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The independent effect of cancer on outcomes: a potential limitation of surgical risk prediction

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Abstract

BACKGROUND—Cancer patients are often thought to have worse surgical outcomes. There is a growing view that risk models do not adequately predict these outcomes. This study aims to compare the use of common risk models for benign versus malignant gastrointestinal disease.

MATERIALS AND METHODS—The NSQIP 2005–2015 participant use files were queried for patients undergoing elective surgery for benign and malignant diseases with a primary procedure code for major colon, pancreas, or stomach resection. Multivariate logistic regression was performed to identify independent predictors of mortality and morbidity.

RESULTS—We identified 264,401 cases (111,563 malignant). The gastrointestinal cancer population was disproportionately male, older than 65, non-white, and less functionally independent. Comorbidities more common in the cancer population included diabetes, hypertension, dyspnea, and COPD. Cancer patients had a longer length of stay (+0.9 days), higher mortality rate (1.7% vs. 1.1%), and higher complication rate (27.4% vs. 23.2%). NSQIP prediction models for complications in cancer versus non-cancer patients underperformed for predicting mortality ($p < 0.001$). Multivariate regression demonstrated that a diagnosis of cancer requiring surgery independently conferred an 18% increased odds of death, a 9% increased odds of a

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AUTHOR CONTRIBUTIONS

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Acquisition of data: Leeds, Canner

Analysis and interpretation of data: Leeds, Canner, Efron, Ahuja, Haut, Wick, Johnston

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DATA ACCESS

I. L. had full access to all the data and takes responsibility for the integrity of the data and accuracy of the data analysis.

DISCLOSURES

No author has a financial or personal relationship with other people or organizations that could inappropriately influence the work reported here.

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complication, and an 8% increased odds of multiple complications compared to patients with benign disease.

CONCLUSIONS—NSQIP prediction models less effectively evaluate the risk of death in cancer patients as compared to patients with benign disease. A diagnosis of cancer is independently associated with an increased risk of surgical complications. Incorporating cancer diagnosis into surgical risk models may better inform patient and surgeon expectations.

Keywords

surgery; morbidity; risk; neoplasms; logistic regression; outcomes assessment

INTRODUCTION

The incidence of cancer continues to rise in the United States with a further expected 45% increase over the next 25 years.¹ For surgeons, this trend is particularly important as more patients will require supportive decision making regarding risk for cancer-related surgical care.² Patients may not fully understand surgical treatment options and are more likely to follow surgeons' recommendations without effective shared decision making. Risk counseling has been demonstrated to reduce decisional conflict.^{3–6}

Large datasets in surgical quality improvement have proliferated to provide patient-specific surgical risk prediction with an aim to improve outcomes through enhanced decision-making. Early efforts focused on procedure- or specialty-specific perioperative risk,^{7,8} but standardization and simplification of risk models have been more characteristic of the recent trend.^{9,10} Within the last decade, the American College of Surgeons' (ACS) National Surgical Quality Improvement Program (NSQIP) and its associated all-procedure risk calculator have set the standard in terms of both scale and ease of use.^{8,11} Risk prediction models have been assessed in cancer-only populations, and it has been shown that these models do not perform as well in a highly specific cancer surgery contexts often lacking complete information on cancer type, stage, etc.^{12,13} Much of the prior work assessing risk prediction has focused on systematic revisions needed in data collection to reduce the risk modeling variability in a cancer surgery patient population (e.g., oncologic omissions such as cancer staging and neoadjuvant chemotherapy).^{14–17} However, a clinically practical question remains unanswered. What is the comparative performance of risk models in cancer versus benign disease populations? Given the risk models currently available today such as the NSQIP all-procedure risk calculator and their known limitations for cancer surgery patients, understanding this difference may allow for the surgeon to better appreciate the risks in undertaking operative interventions in patients with malignancy.

The purpose of this study was to assess the effect of a cancer diagnosis as a binary variable on the risks associated with major gastrointestinal surgery and to provide practical information for the risk counseling of these patients. We hypothesized that there would be a significant worsening in outcomes for in cancer patients.

MATERIALS AND METHODS

Data source

All data were obtained from the 2005–2015 ACS NSQIP participant use files.¹⁸ The development of this national dataset has been previously described.¹⁹ All major colon, pancreas, and stomach elective resections were included based on the record's primary Current Procedural Terminology code (including 44139–41, 44143–7, 44150–1, 44155–8, 44160, 44799, 45121, 44204–8, 44210–3, 43177, 43118, 43121, 43123, 43620, 43621, 43622, 43631, 43632, 43633, 43634, 43635, 43638, 43639, 48150–4, 48140, 48145, 48146, 48155). Surgery for intended gastrointestinal oncologic indication was determined from associated ICD-9 diagnosis code (including 150–159). Emergent cases and those not operated on the same day as admission were excluded. Mirroring the current version of the ACS NSQIP Surgical Risk Calculator (<http://riskcalculator.facs.org>), we included 17 of the 18 preoperative variables (excluded emergent surgery dummy variable; added patient race variable). Laboratory variables were excluded due to their lack of contribution to predictive models in surgery.²⁰ Predicted mortality and morbidity and all 30-day outcomes (mortality, morbidities, length of stay) were obtained from the same dataset. A complication was defined as the occurrence of any NSQIP-reported postoperative morbidity. The Johns Hopkins University School of Medicine Institutional Review Board approved this study.

