Re-operation within 30 days of radical cystectomy: Identifying high-risk patients and complications using American College of Surgeons National Surgical Quality Improvement Program database

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Abstract

Introduction: Radical cystectomy (RC) is a highly morbid procedure, with 30-day complication rates approaching 31%. Our objective was to determine risk factors for re-operation within 30 days following a RC for non-metastatic bladder cancer.

Methods: We included all patients who underwent a RC for non-metastatic bladder cancer using The American College of Surgeons National Surgical Quality Improvement Program database between January 1, 2007 and December 31, 2014. Logistic regression analyses were used to evaluate predictors of re-operation.

Results: A total of 2608 patients were included; 5.8% of patients underwent re-operation within 30 days. On multivariable analysis, increasing body mass index (BMI) (odds ratio [OR] 1.04, 95% confidence interval [CI] 1.01–1.07), African American race (vs. Caucasian OR 2.29, 95% CI 1.21–4.34), and history of chronic obstructive pulmonary disease (COPD) (OR 2.33, 95% CI 1.45–3.74) were significant predictors of re-operation within 30 days of RC. Urinary diversion type (ileal conduit vs. continent) and history of chemotherapy or radiotherapy within 30 days prior to RC were not. Patients who underwent re-operation within this timeframe had a significantly higher mortality rate (4.0% vs. 1.6%) and were more likely to experience cardiac (7.2% vs. 1.9%), pulmonary (23.0% vs. 3.0%), neurological (2.0% vs. 0.49%), and venous thromboembolic events (10.5% vs. 5.4%), as well as infectious complications (64.5% vs. 24.1%), with a significantly longer hospital length of stay (16.5 vs. 7.0 days).

Conclusions: Recognizing increasing BMI, COPD, and African American race as risk factors for re-operation within 30 days of RC will allow urologists to preoperatively identify such high-risk patients and prompt them to adopt more aggressive approaches to minimize postoperative surgical complications.

Introduction

Radical cystectomy (RC) with pelvic lymph node dissection remains the gold standard treatment for non-metastatic, muscle-invasive and high-risk non-muscle-invasive bladder tumors, such as bacillus Calmette-Guérin (BCG)-refractory tumors.[1,2] This procedure, however, is highly morbid, with 30-day overall complication, transfusion, prolonged hospitalization, re-admission, and perioperative mortality rates reported at 31.1%, 24.4%, 25.9%, 20.2%, and 2.7%, respectively.[3] Re-operation within 30 days of RC is a notable complication that may be associated with higher wound complications rates, hospital length of stay, and mortality rates,[4] underlying the significant health and financial consequences of this complication. Efforts to identify patients at higher risk of re-operation within 30 days of RC, particularly at a multi-institutional level, are needed to implement pre- and postoperative strategies to minimize this complication. Our goal was to identify predictors of re-operation within 30 days of RC using a national, validated database.

Methods

Study design, setting, and participants

We used the American College of Surgeons National Surgical Quality Improvement Program Database (NSQIP), which is a nationally validated, risk-adjusted, outcomes-based program,[5] to identify patients undergoing an RC (common procedural terminology codes: 51590, 51595, 51596) with a post-procedural diagnosis of bladder cancer (International Classification of Diseases-9 code: 188.x), between January 1, 2007 and December 31, 2014. Patients missing important baseline characteristics and outcome measures were exclud-

ed from the cohort. This study was exempt from required ethics board approval at our institutions.

Study outcomes

The primary study outcome was re-operation within 30 days of RC. Of note, reason for or type of re-operation performed was not available for this dataset. Secondary outcomes were adverse events within 30 days of surgery, including: mortality, cardiac, neurological, pulmonary, venous thromboembolic, and infectious events, and prolonged hospital length of stay (i.e., greater than seven days).

Study variables

Baseline patient characteristics were abstracted from the NSQIP database and included: patient age, gender, race, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status classification system score, history of cardiac, neurological, chronic obstructive pulmonary disease (COPD), and diabetes mellitus (DM) diagnoses, need for dialysis, active smoking, chronic steroid use, preoperative chemotherapy or radiotherapy (both within 90 days of surgery), preoperative serum albumin (surrogate for preoperative nutritional status), preoperative functional status (independent vs. partially/totally dependent), and type of diversion created (ileal conduit vs. continent diversion). Pathological information was not available for this dataset.

