Techniques in Coloproctology (2018) 22:191–199
https://doi.org/10.1007/s10151-018-1761-x

ORIGINAL ARTICLE

The impact of complications after elective colorectal resection within an enhanced recovery pathway

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Received: 10 August 2017 / Accepted: 5 February 2018 / Published online: 5 March 2018

Abstract

Background Despite the implementation of enhanced recovery pathways (ERP), morbidity following colorectal surgery remains high. The aim of the present study was to estimate the impact of postoperative complications on excess hospital length of stay (LOS) in patients undergoing elective colorectal resection.
Methods A retrospective study of patients undergoing elective colorectal surgery at a single institution from 2003 to 2010 was performed. Patients managed by an ERP were compared to conventional care (CC), matched by propensity score radius matching. Complications were defined a priori. Excess (independent effect on LOS from multivariate analysis) and attributable (absolute number of additional bed days) LOS of common postoperative complications determined the impact of complications on bed utilization. Multivariate analysis was performed using multiple linear regression.
Results A total of 810 propensity-score-matched patients were included (ERP = 472, CC = 338). Complications were significantly lower in the ERP group compared to the CC group (20 vs. 31%, $p < 0.001$). Median LOS decreased from 7 days in the CC group to 5 days in the ERP group [adjusted decrease in mean LOS of 2.8 days (95% CI 0.8, 4.8)]. Anastomotic leak, myocardial infarction and *C. difficile* infection had the highest excess LOS for both the ERP and CC groups. However, impaired gastrointestinal function had a higher impact on theabsolute number of hospital bed days in the ERP group, as high as anastomotic leak (72.7 vs. 73.5 days respectively), while in the CC group the impact of gastrointestinal dysfunction was less of that of anastomotic leak (50.6 vs. 78.9 days respectively).
Conclusions In the setting of an ERP, postoperative complications have significant impact on total bed utilization. Impaired gastrointestinal function, given its high incidence, accounted for almost the same number of additional hospital bed days as anastomotic leak in the ERP group and is a target for quality improvement.

Keywords Treatment outcome · Epidemiology · Enhanced recovery pathway · Preoperative care · Length of stay · Postoperative complications

Introduction

Despite advances in surgical care, the rate of complications after colorectal surgery remains significant. In a report based on the American College of Surgeon's National Surgical Quality Improvement Program (NSQIP), colectomy accounted for the highest percentage of adverse events (24.3%) despite accounting for only 9.9% of all general surgery procedures over the study period [1]. In the same study, colectomy was ranked first for highest morbidity, mortality and excess length of stay (LOS) of all general surgical procedures. Postoperative complications on average increase hospital costs by 78% and LOS by 114% [2]. Infectious, cardiac and respiratory complications account for the highest proportion of excess cost and LOS in non-cardiac surgery [3].

An enhanced recovery pathway (ERP) is a multidisciplinary process of care integrating evidence-based interventions in all phases of perioperative management, designed to minimize physiological stress on the patient undergoing colorectal surgery. The primary objective of an ERP is to improve

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quality and efficiency of care by decreasing complications and improving physiological recovery, reducing the need for hospitalization. A meta-analysis of randomized clinical trials comparing ERP to conventional care (CC) reported a reduction in LOS and the incidence of minor complications, although no difference in the incidence of major complications was noted [4]. However, it was unclear which types of complications were reduced with an ERP and whether the impact of specific complications on LOS was affected by the presence of an ERP. For example, consider superficial surgical site infection (SSI). The introduction of an ERP may affect the incidence of infections or simply shift the setting of diagnosis and treatment from the in-patient to the out-patient setting, or both; this has implications for the organization of surgical care after the introduction of an ERP. Therefore, we estimated the impact of postoperative complications on excess hospital LOS in patients undergoing colorectal surgery within an ERP compared to CC by identifying complications that have the highest incidence and greatest independent resource consumption in the two settings.

Materials and methods

Patients

All patients undergoing elective colorectal surgery performed at a single university-affiliated institution from 2003 to 2010 were identified from an operating room database and audited. Patients were excluded if no colonic or rectal resection and/or no anastomosis were performed. An ERP was first implemented in 2005 and consisted of a structured, multidisciplinary approach applying evidence-based practices for perioperative management. The elements of an ERP are described in detail elsewhere [5, 6], but the main goals of the program are pain-free and stress-free surgery with reduced complications and faster recovery.

