection	20 (6)
Total proctocolectomy ± IPAA	23 (7)
Other colorectal procedure*	11 (3)
Associated major procedures	10 (3)
Surgical approach	
Open	69 (20)
Laparoscopic	250 (72)
Laparoscopic converted to open	28 (8)
New stoma formation	90 (26)
Duration of surgery (minutes), median (IQR)	184 (136–261)
Blood loss (ml), median (IQR)	100 (100–300)
Intraoperative fluid infusion, mean (95 % CI)	
Overall (ml)	2105 (1973–2237)
Maintenance fluids (ml/kg per hour)	7.4 (6.8–8)
Use of vasopressors	34 (10)
Main type of anesthesia	
Inhalational	320 (92)
TIVA	27 (8)
Intraoperative complications	
Clinically significant hemorrhage	16 (5)
Cardiac or respiratory complication	4 (1)
Bowel injury	3 (1)
Urinary tract injury	1 (0)
Other	3 (1)
Late discharge from PACU (after 6 pm)	105 (30)

Values are number of patients (%) otherwise noted; *TIVA* total intravenous anesthesia, *IPAA* ileal pouch–anal anastomosis, *PACU* post-anesthesia care unit

* Includes reversal of Hartmann's procedure ($n = 5$), takedown of end ileostomy + ileorectal anastomosis ($n = 3$), enterocutaneous fistula repair ($n = 1$), and fashioning of diverting transverse colostomy ($n = 1$)

Table 4 shows adherence rates for single ERP elements. Overall, patients were adherent to median 18 (16–20) elements. Median adherence was similar for preoperative, intraoperative, and postoperative elements (75, 78, and 80 percent, respectively). The only elements with poor adherence (<50 %) were intraoperative balanced intravenous infusions and intake of oral nutritional supplementation on the day of surgery postoperatively.

Table 5 reports postoperative outcomes. One hundred fifty-six (45 %) patients had a successful recovery with early discharge, no readmission and no complications. Median length of primary hospital stay was 4 days (3–7); 135 (39 %) patients were discharged within the third day after surgery. One hundred seventy-five (50 %) patients experienced at least one complication within 30 days after surgery, and 56 (16 %) patients were treated for a complication after discharge. Hospital readmissions at 30-days occurred in 44 (13 %) patients. Most common reasons for readmission were intraperitoneal or pelvic abscess ($n = 10$, 23 %), bowel obstruction ($n = 7$, 16 %), anastomotic leak ($n = 6$, 14 %), and other gastrointestinal complications ($n = 6$, 14 %).

Table 4 Patient compliance to enhanced recovery program elements

Enhanced recovery program element	$n = 347$
Preoperative	
Preadmission education	347 (100)
Selective MBP	246 (71)
Carbohydrate loading	213 (61)
No long-acting sedation	347 (100)
Intraoperative	
Antibiotic prophylaxis	345 (99)
Epidural anesthesia	253 (73)
Laparoscopic approach	250 (72)[†]
Balanced IV fluids	90 (26)
PONV prophylaxis	320 (92)
Normothermia	223 (64)
Avoidance of abdominal or pelvic drainage	298 (86)
TED prophylaxis	346 (100)
Avoidance of nasogastric tube	344 (99)
Postoperative	
Opioid-sparing multimodal analgesia	341 (98)
Oral liquids on POD 0	309 (89)
Oral nutritional supplements on POD 0	146 (42)
Early mobilization out of bed	275 (79)
Early termination of IV fluid infusion	201 (58)
Early termination of urinary drainage	298 (86)
Free diet on POD 1	282 (81)
Chewing gum	217 (63)[‡]
Laxative	210 (61)
Transition to oral analgesia by POD 2	255 (73)

Values are number of patients (%)

MBP mechanical bowel preparation, *IV* intravenous, *PONV* postoperative nausea and vomit, *TED* thromboembolic disease, *POD 0* postoperatively on day of surgery, *POD 1* postoperative day 1, *POD 2* postoperative day 2

[†] Refers to successful completion of laparoscopic resection

[‡] Missing data for 108 patients (31 %)

The impact of overall adherence on outcomes

Figure 1 shows the significant association between overall adherence to ERP elements and recovery outcomes. There was a positive association between adherence and successful recovery (adjusted OR 1.39 (95 % CI 1.24–1.57) for every additional element, $p < 0.001$). An inverse relationship was found between adherence and LOS (11 % reduction, 95 % CI −14 to −8 %, $p < 0.001$), 30-day postoperative morbidity (OR 0.78, 95 % CI 0.70–0.87, $p < 0.001$), and the CCI (17 % reduction, 95 % CI −23 to −10 %, $p < 0.001$). There was no association between overall adherence to ERP and hospital readmission (adjusted OR 1.03 (95 % CI 0.89–1.18) for every additional element, $p = 0.726$).

