Cystectomy for benign disease: readmission, morbidity, and complications

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Introduction: *We sought to elucidate outcomes and risks associated with cystectomy and urinary diversion for benign urological conditions compared to malignant conditions.*

Materials and methods: *We identified patients who underwent cystectomy and urinary diversion for benign and malignant diseases through the American College of Surgeons National Surgery Quality Improvement Program database for the period 2007-2015. Patients were selected for inclusion based upon their current procedure terminology and International Classification of Disease, Ninth revision codes. Primary outcome was 30 day morbidity including return to the operating room (OR); infectious, respiratory, and/or cardiovascular complications; readmission to the hospital; and mortality. Multivariable regression analyses were performed to identify associated factors.*

Results: *A total of 317 patients underwent cystectomy and urinary diversion for benign disease, and 5510 patients underwent radical cystectomy with urinary diversion for cancer. Rates of major morbidity (43.2% versus 38.6%), mortality (0.9% versus 1.9%), return to OR (5% versus 5.8%), readmission (19.7% versus 21.4%), postoperative sepsis (14.5% versus 12%), and wound complications (16.1% versus 14.2%) were similar among patients undergoing cystectomy for benign and malignant conditions. In the group with cystectomy for benign conditions, smoking (OR: 3.11) and longer operative duration (OR: 1.06) were significantly associated with increased overall morbidity. Wound complications were significantly higher in smokers (OR: 3.09) and with an ASA ≥ III (OR: 5.71)*

Conclusions: *Patients undergoing cystectomy and urinary diversion for benign disease are at similar risk for 30 day morbidity and mortality as patients undergoing surgery for malignant conditions. Risk factors are identified that can potentially be targeted for morbidity reduction.*

Key Words: cystectomy, readmission, morbidity

Introduction

Cystectomy for benign disease is the final surgical option for patients with end-stage bladders who have failed conservative measures.[1,2] Common diagnoses for patients undergoing cystectomy for benign disease include neurogenic bladder, incontinence, terminal fistula disease, end-stage radiation cystitis, and interstitial cystitis.[3] In many of these patients, cystectomy is aimed toward improving quality of life.

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However, there is significant morbidity associated with radical cystectomy for malignant conditions.[4-6] The risks and complication rates for patients undergoing cystectomy and urinary diversion for benign disease (CUBD) are less defined. Due to differences in patient characteristics and operative techniques, cystectomy for benign conditions theoretically may have lower morbidity and mortality compared to cystectomy for malignant indications, however, objective data are lacking.

Urologists often rely on data from radical cystectomy (RC) studies to counsel patients considering CUBD. Majority of available data on CUBD comes from single institution retrospective reviews with small sample sizes.[7-9] A comprehensive knowledge of surgical complications and their predictors in these patients

would help improve patient counseling and setting expectations. In this study, we describe and compare patient characteristics, 30 day morbidity, readmission, and mortality rate for patients undergoing cystectomy for benign and malignant conditions. Finally, we attempt to identify risk factors associated with increased complications in patients undergoing cystectomy for benign diseases to help with risk-stratified patient counseling.

Materials and methods

American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP)

We utilized the ACS-NSQIP database to identify patients undergoing cystectomy and urinary diversion between 2007 and 2015. ACS-NSQIP is a nationally validated, outcomes-based program which is intended to measure and improve the quality of surgical care. The data are collected from 766 academic and community hospitals in the United States and Canada. Each institution has a trained surgical clinical reviewer who collects and tracks 30 day outcomes; data are audited annually to ensure accuracy.[10,11] Hospitals participating in the ACS-NSQIP are given access to Participant Use Data Files (PUFs), an aggregate collection of deidentified data intended to promote research and advance the quality of patient care. The necessary Institutional Review Board approval was obtained for use of the data for this study.