Analysis

Individuals were stratified by their binary indication for surgery (e.g., cancer versus benign). Those with and without a surgical cancer diagnosis were directly compared with univariable analysis. Binary and categorical variables were assessed using test and continuous variables' association were calculated using Wilcoxon-Mann-Whitney tests. Multivariable regression methods were employed in a manner similar to prior prediction model building.^{8,11} A backward stepwise logistic – and ordered logistic where appropriate – regression was then performed to assess independent predictors of mortality, morbidity, and length of stay. An organ-specific indicator variable was included to independently model for each distinct organ-specific procedure type included in the study population. Heterogeneity in the cancer patient versus benign disease population's demographics and comorbidities identified during univariable analysis led to *post hoc* propensity score matching being performed with weighted propensity scores based on the significant univariable findings below (e.g., sex, age, ASA score, specific comorbidities). Subgroup analysis by procedure was also performed to assess for asymmetric effects by procedure type. All statistical analyses were performed in Stata® 14.2 (StataCorp, College Station, TX).

Existing Risk Prediction Models

The ACS NSQIP participant use file includes a predicted risk of mortality and morbidity for each patient. The selection and construction of these risk models has been previously described.^{21–23} These variables were directly compared to the new multivariable regression described above using goodness-of-fit testing (e.g., c-statistic, Brier score) and observed-to-expected outcomes correlations were compared using Fisher's *r* to *Z* transformation.

RESULTS

We identified 264,401 cases of which 111,563 (42.2%) were for a malignant surgical indication, and 152,838 (57.8%) were for benign disease. A summary and comparison of these populations is provided in Table 1. The two populations were heterogeneous with a greater proportion of the total for the cancer surgery population being male (51.9% versus 45.6%, $p < 0.001$), older (56.2% versus 36.6% older than 65 years, trend $p < 0.001$), non-white (23.8% versus 22.2%, $p < 0.001$), and functionally impaired (3.1% versus 2.9%, $p < 0.001$). Overall, the malignant disease group was sicker by ASA class (median 3 versus 2, $p < 0.001$ for mean), and also had more hypertension (55.0% versus 45.3%, $p < 0.001$), diabetes (20.0% versus 13.5%, $p < 0.001$), congestive heart failure (0.8% versus 0.5%, $p < 0.001$), dyspnea on exertion (9.8% versus 6.8%, $p < 0.001$), and chronic obstructive pulmonary disease (5.3% versus 4.4%, $p < 0.001$). Comorbidities more common in the benign gastrointestinal surgery group included greater steroid use (9.1% versus 2.5%, $p < 0.001$), chronic sepsis (3.2% versus 0.3%, $p < 0.001$), tobacco use (19.6% versus 15.2%, $p < 0.001$), acute renal failure (0.2% versus 0.1%, $p < 0.001$), and body mass index (median 27.5 versus 27.2, $p < 0.001$ for mean).

These two populations also had heterogeneous outcomes (Table 2) with the cancer surgery population demonstrating greater complication rates (27.4% versus 23.2%, $p < 0.001$), pneumonia incidence (2.9% versus 2.2%, $p < 0.001$), failed extubations (2.5% versus 1.7%, $p < 0.001$), renal failure (1.5% versus 1.1%, $p < 0.001$), cardiac events (1.5% versus 0.8%, $p < 0.001$), bleeding (9.4% versus 5.8%, $p < 0.001$), venous thromboembolism (1.5% versus 1.3%, $p < 0.001$), and postoperative septic shock (2.1% versus 1.6%, $p < 0.001$). In addition to an increased complication rate, the cancer surgery group also demonstrated a larger number of complications per patient (mean 0.47 versus 0.39, $p < 0.001$), length of stay (median 6 versus 5 days, $p < 0.001$ for mean), and mortality rate (1.7% versus 1.1%, $p < 0.001$). In the cancer surgery group, the observed-to-expected mortality and morbidity correlations in the cancer surgery group were lower than the benign disease population's suggesting less correlation between NSQIP risk-adjusted mortality probability estimates and actual mortality and morbidity (respectively, 0.22 versus 0.33, $p < 0.001$; 0.28 versus 0.29, $p < 0.001$)).

Tables 3, 4, and 5 summarize the multivariable regression for 30-day mortality, complication rate, and total number of complications. When controlling for other preoperative variables and procedure type, there remained an 18% (OR = 1.18, 95% CI = 1.10–1.28) increase in the odds of death, a 9% (OR = 1.09, 95% CI = 1.07–1.11) increase in the odds of a complication, and an 8% (OR = 1.08, 95% CI = 1.06–1.11) increase in the number of complications in the cancer surgery population versus the benign disease group. Logistic regression was repeated with frequency weights applied based on propensity scoring, and significant variables and effect sizes were identical (Appendix 1). Subgroup analysis by procedure type also demonstrated consistent findings.

