Predicting primary postoperative pulmonary complications in patients undergoing minimally invasive surgery for colorectal cancer

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Abstract

Objective To determine the risk factors for developing primary postoperative pulmonary complications (PPC) in patients undergoing minimally invasive colorectal surgery (MIS) for the treatment of cancer and to identify the potential indicators for more extensive preoperative evaluation.

Materials and methods The ACS-NSQIP[®] database was interrogated to capture patients who had elective colon or rectal cancer and underwent MIS between 2012 and 2017. Patients who had primary PPC including pneumonia, unplanned intubation and/or failure to wean from mechanical ventilation for > 48 h were compared to patients without PPC. Significant risk factors for PPC were retained to build a predictive risk model through logistic regression analysis. The model was then internally validated using 2018 data.

Results Of 50,150 patients identified, 637 (1.3%) had PPC. The final risk prediction model included six variables: history of chronic obstructive pulmonary disease, age, smoking status, functional health status, pre-operative congestive heart failure, and American Society of Anesthesiology class ≥ 3 . The model achieved good calibration (Hosmer–Lemeshow goodness-of-fit test, $p = 0.614$) and discrimination (c statistics = 0.757). Internal validation achieved similar discrimination (c statistics = 0.798).

Conclusion Primary postoperative pulmonary complications affected 1.3% of patients undergoing MIS for colon or rectal cancer. The novel predictive risk score showed good discrimination and may help to identify patients who may benefit from perioperative optimization.

Keywords Colorectal surgery · Minimally invasive surgery · Colorectal cancer · Respiratory complications · Pneumonia · Unplanned intubation · Failure to wean from mechanical ventilation

Introduction

Postoperative pulmonary complications (PPC) are infrequent but critically important after colorectal surgery [1]. Approximately 20% of patients who have PPC will die within 30 days, in comparison to 0.2–3% who do not develop PPC [2]. Affected patients also have increased length of stay and associated cost of care [3, 4].

The impact of risk factors on postoperative respiratory function and complications has yet to be defined in the setting of minimally invasive surgery (MIS). The use of carbon dioxide pneumoperitoneum with laparoscopy reduces lung compliance and functional residual capacity, which in turn increases the risk of hypoxemia [5, 6]. As such, open techniques have historically been recommended for patients deemed high-risk.

Despite these concerns, several studies have reported that MIS does not increase PPC [2, 7]. Furthermore, MIS is associated with decreased pain, accelerated functional recovery, and shorter length of stay when compared to open surgery [8–10]. Laparoscopic colonic surgery is linked to a lower risk of postoperative respiratory complications, decreased postoperative morbidity, and a shorter length of stay compared with open colonic surgery [11–15].

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To date, the identification of factors associated with PPC within a MIS framework has yet to be defined. This study aimed to document characteristics of patients who had PPC following minimally invasive colorectal cancer surgery. A tool to predict PPC was then built from this information.

Methods

Data source

Data were obtained from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. ACS-NSQIP program is a nationally validated, and outcome-based program which was developed to measure and improve the quality of surgical care. Patients' data are collected by trained clinical abstractors based on a predesigned data extraction sheet. Data from all participating institutions are collected and 20% of the patients are retained in the final files.

Cohort

All patients who had minimally invasive colon or rectal surgery between January 2012 and December 2017 were identified using the Current Procedure Terminology (CPT) codes: 44,204, 44,205, 44,206, 44,207, 44,208, 44,210, 44,211, 44,212, 45,395, and 45,397. Patients with colon or rectal cancer were identified using the International Classification of Diseases (ICD) codes: ICD-9-CM 153.x, 230.3, and 230.4; and ICD-10-CM D01.0, D01.1, D01.2, C18.x, C19, and C20. Patients were excluded if they had emergent or non-elective (urgent) surgery, a concurrent operation under a different attending or an American Society of Anesthesiology Class (ASA) V. Patients who had major complications before the onset of respiratory complications were also excluded. These included cardiac arrest requiring resuscitation, myocardial infarction, pulmonary embolism, septic shock, reoperation, and organ space infection due to leak.

