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Does adherence to perioperative enhanced recovery pathway elements influence patient-reported recovery following colorectal resection?

Nicolò Pecorelli[1,4] · Saba Balvardi[1] · A. Sender Liberman[2] · Patrick Charlebois[2] · Barry Stein[2] · Franco Carli[3] · Liane S. Feldman[1,2] · Julio F. Fiore Jr.[1,2]

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Abstract

Introduction Patient-reported outcome measures (PROMs) are pivotal to promote patient-centered perioperative care. Adherence to enhanced recovery programs (ERPs) is associated with improved clinical outcomes (i.e., morbidity, length of stay), but the impact of adherence on PROMs is uncertain. The objective of this study was to evaluate the extent to which adherence to an ERP for colorectal surgery is associated with postoperative recovery as assessed using PROMs.

Methods and procedures 100 patients were included [median age 63 (IQR 50–71) years, 81 laparoscopic, 37 rectal surgery]. Overall adherence to the ERP and adherence to specific ERP elements were analyzed. Adjusted linear regression was used to evaluate the association of adherence with PROMs assessing early recovery [Abdominal surgery impact scale (ASIS) and Multidimensional fatigue inventory (MFI) on POD2] and late recovery (Duke Activity Status Index, RAND-36 Physical and Mental Summary Scores, Life-Space Mobility Assessment at 4 weeks after surgery). Missing data were addressed using multiple imputations.

Results Median adherence to the ERP was 80% (16/20 elements, IQR 70–90%). Overall adherence was associated with ASIS scores on POD2 (4% increase per additional element, 95% CI 1–8%; $p=0.018$). When specific ERP elements were analyzed, ASIS scores were associated with adherence to PONV prophylaxis (34% increase, 95% CI 5–63%; $p=0.023$) and early solid food diet (20% increase, 95% CI 5–35%; $p=0.009$). MFI General fatigue and MFI Mental fatigue scores on POD2 were associated with adherence to PONV prophylaxis (36% decrease, 95% CI −64 to −8%, $p=0.014$ and 22% decrease, 95% CI −44 to −8%, $p=0.042$). Overall adherence and adherence to specific elements were not associated with PROMs at 4 weeks after surgery.

Conclusion Our findings suggest that, from the perspective of patients, adherence to an ERP for colorectal surgery impacts early, but not late postoperative recovery. This result may reflect the lack of PROMs able to validly measure postoperative recovery beyond hospital discharge.

Keywords Patient-reported outcome measures · Postoperative recovery · Enhanced recovery · Outcome and process assessment (Health Care) · Colorectal surgery

Enhanced recovery programs (ERPs) are structured perioperative care pathways including multiple evidence-based interventions aimed to reduce postoperative organ dysfunction and accelerate recovery [1]. This novel concept of care represents an effective and cultural-shifting innovation especially in colorectal surgery, where a large body of evidence supports the use of ERPs to improve postoperative outcomes compared to usual care [2].

Adherence to ERP elements (interventions) represents a key process metric to guide the effective implementation of ERPs [3]. A recent systematic review found that reduced

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✉ Julio F. Fiore Jr.
julio.fiorejunior@mcgill.ca

Extended author information available on the last page of the article

ERP adherence is associated with increased hospital stay, complications, and readmissions after laparoscopic colorectal resection [4]. Several cohort studies have identified specific ERP elements predicting better postoperative outcomes, including perioperative intravenous fluid management, early mobilization, and solid food diet after surgery [5, 6]. Nonetheless, in these studies, recovery has been mainly assessed using clinical outcome measures such as length of hospital stay (LOS), postoperative morbidity, and readmission rates, which do not reflect the complexity of the recovery process and fail to capture the perspective of patients [7, 8].

Postoperative recovery is a highly dynamic process comprising multiple dimensions of health (e.g., symptom experiences, functional status, and well-being); therefore, it cannot be easily captured by a single metric [9]. Following the principles of patient-centered care [10], recent literature advocates the addition of patient-reported outcome measures (PROMs) in the evaluation of recovery [11–13]. The main advantage of using PROMs as a recovery metric is that they use information coming directly from the patients without interpretation by a clinician or anyone else [12]. In addition, PROMs allow a broad assessment of health status across various domains and engage patients as the main stakeholders in the recovery process.

