Timing of Complications and Length of Stay after Rectal Cancer Surgery

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- BACKGROUND:** Enhanced recovery pathways have been shown to improve short-term outcomes after colorectal surgery. Occurrence of complications can lead to prolonged length of stay (LOS). The goal of this study was to examine whether shorter time to occurrence of complications was associated with a shorter hospital LOS in rectal cancer patients undergoing minimally invasive surgery, taking into account the perioperative pathway.
- STUDY DESIGN:** This retrospective study included consecutive patients undergoing rectal cancer resection from 2005 to 2011 at a single institution. Enhanced recovery pathway was introduced in 2009. Complications and date of occurrence were reviewed. The impact of perioperative care modalities and comorbidities was evaluated using competing risk models with occurrence of complications and LOS as time-dependent outcomes measured as time from surgery.
- RESULTS:** A total of 346 patients were included in the analysis with 78 patients treated with enhanced recovery pathway, and 268 with established care. The overall complication rate was 22.3% (77 patients with ileus, wound infection, leak, abscess, small bowel obstruction, reoperation for bleeding, and renal failure). Median time to occurrence of a complication was 3 days post operation. The time to complication diagnosis was associated with shorter time to discharge after the advent of the complication (hazard ratio = 0.84; 95% CI, 0.73–0.96; $p = 0.01$). Enhanced recovery pathway was associated with a shorter LOS for patients without complications compared with the established pathway (hazard ratio = 2.81; 95% CI, 2.09–3.78; $p < 0.001$) after adjusting for comorbidities in a competing risk model.
- CONCLUSIONS:** Early diagnosis of postoperative complications is associated with a shorter LOS after rectal cancer surgery. Enhanced recovery pathway can facilitate a faster recovery in the presence of comorbidities. (J Am Coll Surg 2014;218:914–919. © 2014 by the American College of Surgeons)
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A number of factors contribute to a patient's length of stay (LOS) after bowel surgery. These factors include pre-existing patient conditions, surgical and anesthesia factors, development of postoperative ileus, and other

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postoperative complications. Pre-existing conditions can be an important factor in the analysis of adverse outcomes.¹ The majority of patients have chronic illnesses and might be at a higher risk for postoperative complications or prolonged LOS. Accurately assessing comorbid conditions can impact treatment decisions and prognosis^{2–5} and improve patient safety.

Because complications affect LOS, the time to occurrence should be taken into account in multi-state or competing risk models with LOS as one of the primary outcomes and postoperative complications as competing risks. Such models can be used to describe the recovery process over time. Multi-state models are applicable for surgical cohorts and statistical software is available, but so far they have not been widely adopted.^{6–8}

The goal of this study was to examine whether shorter time to occurrence of complications in hospital was associated with a shorter LOS in rectal cancer patients undergoing minimally invasive surgery, taking into account the

perioperative pathway. Preoperative variables and the perioperative care pathway instituted were evaluated as explanatory factors for the variability in LOS.

METHODS

Patients and inclusion criteria

All patients older than 17 years undergoing minimally invasive resection for rectal cancer from February 2005 until December 2011 were included in this analysis. A total of 349 patients were identified, 2 were excluded from the final database because their surgery was palliative. There were 346 patients with research authorization that could be matched to billing data and comorbidity information. All patients underwent either hand-assisted, laparoscopic-assisted, or robotic-assisted rectal resections. The IRB approved this retrospective study.

Patient comorbidities at admission, including diabetes, chronic renal insufficiency, and cardiovascular diseases, were captured using billing data. Administrative (billing) data include the identification of the problem or problems (diagnoses) leading to the health care service being delivered in a standard diagnostic code (ICD-9-CM in the United States) and can include additional diagnosis codes to reflect comorbidities. Complications considered were postoperative ileus, abscess, leak, wound infection, small bowel obstruction, reoperation for bleeding, and renal failure. Ileus was defined as inability to tolerate oral intake for longer than 5 days with nausea and vomiting and/or requiring the insertion of a nasogastric tube at any time. Thirty-day results were obtained through direct patient contact at the Mayo clinic or through routine phone follow-up.

Patients were treated with either enhanced recovery pathway (ERP) or an established care pathway (control) as a defined order set. The ERP consists of preoperative, intraoperative, and postoperative elements.^{9,10} Enhanced recovery pathway was introduced in the practice in 2009 and was an important factor to consider in this study.

