Assessment of complications following urinary diversion for benign indications

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Introduction: *To evaluate complications following urinary diversion for non-malignant conditions.*

Materials and methods: *We performed a retrospective review of patients undergoing urinary diversion for benign indications between 2000 and 2017. Data collected including patient demographic and clinical characteristics, surgical characteristics, and complications. Complications were graded using Clavien-Dindo classification and were categorized as early versus delayed (≤ versus > 90 day postoperatively). Logistic regression assessed for predictors of developing any postoperative complication.*

Results: *A total of 68 patients were identified for study analysis with median follow up of 24 (7-72) months. Sixty-eight and 25% of patients underwent diversion for neurogenic bladder and complications related to pelvic radiation, respectively. A majority (90%) underwent ileal conduit with the remainder undergoing continent diversion. A total of 121 complications were identified, comprising 50 early and 72 delayed. Overall, 77% of patients had at least one complication during the follow up period. Fifty-one percent of patients experienced early complication, while 66% of patients experienced delayed complications. Complications of Clavien-Dindo Score ≥ IIIB were seen in 48% of patients. The most common early complication was wound infection (12%); delayed was urinary tract infection (39%). Multivariable logistic regression modeling found no independent predictors of complication, although the best-fit model included BMI, diabetes, presence of multiple comorbidities, and operative time (hr) as positive predictors of complication.*

Conclusion: *Our study demonstrates that urinary diversion for benign etiologies is associated with a significant rate of complication. A large percentage of these complications occur in the delayed period and are classified as severe complications.*

Key Words: urinary diversion, benign disease, cystectomy

Introduction

Urinary diversion is most commonly performed in the setting of cystectomy for treatment of malignant disease. However, urinary diversion is also indicated in the treatment of refractory benign disease. Accordingly, urinary diversion may be performed in the treatment of neurogenic bladder, urinary incontinence, radiation-related bladder complications, and other complex pathology of the bladder. Investigation demonstrates that functional and quality of life outcomes following diversion in this patient population are excellent.[1,2]

Complication rates following cystectomy and urinary diversion for malignant disease are widely reported. As such, complication rates over 60% are reported in large series and often include a high rate of severe complications.[3,4] In contrast, there are limited series evaluating complications in patients undergoing diversion for benign etiology. Focused study is important as this patient population is heterogeneous and has unique characteristics and comorbidities that may affect surgical complications.

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Diversion in these cases may be done with or without cystectomy. Supratrigonal cystectomy has been recommended in these cases under the assumption that this approach may decrease morbidity.[5] However, limited data is available to understand whether this approach is indeed associated with lower risk or to compare complication rates in patients undergoing diversion with cystectomy versus with bladder preservation.

We aimed to assess complication rates in patients undergoing urinary diversion for benign disease with specific focus on timing and classification of the complication. We also sought to assess for predictors of developing any postoperative complication.

Materials and methods

We performed a retrospective review of patients undergoing urinary diversion for benign indications at a single institution between January 2000 and December 2017. After institutional review board approval, we queried the University of Virginia clinical repository database for patients with CPT Codes 50820, 51590, 51596, 51570, 51550, or 51555 over this time period. The resulting list of patients was then screened to exclude those who were diverted for oncologic reasons. Data were collected including patient demographic and clinical characteristics, with focus placed on surgical characteristics and postoperative complications. Pyelonephritis and sepsis of urinary tract were categorized as urinary tract infections. Complications were graded according to the Clavien-Dindo classification and were classified as early (≤ 90 day postoperatively) or delayed (> 90 days postoperatively).[6]

Data analysis was performed using R statistical software (V3.3.2). Data are presented as median (interquartile range (IQR)). Comparisons between groups were made using Chi-squared, Fisher's Exact, Wilcoxon Rank Sum or Kruskal-Wallis tests as appropriate. Univariate and multivariate logistic regression was used to assess for predictors of developing complications after urinary diversion.

Multivariable logistic regression of the odds of developing any complication after benign urinary diversion was then performed using those variables with $p < 0.15$ on univariable modeling of the outcome. The multivariable model was fitted in stepwise manner using StepAIC function from the MASS package in R and goodness of fit was further assessed with rms package.[7,8] All tests were performed with $\alpha = 0.05$.