Outcomes

Our primary outcome was development of primary PPC defined as pneumonia, unplanned reintubation, or failure to wean from the ventilator within the participant data use file (PUF). Primary PPC was defined as a pulmonary complication that preceded another known major complication. Pneumonia is only reported in the presence of radiological features in combination with signs, symptoms, or laboratory confirmation. Unplanned reintubation was defined as unintended endotracheal intubation and mechanical ventilation after extubation. Failure to wean was ascribed if mechanical ventilation was required for a total cumulative time of more

than 48 h. Our secondary outcome was a 30-day mortality rate.

Statistical analysis

Data were reported as frequency and proportions for categorical variables and median (interquartile range) for continuous variables. Demographics and pre-operative characteristics were compared between patients who had PPC and patients who did not have PPC using the Chi-Square test or Fisher's exact test for categorical variables and Mann–Whitney *U* test for continuous variables.

A multivariable logistic regression with stepwise variable selection was then used to build a prediction model for the primary outcome (PPC). Independent risk factors associated with a PPC ($p < 0.1$) in the univariate analysis were entered in the initial model. With a backward elimination procedure, only significant risk factors ($p < 0.05$) were kept. Then, a forward stepwise selection method was utilized which achieved the same model. Once a stable model was built, all eliminated variables were rechecked none of which had a significant effect on the model. Odds ratios (OR) with 95% confidence intervals (CI) were used to measure the magnitude of the association.

The proposed prediction model was then internally validated using the PUF 2018. Hosmer Lemeshow goodness-of-fit test was used to test the calibration of the proposed score in both datasets. A *c* statistics obtained from the receiver operating characteristic (ROC) curve was then used to assess the discriminative ability of the model in both datasets. The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, Version 25; SPSS, Inc., Armonk, NY, USA). In our analysis, an alpha level of less than 0.05 was considered statistically significant.

Results

Some 50,150 patients from the ACS NSQIP program were included from 2012 to 2017. Of these patients, 420 (0.8%) developed pneumonia, 260 (0.5%) developed unplanned reintubation, and 57 (0.1%) patients needed mechanical ventilation for more than 48 h. Collectively, 637 (1.3%) developed PPC. Patients who developed respiratory complications were more likely to be male, older, and with more co-morbidities as outlined in Table 1. Patients who had a PCC had a higher 30-day mortality rate compared to patients who did not have a PCC (17.5% vs 0.2%; $p < 0.0001$).

Of all the examined variables, the final risk assessment model for prediction of PCC development included six risk factors: a history of chronic obstructive pulmonary disease, age, smoking status, functional health status,