Statistical methods

Continuous variables were reported using medians and interquartile ranges (IQR), while categorical variables were described using proportions. Univariable analysis was performed using the Chi-squared and Fisher's exact test, where appropriate, for categorical variables, with the Student's t-test and Wilcoxon rank-sum test used to compare continuous variables. Multivariate logistic regression analysis accounting for clinical factors identified a priori as potentially influencing rates of re-operation (age, gender, BMI, race, ASA score, history of DM, history of COPD, active smoking, chronic steroid use, functional status, and type of diversion) was used to evaluate predictors/risk factors for re-operation within 30 days of RC. All statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC, U.S.).

Results

We identified 2608 patients undergoing RC for bladder cancer during the study time frame. Median patient age was 69.0 years (IQR 61.0–76.0); 82.4% of patients were male, 89.0% were Caucasian, and 79.5% received an ileal conduit at time of surgery. A total of 152 patients (5.8%) underwent re-operation within 30 days of RC.

On univariate analysis, race (10.9% of African Americans vs. 5.1% of Caucasians and 4.0% of other races, p=0.04), history of COPD (12.3% vs. 5.3%, p<0.01), and higher BMI (29.1 kg/m^2 for those with re-operation within 30 days vs. 27.8, p=0.017) were associated with higher re-operation rates. Choice of urinary diversion, preoperative chemotherapy or radiotherapy use, serum albumin, gender, ASA score, cardiac, neurological, and DM histories, need for dialysis, active smoking, chronic steroid use, and preoperative functional status were not significantly different between patients who did and did not undergo re-operation within 30 days of RC (Table 1).

On multivariable analysis, increasing BMI (odds ratio [OR] 1.04, 95% confidence interval [CI] 1.01–1.07), African American race (vs. Caucasian OR 2.29, 95% CI 1.21–4.34), and history of COPD (OR 2.33, 95%CI 1.45–3.74) were the only significant predictors for higher risk of re-operation within 30 days of RC (Table 2).

Patients who underwent re-operation were significantly more likely to experience the following adverse events within 30 days of RC: mortality (4.0% vs. 1.6%), cardiac (7.2% vs. 1.9%), neurological (2.0% vs. 0.5%), pulmonary (23.0% vs. 3.0%), and venous thromboembolic events (10.5% vs. 5.4%), sepsis (43.4% vs. 11.9%), pneumonia (13.2% vs. 2.8%), wound infections (48.0% vs. 11.0%), and prolonged hospital length of stay, with median length of stay of 16.5 days (IQR 8.0–26.5) compared to 7.0 days (6.0–10.0) for patients who did not undergo re-operation (Table 3).

Discussion

Based on this large, multi-institutional cohort, more than one in 20 patients (5.8%) undergoing RC for bladder cancer will undergo re-operation within 30 days. Patients who are African American, have COPD, and have a higher BMI experience an increased likelihood of re-operation. Such re-operation is associated with a 2.5-fold increased risk of death, a 3.8-fold increased risk of experiencing a cardiac event, and a significantly longer hospital length of stay (16.5 vs. 7.0 days), which highlights the health and financial consequences of this worrisome complication.

Multiple studies have evaluated the impact of obesity on postoperative complications following RC, with Arora et al and Al-Daghmin et al demonstrating that increasing obesity was associated with a progressively worsening 30-day complication rate[6] and a higher re-admission rate,[7] respectively. Interestingly, 13.4% of obese patients had hypoalbuminemia,[6] a marker of malnutrition. Hypoalbuminemia was shown to be independently associated with a 2.33-fold higher mortality rate,[6] yet in our study, there were no significant differences in albumin levels between the two

Table 1. Baseline characteristics of bladder cancer patients with and without re-operation within 30 days of radical cystectomy (n= 2608)