The morbidity and mortality rate regression models were also compared to the risk predictor variables included in the ACS NSQIP participant use file. Goodness-of-fit testing with Brier

scores and c statistics is reproduced in Appendix 2 and demonstrated similar rates of predictive ability between ACS NSQIP models and the models created in this study.

DISCUSSION

The purpose of this study was to assess the utility of risk prediction when comparing surgery for cancer to a benign disease indication. We used short-term surgical outcomes for those undergoing gastrointestinal surgery as a comparable population cohort once controlling for procedure-specific risks. This study represents the first time that national surgical 30-day follow-up data was compared directly between cancer and non-cancer patients to assess the feasibility of risk prediction in these distinct populations. Our findings suggest that a cancer diagnosis confers an independent cancer risk for morbidity that is not addressed in existing risk prediction models.

Although previous work did not use a non-cancer comparison group, our results are consistent with the limited alignment of existing risk models previously observed in cancer populations.^{12,13} Our results also confirm that cancer and benign disease patients undergoing the same surgery are intrinsically different populations with different postoperative risks. Furthermore, the statistical model building performed here demonstrates that the increased variability, mortality, and morbidity seen in cancer surgery patients cannot be explained away with subset analysis. These findings provide support for the assumptions of proposed changes^{14–16,24} to current prediction models for cancer operations that there are currently unknown predictive factors that may explain this population's postoperative variation.

Our findings are also consistent with the evolving understanding of the role solid tumors play systemically at diagnosis. Longstanding clinical observations suggest that systemic metabolic processes underlie cancer pathogenesis,^{25–27} These theories have more recently been reinforced with increasing biological evidence that cancer alters the body's immunologic and biosynthetic mechanisms.^{28,29} Given these systemic alterations in cancer patients and the need for physiologic reserve with invasive procedures, it is not surprising that short-term surgical outcomes are affected. For example, a dysfunctional immune system would be less effective at preventing post-operative sepsis,³⁰ and cancer-induced coagulopathy may increase the risk of hemorrhage.

Although the increased risk variation in cancer surgery using risk models has been recognized, this study is the first to use NSQIP data to compare post-operative outcomes directly between cancer and benign disease surgery patients. These findings represent a very practical “real-world” setting for the surgeon who operates on both malignant and benign surgical disease. With internet access alone, a surgeon today can provide a new patient presenting to clinic with evidence-based, individualized risk predictions of post-operative surgical course that include predicted length of stay, complication-specific morbidity rates, and comparisons to the average population. Our analysis demonstrates that existing risk prediction models may not sufficiently account for the role of a cancer diagnosis. Although proxies for a cancer diagnosis such as NSQIP variables for disseminated malignancy and ascites influence these models, our analysis suggests there is a critical degree of granularity

missing when evaluating these patients. Put another way, we have shown that a cancer diagnosis requiring surgery confers as great an increased risk of worse short-term surgical outcomes as other variables included in current prediction models such as hypertension and diabetes. However, cancer is notably absent from these models.

More globally, given the significant differences in health status at baseline for these patients, research is needed to evaluate potential interventions to “normalize” patients with cancer and to understand the possible effectors driving this phenomenon. Efforts are already under way to improve cancer patients’ overall health status to reduce postoperative complications.³¹ The Lung Cancer Exercise Training Study is currently randomizing patients to various exercise modalities to improve physiologic reserve following partial lung resection.³² Preoperative interventions to “prehabilitate” colorectal patients prior to surgery are currently under investigation with early results demonstrating improved postoperative outcomes following an improvement in preoperative activity levels.³³ Additionally, these efforts have also demonstrated the need for continuous improvement of risk prediction models as further data has refined all-procedure risk prediction over time.¹⁷

When discussing individualized risks with patients preoperatively, such a distinction will be important in that it recognizes that even the best all-procedure risk models available are unable to fully account for the increased variability and negatively biased outcomes of those with cancer. For surgeons using publicly available risk calculators and their patients, this gap in our current prediction knowledge will be an important caveat. Even for surgeons who provide risk counseling on *gestalt* alone, these findings can be incorporated into one’s usual heuristic thinking recognizing there is an increased degree of randomness for outcomes of cancer surgery patients.^{34–36}

Although not tested here, an important area of future research is whether other recent simplified risk prediction tools may also be vulnerable to the inherent variability of cancer surgery. For example, simplified clinical review (e.g., the Surgical Risk Preoperative Assessment System), timed stair-climbing, and frailty assessment have been suggested as alternative methods of risk prediction.^{9,10,37,38} Performance of these other models within cancer patient populations has not been rigorously assessed to date, and the findings here suggest these alternative measures may be equally problematic to predict the inherent excessive variability of cancer surgery outcomes. Many of these risk models advocate for the immediate use of these models at the bedside through incorporation into electronic health record platforms.^{9,39} However, it remains unresolved how to not only communicate risk but also the degree of uncertainty around that risk. Such an element of risk counseling is intuitively important but is also likely one of the most difficult concepts to convey. Future risk tools may need to incorporate a mechanism to explicitly signal uncertainty and may benefit from delineation of risks by their uncertainty and modifiability.