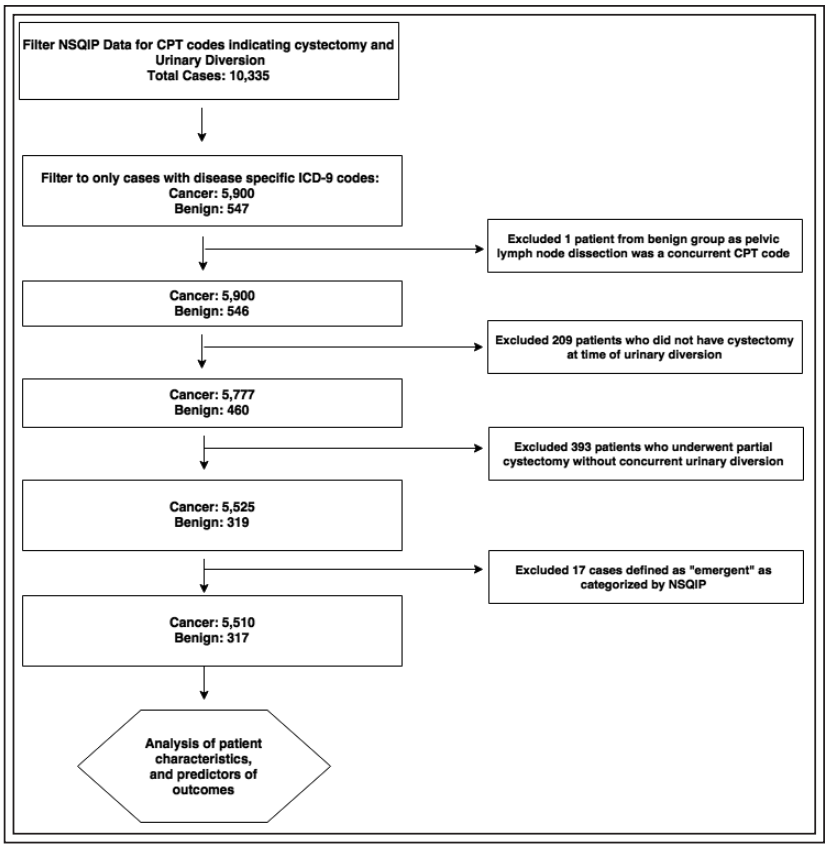

Figure 1. Patient selection schema.

Patient population

The ACS-NSQIP database was queried for cystectomy and urinary diversion from 2007 to 2015 using Common Procedural Terminology (CPT) codes. Procedures included ureteroileal conduit, continent bowel bladder, partial cystectomy, complicated partial cystectomy, cystectomy complete, cystectomy complete with ureterosigmoidostomy, cystectomy complete with ureteroileal conduit or sigmoid bladder, and cystectomy complete with continent diversion. Out of the patients that underwent the above procedures, patients with diagnoses for benign disease were identified according to their documented primary International Classification of Diseases, Ninth revision codes (ICD-9). The ICD-9 codes identified diagnoses including chronic interstitial cystitis, radiation cystitis, cystitis unspecified, intestinovesical fistula, vesical fistula, neurogenic bladder, urethral fistula, female genital fistula, and urinary incontinence. Patients with an ICD-9 code suggesting concurrent bladder cancer, partial cystectomy without urinary diversion, and pelvic lymph node dissection were excluded from the benign study group. The cohort of patients undergoing cystectomy for malignant indications were identified in a similar fashion based on the ICD-9 and CPT codes. See Figure 1 for patient selection schema.

The primary outcome was 30 day major morbidity and mortality. Major morbidity included readmission, return to the OR, urinary tract infection (UTI), pneumonia, pulmonary embolism/DVT, intubation/vent > 48 hrs, cardiovascular events, sepsis/septic shock, renal failure, and wound complications. Requirement for postoperative transfusion was assessed separately.

Differences in the patient characteristics and outcomes between the benign and cancer group were assessed using chi-square and Fisher's exact tests for categorical data; and Mann-Whitney U test for continuous variables. Variables explored included patient characteristics (age,

race, BMI, smoking status, diabetes, COPD, weight loss, dyspnea, steroid use, functional dependence), lab values (albumin, hematocrit, platelets, sodium, white blood cell count, bilirubin, BUN, creatinine), and operative characteristics (operative time, primary CPT code, ASA class, wound classification). Potential covariates included: Age > 70, smoking, history of COPD, steroid use, preoperative weight loss > 10% in last 6 months, preoperative sepsis, Albumin < 3.5, Hematocrit < 30, operative duration, and ASA Class > II. Multivariable regression models along with an AIC-based stepwise procedure were used to identify the group of variables most predictive of morbidity and length of stay. Logistic regression models were used for binary outcomes and a general linear regression model was used for length of stay (LOS). Since the distribution of length of stay was heavily right skewed which can lead to poor model estimates, it was transformed by adding 1 (since there were some LOS values of 0) and then taking the natural logarithm. All model estimates were reported by exponentiated beta estimates, which can be interpreted as odds ratios in the logistic regression models and as the multiplicative change in the geometric mean of LOS in the LOS model. Statistical significance was set at $p < 0.05$. All analyses were done in R programming language, version 3.4.2 (R Core Team; Vienna, Austria). Graphics were produced using the R package ggplot2, version 2.2.1 (Springer-Verlag New York, USA).