Statistical analysis

Continuous variables were summarized as mean (SD) or median (quartiles) as appropriate and compared with a 2-sided *t*-test or Wilcoxon rank sum test. Categorical variables were described as frequencies (percentages) and compared with a chi-square test or Fisher's exact test. Comparisons for small samples with sparse structures (complications) were performed using Firth's penalized likelihood procedure that corrects for bias.¹¹

Length of stay was defined as the time from surgery to discharge. Multivariable logistic regression models were used for binary outcomes, such as LOS longer than 3 days. Complications and LOS are not independent end points. It is useful to define surgical complications as a

competing risk to discharge. Therefore multi-state models were used to examine associations of factors on time to occurrence of complications or time to discharge, where time refers to the time since surgery. Surgery was the initial state; discharge the primary end point modeled as a terminal event, and occurrence of complications a time-dependent intermediate state. Although survival analysis models estimate hazard ratios to characterize the transition time between 2 states (alive to death), this multi-state model approach enabled us to estimate hazard ratios for risk factors separately for each transition, surgery to discharge, surgery to occurrence of complication, and discharge after a complication. A clock forward approach was used for the time scale where time is measured from the date of surgery. For example, if a patient was diagnosed with a complication 2 days after surgery and then was discharged 5 days later, time to discharge is 7 days. A Markov proportional hazards model was used to estimate the hazard ratios for predictors at transitions from surgery to discharge, surgery to complications, or complications to discharge.¹² In particular, the hazard function for transition from state *i* to state *j* is given by $\lambda_{ij}(t) = \lambda_{ij,0}(t) \exp(X_{ij}\beta)$, where X_{ij} are transition-specific covariates and $\lambda_{ij,0}$ is the baseline hazard for the transition from *i* to *j*. We investigated whether the time a patient experienced a complication was associated with time to subsequent discharge. Proportional hazard assumptions were evaluated with scaled Schoenfeld residuals.

In a subgroup of patients with complications, a generalized linear model with a log link function was used to estimate the association of time to first occurrence of a complication with LOS, and the appropriate distribution of LOS was determined with the modified Park test¹³ adjusted for comorbidities.

A level of 0.05 was considered statistically significant. All analyses were performed using R version 2.15.3¹⁴ and the multi-state analysis package *mstate* version 0.2.6.¹⁵

RESULTS

A total of 346 patients with rectal cancer undergoing minimally invasive surgery from 2005 to 2011 were included in the analysis. Patients underwent 1 of 3 procedures, low anterior resection (*n* = 250), abdominoperineal resection (*n* = 68), and proctocolectomy (*n* = 28). Mean age was 58.9 years (SD 14 years) for the entire cohort. The majority of the patients were American Society of Anesthesiologists (ASA) physical status score 1 or 2 (72.5%). Prevalence of comorbidities was 12.1% for diabetes, 12.4% for cardiovascular disease, and 2.3% for renal insufficiency. There were no statistically significant differences in age, sex, body mass index, neoadjuvant therapy, or primary

Table 1. Baseline Patient Characteristics of Rectal Cancer Patients Undergoing Minimally Invasive Resection, 2005–2011

Patient characteristics	Complications after surgery (n = 77)	No complications after surgery (n = 269)	Total (n = 346)	p Value
Age, y, mean (SD)	60.1 (16.0)	58.5 (13.0)	58.9 (13.7)	0.43
Body mass index, kg/m ² , mean (SD)	27.6 (5.0)	27.2 (4.9)	27.2 (5.0)	0.49
Sex, n (%)				0.07
Male	59 (76.6)	176 (65.4)	235 (67.9)	
Female	18 (23.4)	93 (34.6)	111 (31.1)	
ASA, n (%)				0.006
1 or 2	46 (59.7)	205 (76.2)	251 (72.5)	
3 or 4	31 (40.3)	64 (23.8)	95 (27.5)	
Primary procedure, n (%)				0.31
LAR	58 (75.3)	192 (71.4)	250 (72.3)	
APR	11 (14.3)	57 (21.2)	68 (19.7)	
Proctocolectomy	8 (10.4)	20 (7.4)	28 (8.1)	
Perioperative pathway, n (%)				0.35
ERP	14 (18.2)	64 (23.8)	78 (22.5)	
Established	63 (81.8)	205 (76.2)	268 (77.5)	
Neoadjuvant therapy, n (%)	38 (49.4)	123 (45.7)	161 (46.5)	0.61
Conversion to open, n (%)	18 (23.4)	29 (10.8)	47 (13.6)	0.008
Diabetes, n (%)	14 (18.2)	28 (10.4)	42 (12.1)	0.08
Obese (BMI >30), n (%)	21 (27.3)	62 (23.0)	83 (24.0)	0.45
Cardiovascular disease, n (%)	4 (5.2)	17 (6.3)	43 (12.4)	>0.99
Chronic renal insufficiency, n (%)	5 (6.5)	3 (1.1)	8 (2.3)	0.011

APR, abdominoperineal resection; ASA, American Society of Anesthesiologists physical status score; BMI, body mass index; ERP, enhanced recovery pathway; LAR, low anterior resection.

procedure between patients with or without postoperative complications (Table 1). There were 268 patients treated with established care and 78 patients on ERP. Neoadjuvant therapy was received by 46.5% of the patients.