This study is not without its limitations. This study was not able to address long-term outcomes of the surgeries examined. The information on both patient’s preoperative health as well as post-operative outcomes both come from a national database that is vulnerable to between-institution reporting differences as well as heterogeneity in data capture abilities of the individual clinical reviewers. Fortunately, the lack of complete data capture if occurring

should be equally likely across all records and therefore would favor the null hypothesis. Another limitation of this study is the comparison of a *de novo* multivariable regression model to the ACS NSQIP risk prediction model whose specific methodology is not publicly reported.⁴⁰

Finally, interpreting diagnostic indication has been simplified for the purpose of this analysis. Both benign and cancer diseases were grouped together without further information about the severity of disease or subtype (e.g., inflammatory versus infectious benign disease). Since operations were grouped by CPT code in this study, it is possible that cancer diagnosis is serving as a proxy measure of residual confounding where cancer operations tend to be more extensive resections than benign disease. Although our own personal experience is not consistent with this consideration (e.g., chronic pancreatitis or severe diverticulitis are no easier than their malignant comparators), even if it were the case that the differences reported here were due to varying *intraoperative* complexity, it does not negate our conclusions. Additionally, current prediction models do not readily account for planned operative complexity and group by CPT codes in a similar manner to our study methodology. Therefore, for the general surgeon who sees both malignant and benign disease, he or she must account for limitations in current risk prediction models that do not adequately discriminate between these operative indications. Further discerning disease-specific risk factors for a patient will ultimately need to balance increased complexity of the risk models versus practical usability.

CONCLUSIONS

There is increased outcomes variability within the cancer surgery patient population when compared to benign surgical disease patients. This variation cannot be fully explained by current risk prediction model methodologies, and there are likely additional preoperative variables needed to improve the performance of these models in cancer patients. Current prediction models also less effectively evaluate the risk of death and complications in cancer patients. Finally, a diagnosis of cancer independently increases the risk of complications and 30-day mortality from surgical resection, and additional counseling regarding the uncertainty of short-term outcomes for cancer surgery may be needed. Prospective studies are planned to examine this phenomenon further.

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APPENDIX 1

Due to the observed heterogeneity of the study population illustrated in Table 1, we performed propensity score matching described below and the repeated the main text's statistical. This mirrored analysis is described through the series of complementary tables below. Propensity score matching was performed using the *teffects* package within Stata® 14.2 (StataCorp, College Station, Texas). Covariates matched included sex, race, age, functional status, ASA class, use of chronic steroids, and presence of ascites preoperatively. Patients unable to be matched were excluded from further analysis. A total of 35,839 (23.5%) of benign patients were successfully matched to the cancer patient group.

Figure A1. Distribution of aggregate covariate similarity pre- and post-propensity score matching when modeling the risk of death at 30 days

*By Stata nomenclature, the “treated” group represents those with surgery for a cancer indication.

Figure A2. Distribution of aggregate covariate similarity pre- and post-propensity score matching when modeling the risk of any complication at 30 days

*By Stata nomenclature, the “treated” group represents those with surgery for a cancer indication.

Table A1

Population preoperative characteristics for gastrointestinal surgery in NSQIP (2005–2015 with propensity score matched benign group)

	Surgery for GI Cancer (n = 111,563)	Surgery for Benign GI Disease (n = 35,839)	p
Gender			<0.001
Male	57,879 (51.9%)	16,480 (46.0%)	
Female	53,684 (48.1%)	19,359 (54.0%)	
Age			<0.001
< 65	48,945 (43.8%)	22,101 (61.6%)	
65–74	31,024 (27.8%)	8,538 (23.8%)	
75–84	23,876 (21.4%)	4,356 (12.1%)	
> 84	7,828 (7.0%)	877 (2.4%)	
Race			<0.001
White	79,272 (76.2%)	26,792 (76.9%)	
Black	10,745 (10.0%)	2,997 (8.6%)	