TABLE 1. **Preoperative and operative characteristics of benign and cancer cohorts undergoing cystectomy**

	Benign n = 317 (%)	**Cancer n = 5,510 (%)**	**p value**
Patient age,	60	70	< 0.001
Median (quartiles)	(48, 70)	(62, 76)	
Female	138 (43.5)	1,008 (18.3)	< 0.001
White race	273 (86.1)	5,168 (93.8)	< 0.001
BMI > 30	128 (40.3)	1,873 (34.0)	0.02
Diabetes	57 (18.0)	1,119 (20.3)	0.35
Current smoker	65 (20.5)	1,344 (24.4)	0.12
Functionally dependent	63 (20.1)	105 (1.9)	< 0.001
History of severe COPD	13 (4.1)	473 (8.6)	0.006
Hypertension requiring medication	159 (50.2)	3,372 (61.2)	< 0.001
Steroid use for chronic condition	16 (5.0)	187 (3.4)	0.17
Body weight loss > 10% in last 6 months	17 (5.4)	158 (2.9)	0.01
Hematocrit < 30	46 (14.5)	452 (8.2)	< 0.001
Transfusion, preop	18 (5.7)	88 (1.6)	< 0.001
Sepsis, preop	9 (2.8)	72 (1.3)	0.042
Albumin < 3.5 gm/dL	95 (29.9)	782 (14.2)	< 0.001
Operation duration,	333	337	0.06
Median (quartiles)	(257, 404)	(263, 425)	
ASA class			< 0.001
I-II	51 (16.1)	1,394 (25.3)	
III	250 (78.8)	3,796 (68.9)	
IV-V	16 (5.1)	320 (5.8)	
Wound class			< 0.001
Clean	2 (0.6)	83 (1.5)	
Clean/contaminated	272 (85.8)	5,124 (93.0)	
Contaminated	32 (10.1)	281 (5.1)	
Dirty/infected	11 (3.5)	22 (0.4)	

BMI = body mass index; COPD = chronic obstructive pulmonary disease; ASA = American Society of Anesthesiologists

Results

Patients undergoing cystectomy for benign conditions (n = 317) and for malignant conditions (n = 5510) were identified. Patient characteristics are noted in Table 1. As compared to the cancer cohort, patients undergoing cystectomy for benign indications were more likely to be young, obese, functionally dependent, anemic, hypoalbuminemic, and have a higher ASA class; see Table 1.

In patients undergoing cystectomy for benign disease, the most common indication was neurogenic bladder (42%), followed by radiation cystitis (17%). The majority of patients underwent ileal conduit urinary diversion (79.5%) and the use of continent diversion was limited (11.5%). Median operative time was 333 minutes (IQR: 257-404).

In the benign cystectomy cohort, major morbidity was experienced by 137 patients (43.2%) within 30 days of surgery. Three patients (0.9%) died within 30 days of the operation. Common complications included readmission and infectious complications including wound infection (16.1%), sepsis (14.5%), urinary tract infection (10.7%), and pneumonia (3.2%). Furthermore, 36.6% of the patients required transfusion in the postoperative period.

Benign and cancer cohorts showed similar rates of major morbidity, mortality, readmission, and return to the OR; see Table 2. Although incidence of overall morbidity was similar, patients undergoing cystectomy for benign indications were different in the number of morbidities suffered (p = 0.03) compared to cancer cohort. Interestingly, patients undergoing cystectomy for benign indications had longer LOS (median 8 days versus 7 days).

We explored the factors associated with perioperative complications in patients undergoing cystectomy for benign indications using multivariable analyses;

