

# Female Urology, Urodynamics, Incontinence, and Pelvic Floor Reconstructive Surgery

## Female Urethral Diverticula: Diagnosis, Pathology, and Surgical Outcomes at an Academic, Urban Medical Center



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<b>OBJECTIVE</b>	To describe the outcomes of a series of women diagnosed with a urethral diverticulum at an urban tertiary care center.
<b>METHODS</b>	An Institutional Review Board-approved review of a series of 78 women with a diagnosis of urethral diverticulum from 2009 to 2015 was performed. Clinical, radiographic, and pathologic data was collected by retrospective review of patient medical records. Data regarding treatment selection and postoperative outcomes were collected. A multivariable logistic regression was performed to identify preoperative variables that were associated with undergoing surgical resection.
<b>RESULTS</b>	Of the 78 patients reviewed, the median age was 45.5 years (interquartile range (IQR) 36.0-53.8), median body mass index was 30.4 (IQR 24.8-34.4). The most common presenting symptoms included: incontinence (39%), recurrent urinary tract infections (23%), dysuria (18%), discharge (13%), dyspareunia (12%), and hematuria (9%). Additionally, 16 (21%) women were asymptomatic. Of these 78 cases, 40 underwent surgical excision (51%). Of the remaining 38, 13 were symptomatic and lost to follow-up, 23 were managed expectantly, and 2 underwent surgery after the study period. Review of the pathology results revealed that the most common finding was squamous metaplasia (31%). There was 1 adenocarcinoma in the series (2.5%). Of the 40 patients who had surgery, 3 (7.5%) had a diverticular recurrence and 5 (12.5%) developed stress urinary incontinence. The median follow-up was 7.5 months (IQR 1-20.25 months).
<b>CONCLUSION</b>	A variety of presenting symptoms existed for women with a urethral diverticulum seeking medical care at an urban medical center. When controlling for age, body mass index, and race, the presence of preoperative symptoms was associated with undergoing surgical resection. UROLOGY 128: 42–46, 2019. © 2019 Elsevier Inc.

Female urethral diverticula (UD) are outpouchings of urethral lumen into the periurethral space.<sup>1,2</sup> The prevalence of UD ranges from 0.6% to 4.7%.<sup>3,4</sup> Classically, the clinical symptom triad is described as

dysuria, dyspareunia, and postvoid dribbling.<sup>5</sup> However, in practice, the clinical presentation can vary dramatically with some patients reporting no symptoms at all.<sup>6</sup> Though UD are most often benign, malignancy has been described with a reported incidence between 3% and 6%.<sup>7,8</sup> The diagnosis of UD is typically made by a detailed history and physical examination. Imaging can facilitate diagnosis when uncertainty exists and aid in surgical planning. Imaging options include voiding cystourethrogram, positive-pressure urethrography, ultrasonography, and magnetic resonance imaging (MRI).<sup>9</sup> MRI is currently considered the gold standard.<sup>10-12</sup>

Surgical resection is the primary approach to treating UD beyond expectant management.<sup>4,13</sup> Several surgical techniques have been described with transvaginal diverticulectomy being performed most commonly. However, the outcome data regarding surgical technique have never been truly compared as the data have been variably

**Financial Disclaimer/Conflict of Interest:** None.

**Funding:** There are no financial disclosures.

This work was presented as a poster at Pelvic Floor Disorders Week, American Urogynecologic Society, Denver, CO, USA, in September 2016.

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Submitted: August 9, 2018, accepted (with revisions): December 4, 2018

reported and the rarity of UD makes it challenging to study prospectively.<sup>14</sup> In addition, there is also limited data on factors that influence physician and patient decision making with respect to management of UD. In this study, we describe the diagnosis and treatment of UD in our patient population with a focus on factors influencing patient selection for surgical intervention and outcomes following surgery.

## METHODS

After Institutional Review Board review, the electronic medical record was queried for cases of female urethral diverticulum using the International Statistical Classification of Diseases (ICD)-9 code(s) for urethral diverticulum between the years 2009 and 2015 via an in-house developed electronic medical record search program called Clinical Looking Glass.<sup>15</sup> Cases were identified by chart review. The report of clinical symptoms, radiologic findings, pathology results, and postoperative outcomes were extracted from the medical record by 2 of the study's authors (J.P. and M.L.). To be included in the final cohort, the presence of a urethral diverticulum had to be documented in an imaging study.