	Surgery for GI Cancer (n = 111,563)	Surgery for Benign GI Disease (n = 35,839)	p
Hispanic	11,826 (11.1%)	4,218 (12.1%)	
Other	5,182 (4.8%)	816 (2.3%)	
Functional Status			<0.001
Independent	107,918 (96.9%)	34,746 (97.2%)	
Partially dependent	2,497 (2.2%)	604 (1.7%)	
Totally dependent	945 (0.9%)	390 (1.1%)	
ASA Class, (Mean/Median)	2.6/3	2.5/2	<0.001
Comorbidities			
Chronic steroids	2,916 (2.6%)	3,013 (8.4%)	<0.001
Ascites	710 (0.6%)	186 (0.5%)	0.013
Systemic sepsis			<0.001
SIRS	1,487 (1.3%)	626 (1.8%)	
Sepsis	310 (0.3%)	363 (1.0%)	
Septic shock	24 (0.0%)	78 (0.2%)	
Ventilator dependent	41 (0.0%)	78 (0.2%)	<0.001
Disseminated cancer	8,128 (7.3%)	1,040 (2.9%)	<0.001
Diabetes			<0.001
Non-insulin dependent	14,552 (13.0%)	3,284 (9.2%)	
Insulin dependent	7,785 (7.0%)	1,689 (4.7%)	
Hypertension on meds	61,442 (55.0%)	16,701 (46.6%)	<0.001
Congestive heart failure	909 (0.8%)	191 (0.5%)	<0.001
Dyspnea			<0.001
With activity	10,309 (9.2%)	2,307 (6.4%)	
At rest	691 (0.6%)	188 (0.5%)	
Active tobacco use	17,010 (15.2%)	6,818 (19.0%)	<0.001
Chr. obstruct. pulm. dis.	5,924 (5.3%)	1,532 (4.3%)	<0.001
Dialysis	460 (0.4%)	210 (0.6%)	<0.001
Acute renal failure	128 (0.1%)	61 (0.2%)	0.011
BMI (Mean/Median)	28.1/27.2	28.5/27.6	<0.001
Procedure Performed			
Colectomy	83,501 (81.2%)	30,792 (85.8%)	<0.001
Pancreatectomy	22,681 (20.3%)	4,112 (11.5%)	<0.001
Gastrectomy	5,491 (4.9%)	968 (2.7%)	<0.001

Of note, statistically significant differences are still reflected in Table A1 due to the omission of propensity weighted estimates.

Table A2

Postoperative outcomes for gastrointestinal surgery in NSQIP (2005–2015 with propensity score matched benign group)

	Surgery for GI Cancer (n = 111,563)	Surgery for Benign GI Disease (n = 35,839)	p
LOS Mean	8.3	7.4	<0.001
LOS Median	6 (IQR = 4 –9)	5 (IQR = 4–8)	
Death	1,934 (1.7%)	361 (1.0%)	<0.001
Morbidity			
Any Complication	30,637 (27.4%)	8,364 (23.3%)	<0.001
Superficial SSI	7,342 (6.6%)	2,253 (6.3%)	0.050
Deep SSI	1,497 (1.3%)	505 (1.4%)	0.338
Organ Space SSI	5,919 (5.3%)	1,843 (5.1%)	0.230
Wound Disruption	1,253 (1.1%)	386 (1.1%)	0.470
Pneumonia	3,222 (2.9%)	754 (2.1%)	<0.001
Reintubation	2,814 (2.5%)	566 (1.6%)	<0.001
Pulmonary Embolism	925 (0.8%)	236 (0.7%)	0.001
Prolonged Mechanical Ventilation (> 48 hours)	2,514 (2.3%)	641 (1.8%)	<0.001
Progressive Renal Failure	893 (0.8%)	220 (0.6%)	<0.001
Acute Renal Failure	766 (0.7%)	151 (0.4%)	<0.001
Urinary Tract Infection	3,609 (3.2%)	1,078 (3.0%)	0.033
Cerebrovascular accident	367 (0.3%)	64 (0.2%)	<0.001
Cardiac arrest	762 (0.7%)	141 (0.4%)	<0.001
Myocardial infarction	833 (0.8%)	175 (0.5%)	<0.001
Bleeding w/transfusion	10,505 (9.4%)	2,185 (6.1%)	<0.001
Deep vein thrombosis	1,629 (1.5%)	458 (1.3%)	0.011
Sepsis	5,010 (4.5%)	1,545 (4.3%)	0.152
Septic Shock	2,301 (2.1%)	542 (1.5%)	<0.001
Total # Complications, Mean	0.47	0.39	<0.001
Total # of Complications, Median	0 (IQR = 0 – 1)	0 (IQR = 0 – 0)	
Any readmission	6,631 (5.9 %)	2,237 (6.2%)	0.039
Observed Expected Mortality Correlation	0.22	0.32	<0.001
Observed Expected Morbidity Correlation	0.28	0.29	<0.001

Table 3A

Multivariable logistic regression with propensity score matching for death within 30 days of operation, controlled for procedure type