TABLE 2. **Postoperative outcomes and complications**

	Benign n = 317 (%)	**Cancer n = 5,510 (%)**	**p value**
Mortality, 30 day	0.9%	1.9%	0.33
Postop LOS, days, Median (quartiles)	8.0 (7.0, 11.0)	7.0 (6.0, 10.0)	< 0.001
Postop transfusion	116 (36.6)	2,138 (38.8)	0.46
No. of Morbidities			0.03
0	180 (56.8)	3,383 (61.4)	
1	70 (22.1)	909 (16.5)	
2+	67 (21.1)	1,223 (22.2)	
Major morbidity (any of the following)	137 (43.2)	2,127 (38.6)	0.11
Readmission	62 (19.7)	1179 (21.4)	0.53
Return to OR	16 (5.0)	320 (5.8)	0.65
UTI	34 (10.7)	512 (9.3)	0.47
Pneumonia	10 (3.2)	187 (3.4)	0.97
Pulmonary embolism/DVT	14 (4.4)	281 (5.1)	0.70
Intubation/Vent > 48 hrs	12 (3.8)	209 (3.8)	1.00
Cardiovascular events	5 (1.6)	154 (2.8)	0.27
Sepsis/septic shock	46 (14.5)	661 (12.0)	0.20
Renal failure	5 (1.6)	187 (3.4)	0.10
Wound complications (any of the following)	51 (16.1)	782 (14.2)	0.38
Superficial SSI	27 (8.5)	320 (5.8)	0.06
Deep SSI	6 (1.9)	105 (1.9)	1.00
Organ/space SSI	15 (4.7)	309 (5.6)	0.57
Wound dehiscence	6 (1.9)	154 (2.8)	0.44

LOS = length of stay; OR = operating room; DVT = deep vein thrombosis; SSI = surgical site infection

TABLE 3. **Factors associated with postoperative complications with simple cystectomy (n = 317)**

		Predictors of morbidity	
Variable	**Odds ratio**	**95% confidence interval**	**p value**
Current smoking	3.11	(1.74, 5.69)	0.0002
Operative duration (30 min.)	1.06	(1.00, 1.12)	0.0386
	Predictors of the natural logarithm of postoperative length of stay		
Variable	**Exponentiated Beta**	**95% confidence interval**	**p value**
ASA class ≥ III	1.15	(1.00, 1.33)	0.0436
	Predictors of wound complications		
Variable	**Odds ratio**	**95% confidence interval**	**p value**
Current smoking	3.09	(1.53, 6.21)	0.0015
ASA class ≥ III	5.71	(1.65, 36.04)	0.0198
	Predictors of perioperative transfusion		
Variable	**Odds ratio**	**95% confidence interval**	**p value**
Preoperative weight loss	3.37	(1.16, 11.16)	0.0317
Hematocrit < 30	2.93	(1.49, 5.85)	0.0019
Operative duration (30 min.)	1.10	(1.04, 1.17)	0.0014

Table 3. Smoking and longer operative duration were significantly associated with increased overall morbidity. Current smokers were three times as likely to experience complications postoperatively (OR: 3.11). Additionally, longer operative times were associated with higher odds of experiencing complications. For every 30 minute increase in operative duration, there were 6% increased odds of having any complication (OR: 1.06).

Smoking (OR: 3.09) and ASA ≥ III (OR 5.71) were associated with increased odds of postoperative wound complications; Table 3. A total of 116 patients (36.6%) required transfusion in the perioperative period. Logistic regression showed that preoperative weight loss (OR 3.37), lower hematocrit (OR 2.93), and longer OR times (OR 1.10 for each 30 minute increase) were associated with increased odds of requiring transfusion.

Median length of stay for all patients was 8 days (IQR: 7-11). On linear regression analysis, higher ASA class > III was significantly associated with longer postoperative LOS; Table 3.

Discussion

Research on benign cystectomy outcomes is sparse in comparison to that of radical cystectomy. Most studies looking at benign cystectomy come from single institution experiences or review of administrative data. While some studies look at specific patient populations (radiation cystitis, fistula disease), others look broadly at patients undergoing CUBD with studies ranging from 19-139 patients.[7,8,12] Thirty day complication rates for these studies range from 39%-73% with postoperative LOS ranging from 7-12 days. Patients seeming to be at a higher risk for complications are those with comorbid conditions and history of fistula disease secondary to radiotherapy.[7,8] Larger scale studies are based upon administrative data and lack longitudinal data on complications and readmissions.