Predictors of recovery outcomes

Table 6 reports univariate logistic regression for predictors of successful recovery including patient- and procedure-related confounding factors such as age, gender, ASA score, type of surgery, and intraoperative complications. At multivariate analysis (Table 7), laparoscopy (OR 4.32, 95 % CI 2.26–8.27, $p < 0.001$), early mobilization out of bed (OR 2.25, 95 % CI 1.13–4.47, $p = 0.021$), and early termination of IV fluid infusion (OR 2.00, 95 % CI 1.16–3.45, $p = 0.013$) were significantly associated with successful recovery. These factors were also key elements associated with reduction in LOS, 30-day postoperative morbidity and complication severity index as measured by the CCI. In addition, intraoperative balanced IV fluids were associated with a 21 % reduction in LOS, while epidural anesthesia prolonged LOS by 19 %.

Sensitivity analysis

Excluding patients who experienced intraoperative or early complications ($n = 71$), the positive association between overall adherence to the pathway and successful recovery remained significant (OR 1.37 (95 % CI 1.20–1.57) for every additional element, $p < 0.001$). At multivariate analysis, laparoscopy (OR 4.61, 95 % CI 2.28–9.33, $p < 0.001$) and early mobilization (OR 2.22, 95 % CI 1.06–4.66, $p = 0.035$) were the only factors significantly associated with successful recovery.

Discussion

This study relying on prospectively collected data in a tertiary Canadian university hospital showed that increased adherence to ERP interventions is independently associated with successful recovery, reduced LOS, and complications following bowel surgery. In this large series of patients treated between 2012 and 2014, where mean adherence to the pathway was high, laparoscopic surgery, early mobilization out of bed, and perioperative fluid management resulted as key elements correlating with improved postoperative outcomes.

When compared to traditional perioperative care, ERPs in colorectal surgery have been shown to improve postoperative outcomes in terms of accelerating recovery, reducing LOS, medical complications [25], and societal costs [11]. Positive results for ERPs seem to be achieved regardless of the number, type, or the combination of interventions implemented in different series [3]. This may suggest that it is not the effect of single ERP elements or the number of elements, but simply the coordination of care into an organized pathway that reduces variability and

Table 5 Postoperative recovery outcomes

Variables	$n = 347$
Successful recovery*	156 (45)
Length of primary hospital stay, median days (IQR)	4 (3–7)
Length of total hospital stay, median days (IQR)	4 (3–9)
30-day postoperative complications at all	175 (50)
During primary stay	146 (42)
Post-discharge	56 (16)
Timing of first complication (hours), median (IQR)	39 (19–80)
Within 24 h postoperatively	60 (17)
Type of postoperative complications	
Medical complications	93 (27)
Cardiovascular	20 (6)
Respiratory	21 (6)
Other	69 (20)
Infectious complications	72 (21)
Surgical complications	110 (32)
Anastomotic leak	18 (5)
Bleeding	13 (4)
Ileus	71 (20)
Other	19 (5)
30-day reoperations	19 (5)
30-day severe complications (Clavien III-V)	43 (12)
30-day comprehensive complication index, median (IQR)	8.6 (0–22.6)
30-day emergency department visits	68 (20)
30-day hospital readmissions	44 (13)

Values are number of patients (%) otherwise noted; POD, postoperative day; IQR (25th percentile–75th percentile). Single complications do not add up to the total number of complications as patients may have more than one complication

* Defined as length of primary hospital stay $\leq$ 4 days, no 30-day postoperative complications, and no hospital readmissions