Variables	Odds Ratio	95% Confidence Interval	P Value
Cancer diagnosis	1.09	(1.02–1.17)	0.015
Procedure Control			
Pancreas	Ref		
Colon	0.57	(0.52–0.62)	<0.001
Stomach	1.01	(0.86–1.19)	0.878
Male sex	0.71	(0.67–0.77)	<0.001
BMI	0.99	(0.98–0.99)	<0.001
Age	1.05	(1.05–1.06)	<0.001
Functional status	0.41	(0.37–0.45)	<0.001
ASA Class	2.12	(1.98–2.26)	<0.001
Chronic steroid use	1.50	(1.26–1.77)	<0.001
Hypertension	1.27	(1.16–1.38)	<0.001
Diabetes	1.12	(1.03–1.21)	0.007
COPD	1.35	(1.21–1.50)	<0.001
Ascites	5.30	(4.39–6.40)	<0.001
Sepsis	2.90	(2.52–3.33)	<0.001
Ventilator dependent	2.55	(1.25–5.22)	0.010
Active smoker	1.24	(1.12–1.38)	<0.001
Acute renal failure	1.46	(0.89–2.39)	0.130
Dialysis	2.07	(1.56–2.74)	<0.001
Congestive HF	1.69	(1.42–2.02)	<0.001
Dyspnea	1.65	(1.51–1.81)	<0.001

Table A4

Multivariable logistic regression with propensity score matching for any complication within 30 days of operation, controlled for procedure type

Variables	Odds Ratio	95% Confidence Interval	P Value
Cancer diagnosis	1.07	(0.72–0.80)	<0.001

Variables	Odds Ratio	95% Confidence Interval	P Value
Procedure Control			
Stomach	Ref		
Colon	0.76	(1.04–1.10)	<0.001
Pancreas	1.79	(1.69–1.90)	<0.001
Male sex	0.95	(0.93–0.97)	<0.001
White race	1.07	(1.05–1.08)	<0.001
Age	1.00	(1.00–1.01)	<0.001
Functional status	0.62	(0.58–0.66)	<0.001
ASA Class	1.53	(1.50–1.56)	<0.001
Ascites	2.10	(1.84–2.39)	<0.001
Sepsis	2.29	(2.13–2.46)	<0.001
Active smoker	1.15	(1.11–1.18)	<0.001
Diabetes	1.08	(1.05–1.11)	<0.001
Chronic steroid use	1.49	(1.41–1.56)	<0.001
BMI	1.01	(1.01–1.01)	<0.001
Hypertension	1.03	(1.01–1.07)	0.004
Congestive HF	1.35	(1.19–1.52)	<0.001
Ventilator dependent	2.04	(1.40–2.96)	<0.001
Dyspnea	1.25	(1.20–1.29)	<0.001
COPD	1.22	(1.16–1.28)	<0.001

Table A5

Multivariable ordered logistic regression with propensity score matching for number of complications within 30 days of operation, controlled for procedure type

Variables	Odds Ratio	95% Confidence Interval	P Value
Cancer diagnosis	1.06	(1.03–1.09)	<0.001
Procedure Control			
Stomach	Ref		
Colon	0.72	(0.68–0.76)	<0.001
Pancreas	1.74	(1.65–1.85)	<0.001
Male sex	0.93	(0.91–0.95)	<0.001
White race	1.07	(1.05–1.08)	<0.001

Variables	Odds Ratio	95% Confidence Interval	P Value
Age	1.00	(1.00–1.01)	<0.001
Functional status	0.58	(0.55–0.61)	<0.001
ASA Class	1.54	(1.51–1.58)	<0.001
Ascites	2.16	(1.91–2.45)	<0.001
Sepsis	2.35	(2.19–2.51)	<0.001
Active smoker	1.15	(1.12–1.19)	<0.001
Ventilator dependent	1.40	(1.06–1.86)	0.018
Acute renal failure	1.23	(0.95–1.60)	0.115
Diabetes	1.07	(1.04–1.10)	<0.001
Chronic steroids	1.50	(1.42–1.57)	<0.001
BMI	1.01	(1.01–1.01)	<0.001
Hypertension	1.04	(1.02–1.07)	0.001
Congestive HF	1.28	(1.14–1.44)	<0.001
Dyspnea	1.26	(1.21–1.31)	<0.001
COPD	1.25	(1.19–1.32)	<0.001

APPENDIX 2

Table A6

Goodness-of-fit testing NSQIP Risk Prediction versus Cancer-controlled Logistic Regression within a cancer surgery population

	c-statistic	Brier Score
Mortality		
NSQIP	0.83	0.0088
Cancer-controlled	0.82	0.0090
Morbidity		
NSQIP	0.71	0.1710
Cancer-controlled	0.66	0.1694

From Bilimoria, NSQIP adjustment, JACS 2014

The c-statistic is a measure of discrimination, that ranges from 0.5 (chance) to 1.0 (perfect), which reflects the extent to which cases are properly classified as having or not having an event. The Brier score describes the averaged squared difference between patients' predicted

probability and the actual outcome (0 for a non-event and 1, for an event). If all patients without an event are assigned a predicted probability of 0, and all patients with an event are assigned a predicted probability of 1, the Brier Score will be 0, indicating perfect prediction. For the null model Brier Score, the overall event rate (say, 0.05 for a 5% mortality rate) is assigned to each patient.