Our study used ACS-NSQIP database to investigate the outcomes and morbidity for patients undergoing cystectomy for benign indications. We note that patients undergoing benign cystectomy are at significant risk for postoperative complications. The incidence of morbidity and mortality was similar in the benign and cancer cohort undergoing cystectomy. These outcomes are comparable to the previous publications on radical cystectomy.[4,6,13]

Previous studies in the literature have reported variable complication rates after simple cystectomy. The rates vary primarily due to differences in the classification of the morbidities and follow up time interval. Brown et al[14] used the Healthcare Cost and Utilization Project Nationwide Inpatient Sample to review more than 15,000 patients who underwent urinary diversion with or without concomitant cystectomy for end-stage lower urinary tract dysfunction. They noted a higher complication rate for patients undergoing cystectomy at the time of urinary diversion compared to those with diversion alone (35.0% and 30.6%, respectively).[8]

Therefore, cystectomy may be correctly omitted in carefully selected patients in order to reduce the risk of perioperative complications. Notably, this study did not capture post-discharge data, thereby likely underestimating morbidity for a procedure in which a significant proportion of complications occur after discharge. In contradistinction, a smaller case series by Neulander et al[15] purported to show reduced morbidity in 19 patients undergoing supratrigonal cystectomy and urinary diversion for benign disease; suggesting that cystectomy should be done to avoid future complications such as pyocystis. Other studies on supratrigonal cystectomy have shown a reduction in operative time and theorized lower morbidity with improved outcomes. While this seems intuitive, it has yet to be proven on a large scale.[12] A recent study by Aisen et al found similar results using the NSQIP database that included patients from 2005-2014.[16] We believe that our study incorporates cleaner data, allowing for more focused results. Benign cystectomy was rarely recorded in NSQIP prior to 2007 and the data during this time is often incomplete. Our data includes patients from 2007-2015 with more complete outcomes data. Furthermore, our study excludes patients who underwent "emergent" cystectomy which fundamentally have a higher complication rate.[17] Including these patients does not represent the intended study population and could inflate their complication rates. In general, the literature seems to agree that CUBD is a relatively morbid procedure but is an option for the appropriately selected patient to improve health-related quality of life.[18]

In our analysis we were able to identify factors associated with complications. Smoking was associated with a higher overall complication rate as well as wound-related complications. Longer operative times were also associated with an increase in complications, a finding that has been reported in prior urologic studies.[9,19] It is important not to conflate this association with causation, however, as an increased operative duration may be due to several intangible confounders like prior radiation, prior surgery, and difficult anatomy that may be independently associated with complications. In contrast to the previously reported bladder cancer cohorts, we did not find hypoalbuminemia to be associated with increased morbidity, possibly due to the smaller sample size in our cohort.[13] We categorized postoperative transfusion requirement as a distinct outcome rather than merge it under the overall morbidity rubric. This allowed us to separately analyze transfusion and non-transfusion related complications and identify different but overlapping risk factors. We noted that preoperative anemia and preoperative weight loss were associated with increased odds of transfusion, and both can be considered surrogates for nutritional depletion. Notably, one-third of the patients in our benign cohort had hypoalbuminemia, providing opportunities for nutritional optimization before surgery. Identifying these factors is useful to counseling patients on expectations and targeting modifiable variables to reduce risk.

There is growing policy and public health interest in reducing perioperative complications and readmissions as a means to improving clinical outcomes and reducing costs. As we continue the paradigm shift toward value-based care, identifying preoperative predictors of morbidity and LOS will be important in developing care pathways to help mitigate risk, decrease cost, and improve outcomes.

Strengths of this study include the utilization of ACS-NSQIP, a nationally validated prospectively maintained, risk-adjusted database as opposed to administrative databases.[10] The limitations of this study are those inherent to the ACS-NSQIP database. While the occurrence of any outcomes or complications in NSQIP is audited for integrity, the potential for coding errors exist.[20,21] As with any non-randomized study, we are unable to account for unmeasured confounders. Clinical details including preoperative characteristics and postoperative outcomes are less granular than with chart review, and furthermore, our data are also currently limited to 30 days from surgery.

One unique limitation pertains to the specifics of the operative steps. In this cohort, 79% of patients had the CPT code 51590 (cystectomy complete with ureteroileal conduit) – which implies that these patients essentially underwent a radical cystectomy, albeit for a benign indication leading to misclassification bias. This may be because at some institutes, CUBD is performed by urologic oncologists, who transfer their operative preferences to this patient population. This highlights some of the difficulties in studying patients undergoing CUBD - the heterogeneity of the patient population, as well as variability in surgeon and surgical details. However, this also represents the real-world scenario in which CUBD is performed in disparate patients with differing techniques and variable settings.