Table 1 Baseline and surgical characteristics

	Respiratory complications			<i>p</i> value
	Yes	No	Total	
Number of patients	637	49,513	50,150	
Gender				< 0.0001
Female	256 (40.2%)	23,774 (48.0%)	24,030 (47.9%)	
Race				< 0.0001
White	445 (69.9%)	34,797 (70.3%)	35,242 (70.3%)	
African American	55 (8.6%)	4215 (8.5%)	4270 (8.5%)	
Asian	10 (1.6%)	2541 (5.1%)	2551 (5.1%)	
American Indian or Alaska Native	3 (0.5%)	185 (0.4%)	188 (0.4%)	
Native Hawaiian or Pacific Islander	0	170 (0.3%)	170 (0.3%)	
Unknown/not reported	124 (19.5%)	7605 (15.4%)	7729 (15.4%)	
Hispanic				< 0.0001
Yes	15 (2.4%)	2410 (4.9%)	2425 (4.8%)	
No	499 (78.3%)	40,262 (81.3%)	40,761 (81.3%)	
Unknown	123 (19.3%)	6841 (13.8%)	6964 (13.9%)	
BMI, kg/m ²				0.146
Normal (BMI 18.5–25)	201 (31.6%)	14,287 (28.9%)	14,488 (28.9%)	
Under weight (BMI < 18.5)	13 (2.0%)	866 (1.7%)	879 (1.8%)	
Over weight (BMI 25–30)	202 (31.7%)	17,388 (35.1%)	17,590 (35.1%)	
Class I obesity (BMI 30–35)	119 (18.7%)	10,078 (20.4%)	10,197 (20.3%)	
Class II obesity (35–40)	60 (9.4%)	4134 (8.3%)	4194 (8.4%)	
Class III obesity (BMI > 40)	36 (5.7%)	2541 (5.1%)	2577 (5.1%)	
Missing	6 (0.9%)	219 (0.4%)	225 (0.4%)	
Age, years				< 0.0001
< 50	24 (3.8%)	5795 (11.7%)	5819 (11.6%)	
50–59	47 (7.4%)	10,960 (22.1%)	11,007 (21.9%)	
60–69	122 (19.2%)	13,518 (27.3%)	13,640 (27.2%)	
70–79	225 (35.3%)	12,004 (24.2%)	12,229 (24.4%)	
80–89	187 (29.4%)	6429 (13.0%)	6616 (13.2%)	
≥ 90	32 (5.0%)	806 (1.6%)	838 (1.7%)	
DM				< 0.0001
No diabetes	498 (78.2%)	40,510 (81.8%)	41,008 (81.8%)	
Insulin dependent	59 (9.3%)	2631 (5.3%)	2690 (5.4%)	
Non-insulin dependent	80 (12.6%)	6372 (12.9%)	6452 (12.9%)	
Current smoker	112 (17.6%)	6099 (12.3%)	6211 (12.4%)	< 0.0001
COPD	130 (20.4%)	2105 (4.3%)	2235 (4.5%)	< 0.0001
Dyspnea				< 0.0001
No	510 (80.1%)	46,147 (93.2%)	46,657 (93.0%)	
Yes, at rest	13 (2.0%)	156 (0.3%)	169 (0.3%)	
Yes, at moderate exertion	114 (17.9%)	3210 (6.5%)	3324 (6.6%)	
Functional status				< 0.0001
Independent	587 (93.3%)	48,627 (98.6%)	49,214 (98.1%)	
Partially dependent	37 (5.9%)	623 (1.3%)	660 (1.3%)	
Totally dependent	5 (0.8%)	68 (0.1%)	73 (0.1%)	
Ventilator dependent	2 (0.3%)	3 (0.0%)	5 (0.0%)	< 0.0001
Ascites	3 (0.5%)	60 (0.1%)	63 (0.1%)	0.013
CHF	27 (4.2%)	315 (0.6%)	342 (0.7%)	< 0.0001
Antihypertensive therapy	457 (71.7%)	25,560 (51.6%)	26,017 (51.9%)	< 0.0001
Hemodialysis	4 (0.6%)	183 (0.4%)	187 (0.4%)	0.288
Disseminated cancer	52 (8.2%)	2706 (5.5%)	2758 (5.5%)	0.003

Table 1 (continued)

	Respiratory complications			<i>p</i> value
	Yes	No	Total	
Open wound/wound infection	8 (1.3%)	181 (0.4%)	189 (0.4%)	< 0.0001
Steroid use for chronic condition	37 (5.8%)	1300 (2.6%)	1337 (2.7%)	< 0.0001
> 10% weight loss in the last 6 months	27 (4.2%)	1495 (3.0%)	1522 (3.0%)	0.075
Bleeding disorder	28 (4.4%)	1121 (2.3%)	1149 (2.3%)	< 0.0001
Transfusion of ≥ 1 unit of pRBCs 72 h prior to surgery	18 (2.8%)	331 (0.7%)	349 (0.7%)	< 0.0001
ASA class				< 0.0001
I and II	119 (18.7%)	22,585 (45.7%)	22,704 (45.3%)	
III and IV	518 (81.3%)	26,870 (54.3%)	27,388 (54.7%)	
Preoperative laboratories; median (IQR)				
Albumin, g/dL	3.8 (3.4–4.1)	4 (3.7–4.3)	4 (3.7–4.3)	< 0.0001
Hematocrite, %	35.8 (31.5–40.5)	38.5 (34.2–41.9)	38.7 (34.5–42)	< 0.0001
Platelets, 1000/ μ L	245 (195–320)	249 (204–306)	248 (204–304)	< 0.0001
Operation time	162 (117–222)	168 (122–234)	165 (120–229)	0.210
30-Day mortality	94 (14.8%)	118 (0.2%)	212 (0.4%)	< 0.0001