Patients enrolled in the ERP at our institution received preoperative teaching regarding all aspects of care, including multimodal analgesia, early postoperative oral intake and ambulation, as well as the target discharge date of 3 days after surgery [7]. Initially, all patients received thoracic epidural analgesia; however, by 2010 it was only performed in rectal cases, with the remainder of patients receiving multimodal analgesia including patient-controlled analgesia, nonsteroidal anti-inflammatory drugs and gabapentin. All patients received prophylactic intravenous antiemetics for postoperative nausea and vomiting. Intravenous fluids were administered at a rate of 6 mL/kg/h intraoperatively and in the post-anesthesia care unit. Postoperative fluid management specified the cessation of intravenous fluid upon arrival to the surgical ward, although the catheter remained in place ("heplock IV"). Patients were given a clear fluid diet on the evening of surgery, progressing to full diet on the first postoperative day, and were encouraged to be out of bed for a minimum of 8 h per day. Peripherally acting mu-opioid-receptor antagonists were not approved for use in Canada at the time of ERP implementation. Target discharge from hospital was 3 days after surgery, but discharge required that the patient was tolerating solid diet without nausea and vomiting, had adequate pain control and had passage of flatus. Patients were highly selected and enrolled as per the surgeon's discretion when the ERP was first implemented in 2005 and gradually enrollment increased with time.

Outcome measures

Preoperative and operative characteristics and short-term postoperative outcomes were collected. All postoperative complications within 30 days of the index operation were defined a priori and graded as per the Clavien classification [8]. Impaired gastrointestinal (GI) function was defined as either two or more episodes of nausea and vomiting after beginning oral intake or as the insertion of a nasogastric tube for the indication of nausea or vomiting without evidence of concomitant intraabdominal or infectious processes. Anastomotic leak was defined by the presence of a perianastomotic abscess on a computed tomography scan of the abdomen or intraoperative confirmation. Acute myocardial infarction was defined by electrocardiographic ischemic changes associated with an increase in cardiac troponins, along with consistent symptomology. Respiratory complications included pneumonia, pulmonary embolism or symptomatic pleural effusion or pulmonary edema. SSI was defined as per the Center for Disease Control [9]. Urinary tract infection was defined by a positive urine culture. *Clostridium difficile* infection was defined as diarrhea and a positive *C. difficile* toxin assay. The number of additional minor (Clavien I–II; requiring bedside or pharmacologic treatment only) and major (Clavien III+; requiring radiologic, endoscopic or surgical intervention, intensive care or death) complications per patients was also collected [10]. Hospital LOS was calculated from the date of elective surgery until hospital discharge or in-hospital death. LOS also included the duration of hospitalization if the patient was re-admitted within 30 days of the index operation.

Statistical analysis

In order to reduce bias in this observational study, propensity score radius matching was performed to identify the intervention (ERP) and the control (CC) groups. In this procedure, a multiple logistic regression model was fitted using the intervention as the dependent variable and calculated the probability of receiving ERP based on the characteristics of each patient (age, gender, body mass index, American Society of Anesthesiologists (ASA) grade, indication for surgery, procedure type and previous major abdominal surgery). Radius matching then matched each patient in the ERP group to all patients in the control group within 0.2 of the standard deviation of the logit of the propensity score [11, 12]. Patients in either group who did not have any suitable matches were excluded from the analysis.

Baseline summary statistics of demographic and clinical variables were then calculated. Univariate analyses were performed using the χ^2, Student's *t*, ANOVA or the Mann–Whitney *U* tests as appropriate. Multivariate analysis was performed to analyze the impact of the most common complications on LOS. The point estimate of a specific complication on multivariate analysis was defined as the excess LOS (for a single occurrence of the complication). LOS was positively skewed and therefore was log-transformed when used as the dependent variable in a multiple linear regression model for each group (ERP and CC). Each complication was entered as a separate variable in the multivariate regression analysis, along with the following a priori defined confounders: age, gender, ASA grade, laparoscopic approach, the year of operation and if a new stoma was fashioned in the index operation. No interaction terms were used. The number of bed days occupied as a direct result of a specific complication was defined as the attributable LOS. It was calculated by the following formula:

$$\text{Attributable LOS} = \text{Excess LOS for each complication} \times \text{number of occurrences},$$

and then standardized to a standard population of 100 to facilitate comparison between the two groups. Statistical significance was defined using $\alpha = 0.05$. Data are presented as percentage (*n*), mean (SD) or median [IQR]. Statistical analyses were performed using STATA 12 (College Station, TX, USA).