Table 1

Population preoperative characteristics for gastrointestinal surgery in NSQIP (2005–2015)

	Surgery for GI Cancer (n = 111,563)	Surgery for Benign GI Disease (n = 152,838)	p
Gender			<0.001
Male	57,879 (51.9%)	69,624 (45.6%)	
Female	53,684 (48.1%)	83,214 (54.5%)	
Age			<0.001
< 65	48,945 (43.8%)	97,000 (63.4%)	
65–74	31,024 (27.8%)	34,923 (22.8%)	
75–84	23,876 (21.4%)	17,669 (11.6%)	
> 84	7,828 (7.0%)	3,399 (2.2%)	
Race			<0.001
White	79,272 (76.2%)	115,001 (77.8%)	
Black	10,745 (10.0%)	12,899 (8.7%)	
Hispanic	11,826 (11.1%)	16,498 (11.2%)	
Other	5,182 (4.8%)	3,382 (2.3%)	
Functional Status			<0.001
Independent	107,918 (96.9%)	148,016 (97.1%)	
Partially dependent	2,497 (2.2%)	2,797 (1.8%)	
Totally dependent	945 (0.9%)	1,595 (1.1%)	
ASA Class, (Mean/Median)	2.6 / 3	2.5 / 2	<0.001
Comorbidities			
Chronic steroids	2,916 (2.6%)	13,890 (9.1%)	<0.001
Ascites	710 (0.6%)	879 (0.6%)	0.044
Systemic sepsis			<0.001
SIRS	1,487 (1.3%)	3,122 (2.1%)	
Sepsis	310 (0.3%)	1,671 (1.1%)	
Septic shock	24 (0.0%)	14 (0.1%)	
Ventilator dependent	41 (0.0%)	384 (0.3%)	<0.001
Disseminated cancer	8,128 (7.3%)	4,372 (2.9%)	<0.001
Diabetes			<0.001
Non-insulin dependent	14,552 (13.0%)	13,565 (8.9%)	
Insulin dependent	7,785 (7.0%)	7,004 (4.6%)	
Hypertension on meds	61,442 (55.0%)	69,329 (45.3%)	<0.001
Congestive heart failure	909 (0.8%)	802 (0.5%)	<0.001
Dyspnea			<0.001
With activity	10,309 (9.2%)	9,581 (6.3%)	
At rest	691 (0.6%)	831 (0.5%)	
Active tobacco use	17,010 (15.2%)	29,943 (19.6%)	<0.001

	<u>Surgery for GI Cancer (n = 111,563)</u>	<u>Surgery for Benign GI Disease (n = 152,838)</u>	<u>p</u>
Chr. obstruct. pulm. dis.	5,924 (5.3%)	6,695 (4.4%)	<0.001
Dialysis	460 (0.4%)	911 (0.6%)	<0.001
Acute renal failure	128 (0.1%)	300 (0.2%)	<0.001
BMI (Mean/Median)	28.1 / 27.2	28.5 / 27.5	<0.001
Procedure Performed			
Colectomy	83,501 (81.2%)	131,472 (85.9%)	<0.001
Pancreatectomy	22,681 (20.3%)	17,216 (11.3%)	<0.001
Gastrectomy	5,491 (4.9%)	4,303 (2.8%)	<0.001

Table 2

Postoperative outcomes for gastrointestinal surgery in NSQIP (2005–2015)

	Surgery for GI Cancer (n = 111,563)	Surgery for Benign GI Disease (n = 152,838)	p
LOS Mean	8.3	7.4	<0.001
LOS Median	6 (IQR = 4–9)	5 (IQR = 4–8)	
Death	1,934 (1.7%)	1,607 (1.1%)	<0.001
Morbidity			
Any Complication	30,637 (27.4%)	35,423 (23.2%)	<0.001
Superficial SSI	7,342 (6.6%)	9,821 (6.4%)	0.109
Deep SSI	1,497 (1.3%)	2,173 (1.4%)	0.083
Organ Space SSI	5,919 (5.3%)	7,624 (5.0%)	<0.001
Wound Disruption	1,253 (1.1%)	1,758 (1.2%)	0.517
Pneumonia	3,222 (2.9%)	3,297 (2.2%)	<0.001
Reintubation	2,814 (2.5%)	2,527 (1.7%)	<0.001
Pulmonary Embolism	925 (0.8%)	913 (0.6%)	<0.001
Prolonged Mechanical Ventilation (> 48 hours)	2,514 (2.3%)	2,834 (1.9%)	<0.001
Progressive Renal Failure	893 (0.8%)	934 (0.6%)	<0.001
Acute Renal Failure	766 (0.7%)	694 (0.5%)	<0.001
Urinary Tract Infection	3,609 (3.2%)	4,544 (3.0%)	<0.001
Cerebrovascular accident	367 (0.3%)	285 (0.2%)	<0.001
Cardiac arrest	762 (0.7%)	638 (0.4%)	<0.001
Myocardial infarction	833 (0.8%)	623 (0.4%)	<0.001
Bleeding w/transfusion	10,505 (9.4%)	8,716 (5.7%)	<0.001
Deep vein thrombosis	1,629 (1.5%)	1,928 (1.3%)	<0.001
Sepsis	5,010 (4.5%)	6,715 (4.4%)	0.230
Septic Shock	2,301 (2.1%)	2,401 (1.6%)	<0.001
Total # Complications, Mean	0.47	0.39	<0.001
Total # of Complications, Median	0 (IQR = 0 – 1)	0 (IQR = 0 – 0)	
Any readmission	6,631 (5.9 %)	9,098 (6.0%)	0.924
Observed: Expected Mortality Correlation	0.22	0.33	<0.001
Observed: Expected Morbidity Correlation	0.28	0.29	<0.001