COPD chronic obstructive pulmonary disease, *BMI* Body Mass Index, *DM* diabetes mellitus, *CHF* congestive heart failure, *pRBCs* packed red blood cells, *ASA* American Society of Anesthesiologist

congestive heart failure within 30 days prior to surgery, and ASA class (Table 2).

The multiple logistic regression equation was as follows:

$$L = -5.932 + (1.157 \times \text{presence of COPD}) + (-0.109 \times \text{age: 50 to 59}) + (0.469 \times \text{age: 60 to 69}) + (1.112 \times \text{age: 70 to 79}) + (1.484 \times \text{age: 80 to 89}) + (1.789 \times \text{age} \geq 90) + (0.578 \times \text{current smoker}) + (0.857 \times \text{functional status partially dependent}) + (1.227 \times \text{functional status totally dependent}) + (1.015 \times \text{CHF}) + (0.743 \times \text{ASA III_IV}).$$

dependent) + (1.227 $\times$ functional status totally dependent) + (1.015 $\times$ CHF) + (0.743 $\times$ ASA III_IV).

The estimated probability of 30-day PPC was calculated using the following formula:

Estimated probability of composite adverse event = $\text{EXP}[L] / (1 + \text{EXP}[L])$.

As shown in Table 3, the model demonstrated good calibration (Hosmer–Lemeshow goodness-of-fit test, $\chi^2 = 6.297$,

Table 2 Predictors of postoperative respiratory complications: results of multivariable logistic regression analysis in PUF 2012–2017

	β -coefficient	OR	95% CI
History of COPD	1.157	3.179	(2.575–3.925)
Age; years			
< 50 (reference)			
50–59	– 0.109	0.897	(0.547–1.470)
60–69	0.469	1.599	(1.027–2.490)
70–79	1.112	3.041	(1.980–4.672)
80–89	1.484	4.410	(2.844–6.840)
≥ 90	1.789	5.981	(3.452–10.365)
Current smoker within one year	0.578	1.783	(1.429–2.225)
Functional health status prior to surgery			
Independent (reference)			
Partially dependent	0.857	2.356	(1.653–3.358)
Totally dependent	1.227	3.411	(1.327–8.770)
CHF within 30 days prior to surgery	1.015	2.758	(1.815–4.192)
ASA classification			
(III and IV) vs (I and II)	0.743	2.102	(1.702–2.596)
Constant	– 5.932		

PUF participant user files, *COPD* chronic obstructive pulmonary disease, *DM* diabetes mellitus, *CHF* congestive heart failure, *ASA* American Society of Anesthesiologist,

Table 3 Calibration and discriminatory statistics for the regression model

	<i>c</i> statistic	Standard error ^a	Asymptotic 95% confidence interval	<i>p</i> value
PUF (2012–2017): model development data set	0.757	0.010	0.738–0.776	< 0.0001
PUF 2018: model validation data set	0.798	0.017	0.765–0.832	< 0.0001

PUF participant user files

^aUnder the nonparametric assumption

p value = 0.614) and discrimination (*c* statistic = 0.757). The generated model based on 2012–2017 ACS-NSQIP® was then internally validated using the 2018 ACS-NSQIP® data which showed relatively similar performance (*c* statistic = 0.798) (Fig. 1).

The performance of the risk prediction model at different cut-off points is shown in Table 4. Using the predicted probability of $\geq 1.96\%$ as a cut-off value, the model achieved a specificity of 83.7% for detecting the PPC. In other words, those with a predicted probability of $\geq 1.96\%$ were at higher risk of having pulmonary complications.