Results

Review identified 68 patients for study analysis undergoing diversion by seven surgeons between January 2000 and December 2017. Demographic and clinical characteristics are presented in Table 1. This cohort demonstrated a median of age of 52 (38-63) years with median body mass index (BMI) 28.5 (23-37) kg/m^2. The majority were women (74%). Median follow up was 23.5 (7-72) months. A significant number and variety of comorbidities were seen. Indications for urinary diversion are summarized in Table 1 as well. Sixty-eight percent underwent diversion for

TABLE 1. **Demographic and clinical characteristics**

Female	50 (74%)
Male	18 (26%)
Age	52 [38, 63]
BMI (kg/m^2)	28.5 [23, 37]
Smoker	
Current	18 (29%)
Former	14 (23%)
Comorbidities	
CKD	19 (28%)
Cardiac*	9 (13%)
COPD	2 (3%)
Diabetes	19 (28%)
Liver**	5 (7%)
Anticoagulant***	10 (15%)
Multiple****	14 (21%)
Indication for diversion†	
Neurogenic bladder	46 (68%)
Poor compliance	24 (52%)
Bladder neck erosion	8 (17%)
Refractory UUI	6 (13%)
Sacral decubitus ulcers	8 (17%)
Radiation	17 (25%)
Poor compliance	5 (29%)
Fistula	9 (53%)
Stricture	2 (11%)
Cystitis	1 (6%)
Other	5 (7%)

BMI = body mass index; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease;
*cardiac disease including prior myocardial infarction; **chronic liver disease; ***anticoagulant, systemic anticoagulation in pre-operative period. ****multiple, more than 1 of the comorbidities listed above in table. †primary indication for diversion. Data represented as n (%)

TABLE 2. **Complication severity***

Clavien-Dindo score	Early (< 90 d) n = 68	Late (> 90 d) n = 56	Total n = 68
≤ IIIa	24 (35%)	16 (29%)	21 (31%)
IIIb-IVb	7 (10%)	23 (41%)	30 (44%)
V	3 (4%)	2 (4%)	5 (7%)

*represents the highest complication grade suffered by a patient. Data presented as n (%) where n is number of patients in the cohort.

neurogenic bladder as related to spinal cord injury (n = 24), spina bifida (n = 8), multiple sclerosis (n = 6), and other etiology (n = 8). Indications for diversion in those with neurogenic bladder related issues included poor bladder wall compliance, refractory urge incontinence, bladder neck erosion, sacral decubitus ulcers in the setting of incontinence, and inability to manage clean intermittent catheterization. Many of the neurogenic bladder patients (89%) had multiple indications for diversion. In addition, 25% of the overall cohort underwent diversion for complications specific to pelvic radiation and related issues including fistula, urethral or ureteral stricture disease, and hemorrhagic radiation cystitis.

Most patients underwent ileal conduit (90%) with a subset undergoing simultaneous supratrigonal cystectomy (STC) (16%). The remainder underwent continent diversion, including ileovesicostomy and ileocolic reservoir. The median operative time and hospitalization duration was 258 (232-350) minutes and 7 (6-10) days, respectively. Concurrent procedures were performed in 26% of patients and included lysis of adhesions and diverting colostomy.

Postoperative complications are detailed in Table 2 and Table 3. A total of 121 complications were identified, comprising 50 early and 72 delayed. Seventy-eight percent of patients had at least one complication during the follow up period. Fifty percent of patients experienced early complications, while 66% experienced delayed complications. Complications of Clavien-Dindo Score ≥ IIIB were seen in 48.5% of patients.

The most common early complications included wound infection (12%), prolonged ileus (9%), and urinary tract infection (UTI) (6%). Urinary tract infection (39%), nephrolithiasis (29%) and ureteroenteric anastomotic stricture (18%) were the most frequent delayed complications. Six patients underwent subsequent supratrigonal cystectomy for pyocystitis. Five deaths were classified as complications of urinary diversion. Three early mortalities resulted from sepsis related to bowel leak or rhabdomyolysis. Two delayed mortalities resulted from sepsis. An additional 5 patient deaths unrelated to diversion occurred during the follow up period.