Variable	Patients with re-operation (n=152)	Patient without re-operation (n=2456)	p[a]
Age in years, median (IQR)	69.0 (61.0–76.0)	69.0 (61.0–76.0)	0.88
Gender, n (%)			0.40
Male	129 (84.9%)	2019 (82.2%)	
Female	23 (15.1%)	437 (17.8)	
Race, n (%)			0.04*
African American	12 (7.9%)	98 (4.0%)	
Caucasian	133 (87.5%)	2189 (89.1%)	
Other	7 (4.6%)	169 (6.9%)	
BMI in kg/m^2, median (IQR)	29.1 (25.2–33.2)	27.8 (24.7–31.4)	0.02*
ASA, n (%)			0.17
1	0 (0%)	5 (0.2%)	
2	30 (19.7%)	537 (21.9%)	
3	107 (70.4%)	1775 (72.3%)	
4	15 (9.9%)	139 (5.7%)	
Cardiac history, n (%)	8 (5.3%)	107 (4.4%)	0.60
Neurologic history, n (%)	0 (0%)	26 (1.1%)	0.40
History of COPD, n (%)	25 (16.5%)	179 (7.3%)	<0.01*
Diabetes mellitus, n (%)	31 (20.4%)	495 (20.2%)	0.94
Dialysis, n (%)	0(0%)	6 (0.2%)	0.70
Active smoking, n (%)	47 (30.9%)	605 (24.6%)	0.08
Chronic steroid use, n (%)	9 (5.9%)	80 (3.3%)	0.08
Preoperative chemotherapy, n (%)	2 (1.3%)	77 (3.1%)	0.20
Preoperative radiotherapy, n (%)	0 (0%)	2 (0.1%)	0.89
Preoperative serum albumin in g/dL, median (IQR)	4.0 (3.7–4.3)	4.0 (3.7–4.3)	0.24
Preoperative functional status, n (%)			0.67
Independent	150 (98.7%)	2412 (98.2%)	
Partially/totally dependent	2 (1.3%)	44 (1.8%)	
Urinary diversion, n (%)			0.09
Ileal conduit	129 (84.5%)	1944 (79.2%)	
Continent diversion	23 (15.1%)	512 (20.9%)	

[a]Using Chi-squared or Fisher's exact test for categorical variables and student's t-test for continuous variables. *Denotes p<0.05. ASA: American Society of Anesthesiologists; BMI: body mass index; COPD: chronic obstructive pulmonary disease; IQR: interquartile range.

groups. Future studies that investigate the significance of other preoperative nutritional markers, such as pre-albumin, a non-specific marker of short-term nutritional status,[8] may further highlight the significance of preoperative nutritional status on post-RC outcomes.

A history of COPD was one of the most prominent predictors of re-operation following RC, with a 2.33-fold increased risk of re-operation. Such patients are classically

Table 2. Multivariable regression model evaluating predictors of re-operation within 30 days of radical cystectomy

Variable	Odds ratio	95% confidence interval
Age	1.01	0.99–1.03
Gender (male vs. female)	1.34	0.84–2.13
Race (African American vs. Caucasian)	2.29	1.21–4.34
Race (Other vs. Caucasian)	0.70	0.31–1.52
Body mass index	1.04	1.02–1.07
ASA (2 vs. 1)	0.95	0.62–1.46
History of diabetes mellitus	0.88	0.57–1.34
Active smoking	1.46	0.99–2.17
History of COPD	2.33	1.45–3.74
Chronic steroid use	1.75	0.85–3.63
Functional status (partially/totally dependent vs. independent)	0.72	0.17–3.11
Type of diversion (continent vs. ileal conduit)	0.73	0.45–1.18

ASA: American Society of Anesthesiologists; COPD: chronic obstructive pulmonary disease.

underweight, malnourished, have poor pulmonary reserve,[9] and poor exercise tolerance,[10] which predispose to poor postoperative outcomes. Moreover, these patients may have a chronic cough, which may mechanically contribute to

Table 3. Adverse events following radical cystectomy for bladder cancer patients with and without re-operation within 30 days of surgery

Adverse events	Patients with re-operation (n=152)	Patient without re-operation (n=2456)	p[a]
Mortality	6 (4.0%)	38 (1.6%)	0.03*
Cardiac event	11 (7.2%)	46 (1.9%)	<0.01*
Neurologic event	3 (2.0%)	12 (0.5%)	0.02*
Pulmonary event	35 (23.0%)	73 (3.0%)	<0.01*
Venous thromboembolic event	16 (10.5%)	132 (5.4%)	0.01*
DVT	9 (5.9%)	89 (3.6%)	0.15
PE	9 (5.9%)	59 (2.4%)	0.01*
Any infection	98 (64.5%)	593 (24.1%)	<0.01*
Sepsis	66 (43.4%)	293 (11.9%)	<0.01*
Pneumonia	20 (13.2%)	69 (2.8%)	<0.01*
Urinary tract infection	22 (14.5%)	210 (8.6%)	0.013*
Wound infection	73 (48.0%)	271 (11.0%)	<0.01*
Superficial SSI, n (%)	20 (13.2%)	(143 (5.8%)	<0.01*
Deep incisional SSI, n (%)	17 (11.2%)	34 (1.4%)	<0.01*
Organ space SSI, n (%)	40 (26.3%)	108 (4.4%)	<0.01*
Prolonged hospital length of stay, n (%)	124 (81.6%)	1164 (47.4%)	<0.01*
Length of stay, median (IQR)	16.5 (8.0–26.5)	7.0 (6.0–10.0)	<0.01*