Although a large number of studies assessed the influence of ERP adherence on postoperative outcomes after colorectal surgery, to date, no study has explored the impact of adherence on recovery from the patient's perspective. Therefore, the objective of this study was to evaluate the extent to which adherence to an ERP for colorectal surgery is associated with patient-reported recovery, as measured by a variety of PROMs.

Methods

This study was conducted and reported following the STROBE guidelines for observational cohort studies [14].

Participants and setting

This study involved 100 adult patients undergoing elective colorectal resection at a Canadian university hospital between July 2014 and July 2015. This study involved the secondary analysis of data collected for a recently completed randomized controlled trial (RCT) that evaluated the impact of staff-directed facilitation of early mobilization in the context of an ERP. The RCT protocol and results can be found in a previous publication [15]. Patients with metastatic disease, inability to fully mobilize preoperatively (e.g., neurological or musculoskeletal diseases), inability to understand English or French, and planned admission to ICU immediately after surgery were excluded. Institutional review board was granted (MUHC Research Ethics Board ref. 13-329-SDR), and all patients provided informed consent. All patients were treated within an ERP including multiple perioperative care elements with targeted discharge on postoperative day (POD) 3, as previously described [5].

Clinical and adherence data

Patient characteristics (e.g., age, sex, diagnosis, comorbid conditions), surgical data (e.g., type of surgery performed, technical details), and postoperative clinical outcomes (LOS, 30-day complications, 30-day readmissions) were obtained from medical records. Complications were recorded based on pre-defined criteria [15], graded using the Dindo–Clavien classification and summarized into a numeric score (1–100) using the Comprehensive Complication Index (CCI) [16]. LOS was calculated by subtracting the date of hospital discharge from date of surgery as recorded in the patients' electronic health record.

Adherence to each ERP component was defined as the successful completion of a planned intervention (e.g., a patient planned to have postoperative nausea and vomit (PONV) prophylaxis actually received anti-emetics intraoperatively). For the purpose of this study, we assessed the adherence to 20 perioperative elements that were evaluated on a daily basis by a clinical auditor. Definitions for each measure of adherence are detailed in Table 1. Adherence to intraoperative intravenous infusions followed recent recommendations [17], 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/hr for laparoscopic surgery and ≤ 5 ml/kg/hr for open surgery [17]. A patient was considered adherent to PONV prophylaxis if they received at least one anti-emetic medication (e.g., dexamethasone, ondansetron) during surgery. Patient's overall adherence was defined as the total number of ERP components to which the patient complied.

Patient-reported outcome measures

Recovery from the perspective of patients was evaluated using 5 different PROMs; the Abdominal surgery impact scale (ASIS), the Multidimensional fatigue inventory (MFI-20), the RAND-36, the Duke Activity Status Index (Duke scale), and the Life-Space Mobility (LSM) scale. Main characteristics of these PROMs are listed in Table 2.

Short-term recovery was assessed using the ASIS and MFI-20 administered preoperatively and during hospital stay on POD 2. These PROMs use a short recall period (i.e., period of time patients are asked to consider when completing the questionnaire) of 24 h and use questions that are applicable to hospitalized patients, allowing an

Table 1 Perioperative ERP interventions and definition of adherence

ERAS 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 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
Balanced intravenous fluids	Maintenance fluids excluding replacement of blood loss: for laparoscopy < 3 ml/kg/h; for open surgery < 5 ml/kg/h
PONV prophylaxis	Multimodal prophylaxis administered according to Apfel score
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 drainage	Nasogastric tube removed at the end of general anesthesia
Postoperative	
Oral liquids early after surgery	Patient had oral fluids on the day of surgery postoperatively
Oral nutritional supplements on POD0	Patient received one or more nutritional drinks on the day of surgery postoperatively
Early mobilization out of bed	Patient mobilized out of bed at least 6 h on POD 1
Early termination of IV fluid infusion	Termination of intravenous fluid infusion by POD 1
Early termination of urinary drainage	Termination of urinary drainage by POD 1
Early solid food diet	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 started by POD 1
Transition to oral analgesia by POD 2	Successful termination of thoracic epidural or intravenous PCA analgesia and transition to oral analgesics by POD 2