Results

A total of 810 propensity-score-matched patients underwent elective colorectal resection from 2003 to 2010, including 472 in the ERP group and 338 in the CC group. The model diagnostics of the multiple logistic regression used to calculate propensity scores reported excellent discrimination (area under the receiver operating characteristic (ROC) curve 0.87, 95% CI 0.85, 0.89) and goodness of fit (Hosmer–Lemeshow χ^2 statistic = 5.8, $df = 8$, p value = 0.669). Patient and operative characteristics are reported in Table 1. There were significant differences in the use of laparoscopy and percentage of patients with a new stoma between the two groups, with more patients treated with laparoscopy and fewer new stomas in the ERP group.

Table 1 Comparison of patient characteristics between the conventional care and enhanced recovery pathway groups

	Conventional care ($n = 338$)	Enhanced recovery pathway ($n = 472$)	p value
Age category			0.822
Less than 60 years	142 (42%)	202 (43%)	
60–75 years	130 (38%)	172 (36%)	
Greater than 75 years	66 (20%)	98 (21%)	
Male gender	349 (60%)	270 (57%)	0.416
Body mass index, kg/m^2 (SD)	25.79 (4.9)	25.9 (5.1)	0.992
ASA physical status			0.058
1	46 (14%)	94 (20%)	
2	211 (62%)	267 (57%)	
3+	81 (24%)	111 (24%)	
Comorbidities			
Ischemic heart disease	35 (10%)	56 (12%)	0.502
Diabetes	37 (11%)	51 (11%)	0.949
Pulmonary	76 (22%)	105 (22%)	0.936
Charlson comorbidity index, points (SD)	1.7 (1.6)	1.6 (1.6)	0.795
Histology			0.164
Malignancy	207 (61%)	283 (60%)	
Inflammatory bowel disease	26 (8%)	55 (12%)	
Other	105 (31%)	134 (28%)	
Laparoscopy	19 (6%)	348 (74%)	< 0.001
Rectal procedure	151 (45%)	212 (45%)	0.946
New stoma	124 (37%)	102 (21%)	< 0.001

ASA American Society of Anaesthesiologists

An ERP was introduced in 2005, and the proportion of patients undergoing elective colorectal resection treated on the pathway increased over time from 25% (39/159) of all elective colorectal resections in 2005 to 92% (167/181) in 2010 (p trend < 0.001). There were significant differences in the usage of ERP elements between the ERP and CC groups (Table 2); however, compliance was poor with the order to stop continuous IV fluids on the evening after surgery. Approximately one-third of patients tolerated a clear fluid diet on the day of surgery, and a similar number of patients started solid food on the first postoperative day (Table 2). However, patients tolerated full diet earlier in the ERP group than in the CC group (Table 2). In the ERP group, 28% (122/472) of patients were discharged by the third postoperative day target, and a further 34% (161/472) were discharged on the fourth or fifth postoperative day. Comparatively, only 38% (129/338) of patients in the CC group were discharged by the fifth postoperative day.

A total of 610 complications occurred in 359 patients (Table 3). The incidence of 30-day postoperative complications was significantly lower in the ERP group than in the CC group (38 vs. 54%, p value < 0.001). Median overall LOS decreased from 7 days in the CC group to 5 days in the ERP group (p < 0.001). This effect was mainly found in uncomplicated patients, as no difference in LOS was found once complications occur, even when stratified by severity (Table 3). Among surgical complications, the incidence of superficial SSI was significantly lower in the ERP group. On multiple regression analysis, both laparoscopy (OR 0.32, 95% CI 0.19–0.56) and ERP (OR 0.56, 95% CI 0.32–0.99) were independent risk factors for superficial SSI, further adjusting for age, gender, body mass index, comorbidities, year of operation, indication

Table 2 Comparison of enhanced recovery pathway elements in the conventional care and enhanced recovery pathway groups

	Conventional care (n = 338)	Enhanced recovery pathway (n = 472)	p value
Thoracic epidural analgesia	281 (83%)	325 (69%)	< 0.001
Laparoscopic approach	19 (6%)	348 (74%)	< 0.001
Cessation of IV fluids on day of surgery	2 (1%)	72 (16%)	< 0.001
Tolerated clear fluid diet on day of surgery	19 (6%)	136 (29%)	< 0.001
Solid diet on first postoperative day	12 (4%)	157 (33%)	< 0.001
Median day tolerating solid diet, day [IQR]	4 [3–7]	2 [1–4]	< 0.001
Foley removed on first postoperative day	57 (18%)	275 (63%)	< 0.001