Univariable and multivariable analysis of predictors of any complication are shown in Table 4. Prior to modeling, comparison testing was performed. This demonstrated BMI, diabetes, and presence of multiple comorbidities each positively associated with higher risk of complication ($p < 0.05$), which was corroborated on

TABLE 3. **Type of complication***

	Early (< 90 d) n = 68	Late (> 90 d) n = 56	Total n = 68
Prolonged ileus	6 (9%)	NA	6 (8%)
Wound	8 (12%)	NA	8 (15%)
Urinary tract infection	4 (6%)	22 (39%)	26 (38%)
SBO	2 (3%)	5 (8%)	7 (10%)
Hernia	0 (0%)	6 (10%)	6 (9%)
Stricture	0 (0%)	10 (18%)	10 (15%)
Stones	0 (0%)	16 (29%)	16 (24%)
Pyocystitis requiring delayed STC	0 (0%)	6 (13%)	6 (11%)

*complications occurring in less than 5 patients are excluded. Data presented as n (%).

TABLE 4. **Predictors of any complication**

Univariate analysis	**OR**	**95% CI**	**p value**
Age	1.00	0.96-1.04	0.98
BMI (kg/m^2)	1.10	1.01-1.24	0.02
Smoker			
Former	0.04	0.10-1.58	0.54
Current	0.50	0.10-2.38	0.38
Diabetes	7.20	1.29-135.6	0.02
Multiple comorbidities	***	***	< 0.01
Neurogenic bladder	1.54	0.45-5.03	0.48
Radiation	0.59	0.17-2.17	0.41
Continent diversion	1.79	0.27-35.2	0.58
STC	3.67	0.58-67.7	0.19
Concurrent procedure	1.11	0.37-3.44	0.86
Operative time (hr)	1.52	0.99-2.81	0.06
Final multivariable model of any complication			
	OR	**95% CI**	**p value**
BMI (kg/m^2)	3.70	0.80-17.1	
Diabetes	2.70	0.21-33.2	0.003
Multiple comorbidities	1806	***	
Operative time (hr)	1.70	0.80-37.3	

BMI = body mass index; STC = supratrigonal cystectomy.
Multiple comorbidities, greater than one of diabetes, heart disease, chronic kidney disease, liver disease, chronic obstructive pulmonary disease, or use of systemic anticoagulation preoperatively.
***all patients with multiple comorbidities had a complication postoperatively, which resulted in unreliable OR and 95% confidence intervals specific values.

subsequent univariate logistic regression. In addition to these variables, predictors demonstrating a trend towards significance ($p < 0.15$) on univariable modeling were also included in multivariable modeling. The final model with best fit included BMI, diabetes, multiple comorbidities, and operative time, although no independent predictors reached statistical significance (overall model $p = 0.002$, pseudo $R2 = 0.53$). Subset univariable analysis of predictors for high grade delayed complication (Clavien-Dindo score > IIIa) suggested radiation as negative predictor (OR 0.28, $p = 0.046$) and neurogenic bladder as positive predictors (OR 3.33, $p = 0.038$). Other subset analyses of more specific complications (death; early versus delayed complications) did not demonstrate statistical significance associated with any predictor.

Discussion

The majority of published studies focus on outcomes following urinary diversion related to cystectomy in the setting of oncologic disease. Although diversion for benign disease is technically similar, focused investigation is important as this patient population may have unique characteristics that affect surgical outcomes and complications. For example, cancer has been described as a disease of aging and these surgical patients thus often have significant comorbid disease that increases surgical risk.[9] Accordingly, Shabsigh and colleagues report a mean age of 68 in a series of 1142 patients undergoing radical cystectomy for bladder cancer.[10] The study population demonstrated a significant degree of associated comborbidity, with an age adjusted Charlson-Romano morbidity index ≥ 2 and ASA score ≥ 3 in 64% and 43% of patients, respectively.

In contrast, diversion for benign disease is often seen in younger patients as related to neurologic injury and thus carries different surgical risk. For this reason, we sought to evaluate complications following urinary diversion for non-malignant conditions and our study revealed several interesting findings. Consistent with

prior discussion, the mean age of our study population was younger (52 years). In addition, the indication for diversion was related to the management of neurogenic bladder in a majority of cases. Diversion in neurogenic bladder patients may be indicated for upper tract damage, recurrent UTI, fistula formation, and refractory urinary incontinence.[11] Fortunately, prior investigation suggests that the rate of patients with neurogenic bladder requiring diversion is low. Accordingly, Cheng et al reported that, of 2569 patients followed for spinal cord injury, only 0.5% required diversion.[12]