Conclusion

Cystectomy for benign disease is a morbid procedure with a high risk of readmission and infectious complications. Smoking, longer operative times, higher ASA class, and pre-op weight loss are associated with increased postoperative complications. These should serve as benchmark data for complications after CUBD and help identify areas for further research as well as interventions to improve outcomes and reduce costs. □

References

1. Gormley EA, Lightner DJ, Burgio KL et al; American Urological Association; Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. *J Urol* 2012;188(6 Suppl):2455-2463.
2. Hanno PM, Burks DA, Clemens JQ et al. AUA guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome. *J Urol* 2011;185(6):2162-2170.
3. Isharwal S, Gupta S. Management of end-stage radiation cystitis in the cancer survivor. *Curr Bladder Dysfunction Reps* 2016;11(2):98-104.
4. Stimson CJ, Chang SS, Barocas DA et al. Early and late perioperative outcomes following radical cystectomy: 90-day readmissions, morbidity and mortality in a contemporary series. *J Urol* 2010;184(4):1296-1300.
5. Gore JL, Lai J, Gilbert SM; Urologic Diseases in America Project. Readmissions in the postoperative period following urinary diversion. *World J Urol* 2011;29(1):79-84.
6. James AC, Izard JP, Holt SK et al. Root causes and modifiability of 30-day hospital readmissions after radical cystectomy for bladder cancer. *J Urol* 2016;195(4 Pt 1):894-899.
7. Cohn JA, Large MC, Richards KA, Steinberg GD, Bales GT. Cystectomy and urinary diversion as management of treatment-refractory benign disease: the impact of preoperative urological conditions on perioperative outcomes. *Int J Urol* 2014;21(4):382-386.
8. Brown ET, Osborn D, Mock S et al. Perioperative complications of conduit urinary diversion with concomitant cystectomy for benign indications: a population-based analysis. *Neurourol Urodyn* 2017;36(5):1411-1416.
9. Osborn DJ, Dmochowski RR, Kaufman MR, Milam DF, Mock S, Reynolds WS. Cystectomy with urinary diversion for benign disease: indications and outcomes. *Urology* 2014;83(6):1433-1437.
10. ACS National Surgical Quality Improvement Program. Available from URL: https://www.facs.org/quality-programs/acs-nsqip. Accessed January 5, 2018.
11. Hall BL, Hamilton BH, Richards K, Bilimoria KY, Cohen ME, Ko CY. Does surgical quality improve in the American College of Surgeons National Surgical Quality Improvement Program: an evaluation of all participating hospitals. *Ann Surg* 2009;250(3):363-376.
12. Rowley MW, Clemens JQ, Latini JM, Cameron AP. Simple cystectomy: outcomes of a new operative technique. *Urology* 2011;78(4):942-945.
13. Johnson DC, Riggs SB, Nielsen ME et al. Nutritional predictors of complications following radical cystectomy. *World J Urol* 2015; 33(8):1129-1137.
14. Brown ET, Osborn D, Mock S et al. Temporal trends in conduit urinary diversion with concomitant cystectomy for benign indications: a population-based analysis. *Urology* 2016;98:70-74.
15. Neulander EZ, Rivera I, Eisenbrown N, Wajsman Z. Simple cystectomy in patients requiring urinary diversion. *J Urol* 2000; 164(4):1169-1172.
16. Aisen CM, Lipsky MJ, Tran H, Chung DE. Understanding simple cystectomy for benign disease: a unique patient cohort with significant risks. *Urology* 2017;110:239-243.
17. Linder BJ, Tarrell RF, Boorjian SA. Cystectomy for refractory hemorrhagic cystitis: contemporary etiology, presentation and outcomes. *J Urol* 2014;192(6):1687-1692.
18. Al Hussein Al Awamlh B, Lee DJ, Nguyen DP, Green DA, Shariat SF, Scherr DS. Assessment of the quality-of-life and functional outcomes in patients undergoing cystectomy and urinary diversion for the management of radiation-induced refractory benign disease. *Urology* 2015;85(2):394-400.
19. De Nunzio C, Cindolo L, Leonardo C et al. Analysis of radical cystectomy and urinary diversion complications with the Clavien classification system in an Italian real life cohort. *Eur J Surg Oncol* 2013;39(7):792-798.
20. Sellers MM, Merkow RP, Halverson A et al. Validation of new readmission data in the American College of Surgeons National Surgical Quality Improvement Program. *J Am Coll Surg* 2013;216(3):420-427.
21. Steinberg SM, Popa MR, Michalek JA, Bethel MJ, Ellison EC. Comparison of risk adjustment methodologies in surgical quality improvement. *Surgery* 2008;144(4):662-667; discussion 662-667.