POD 0 day of surgery postoperatively, *POD 1* first day after surgery, *POD 2* s day after surgery, *MBP* mechanical bowel preparation, *PONV* postoperative nausea and vomiting, *TED* thromboembolic disease, *PCA* patient-controlled analgesia

estimation of patients' health status in the first postoperative days. Measures taken on POD2 were believed to provide an appropriate snapshot of a patient's health state during hospital stay. ASIS is a PROM developed by Urbach et al. to assess short-term quality of life after abdominal surgery [18, 19]. The questionnaire contains 18 items covering six domains (physical limitations, functional impairment, pain, visceral function, sleep, and psychological function) with responses given using a seven-point Likert scale (from 'strongly disagree' to 'strongly agree'). The ASIS provides an overall score that ranges from 18 to 126 with higher scores indicating better postoperative quality of life. The MFI-20 is a PROM that has been extensively used to measure fatigue in surgical populations [20]. This PROM comprises 20 items and considers fatigue as a multidimensional construct across five domains that are scored separately: general fatigue, physical fatigue, mental fatigue, reduced motivation, and reduced activity [21]. Subscales scores range from 4 to 20, with higher scores indicating more fatigue.

Long-term recovery was evaluated through the administration of the RAND-36, the Duke, and the LSM scale preoperatively and at 4 weeks after surgery. These PROMs have longer recall periods (4 weeks) and include questions that are only applicable to outpatient settings, allowing a better estimate of patients' health status beyond hospital discharge. The RAND-36 is the publicly accessible version of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) [22]. This questionnaire assesses eight domains of health (physical function, role physical, role emotional, social functioning, bodily pain, general health, vitality, and mental health) that are summarized into a physical component and a mental component score ranging from 0 to 100, with higher scores indicating better quality of life. The Duke scale assesses physical function and can predict exercise capacity [23]. In this brief questionnaire,

Table 2 Characteristics of the Patient-reported Outcome measures assessed in this study

Name	Subscales[a]	Time of assessment[b]	Recall period	Rating	Range of scores
Abdominal surgery impact scale (ASIS)	Physical limitations, functional impairment, pain, visceral function, sleep, and mood[c]	Preoperatively, POD 2	24 h	Likert scale (7-point)	Total score: 18–126; Subscales 7–21; (worst–best)
Multidimensional fatigue inventory (MFI-20)	General fatigue, physical fatigue, mental fatigue, impact on activity, impact on motivation	Preoperatively, POD 2	24 h[e]	Ordinal scale (5-point)	Subscales: 4–20 (best-worst)
Duke activity status index	–	Preoperatively, POW 4	Today/present	Dichotomous scale (yes/no)	Total score: 0–58.2 (worst–best)
RAND-36	Physical summary (PCS) and mental summary scores (MCS)[d]	Preoperatively, POW 4	4 weeks	Ordinal scale (3- and 6-point)	Total score: 0–800 Subscales: 0–100 (worst–best)
Life-space mobility assessment	–	Preoperatively, POW 4	4 weeks	Dichotomous scale (yes/no)	Total score: 0–120 (worst–best)

POD postoperative day, *POW* postoperative week

[a]Different health domains that are scored separately within the same PRO

[b]Refers to the timing at which the PRO was administered during this study

[c]Only the overall ASIS score was evaluated in this study

[d]PCS comprises the domains physical functioning, physical role, bodily pain, and general health; MCS comprises the domains vitality, social functioning, emotional role, and mental health

[e]Modified from the original recall period 'lately'

participants report if they are able to perform 12 specific activities of various intensities (i.e., ambulation, personal care, leisure activities). A specific score is given for each positive answer adding up to a total score that ranges from 0 to 58.2. The LSM scale is used to evaluate community mobility [24]. This questionnaire incorporates information about the distance that the person moved during the 4 weeks preceding the assessment (e.g., outside the room, outside the house, outside of town), the frequency and degree of assistance required. Scores obtained for each level (e.g., leaving the bedroom, level 1; leaving the house, level 2) are summed to calculate a total score ranging from 0 to 120. A higher Life-Space score indicates greater mobility within and away from home.