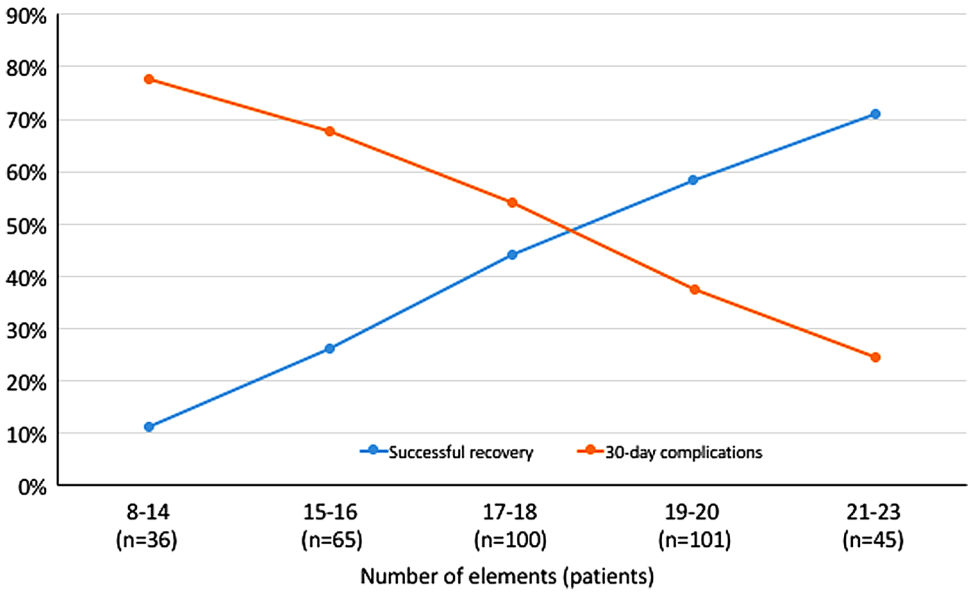

Fig. 1 Relationship between overall adherence to enhanced recovery pathway elements, successful recovery and 30-day complications

Table 6 Univariate analysis for predictors of successful recovery defined as discharge home by postoperative day 4, no 30-day morbidity, and no hospital readmission

Variables	Univariate analysis		
	OR	95 % CI	*p* value
Patient characteristics			
Age ≥ 75 years	0.570	0.340–0.955	0.033
Male gender	0.673	0.440–1.029	0.068
Obesity (BMI ≥ 30)	1.203	0.744–2.094	0.400
ASA physical status 3+	0.403	0.251–0.651	<0.001
Charlson comorbidity index 3+	0.529	0.321–0.868	0.012
Previous abdominal surgery	0.442	0.285–0.685	<0.001
Inflammatory bowel disease	0.491	0.257–0.940	0.032
Procedural factors			
Pelvic surgery	0.495	0.313–0.782	0.003
New stoma	0.370	0.219–0.623	<0.001
Intraoperative complications	0.213	0.072–0.635	0.005
Late discharge from PACU (after 6 pm)	0.647	0.419–1.067	0.091
Enhanced recovery elements			
Selective MBP	1.082	0.679–1.727	0.738
Carbohydrate loading	1.295	0.837–2.005	0.246
Epidural anesthesia	0.564	0.350–0.909	0.019
Laparoscopic surgery	4.977	2.843–8.712	<0.001
Intraoperative balanced IV fluids	1.033	0.638–1.673	0.894
Selective PONV prophylaxis	0.741	0.337–1.626	0.455
Normothermia	0.693	0.455–1.077	0.103
Avoidance of abdominal drainage	3.274	1.612–6.649	0.001
Oral liquids on POD 0	5.031	2.046–12.376	<0.001
Oral nutritional supplements on POD 0	1.492	0.971–2.292	0.068
Early mobilization out of bed	3.022	1.686–5.416	<0.001
Early termination of IV fluid infusion	2.917	1.860–4.575	<0.001
Early termination of urinary drainage	5.057	2.293–11.151	<0.001
Free diet on POD 1	3.695	1.957–6.978	<0.001
Chewing gum	1.381	0.889–2.145	0.151
Laxative	1.686	1.087–2.617	0.020

BMI body mass index, *ASA* American Society of Anesthesiologists, *PACU* post-anesthesia care unit, *MBP* mechanical bowel preparation, *PONV* postoperative nausea and vomit, *POD* postoperative day

is sufficient to improve outcomes. In our study, we assessed the relationship between adherence to ERP elements and postoperative results and identified key processes facilitating recovery in order to consider whether additional resources should be allocated to increase adherence to those elements (e.g., dedicated personnel for patient mobilization).

In previous series, adherence was usually lower for postoperative elements [7, 8, 26]. In fact, compliance with postoperative interventions may be influenced by patient symptoms and by the occurrence of complications. In the current series, adherence was high and similar throughout the different perioperative phases reflecting a well-organized and established clinical pathway. In addition, only early postoperative interventions (i.e., within the first 24 h) were considered in the analysis to limit the potential influence of adverse events on adherence. Low adherence was found for intraoperative fluid infusions and intake of oral nutritional supplements on the day of surgery postoperatively. The former may be related to the lack of a specifically dedicated anesthesia team for colorectal surgery but also to the adoption of a strict definition of adherence following recently published guidelines [27]. The latter represents an organizational problem (e.g., product availability, patient arriving to the surgical ward late in the day). Both elements represent targets for improvement.