Another notable finding to the present study is the significant rate of complications in our cohort. A total of 78% of patients experienced at least one complication during the study period. Prior research detailing complications following diversion for benign disease is limited and conflicting. Chartier-Kastler et al reported an overall complication rate of 36% in 33 patients undergoing ileal conduit for neurogenic bladder management.[13] Similarly, additional small series report low rates of complications following diversion for benign disease.[14] More recent studies demonstrate a much higher rate of complication that ranges from 67%-73% and is more consistent with our findings.[15,16]

Similarly, a significant portion of complications seen in our investigation were severe, with 51% of patients experiencing at least one complication of Clavien-Dindo Score ≥ IIIB. Osborne and colleagues reported that 57% of patients experienced a grade ≥ II Clavien-Dindo complication, with 54 ≥ IIIa complications in a series of 161 patients.[15] Similarly, Cohn et al reported severe (≥ IIIa) complications in 38% of patients within 30 days of surgery.[16] Our study supports these findings and suggests that a significant rate of severe complications is seen following urinary diversion for benign disease.

A paucity of data exists to identify predictors of surgical complications in this patient population. On univariable analysis we found BMI, diabetes, multiple comorbidities, and operative time as possible predictors of complication; although a strong multivariable model was created with these variables ($R2 = 0.53$; $p = 0.003$), none were found as independent predictors within the model. This could be related to collinearity between variables or reflect inherent limitation of logistical regression modeling in small datasets. Interestingly, the identification of operative time as a possible predictor supports prior investigation by Osborne and colleagues demonstrating that longer surgical duration was correlated with a higher incidence of moderate and severe complications in patients undergoing diversion for benign disease.[15]

Our subset analysis suggested radiation-related indication for diversion may predict lower risk of severe complications (Clavien-Dindo > IIIa), while neurogenic bladder related indications may increase the risk. Other investigation has conversely identified a high rate of complication in patients undergoing diversion related to radiation-induced complication.[16] However, predictive analysis by Osborne has shown that surgical indication does not predict for complications.[15] Further study is necessary to determine if surgery indication predicts for postoperative complications.

The role of cystectomy in diversion for benign disease is controversial. It has been argued that cystectomy at the time of diversion is indicated given that failure to remove the bladder can lead to complications including pyocystitis, pain, and hematuria.[17] Indeed, delayed cystectomy rates as high as 25% are reported in small series.[18] In contrast, other authors have reported much lower rates of delayed cystectomy and overall complications related to the native bladder.[19] Lawrence et al reported only a 7% complication rate related to retaining the defunctionalized bladder.[20] All patients were managed conservatively without the need for cystectomy or other surgical management. In our series, 6 (11%) patients undergoing ileal conduit with bladder preservation required cystectomy related to complications of the defunctionalized bladder, suggesting that cystectomy at the time of diversion should be considered. This decision is also made difficult by that lack of supplemental research to understand whether there is significant additional risk of surgical complication related to the cystectomy itself when compared to diversion alone.

Study limitations include its single-center, retrospective nature and related bias. Despite spanning nearly two decades, our follow up was limited to median 23.5 months, likely due to the practice of releasing patients to their local providers when stable due to our institution's wide catchment. We were also limited by data available to us via the University of Virginia clinical repository database. For this reason, our study focused only on surgical complications as our data set does not allow for assessment of functional and quality of life outcomes. Further, study conclusions may be limited by lower patient numbers, especially within subset analysis. Despite this, our study represents one of the largest available to investigate complications following urinary diversion for benign disease. Our data thus add significantly to the literature and suggest a higher incidence and severity of complications in this patient cohort. In addition, our experience provides additional insight into complications in patients undergoing cystectomy versus bladder preservation at the time of urinary diversion. This data is helpful to guide surgical management and patient counseling when considering cystectomy and diversion for benign disease.

Conclusion

In our series, urinary diversion for benign disease is associated with a significant rate of complication. A large percentage of these complications occur in the delayed period and are classified as severe complications. Multivariable logistic regression modeling found no independent predictors of complication, although the best-fit model included BMI, diabetes, presence of multiple comorbidities, and operative time as positive predictors of complication. Further investigation is necessary to better define predictors of complication in this surgical population. □

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