Major complications occurred in 2% of the patients, ileus was diagnosed in 19.9%, 12.4% were readmitted within 30 days of the surgery, and there were 2 deaths within 30 days of surgery. All other complications, such as leak or abscess, occurred within 4 days of surgery, and 50% of ileus occurrences were after 3 days (Fig. 1).

Median time to occurrence of a complication was 3 days. When the first complication was diagnosed within 4 days post operation, overall median LOS was 8 days, compared with a diagnosis after 4 days with overall median LOS 11 days ($p < 0.001$). Longer time to occurrence of a complication was associated with longer remaining time in the hospital after adjusting for ERP, diabetes, older age, and high ASA physical status score (using a generalized linear model with log transformed LOS, exponent of coefficient of the time variable = 1.12; 95% CI, 1.1–1.2, $p < 0.001$). Although there was no significant difference in the incidence of complications between ERP and established care (Table 2), 64% of the complications in ERP patients occurred within 3 days post operation compared with 49% of

complications in the controls (unadjusted odds ratio = 2.41; 95% CI, 0.61–12.03; $p = 0.22$).

Multi-state models

For those patients with surgical complications, a longer time to diagnosis of the complication was associated with an increased LOS after complication (hazard ratio = 0.84; 95% CI, 0.73–0.96; $p = 0.01$). The ERP was associated with a shorter LOS for patients without complications (hazard ratio = 2.81; 95% CI, 2.09–3.78; $p < 0.001$). Diabetes and older age (older than 65 years) were associated with longer LOS (Table 3, Transition 2). The prediction probability to be discharged without a complication on postoperative day 3 was 44% for a patient with the 3 risk factors, ASA physical status score 3 or 4, older than 65 years, and diabetes, in patients with established care. The corresponding probability was 73% for a patient with these characteristics on the ERP.

DISCUSSION

This analysis quantified transition-specific risk estimates in recovery after rectal surgery. To the best of our knowledge, this is the first study estimating the impact of the

Figure 1. Relative frequency histogram of time to occurrence for the first complication for patients with complications ($n = 77$).

timing of postoperative complications on LOS. Principal findings were that early diagnosis of postoperative complications was associated with shorter LOS after occurrence of complications. Median time to complications was 3 days for ERP patients and 4 days for patients on the established care pathway, however, it was not statistically significant. The most frequent complication was postoperative ileus (90%), with a median time to occurrence of 3 days. All remaining serious complications

occurred within 4 days of surgery. These results suggest that earlier identification of ileus and immediate intervention can lead to faster resolution and shorter LOS. Another plausible explanation relates to earlier occurrence of postoperative ileus in ERP patients. Comprehensive care pathways, such as ERP, incorporate a bundle of preventive measures aimed at reducing postoperative ileus. However, about 15% to 20% of patients after colorectal surgery procedures will experience ileus as an inevitable complication, despite multimodal prevention. In these patients, aggressive components of the protocol, such as early food intake and laxative use, are likely to accelerate occurrence of symptoms. Early decompression would therefore result in earlier resolution of the problem and allow for earlier discharge. This can be considered as an advantage of ERP as long as reliable predictors for postoperative ileus are not available.

The ERP was associated with an earlier discharge for patients without complications after adjusting for comorbidities and patient risk factors. This has also been reported in other published cohorts of colorectal surgery patients. There is a paucity of reports on rectal cancer patients, and the lack of stratification between patients with and without complications hinders direct comparisons between studies. In our study of rectal cancer patients with minimally invasive surgery, the median LOS was 5 days overall, 4 days for patients without complications, and 9 days for patients with complications. Hardt and colleagues¹⁶ reported a median LOS of 12.5 days for 36 rectal cancer patients on the fast-track pathway (44% laparoscopic). In the study by Keane and colleagues¹⁷ dealing with rectal or colon cancer

Table 2. Short-Term Outcomes for Rectal Cancer Patients Undergoing Minimally Invasive Resection, 2005–2011