Table 3

Multivariable logistic regression for death within 30 days of operation, controlled for procedure type

Variables	Odds Ratio	95% Confidence Interval	P Value
Cancer diagnosis	1.18	(1.10–1.28)	<0.001
Procedure Control			
Pancreas	Ref		
Colon	0.53	(0.48–0.58)	<0.001
Stomach	0.97	(0.83–1.14)	0.746
Male sex	0.70	(0.65–0.75)	<0.001
BMI	0.99	(0.99–1.00)	0.026
Age	1.05	(1.05–1.05)	<0.001
Functional status	0.38	(0.34–0.42)	<0.001
ASA Class	2.15	(2.01–2.30)	<0.001
Chronic steroid use	1.42	(1.24–1.63)	<0.001
Diabetes	1.09	(1.00–1.18)	0.057
Hypertension	1.19	(1.09–1.30)	<0.001
COPD	1.37	(1.22–1.53)	<0.001
Ascites	4.30	(3.55–5.22)	<0.001
Sepsis	3.22	(2.85–3.65)	<0.001
Ventilator dependent	1.94	(1.44–2.59)	<0.001
Active smoker	1.20	(1.09–1.33)	<0.001
Acute renal failure	1.88	(1.35–2.62)	<0.001
Dialysis	2.27	(1.81–2.84)	<0.001
Congestive HF	1.59	(1.33–1.91)	<0.001
Dyspnea	1.53	(1.39–1.68)	<0.001

Table 4

Multivariable logistic regression for any complication within 30 days of operation, controlled for procedure type

Variables	Odds Ratio	95% Confidence Interval	P Value
Cancer diagnosis	1.09	(1.07–1.11)	<0.001
Procedure Control			
Pancreas	Ref		
Colon	0.45	(0.44–0.46)	<0.001
Stomach	0.60	(0.57–0.63)	<0.001
Male sex	0.98	(0.96–0.99)	0.011
White race	1.06	(1.05–1.07)	<0.001
Age	1.00	(1.00–1.00)	<0.001
Functional status	0.59	(0.56–0.61)	<0.001
ASA Class	1.56	(1.53–1.58)	<0.001
Dialysis	1.13	(1.00–1.27)	0.052
Acute renal failure	1.45	(1.16–1.82)	0.001
Ascites	2.17	(1.95–2.42)	<0.001
Sepsis	2.17	(2.06–2.30)	<0.001
Active smoker	1.14	(1.11–1.17)	<0.001
Diabetes	1.07	(1.05–1.10)	<0.001
Chronic steroid use	1.52	(1.47–1.58)	<0.001
BMI	1.01	(1.01–1.01)	<0.001
HTN	1.04	(1.02–1.06)	<0.001
Congestive HF	1.35	(1.21–1.50)	<0.001
Ventilator dependent	2.47	(1.89–3.23)	<0.001
Dyspnea	1.24	(1.20–1.29)	<0.001
COPD	1.24	(1.19–1.29)	<0.001

Table 5

Multivariable ordered logistic regression for number of complications within 30 days of operation, controlled for procedure type

Variables	Odds Ratio	95% Confidence Interval	P Value
Cancer diagnosis	1.08	(1.06–1.11)	<0.001
Procedure Control			
Pancreas	Ref		
Colon	0.44	(0.43–0.45)	<0.001
Stomach	0.61	(0.58–0.65)	<0.001
Male sex	0.96	(0.94–0.97)	<0.001
White race	1.06	(1.05–1.07)	<0.001
Age	1.00	(1.00–1.00)	<0.001
Functional status	0.55	(0.53–0.58)	<0.001
ASA Class	1.58	(1.55–1.60)	<0.001
Ascites	2.11	(1.91–2.33)	<0.001
Sepsis	2.29	(2.17–2.41)	<0.001
Active smoker	1.09	(1.03–1.17)	0.005
Ventilator dependent	1.80	(1.49–2.18)	<0.001
Dialysis	1.15	(1.02–1.28)	0.019
Acute renal failure	1.42	(1.17–1.73)	<0.001
Diabetes	1.06	(1.03–1.09)	<0.001
Chronic steroids	1.56	(1.42–1.71)	<0.001
BMI	1.01	(1.01–1.01)	<0.001
Hypertension	1.05	(1.02–1.07)	<0.001
Congestive HF	1.30	(1.18–1.43)	<0.001
Dyspnea	1.26	(1.12–1.17)	<0.001
COPD	1.28	(1.23–1.33)	<0.001