Statistical analysis

Statistical analysis was performed using Stata® version 14 software (StataCorp, College Station, TX, USA). All patients who participated in the RCT were included in the study. Descriptive data are reported as median (interquartile range, IQR), unless otherwise specified. Linear regression was used to evaluate the association of overall adherence to ERP elements with PROMs scores and to identify specific ERP components that are significantly associated with PROMs scores. As PROM scores were not normally distributed, they were log-transformed prior to analysis. Regression coefficients were adjusted for baseline PROMs scores and for factors known to influence both adherence to ERP elements and postoperative recovery. These included age, gender, surgical approach (laparoscopic vs. open), surgical site (colon vs. rectum), new stoma formation, American Society of Anesthesiologists score, late arrival at the ward postoperatively, and occurrence of postoperative complications [15, 25–27]. Backward stepwise elimination retaining variables significant at $p < 0.10$ in the multivariate model was used to determine ERP elements independently associated with PROMs scores.

To prevent bias arising from missing data, we conducted multiple imputations of missing PROM scores using chained equations and predictive mean matching. Estimates from 20 imputed datasets were combined using Rubin rules [28]. In instances where patients failed to respond only specific items in a questionnaire, missing items were assigned the mean value of non-missing items within its specific subscale, provided that at least half of the items in the subscale were completed [29]. If more than half of the items in a subscale were incomplete, PROM scores were deemed 'missing.' There were no missing data for adherence measures.

All statistical tests were 2-sided, and a "p" value < 0.05 was considered to indicate statistical significance.

Results

One hundred patients were included in this study. Table 3 reports demographics, operative characteristics, and clinical outcomes of the included patients. Sixteen patients were 75 years or older (16%), 57 were female (57%), 15 had a low preoperative physical status (ASA score III+, 15%), and 57 underwent surgery for a malignancy (57%). Most commonly, patients underwent a colonic resection (63%), and the laparoscopic approach was attempted in 86 (86%) patients and successfully completed in 81 (81%). Postoperatively, complications at 30 days occurred in 46 patients (46%), median LOS was 3 days (3–4), and hospital readmission was necessary for 11 patients (11%).

Table 4 shows adherence rates for single ERP components. Overall, patients where adherent to median 16 (80%) elements (IQR 14–18, 70–90%). Adherence was higher for preoperative and intraoperative (median 100 and 86 percent, respectively) compared to postoperative (55 percent) elements. ERP components with poor adherence (< 50%) included balanced intravenous infusions during surgery, intake of oral nutritional supplementation postoperatively on the day of surgery, and mobilization on POD 1.

Scores obtained for the different PROMs evaluated at baseline and postoperatively are presented in Table 5. All measures showed an expected decline in postoperative values in comparison to baseline, more evident early after surgery (i.e., POD 2), and for the physical domains of health (e.g., MFI physical fatigue, MFI impact on activity, and RAND-36 physical component summary) compared to the mental domains (e.g., MFI mental fatigue domain, and RAND-36 mental component summary).