Outcomes	Enhanced recovery pathway (n = 78)	Established care pathway (n = 268)	Total (n = 346)	p Value
Overall LOS, days, median (1 st , 3 rd quartile)	3 (2, 4)	5 (4, 7)	5 (3, 6)	<0.001
LOS in patients without complications, days, median (1 st , 3 rd quartile)	3 (2, 3), n = 64	4 (3, 5), n = 205	4 (3, 5), n = 269	<0.001
LOS in patients with complications, days, median (1 st , 3 rd quartile)	9 (8, 10.75), n = 14	10 (7, 13), n = 63	9 (7, 13), n = 77	0.18
LOS within 48 hours, n (%)	24 (30.8)	4 (1.5)	28 (8.1)	<0.001*
Any surgical complication, n (%)	14 (17.9)	63 (23.5)	77 (22.3)	0.30
Ileus, n (%)	10 (12.8)	59 (22.0)	69 (19.9)	0.08
Small bowel obstruction, n (%)	0 (0)	1 (0.4)	1 (0.3)	0.18*
Leak or abscess, n (%)	2 (2.6)	7 (2.6)	9 (2.6)	0.60*
Wound infection, n (%)	1 (1.3)	4 (1.5)	5 (1.4)	0.65*
Renal failure, n (%)	3 (3.8)	6 (2.2)	9 (2.6)	0.37*
Readmission 30 days, n (%)	6 (7.7)	37 (13.8)	43 (12.4)	0.16*
Death within 30 days, n (%)	0 (0.0)	2 (0.7)	2 (0.6)	0.80*

*p Values were calculated with Firth's penalized likelihood method to account for bias in sparse structures.

LOS, length of stay from day of surgery to discharge.

Table 3. Transition-Specific Hazard Ratios (95% Confidence Intervals) for the Multi-State Model with 3 Transitions

Patient characteristics	All patients (n = 346)	LOS, HR (95% CI); p value		
		Complications after surgery, HR (95% CI) (n = 77)	Discharge without complications (n = 269)	Discharge after complications (n = 77)
			Transition 2*	Transition 3*
ERP	78 (22.5) [†]	1.73 (0.95–1.36), p = 0.08	2.81 (2.09–3.78); <0.001	1.21 (0.47–2.33); 0.55
Age older than 65 years	120 (34.7) [†]	1.17 (0.72–1.90), p = 0.52	0.71 (0.54–0.93); 0.013	1.13 (0.70–1.81); 0.61
ASA physical status score 3 or 4	95 (27.5) [†]	1.63 (0.99–2.67), p = 0.05	0.95 (0.71–1.28); 0.75	1.33 (0.80–2.22); 0.27
Diabetes	42 (12.1) [†]	1.01 (0.54–1.87), p = 0.98	0.59 (0.40–0.88); 0.010	0.65 (0.34–1.24); 0.19
Time to diagnosis of complications, days	3 (3, 5) [‡]			0.84 (0.73–0.96); 0.01

*Transition 1 from surgery to occurrence of complications, Transition 2 from surgery to discharge, Transition 3 from complications to discharge.

[†]n (%).

[‡]Median (1st, 3rd quartile).

ASA, American Society of Anesthesiologists; ERP, enhanced recovery pathway; HR, hazard ratio; LOS, length of stay.

patients, a comparison of outcomes for ERP patients (n = 80) and established care patients (n = 160) resulted in a median LOS of 7 days for the ERP group. Enhanced recovery pathway patients with open rectal resection (n = 311) for Hendry and colleagues¹⁸ had a median LOS of 7 days. Lawrence and colleagues reported a median LOS of 3 days and a discharge within 2 days in 36% of the 609 laparoscopic colorectal surgery patients.¹⁹ This is comparable with our results, in which 31% of ERP patients were discharged within 2 days, although data reported in Lawrence and colleagues¹⁹ included a patient mix with a diagnosis of colon and rectal cancer, inflammatory bowel disease, and other diagnoses, and our study was focused on rectal cancer patients.

This was a retrospective review and has inherent limitations. The ERP patients had more recent surgery (2009 to 2011) due to the introduction of ERP in 2009, and patients with surgery in 2005 to 2011 were treated with established care. However, the patient cohorts in these time periods were comparable, as indicated by similar median LOS or use of neoadjuvant therapy in the established care group before and after 2009. Shortcomings of using administrative data for comorbidity codes revolve around the accuracy and completeness of the capture of diagnoses in the billing process. In this study, we used only prevalent comorbidities where we were confident of its accuracy. The strengths of this study are the focus on rectal cancer patients undergoing minimally invasive surgery and the time-dependent statistical models that are able to consider the recovery progression process.

CONCLUSIONS

After adjusting for comorbidities such as diabetes, older age, and higher ASA physical status score, early diagnosis of postoperative complications, in particular postoperative ileus, was related to shorter time to discharge after

the occurrence of the complication. In clinical practice it is advisable to have a greater awareness of slow progress or failure to recovery. Additional research is warranted to investigate whether early food intake in patients on ERP can lead to earlier occurrence of complications and earlier resolution and discharge. Use of an ERP is associated with a shorter LOS for patients without complications in a multi-state model with complications and discharge as competing risks.

Author Contributions

Study conception and design: Huebner, Larson

Acquisition of data: Larson

Analysis and interpretation of data: Huebner, Hübner, Cima, Larson

Drafting of manuscript: Huebner, Hübner, Cima, Larson

Critical revision: Huebner, Hübner, Cima, Larson

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