IV intravenous

Table 3 Univariate comparison of 30-day postoperative outcomes between the conventional care and enhanced recovery pathway groups

	Conventional care (n = 338)	Enhanced recovery pathway (n = 472)	p value
Overall complication rate	181 (54%)	178 (38%)	< 0.001
Anastomotic leak	29 (9%)	33 (7%)	0.423
Impaired GI function	69 (20%)	86 (18%)	0.469
Respiratory	28 (8%)	28 (6%)	0.193
Superficial SSI	52 (15%)	35 (7%)	< 0.001
Myocardial infarction	4 (1%)	6 (1%)	0.911
Urinary tract infection	27 (8%)	22 (5%)	0.050
C. difficile infection	7 (2%)	6 (1%)	0.405
Other minor (Clavien I–II)	86 (25%)	81 (17%)	0.013
Other major (Clavien III +)	13 (4%)	21 (4%)	0.529
Readmission	29 (9%)	44 (9%)	0.716
Operative mortality	3 (0.01%)	4 (0.01%)	1.000
Median overall LOS, days [IQR]	7 [5–11]	5 [4–8]	< 0.001
No complications	5 [4, 5]	4 [3–5]	< 0.001
Any complications	10 [8–18]	10 [8–16]	0.259
Minor complications	9 [8–15]	9 [7–12]	0.182
Major complications	13 [8–26.5]	13 [8–22]	0.709

LOS length of stay

for surgery, proctectomy and new stoma). The interaction between laparoscopy and ERP was not significant.

The study cohort used a total of 7502 hospital bed days. The ERP group had more efficient use of hospital bed days, as 472 patients occupied a total of 3713 bed days, whereas the 338 in the CC group occupied 3789 bed days. In both groups, uncomplicated patients used a minority of bed days; however, this proportion (bed days used by uncomplicated patients divided by total bed days) was higher in the ERP group than in the CC group (31 vs. 20%, $p < 0.001$). Therefore, complications accounted for a significant use of hospital bed days (69% of the total bed days in the ERP group and 80% in the CC group). On multivariate analysis, anastomotic leak, *C. difficile* infection and myocardial infarction had the highest excess LOS per complication (Table 4), after adjusting for known confounders, including laparoscopic approach. This effect was similar in both groups. However, compared to the CC group, the excess LOS associated with impaired gastrointestinal (GI) function, respiratory and urinary complications were higher in the ERP group. The relative proportion of excess LOS by complication is shown in Fig. 1.

However, when the attributable LOS was calculated, taking into account the incidence and the impact of each complication, impaired GI function accounted for almost the same number of additional hospital bed days as anastomotic leak in the ERP group (Fig. 2), given the high incidence of the former. Myocardial infarction did not have a substantial impact on additional bed days, given its low incidence. Of note, the attributable LOS for superficial SSI was meaningfully lower in the ERP group than in the CC group.

Discussion

In this study, we characterized the effect of an ERP on postoperative complications, including incidence and impact on resource utilization, reflected by length of stay. We demonstrated where the ERP was associated with improved outcomes by determining the excess LOS for specific complications within CC and ERP. We found that with use of an ERP, efficiency improved, as uncomplicated patients used fewer hospital bed days. After adjusting for confounders such as laparoscopy, the use of an ERP decreased the impact of superficial SSI and did not affect anastomotic leak, but increased the impact of impaired GI function.

In order to accurately estimate the additional number of hospital days utilized as a direct consequence of a complication, we determined the attributable LOS for each group of complications, defined as the product of the point estimate on multiple regression analysis and the incidence of the complication in the overall patient cohort. We chose this methodology over case matching with a specific complication to a non-complicated patient because multiple complications often occurred in the same patient, making it difficult to determine the independent effect of each complication without using multiple regression modeling. We did not adjust for individual patient comorbidities and body mass index given that there was significant colinearity with ASA physical status or no evidence of significant confounding effect.