Table 6 reports unadjusted and adjusted linear regression results analyzing the impact of overall ERP adherence on PROM scores. For early recovery, at multivariate analysis there was a positive association between overall adherence and ASIS score (4% increase per additional element, 95% CI 1–8%; $p = 0.018$). An association of overall adherence with

Table 3 Demographics, operative characteristics, and clinical outcomes of the included patients

	$n = 100$
Age (years)	63 (50–71)
Male sex	43
Obesity (BMI > 30 kg/m^2)	22
Low preoperative physical status (ASA score III+)	15
Charlson comorbidity index ≥ 3	19
Diagnosis	
Malignancy	57
Inflammatory bowel disease	20
Diverticular disease	8
Other benign disease	15
Procedure performed	
Colon resection	63
Rectal resection	37
Laparoscopic approach[a]	81
Formation of a new stoma	28
Duration of surgery (minutes)	202 (156–257)
Estimated blood loss (mL)	100 (50–200)
Epidural analgesia	47
Late arrival at the ward after surgery (after 6 PM)	66
Overall adherence to care elements (n)	16 (14–18)
Overall adherence to care elements (%)	80 (70–90)
Length of hospital stay (days)	3 (3–4)
Any 30-day complication	46
30-day complication severity (comprehensive complication index)	0 (0–12.2)
30-day hospital readmission	11

Data are *n* or median (interquartile range)

BMI body mass index, *ASA* American Society of Anesthesiologists

[a]Surgeries converted from laparoscopic to open surgery were considered as open surgery

Table 4 Patient adherence to enhanced recovery program elements

Enhanced recovery program element	$n = 100$
Preoperative	
Preadmission education	100
Selective MBP	84
Carbohydrate loading	75
No long-acting sedation	99
Intraoperative	
Antibiotic prophylaxis	99
Balanced IV fluids	28
PONV prophylaxis	95
Normothermia	65
Avoidance of abdominal or pelvic drainage	91
TED prophylaxis	99
Avoidance of nasogastric tube drainage	97
Postoperative	
Oral liquids on POD 0	91
Oral nutritional supplements on POD 0	42
Mobilization out of bed on POD 1 for 6 h	43
Early termination of IV fluid infusion	53
Early termination of urinary drainage	83
Free diet on POD 1	58
Chewing gum	91
Laxative	64
Transition to oral analgesia by POD 2	77

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

Table 5 Patient-reported outcome measures throughout the perioperative course

	n	Median (IQR)
Abdominal surgery impact scale (ASIS)[a]		
Preoperative	90	110 (102–120)
Postoperative day 2	96	75 (55–97)
Multidimensional fatigue inventory (MFI-20)[b]		
General fatigue		
Preoperative	98	10 (6–13)
Postoperative day 2	97	13 (10–16)
Physical fatigue		
Preoperative	98	9 (5–12)
Postoperative day 2	97	13 (10–16)
Mental fatigue		
Preoperative	98	9 (8–10)
Postoperative day 2	97	10 (8–12)
Impact on activity		
Preoperative	96	8.5 (6–12)
Postoperative day 2	97	14 (11–17)
Impact on motivation		
Preoperative	98	10 (8–12)
Postoperative day 2	97	11 (10–13)
Self-reported exercise capacity (Duke scale)[c]		
Preoperative	98	50.7 (42.7–58.2)
Postoperative week 4	85	30.2 (20.7–45.7)
Generic health status (RAND-36)[d]		
Physical component summary		
Preoperative	96	51.3 (45.6–55.3)
Postoperative week 4	85	40.4 (33.4–49.1)
Mental component summary		
Preoperative	96	50.3 (43.8–55.3)
Postoperative week 4	85	50.9 (40.4–57.9)
Community mobility (Life-space mobility scale)[e]		
Preoperative	97	84 (60–100)
Postoperative week 4	85	66 (50–90)

[a]Higher scores indicate better health status (range 18 to 126)

[b]Higher scores indicate more fatigue (range 5 to 20)

[c]Higher scores indicate better exercise capacity (range 0 to 58.2)

[d]Higher scores indicate better health status (range 0 to 100)

[e]Higher scores indicate better mobility (range 0 to 120)

MFI general fatigue, mental fatigue, and activity domains was only found at univariate analysis, but there was no significant impact when the analysis was adjusted for confounders. In adjusted analyses, overall adherence had no significant impact on late recovery as measured by the Duke scale, RAND-36, and LSM scores at 4 weeks postoperatively.

