



# Ileus and small bowel obstruction after radical cystectomy for bladder cancer: Analysis from the Nationwide Inpatient Sample



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## ABSTRACT

**Purpose:** To investigate prevalence and predictors of postoperative small bowel obstruction (SBO) and ileus in a large cohort of bladder cancer (BCa) patients treated with radical cystectomy (RC).

**Methods:** All patients within the Nationwide Inpatient Sample who underwent RC for BCa between 2006 and 2012 were identified. First, prevalence of SBO and ileus was analyzed. Second, predictors of these bowel-related complications were identified using multivariable regression analyses. Third, the association between SBO, ileus, and length of stay was evaluated using logistic regression models adjusted for clustering. Prolonged length of stay was defined as hospital stay above mean stay of the population (>10 days). Fourth, the effect of SBO and ileus on mean inpatient cost of healthcare was examined.

**Results:** Of overall 41,498 patients, 1071 (2.6%) experienced SBO, and 11,155 (26.9%) experienced ileus. Predictors of ileus included age, male gender, black race, hospital characteristics, anemia, chronic pulmonary disease, drug abuse, hypothyroidism, fluid and electrolyte disorders, and neurological disorders (all  $p < 0.05$ ). Predictors of SBO included male gender, Asian/Pacific islander race, hospital characteristics, congestive heart failure, fluid and electrolyte disorders, and psychosis (all  $p < 0.05$ ). Postoperative SBO (odds ratio (OR) 19.587; 95% confidence interval (CI): 15.869–24.167) and ileus (OR 5.646; 95% CI: 5.336–5.974) were associated with prolonged length of stay (all  $p < 0.001$ ). Median cost of hospital stay was \$56,315 for patients who developed SBO, \$32,472 for patients who developed ileus, and \$24,600 for patients after cystectomy without ileus or SBO.

**Conclusions:** Significant prevalence of bowel-related complications in patients after RC was observed. These complications are strongly associated with prolonged length of stay and higher healthcare cost. Increasing awareness of SBO and ileus, identification of patients at risk prior to surgery, and implementation of protective strategies are strongly indicated in cystectomy patients.

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## 1. Introduction

Bladder cancer (BCa) is the seventh most common cancer diagnosis in the United States [1]. In 2017, there were an estimated 79,030 new cases and 16,870 new deaths as a result of BCa. 30% of all BCa cases present as muscle-invasive [2,3]. The standard of care for muscle-invasive BCa is a Radical Cystectomy (RC) with urinary diversion, where a segment of the small intestine is used to redirect urine to a stoma created in the abdomen [4]. However, RC is associated with high morbidity rate, as there is a consistent 90-day

complication rate in the range of 28%–64% in nearly all urologist care centers leading to a readmission rate ranging from 26% to 35% [5,6]. Of these reported complications, 29% of are related to the gastrointestinal system in the form of ileus or small bowel obstruction [7]. Ileus being the most frequent complication associated with RC [8].

This study was conducted to determine the prevalence and predictors of ileus and SBO along with their association with length of stay and cost of care. Much of the data concerning complication rates and correlation with increased length of stay/cost of care are lacking at the national level. This necessitates pulling information from nationwide databases, allowing urologists who practice outside of academic centers to better identify with the information. Additionally, this study looks closely at pre-operative chronic

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conditions as predictors of these complications to assist urologists in identifying patients at increased risk of developing SBO or ileus following RC.

## 2. Material and methods

Subjects were identified from the US Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS), sponsored by the Agency for Healthcare Research and Quality. The NIS is a 20% stratified probability sample that encompasses approximately 8 million acute hospital stays per year from 1050 hospitals in 44 states. It is the largest all-payer inpatient care observational cohort in the United States and represents approximately 90% of all hospital discharges. We used the International Classification of Diseases, 9th Revision (ICD-9), procedure code 57.71 associated with bladder cancer (BCa) diagnosis codes 188.0–188.6, 188.8, 188.9, and 233.7 to identify patients treated with radical cystectomy for bladder cancer between 2006 and 2012. Within this patient pool, we then determined prevalence of patients who experienced SBO or ileus following the procedure by using the appropriate ICD-9 code (560.9 for SBO and 537.2, 560.1, 560.31, 777.1, 777.4 for ileus). Next, a multivariate regression analysis was used in order to identify predictors of ileus and SBO after cystectomy controlling for confounders. Modeling was done using stepwise elimination process. The association between SBO, ileus, and length of stay was also evaluated using logistic regression models adjusted for clustering. Prolonged length of stay was defined as hospital stay above mean stay of the population (>10 days). We decided to use 10 days as the cut off because we felt it was a more realistic estimate of the length of stay based on the database we were using for this analysis. The hospital's bed size categories in the NIS are defined using region of the U.S., the urban-rural designation of the hospital, in addition to the teaching status. Rural hospitals were not split according to teaching status, because rural teaching hospitals were rare. A hospital is considered to be a teaching hospital if it has an AMA-approved residency program, is a member of the Council of Teaching Hospitals (COTH) or has a ratio of full-time equivalent interns and residents to beds of 0.25 or higher. In general a small hospital has up to 249 beds. We now include this explanation in methods. Finally, the effect of SBO and ileus on mean inpatient cost of healthcare was examined from this patient population. Costs were derived from total hospital charges using the HCUP cost-to-charge ratio, which allows conversion of charges to the amount that hospitals are reimbursed. Statistical analysis Stratification, clustering, and survey weights were used in accordance with the NIS sampling design.