Despite the high incidence of impaired GI function (17%), our results are consistent with other reported rates and remained consistent over time [13]. This may be a result of our definition, since patients on an ERP begin enteral feeds immediately postoperatively, before resolution of postoperative ileus and early feeding increases the risk of

Table 4 Excess length of stay due to complications, which measures the independent contribution for each complication on length of stay

Complication	Excess LOS, days (95% CI)[a]	
	Conventional care	Enhanced recovery pathway
Anastomotic leak	+ 9.19 (6.66–12.26)	+ 10.51 (8.17–12.25)
Impaired GI function	+ 2.48 (1.54–3.56)	+ 3.99 (3.06–5.03)
Respiratory	+ 1.82 (0.77–3.09)	+ 0.87 (− 0.20–2.17)
Superficial SSI	+ 1.52 (0.59–2.58)	+ 0.91 (0.01–1.98)
Myocardial infarction	+ 4.17 (0.58–9.98)	+ 7.04 (2.94–13.21)
Urinary tract infection/retention	+ 1.85 (0.57–3.41)	+ 3.32 (1.79–5.17)
C. difficile infection	+ 5.89 (2.49–10.77)	+ 5.06 (1.91–9.60)
Other minor (Clavien I–II)	+ 1.83 (1.10–2.65)	+ 1.84 (1.27–2.48)
Other major (Clavien III+)	+ 10.05 (6.97–13.93)	+ 5.13 (3.38–7.22)

GI gastrointestinal, *SSI* surgical site infection

[a]Point estimate from multiple linear regression, adjusted for age category, gender, American Society of Anaesthesiologists physical status, year of operation, laparoscopic approach and if a new stoma was created in the index operation

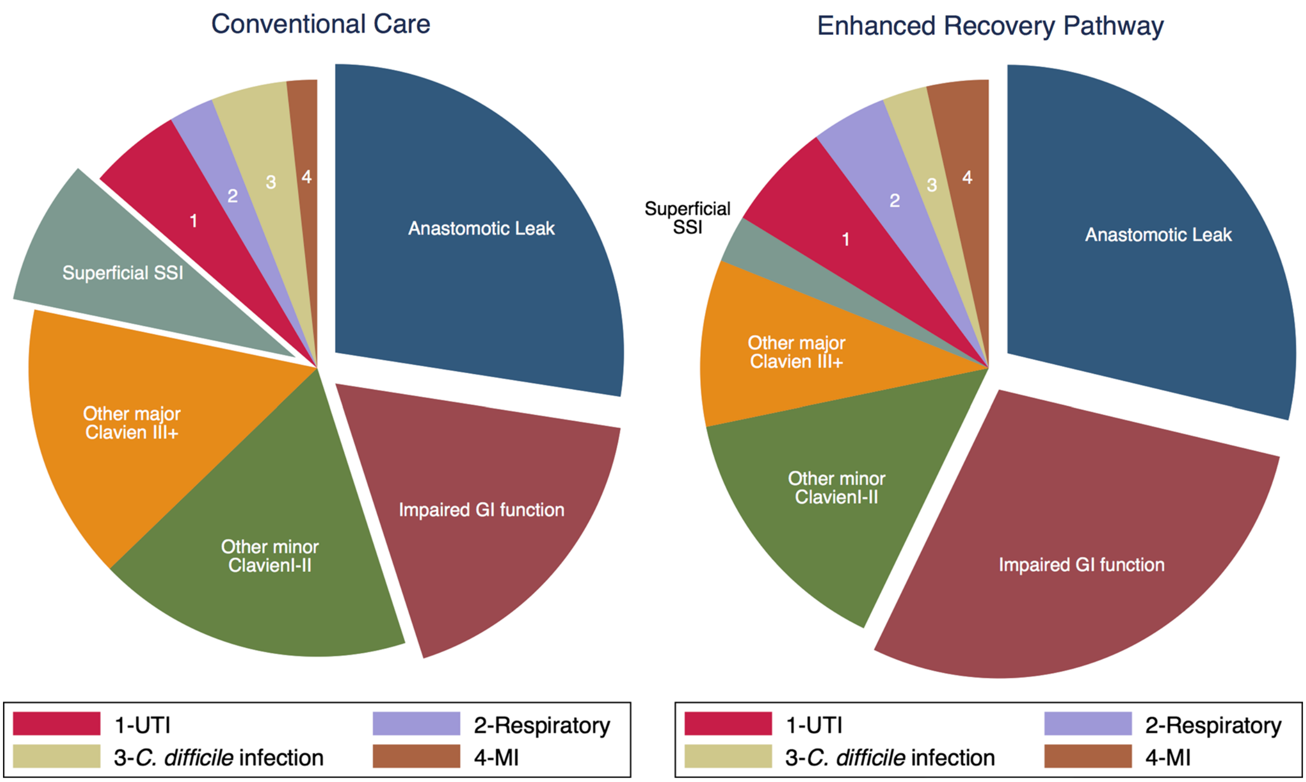
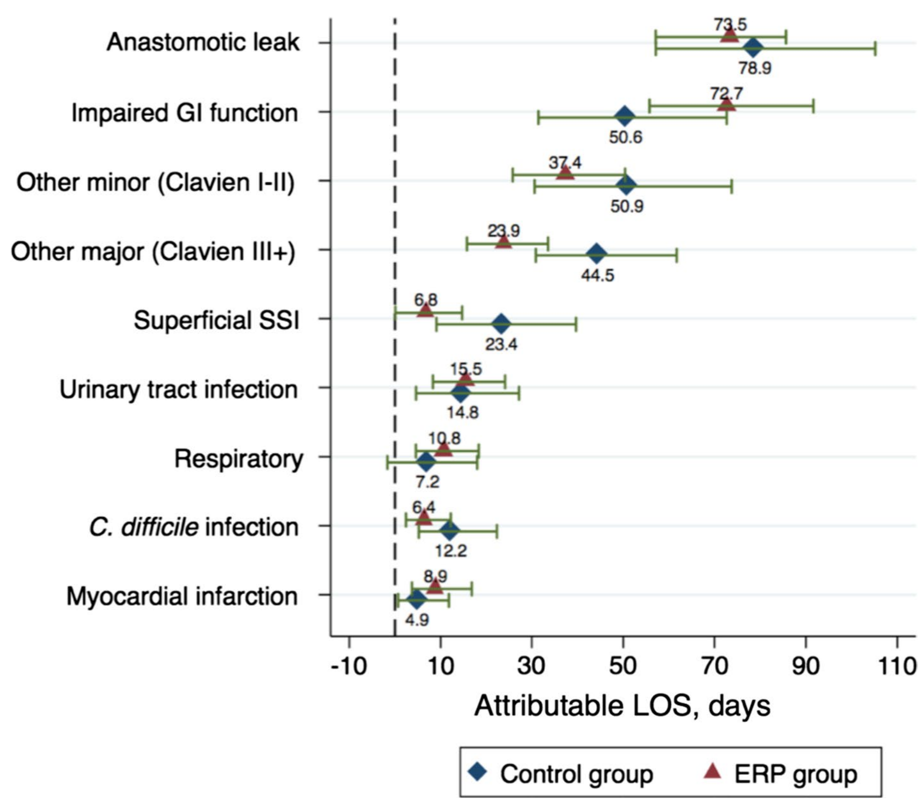