Table 7 shows the results of the regression analysis to identify ERP elements independently associated with PROM scores. On POD2, adherence to PONV prophylaxis was significantly associated with an increase in ASIS scores (34% increase, 95% CI 5–63%; $p=0.023$), and a reduction of the MFI general fatigue (36% decrease, 95% CI −64 to −8%; $p=0.014$) and mental fatigue scores (22% decrease, 95% CI −44 to −8%, $p=0.042$). Patient compliance with early solid food diet also had a positive effect on ASIS (20% increase, 95% CI 5–35%; $p=0.009$) on POD2. No ERP element had a significant influence on late postoperative recovery as measured by Duke scale, RAND-36, and LSM at univariate or multivariate analysis (Supplementary material).

Results from the full multivariate models including the effect of confounding factors influencing postoperative recovery are available in Supplementary material. Notably, occurrence of any postoperative complication was strongly associated with poor recovery. Early after surgery, postoperative morbidity resulted in a 34% reduction (95% CI −48 to −20%; $p<0.001$) in ASIS scores, 20% increase (95% CI 5 to 35%; $p=0.011$) in MFI general fatigue, 36% increase (95% CI 16 to 57%; $p=0.001$) in physical fatigue, and 19% increase (95% CI 6 to 31%: $p=0.004$) for the MFI activity domain. Similarly, for late recovery, postoperative complications were a detrimental factor for Duke scale (33% decrease; 95% CI −64 to −2%; $p=0.034$), RAND-36 physical component summary (25% decrease; 95% CI −36 to −14%; $p<0.001$), and LSM (55% decrease; 95% CI −85 to −25%; $p=0.001$) scores. A new stoma formation was significantly associated with reduced LSM (47% decrease; 95% CI −81 to −13%; $p=0.008$) and RAND-36 Mental summary scores (16% decrease; 95% CI −30 to −1%; $p=0.034$) at 4 weeks.

Discussion

This study analyzing data from a Canadian university hospital showed that overall adherence to ERP interventions was associated with patient-reported early recovery after colorectal surgery but did not influence late recovery as measured by a variety of PROMs. Compliance with perioperative PONV prophylaxis and early return to solid food diet were the only care processes significantly associated with improved PROMs scores early after surgery. Adherence to specific ERP elements was not associated with PROM scores measured at 4 weeks postoperatively These findings suggest that the impact of ERP adherence on recovery from the perspective of patients may be limited to the early postoperative phase.

Measuring adherence to perioperative interventions is pivotal for ERPs, as it reflects how closely patients follow a pathway developed to improve their recovery after surgery. Auditing adherence is important to guide both the implementation and maintenance of ERPs, since it allows to monitor single care processes, identify barriers and facilitators, and make adjustments to the pathway accordingly [30]. In

Table 6 Association between overall adherence to perioperative care elements and recovery as measured by patient-reported outcomes

	Unadjusted coefficient (95% CI)[a]	*p* value	Adjusted coefficient (95% CI)[b]	*p* value
Early recovery (POD 2)				
Abdominal surgery impact scale (ASIS)	0.083 (0.05 to 0.12)	< 0.001	0.042 (0.01 to 0.08)	0.018
Multidimensional fatigue inventory (MFI-20)				
General fatigue	−0.043 (−0.07 to −0.01)	0.010	−0.027 (−0.06 to 0.01)	0.120
Physical fatigue	−0.026 (−0.06 to 0.01)	0.171	−0.014 (−0.06 to 0.03)	0.491
Mental fatigue	−0.027 (−0.051 to −0.01)	0.032	−0.022 (−0.05 to 0.01)	0.096
Impact on activity	−0.029 (−0.05 to −0.01)	0.034	−0.022 (−0.05 to 0.01)	0.139
Impact on motivation	−0.011 (−0.03 to 0.01)	0.280	−0.008 (−0.03 to 0.01)	0.467
Late recovery (postoperative week 4)				
Self-reported exercise capacity (Duke scale)	0.050 (−0.01 to 0.11)	0.109	0.014 (−0.05 to 0.08)	0.672
Generic health status (RAND-36)				
Physical component summary	0.011 (−0.01 to 0.03)	0.371	−0.005 (−0.03 to 0.02)	0.687
Mental component summary	0.014 (−0.01 to 0.04)	0.274	0.001 (−0.03 to 0.03)	0.930
Life-space mobility scale	0.072 (0.01 to 0.14)	0.029	0.036 (−0.03 to 0.10)	0.255