Discussion

This study documents the characteristics of patients who had primary PPC after minimally invasive surgery for colorectal cancer while excluding major postoperative complications that occurred before the onset of PCC. Other major postoperative complications might be a potential cause for the PPC, and as such were excluded from the analysis to provide a precise hands-on predictive tool to identify these patients based on pre-operative data.

Our study population rate of PPC (1.3%) fell below the 2% median incidence of PPC after MIS identified in a 2015 systematic review of randomized controlled trials that compared laparoscopic versus open surgery for colorectal cancer [16]. Some studies included in the systematic review had more broadly encompassing definitions of PPC in comparison to our more narrow definition. The difference may also represent a healthy selection bias given high-risk patients who underwent open surgery were ultimately excluded from our analysis.

Males had a higher preponderance of PPC (59.8%), as did the elderly, those with diabetes, and those with more comorbidities as seen in patients with an ASA score of 3 or more.

Fig. 1 receiver operating characteristic curves**Table 4** Performance of risk calculator at various cut-points

Cut-point	Sensitivity (%)	Specificity (%)	Youden's <i>J</i> ^a
≥ 0.556	88	42	30
≥ 0.934	75.7	64.4	40.1
≥ 1.62	67.2	71.2	38.4
≥ 1.96	50.2	83.7	33.9
≥ 2.45	34.3	92.3	34

^aYouden's *J* test calculated by the following formula: (sensitivity + specificity – 1) to identify the best cut-off point

Expected risk factors and markers of poor respiratory function, such as smoking, dyspnea, and impaired functional status, also increased the risk of PPC. In contrast to former evidence, there was no significant association with BMI [17]. This may speak to the benefit of MIS for obese patients: a smaller incision often results in less pain which allows more optimal respiratory function compared to patients who have a laparotomy [11, 18].

According to our model, if patients have a predicted probability higher than 1.96%, they are at higher risk of primary PPC and, therefore, may warrant greater attention and focus on prehabilitation. Several other studies have devised models for PPC but have covered multi-specialty procedures or multiple disease processes [19–29]. Others focused on a single adverse outcome [19–25]. Furthermore, our uniqueness is different given the fact we excluded the potential main complications after surgery that might predispose to the PPC [2]; our focus was on primary PPC. The predictive potential of our model is high, easy to use, and particularly useful for a colorectal surgical team in pre-operative planning for colorectal cancer.

One of the most significant predictive factors in the score, aside from advancing age and dependence, was a history of severe COPD (OR 3.12, 95% CI 2.53–3.85). COPD is associated with higher rates of in-hospital complications, ICU admission, antibiotic treatment, reintervention, and mortality after colorectal cancer surgery [30]. Although MIS is associated with improved outcomes in patients with COPD [11], perioperative teams still often avoid MIS for fear of worse respiratory outcomes. This study included some 2235 patients with COPD and our score could also be applied to this cohort. In doing so, it may also help clinicians confidently engage in MIS for this subset of patients.

The model is limited having been devised from a retrospective database. The use of a database, such as NSQIP, in itself is limited by the quality of the data. Coding errors can occur for example. However, our model was internally validated using a second dataset from 2018, and predictive performance was closely approximated.

Our methods successfully built an internally validated model to predict postoperative respiratory complications, with good discrimination. Established postoperative pathways, such as ‘Enhanced Recovery’, have significantly reduced PPC [31], in part due to early mobilization, prevention of fluid overload, and avoidance of nasogastric tubes which minimize the risk of bronchoaspiration [32]. Our predictive model could be used to identify at-risk patients to increase postoperative resource allocation to ensure adherence to such pathways and provide pulmonary rehabilitation. Furthermore, the score can be used to guide prehabilitation and inform consent in high-risk patients.

In summary, our study identified a low rate of pulmonary complications after minimally invasive colon and rectal

cancer surgery. The predictive tool may help to mitigate risk through enhancement of preventive measures.

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Compliance with ethical standards

Conflict of interest The authors have no conflict of interest.

Ethical approval Institutional Review Board approval was not required for this study.

Research involving human participants and/or animals This article does not contain any experimental studies with human participants or animals performed by any of the authors.

Informed consent For this study, formal consent is not required.

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