Fig. 1 Relative proportion of the excess length of stay by complication in the conventional care and enhanced recovery pathway groups

Fig. 2 Attributable length of stay for complications that significantly impact length of stay on multivariate analysis (calculated as the product of the number of occurrences and the excess length of stay per complication, standardized to a population of $n = 100$). It represents the absolute number of additional hospital bed days (compared to the expected length of stay for a non-complicated patient with similar characteristics) that were utilized as a direct result of the complication



vomiting, at least in the context of CC [14]. On the other hand, early feeding is a cornerstone of ERP, as evidence suggests it may decrease other complications [14], and preserves nutritional and functional status [15]. Nonetheless, even within a well-developed ERP, only 65% of patients tolerate oral diet by the second postoperative day [16]. With a target discharge on postoperative day 2, intolerance to diet will have an increasingly larger impact on hospital bed utilization within the ERP. We also did not have an approach to feeding intolerance as a component of the ERP, and decisions about treatment such as nasogastric tube insertion were at the discretion of the treating physician and team. There was, however, no difference in nasogastric tube insertion rate between the CC and ERP groups (63 vs. 62%, $p = 0.890$).

Thus impaired GI function remains a priority target for quality improvement for the ERP in that it contributed significantly to increased LOS, and processes of care can be further improved to reduce its impact. Although our ERP incorporated several recommended ileus-prevention techniques, such as avoidance of mechanical bowel preparation, use of opioid-sparing analgesia and emphasis on laparoscopy, adherence was poor for some elements, especially the order to *heplock IV* upon arriving to surgical ward. Other promising interventions such as Doppler-guided fluid management [17] and newer pharmacologic agents [18] were not available in our institution. However, some simple evidence-based interventions, like gum chewing [19], were not used and have been added to the revised ERP introduced in mid-2010. (No patients on the revised pathway were included in this study.) In addition, we have developed an algorithm to guide diagnosis and approach to post-op GI dysfunction for the surgical team; however, its impact remains to be investigated.