Gustafsson and colleagues [7] previously demonstrated that adherence to more than 70 % of the planned care processes was associated with lower morbidity and shorter

Table 7 Multivariate regression models for independent predictors of successful recovery, length of primary hospital stay, 30-day morbidity, and 30-day comprehensive complication index

Outcome measure	Adjusted multivariate models*		
Enhanced recovery program element	OR†/Beta‡	95 % CI	*p* value
Successful recovery[a]			
Laparoscopic surgery	4.322†	2.260 to 8.267	<0.001
Early mobilization out of bed	2.249†	1.130 to 4.474	0.021
Early termination of IV fluid infusion	1.997†	1.158 to 3.445	0.013
Early termination of urinary drainage	2.365†	0.956 to 5.854	0.063
Free diet on POD 1	2.045†	0.952 to 4.393	0.067
Length of primary hospital stay			
Epidural anesthesia	0.186‡	0.034 to 0.339	0.017
Laparoscopic surgery	−0.326‡	−0.481 to −0.172	<0.001
Intraoperative balanced IV fluids	−0.214‡	−0.363 to −0.066	0.005
Early mobilization out of bed	−0.241‡	−0.403 to −0.079	0.004
Early termination of IV fluid infusion	−0.293‡	−0.436 to −0.149	<0.001
30-day morbidity[b]			
Laparoscopic surgery	0.253†	0.140 to 0.456	<0.001
Early mobilization out of bed	0.504†	0.268 to 0.948	0.033
Early termination of IV fluid infusion	0.501†	0.302 to 0.830	0.007
30-day comprehensive complication index			
Laparoscopic surgery	−0.874‡	−1.123 to −0.521	<0.001
Intraoperative balanced IV fluids	−0.542‡	−0.675 to 0.019	0.064
Early mobilization out of bed	−0.443‡	−0.820 to −0.065	0.022
Early termination of IV fluid infusion	−0.859‡	−0.859 to −0.226	0.001

* All models were adjusted for age, gender, ASA score ≥3, pelvic surgery, inflammatory bowel disease

[a] Model statistics: discriminative power AUC: 0.793; Hosmer–Lemeshow goodness-of-fit test $p = 0.626$

[b] Model statistics: discriminative power AUC: 0770; Hosmer–Lemeshow goodness-of-fit test $p = 0.451$

LOS compared to lower adherence. However, they used arbitrary adherence thresholds and did not adjust for the confounding effect of postoperative complications. In our series, patients with higher adherence to the pathway had a greater chance of a successful recovery. In fact, we found a strong association between adherence and outcomes even when patients experiencing intraoperative or early morbidity where excluded from the analysis. For every additional element to which patients were compliant, LOS and 30-day morbidity decreased, confirming results from a large UK study [9] that found a significant inverse relationship between the mean adherence to the ERP and LOS in multiple surgical subspecialties. In our analysis, we chose a composite end point as a proxy for successful postoperative recovery, taking into account not only primary hospital stay and morbidity but also hospital readmission, which is a key post-discharge outcome associated with delayed patient recovery and increased healthcare costs [28]. The use of LOS as measure of postoperative recovery is debated as it may be influenced by non-clinical factors such as surgeon's preference and hospital tradition [29]. An alternative and valid measure of short-term postoperative recovery could have been the time to readiness for discharge (i.e., the time to achieve standardized discharge criteria) [30], but this variable was not part of our database and could not be reliably collected retrospectively.

It is still unclear whether there is an ideal combination of perioperative interventions, or whether there are single items with a greater impact on recovery within an ERP. In a study including mostly open colonic surgery [5], early mobilization, urinary catheter removal, and early oral diet were found as independent predictors of early discharge. However, the lengthy study period including a phase of implementation and the lack of controlling for confounding factors and postoperative complications is a potential source of bias. In a recent multicenter study by the ERAS compliance group [6], where only preoperative and intraoperative items were considered, carbohydrate loading, laparoscopy and restrictive intravenous fluids were found as independent factors associated with reduced LOS and morbidity, while epidural analgesia delayed discharge. In our cohort, laparoscopic approach, early mobilization and discontinuation of intravenous fluids were key elements associated with successful recovery and reduced 30-day morbidity and complication severity. Epidural analgesia

was the only ERP element delaying discharge, corroborating recent evidence from a randomized controlled trial [31]. For laparoscopic colorectal surgery within an ERP, the use of transversus abdominis plane blocks has been proposed as a new opioid-sparing strategy to prevent epidural catheter management issues that may delay discharge [32].