[a]Using Chi-squared or Fisher's exact test for categorical variables and student's t-test for continuous variables. *Denotes p<0.05. DVT: deep vein thrombosis; IQR: interquartile range; PE: pulmonary embolism; SSI: surgical site infection.

poor wound healing. Preoperative rehabilitation/exercise programs for patients with COPD have been proposed by anesthesiologists in an effort to "optimize" respiratory status.[10] This highlights the importance of multispecialty collaboration in the preoperative setting to improve postoperative outcomes. Notably, active smokers did not have significantly increased re-operation rates in our cohort, although this is likely a result of our study sample size/power, as the OR was 1.46 with a 95% CI of 0.99–2.17. Smoking has been previously shown to be associated with increased incidence of Clavien II–V complications following RC.[11]

African American race was found to be a significant risk factor for re-operation following RC, even after adjusting for medical comorbidities with multivariate analysis. African Americans have been shown to have higher clinical grade and stage bladder tumors at presentation, with increased risk of lymph node involvement and metastatic disease.[12,13] Furthermore, there is evidence of racial disparities in the quality of medical care, particularly for bladder cancer patients. African Americans, for example, are less likely to receive neoadjuvant chemotherapy within eight weeks of muscle-invasive bladder cancer diagnosis, which has been shown to be associated with higher risk of tumor upstaging.[14] This combination of biological and resource utilization differences may explain the increased risk of adverse outcomes in African American patients, independent of their medical comorbidities.

Preoperative receipt of chemotherapy or radiotherapy within 90 days of RC was notably not a significant predictor of re-operation. This is consistent with results published by Johnson et al, whereby they demonstrated that neoadjuvant chemotherapy prior to RC does not increase the risk of perioperative morbidity, including re-operation rate.[15] There may be an element of selection bias in these studies, as patients who may seem "fitter" per the physician's judgment are more likely to be referred for preoperative chemotherapy, and these are the patients that are likely to fare better postoperatively.

Our results are consistent with a previously published report investigating perioperative re-operation rates following RC. The reported 90-day re-operation rate was 5.7%, with fascial dehiscence (29%), bowel obstruction (21%), and enteric anastomotic leak (8%) the most common reasons for re-operation.[4] Increasing BMI was also found to be a predictor of re-operation,[4] however, this study did not highlight the significance of race or COPD as predictors of re-operation. Furthermore, the population was from a single institution, which limits the generalizability of these results when compared to data from a national, validated database, such as ACS-NSQIP.

The rate of adverse events for patients who underwent re-operation within 30 days of RC was alarmingly high. In addition to the obvious health burden of such complications, the increased financial burden needs be emphasized. It has been consistently shown that patients with major postoperative complications following abdominal surgery have an almost two-fold increase in direct hospital costs ($56 224 vs $29 038).[16] Thus, there is a crucial need for pre- and immediate postoperative efforts, such as preoperative pulmonary rehabilitation programs,[10] extensive counselling regarding importance of weight loss and smoking cessation, and Enhanced Recovery After Surgery (ERAS) pathways,[17] to minimize postoperative complications in high-risk patients and limit financial costs.

This study is limited by its retrospective nature. We were also unable to evaluate the reason for or type of re-operation. Preoperative pathological information was not available, and this may have influenced the surgeon's surgical approach, leading to heterogeneous results. Furthermore, as NSQIP abstracts data from multiple hospitals and providers, there was no standardized postoperative management plan (such as ERAS pathways), which is likely to have further contributed to the heterogeneity of the results. We did not make a distinction between patients who underwent an open vs. a robotic approach. However, previous studies have demonstrated that the 30-day re-operation rate following a robotic cystectomy was 5.0%,[18] which is similar to our reported rate of 5.8%.

Conclusions

Following RC, 5.8% of bladder cancer patients undergo re-operation within 30 days. Increasing BMI, history of COPD, and African American race are factors independently associated with increased risk of re-operation. Re-operation within 30 days of RC is also associated with significantly increased mortality rates, in addition to various other adverse health consequences. These results highlight the need for identifying at-risk patient demographics and pre- and postoperative optimization of those with modifiable risk factors in order to minimize postoperative complications.

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This paper has been peer-reviewed.

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