## 3. Results

Overall 41,498 patients were identified from the NIS that underwent cystectomy as a primary treatment for bladder cancer between 2006 and 2012. 11,155 (26.9%) of the patients experienced ileus as an adverse outcome of the procedure, while 1071 (2.6%) of the patients experienced SBO. Patient characteristics stratified by these two complications are illustrated in Table 1.

Predictors of ileus on multivariable analysis are illustrated in Table 2. Patient characteristics (older age, male gender, black) were associated with higher odds of developing ileus after cystectomy ( $p < 0.05$ ). Smaller hospitals were not associated with higher odds of developing ileus ( $P > 0.05$ ). Among conditions controlled for, anemia, chronic pulmonary disease, drug abuse, hypothyroidism, fluid and electrolyte disorders, and neurologic disorders were all significant predictors of increase risk of post cystectomy ileus (OR range 1.154 for chronic pulmonary disease to 1.735 for fluid and electrolyte imbalance,  $P < 0.05$ ). Other conditions controlled for

including alcohol abuse, blood loss anemia, diabetes, congestive heart failure, depression, liver disease, peripheral vascular disease, renal failure, and psychosis were not significant predictors of increased risk of post cystectomy ileus ( $p > 0.05$ ).

Predictors of SBO on multivariable analysis are illustrated in Table 3. Patient characteristics (male gender, Asian) were associated with higher odds of developing SBO after cystectomy ( $p < 0.05$ ). Hospital characteristics were not associated with higher odds of developing ileus ( $P > 0.05$ ). Among chronic conditions controlled for, congestive heart failure, fluid and electrolyte disorder, metastatic cancer, and psychosis were all significant predictors of increase risk of post cystectomy SBO (OR range 1.557 for metastatic cancer to 2.440 for fluid and electrolyte imbalance,  $P < 0.05$ ). Other chronic conditions controlled for including alcohol abuse, anemia, chronic pulmonary disease, depression, diabetes, hypothyroidism, neurological disorders, obesity, peripheral vascular disease, and renal failure were not significant predictors of increased risk of post cystectomy SBO ( $p > 0.05$ ).

Predictors of prolonged length of stay (above the mean of 10 days) on multivariable analysis are illustrated in Table 4. Patient characteristics (older age, male gender, black, and Hispanic) were associated with higher odds of prolonged hospital stay after cystectomy ( $p < 0.05$ ). Hospital bed size was not associated with higher odds of developing ileus ( $P < 0.05$ ). Among chronic conditions controlled for, SBO (OR 19.019, 95% CI 15.067–24.008) and ileus (OR 5.634, 95% CI 5.323–5.964) were the strongest predictors of prolonged hospital stay. Almost all of the other chronic conditions we controlled for, with the exception of depression, drug abuse, hypothyroidism and peripheral vascular disease were as well predictors of prolonged hospital stay ( $p < 0.05$ ).

Finally, Median cost of hospital stay was \$56,315 for patients who developed SBO, \$32,472 for patients who developed ileus, and \$24,600 for patients after cystectomy without ileus or SBO.

## 4. Discussion

In spite of the major improvement in surgical technique and perioperative care, RC has continued to be a morbid surgery with significant complications. These complications often lead to prolonged hospital stay, documented to be as high as 9–11 days in many medical centers. Of the complications of RC, gastrointestinal are the most common, specifically ileus [7,9,10]. In this study, we confirm findings from previous studies on the high prevalence of such complications after RC. We also shed light on which preexisting conditions are most associated with ileus and SBO after RC in bladder cancer patients in order for providers to be able to intensify preventive measures in the perioperative period of time.

The rate of ileus in our series (26%) is high compared to previously reported series [11]. However, a uniform definition of ileus is lacking, and the diagnosis of ileus is usually subjective and observer-dependent, explaining the difference in the prevalence of ileus between our series and that of other researchers [8]. Ileus is presumed to result from the stress of surgery, which causes generalized sympathetic stimulation and could initiate a spinal reflex arc that impairs gastrointestinal motility [12,13]. Alternative mechanisms could include manipulation of bowel contents, inflammation from surgery, opiates, retroperitoneal irritation, and local or systemic hormonal or electrolyte imbalances [14]. With this understanding of the causes of ileus, it becomes plausible why risk factors identified in this study are associated with increased risk of post-RC ileus. Previous knowledge of which chronic conditions are significantly associated with ileus could be used to select more aggressive preventive measures in patients at high risk of ileus. Such patients would certainly benefit from enhanced recovery after surgery (ERAS) pathways including pre-operative optimization,

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