Coefficients represent the expected change in the PRO score for one-unit increase in overall adherence

[a]Unadjusted coefficients derived with imputation of missing data

[b]Adjusted coefficients derived with imputation of missing data and adjustment for sex, surgical approach (laparoscopic vs. open), surgical site (colon vs. rectum), American Society of Anesthesiologists score, formation of a new stoma, duration of surgery, late arrival at the ward postoperatively, occurrence of postoperative complications, baseline scores (in deciles)

Table 7 Perioperative ERP components significantly associated with early recovery as measured by patient-reported outcomes on postoperative day 2

	Unadjusted coefficient (95% CI)[a]	*p* value	Adjusted coefficient (95% CI)[b]	*p* value
Abdominal surgery impact scale (ASIS)				
PONV prophylaxis	0.399 (0.03 to 0.77)	0.035	0.340 (0.05 to 0.63)	0.023
Oral liquids on POD 0	0.399 (0.12 to 0.68)	0.005		
Mobilization on POD 1	0.170 (0.01 to 0.34)	0.045		
Early stop of IV fluid infusion	0.222 (0.06 to 0.38)	0.007		
Early solid food diet	0.357 (0.20 to 0.51)	< 0.001	0.200 (0.05 to 0.35)	0.009
Multidimensional fatigue inventory (MFI-20) [c]				
General fatigue				
PONV prophylaxis	−0.359 (−0.67 to −0.04)	0.026	−0.359 (−0.64 to −0.08)	0.014
Early solid food diet	−0.211 (−0.35 to −0.07)	0.003		
Mental fatigue				
PONV prophylaxis	−0.267 (−0.50 to −0.03)	0.026	−0.222 (−0.44 to −0.08)	0.042
Impact on activity				
Early solid food diet	−0.170 (−0.28 to −0.06)	0.004		

Coefficients represent the expected change in the PRO score presence of independent variable

[a]Unadjusted coefficients derived with imputation of missing data

[b]Adjusted coefficients derived with imputation of missing data and adjustment for sex, surgical approach (laparoscopic vs. open), surgical site (colon vs. rectum), American Society of Anesthesiologists score, formation of a new stoma, duration of surgery, late arrival at the ward postoperatively, occurrence of postoperative complications, baseline scores (in deciles)

[c]Higher scores mean more fatigue

fact, a 2017 systematic review found that adherence to ERP elements is the most commonly identified variable associated with improved postoperative outcomes [4]. Recently, two large studies relying on prospectively collected data found that increased adherence to care processes is associated with successful recovery, but this was measured using traditional clinical outcomes (i.e., LOS, complications, and readmissions) [5, 6]. Although relevant from the clinicians'

point of view, these measures fail to take into account the complexity of the construct of recovery and lack the patients' perspective [7].

Of the five PROMs assessed as measures of postoperative recovery in our study, only ASIS on POD 2 was significantly influenced by overall adherence. The ASIS is one of the few PROMs specifically developed to assess postoperative recovery from the perspective of patients undergoing abdominal surgery [19]. It evaluates recovery across six domains (physical limitations, functional impairment, pain, visceral function, sleep, and psychological function) that appear mostly relevant in the early phase of recovery [18]. Recent literature has shown that higher adherence is associated with better pain control, faster return to bowel function, and tolerance of diet, which represent functional domains that are assessed by ASIS [31].