Despite the relatively minor morbidity of primary postoperative ileus compared to anastomotic leak, as reflected in the significantly lower excess LOS (8.0 vs. 2.8 days), when the absolute number of additional hospital days is taken into account, postoperative ileus (+ 298 days) had almost as significant an impact as anastomotic leak (+ 250 days). This finding highlights the limitation of relying only on the relative increase LOS per complication. Other studies have reported a similar significant impact on LOS, as well as significantly increased costs, secondary to postoperative ileus [13, 20]. In addition, while anastomotic leak is a highly morbid complication that has a significant impact on hospital LOS and cost, few, if any, interventions with level I evidence have been demonstrated to be effective in reducing its incidence, other than intraoperative leak testing and defunctioning loop ileostomy for rectal anastomosis after neoadjuvant radiotherapy [21]. In comparison, many different interventions have been reported to reduce postoperative ileus, such as minimally invasive techniques, avoidance of preoperative fasting and mechanical bowel preparation, laxatives, chewing gum, avoidance of over- or under-hydration and non-opioid analgesia [22, 23]. The advent of effective pharmacologic therapies may further help prevent postoperative ileus [18].

Superficial SSIs also decreased with the implementation of the ERP, although this may have been related to laparoscopy. However, both ERP and laparoscopy were independently associated with fewer superficial SSIs on multiple regression analysis. ERPs include standardized antibiotics orders [24] which were not in place in the CC group at the beginning of the study period. The relative impact of the superficial SSIs was also diminished, which may also be a result of the smaller incisions secondary to laparoscopy. Our ERP during this study period also omitted mechanical bowel preparation, although we did not use oral antibiotics even in the CC group. There are recent data that suggest that mechanical bowel preparation with antibiotics may reduce certain complications such as SSIs, ileus and anastomotic leak compared to mechanical bowel preparation alone [25]. It is unclear whether the combination of mechanical bowel preparation and oral antibiotics would have changed the relative impact of complications in this study.

This study has several limitations. First, due to the retrospective nature of the study, certain complications may have been missed because of poor documentation. This may have resulted in a biased estimate of effect of complications on LOS. Also, given that our institution is a regional referral center, some of our patient population originate from remote areas and may have presented to their local health facilities (and not have returned to our institution) with some minor complications that may have occurred after initial discharge. This may have resulted in a falsely low estimate of the incidence of 30-day postoperative complications although it was unlikely to affect major complications that usually result in transfer and readmission for specialized care. There was also a significantly higher use of laparoscopy within the ERP group, even when matched for propensity scores. Therefore, some of the apparent beneficial effects of an ERP may be attributable to laparoscopy rather than the ERP itself. However, there is no clear evidence to suggest decreased morbidity with laparoscopy compared to open colorectal surgery within an ERP. The largest randomized trial comparing laparoscopy and open colorectal surgery with and without an ERP by Vlug et al. [26] reported no differences in overall, minor or major morbidity between laparoscopy and open surgery within an ERP, nor between laparoscopy within an ERP and open surgery without an ERP. Given these previous findings, the estimated excess LOS for complications occurring in both the ERP and CC groups should not be biased by the increased use of laparoscopy in the ERP group.

Conclusions

The incidence of postoperative complications after elective colorectal surgery in the setting of an ERP remains significant. Anastomotic leak and postoperative GI dysfunction had the greatest impact in terms of absolute number of additional hospital bed days utilized. As health-care resources become increasingly limited, more attention is directed toward cost-effective methods to improve quality of care. The identification of complications with the highest incidence and greatest independent impact on resource utilization may pinpoint targets for quality improvement. Whether potentially costly new interventions to reduce postoperative GI dysfunction, such as Doppler-guided fluid therapy and pharmacologic approaches, have a role in colorectal ERPs should be further investigated.

Acknowledgements Salary support for LL was provided by the Fonds de Recherche en Santé—Québec and the McGill Surgeon Scientist program.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study protocol was approved by the institutional review board.

Informed consent For this type of study formal consent is not required.

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