Research shows that laparoscopy in the context of ERPs is associated with reduced pain, ileus [33], and attenuated inflammatory response [34] compared to open surgery. Evidence supports that the combination of laparoscopy and enhanced recovery is associated with improved outcomes. However, ERPs significantly reduce the gap in postoperative results between open and minimally invasive surgery [35]. Early mobilization after surgery is considered a key component of ERPs. It is well known that staying in bed leads to deconditioning that can largely be prevented by physical activity [36]. However, there is little evidence that the implementation of specific interventions to increase mobilization improves outcomes [37]. In our analysis, simply mobilizing out of bed once on the first day after surgery was a significant predictor of early discharge and reduced morbidity. Future studies are warranted to clarify the impact of mobilization on postoperative recovery and verify whether there is a dose–effect relationship.

Adherence to postoperative elements of the pathway may be difficult to interpret as it is confounded by the patient's recovery status. For example, a patient symptomatic for postoperative ileus is less likely to start early oral nutrition and feel like ambulating. Thus, in our regression models, we only considered early postoperative elements (up to 24 h after surgery) that are potentially less influenced by the development of complications and also performed a sensitivity analysis excluding patients with intraoperative or early postoperative morbidity as previously reported by Larson et al. [8]. In this analysis, laparoscopy and early mobilization remained significant factors associated with successful recovery.

Notably, post-discharge complications occurred in 16 % of our cohort resulting in a considerable number of patients returning to the emergency department (ED) (20 %) and eventually being readmitted (13 %). These results corroborate with recent enhanced recovery colorectal surgery series where hospital readmissions ranged between 9 and 13 % [35, 38, 39]. In a previous study, compliance to ERP greater than 93 % was found as a protective factor for readmission [38]. In our series, adherence to ERP had no effect on post-discharge outcomes. More than half of emergency visits resulted in hospital readmission, mostly because of late infectious and surgical complications requiring in hospital management. Patients who returned to the ED but were not readmitted represent a target for quality improvement, as they could have been managed in an outpatient setting or through the local community services or family physicians. Patient information regarding post-discharge care can certainly be improved. In addition, establishing a dedicated follow-up service may also be considered in order to anticipate any serious clinical issue or to prevent unnecessary ED visits.

Strengths and limitations

Although data were prospectively collected and patients were followed by an independent auditor not involved in clinical activities, this analysis carries intrinsic limitations of all observational studies. Sample size may be considered insufficient for the regression analysis we carried out because of the high number of predictors included. However, we limited our series to two consecutive years to avoid time-related bias since ERPs are constantly evolving through time, and new elements are added or removed according to the evidence. Around 20 % of patients who underwent colorectal resection in our institution in the target period were not included in this series as their data were not prospectively collected. These patients were randomly missed because of personnel unavailable to record data. While retrospective chart review can provide reliable postoperative outcome data, it does not provide patient-reported information regarding adherence. Thus, it was decided to exclude these patients from the study to ensure a high quality of the data. Notably, no difference in preoperative characteristics and postoperative outcomes was found between included and excluded patients.

Main strengths of this study were that it followed recent recommendations for reporting and used clear definitions of adherence and outcome measures [40]. In fact, most of the existing works on enhanced recovery fail to thoroughly report the definitions of adherence to each implemented interventions. Other strengths and unique features of this study include the use of sensitivity analysis, and the choice of a composite end point encompassing different clinically relevant recovery outcomes allowing us to better ascertain the role of adherence to ERP elements and its association with postoperative results. Furthermore, all multivariate models were adjusted for relevant factors influencing adherence and postoperative outcomes including patient comorbidities and procedural factors as previously described [21, 41].

The findings of this study confirm the positive impact of ERP interventions on recovery and suggest that auditing adherence to the pathway is a key metric to assess the effectiveness of an ERP. Our results should encourage the allocation of resources toward strategies likely to increase adherence. For example, adopting a structured pathway for all bowel resection patients with standardized sets of perioperative clinical orders minimizes the variability of

patient care favoring adherence to care processes. In addition, reinforcing perioperative education and patient engagement in the pathway may prove effective in improving adherence to elements requiring a high degree of self-management such as mobilization and diet.

Conclusions

In this retrospective study relying on prospectively collected data within an established ERP, increased adherence to enhanced recovery interventions was associated with successful early recovery and a reduction in postoperative morbidity and complication severity. Laparoscopic approach, perioperative fluid management, and patient mobilization were key elements associated with improved outcomes. Our findings suggest that further measures should be implemented to increase adherence to ERP interventions.

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Compliance with ethical standards

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