PONV prophylaxis and early solid food diet were the only ERP components having a significant impact on early recovery. Both components aim at preventing the occurrence of nausea and vomiting and facilitating an earlier return to oral feeding and bowel function. PONV represents a very common adverse event, affecting around 30% patients in the early phase of recovery [32], increasing hospital costs, and reducing patient satisfaction [33]. Not surprisingly, our data also confirmed that the occurrence of PONV has a negative effect on recovery as measured by PROMs on POD 2 (Supplementary material).

Our regression analysis highlights that postoperative complications have an important impact on self-reported recovery after colorectal surgery. This finding confirms recent research showing the adverse effect of postoperative morbidity on generic and cancer-specific PROMs (i.e., EQ-5D; EORTC QLQ Cancer Core-30; and Colorectal-38) up to 3 years after surgery [34]. In our study, complications were the strongest factor associated with reduced physical function on POD2 and at 4 weeks after surgery. These results corroborate with previous studies showing that complications have an important effect on PROMs targeting domains of physical function and also performance-based measures of functional capacity (i.e., 6-min walking test; short physical performance battery tests) [34–36].

To our knowledge, this is the first study analyzing the impact of adherence to ERP interventions on a variety of PROMs reflecting patient recovery after colorectal surgery. A major strength of this work is that adherence was defined thoroughly and measured prospectively, using clear definitions within a randomized controlled study. All regression analyses were adjusted for relevant factors influencing both adherence and postoperative outcomes including patient comorbidities and procedural factors, according to previous research conducted in our center [5, 25].

The main limitation of our study is the use of PROMs that were not specifically developed and validated to measure postoperative recovery, with the exception of ASIS [11]. In fact, a recent systematic review by our group has shown that there is limited evidence supporting the measurement properties of existing PROMs evaluating recovery after abdominal surgery [11]. The absence of valid PROMs is a recognized gap in the literature, and it is fairly common in surgical research to use generic instruments (e.g., quality of life questionnaires) to assess the effectiveness of interventions that are hypothesized to improve recovery (e.g., minimally invasive surgery) [37]. Generic PROM (e.g., RAND-36) are not specifically devised to detect changes in health status after surgery, thus they may not be sensitive to capture significant shifts in the recovery trajectory. Similarly, domain-specific PROMs such as the MFI-20 or LSM only focus on limited aspects of recovery such as fatigue and mobility, failing to include the multiple dimensions of the recovery construct. Importantly, this study involved multiple hypotheses testing which may have lead to spurious significant findings regarding the association of ERP adherence with early recovery. Another limitation of this study is the risk of selection bias, as our sample consisted of patients enrolled in a RCT rather than a consecutive clinical cohort. Additionally, 15% of patients participating in the trial did not respond to the questionnaires 4 weeks postoperatively; however, we conducted multiple imputations to minimize potential bias arising from missing data.

Conclusions

Our findings suggest that, from the perspective of patients, adherence to an ERP for colorectal surgery impacts early, but not late postoperative recovery. It is not clear whether these results reflect a lack of appropriate measures of recovery beyond hospital discharge, or if in fact ERPs have fewer advantages than expected. There remains a need for the development of recovery-specific PROMs with adequate measurement properties to enable patient-centered assessment of postoperative recovery.

Compliance with ethical standards

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Affiliations

Nicolò Pecorelli[1,4] · Saba Balvardi[1] · A. Sender Liberman[2] · Patrick Charlebois[2] · Barry Stein[2] · Franco Carli[3] · Liane S. Feldman[1,2] · Julio F. Fiore Jr.[1,2]

[1] Steinberg-Bernstein Centre for Minimally Invasive Surgery and Innovation, McGill University Health Centre, 1650 Cedar Ave, E19-125, Montreal, QC H3G 1A4, Canada

[2] Department of Surgery, McGill University Health Centre, Montreal, QC, Canada

[3] Department of Anesthesia, McGill University Health Centre, Montreal, QC, Canada

[4] Division of Pancreatic Surgery, Pancreas Translational & Clinical Research Center, San Raffaele Scientific Institute, Milan, Italy