Pertinent demographic data and clinical characteristics were analyzed using descriptive statistics. The cohort was then analyzed to identify factors associated with surgical versus expectant management. For this portion of the analysis, the preoperative covariates selected included the following: age, race, body mass index (BMI), diverticulum size, and the presence (or absence) of preoperative symptoms (dichotomized to any symptoms versus none). Bivariate associations between the outcome variable (surgical resection) and preoperative covariates were assessed. For continuous variables, the Mann-Whitney test was used, as normality could not be assumed for these variables based on histogram inspection. Categorical variables were analyzed using the Pearson's chi-square test or Fisher's exact test as indicated. All variables with significant bivariate associations were included in the full model. Age and race were to remain in the final model due to clinical relevance. Multivariable logistic regression was performed in a backward elimination fashion. No meaningful confounding or interactions were observed during model building. In addition, the Spearman correlation test was used to assess correlation between the independent variables presence of "preoperative

symptoms" and "diverticulum size," and was determined to be poor. (Spearman's  $\rho = 0.086$ ,  $P = .53$ ). Multicollinearity was assessed for all independent variables in the model and not observed. Statistical significance was set at an alpha of 0.05. All analyses were performed using STATA (Stata statistical software version 14.1. College Station, TX).

## RESULTS

A total of 370 patients with a diagnosis code for urethral diverticulum were identified. After reviewing all charts, 78 women met criteria for inclusion. Reasons for exclusion included male, incorrect ICD-9 coding, provisional diagnosis, and incomplete records.

The median age of our population was 45.5 (interquartile range (IQR) 36.0-53.8) and the median BMI was 30.4 (IQR 24.8- 34.4). Thirty-six subjects identified as Black (46%), 9 Hispanic (11%), 5 Caucasian (6%), 1 Asian (1%), and 17 identified as "other" (21%). The most common presenting symptom was urinary incontinence (31 women, 39%). There were 18 women with recurrent urinary tract infection (UTI) (23%), 14 with dysuria (18%), 10 with urethral discharge (13%), 9 with dyspareunia (12%), and 7 with hematuria (9%). An additional 16 women (21%) were completely asymptomatic upon presentation (see Table 1).

All the patients had diagnostic imaging. Seventy-one patients (91%) had a pelvic MRI. 6 patients (8%) had a pelvic ultrasound, and 1 patient (1%) underwent both. Median MRI diameter of the UD was 2.00 cm (IQR 1.25-2.45 cm). Median ultrasound diameter was 2.3 cm (IQR 1.90-2.55 cm).

40 patients (51%) underwent surgical resection and repair by 1 of 6 urology or urogynecology trained surgeons. There were 2 urologists and 4 gynecologists among the surgeons. Of these, 1 of the urologists and 2 of the gynecologists were fellowship trained in Female Pelvic Medicine and Reconstructive Surgery. There were no recorded incidences of intra-operative complications. The remaining 38 patients did not initially undergo surgical repair. Of these, 13 were symptomatic and lost to follow-up, 23 were managed expectantly, and 2 underwent surgery after the study period.

Median follow-up after surgery was 222 days (IQR 55-557). Two patients had postoperative complications: 1 had a UTI and the other had a wound separation. Over the course of follow-up, 3 (8%) patients had a recurrence (none of whom had a second

**Table 1.** Comparison of baseline characteristics of patients who were managed surgically versus managed expectantly

Variables	Total N = 78	Surgically Managed N = 40	Expectantly Managed N = 38	P Value
Median age in y (IQR)	45.5 (36-54)	44 (34.5-49.5)	48 (36-64)	0.19
Median body mass index kg/m <sup>2</sup> (IQR)	30.4 (24.8-34.4)	31.3 (25.6-36.3)	28.6 (24.3-34.0)	0.21
Race				0.17
Hispanic	12.8%	10%	15.8%	
Black	47.6%	52.5%	42.1%	
White	6.4%	5%	7.9%	
Asian	1.2%	2.5%	0%	
Other	20.5%	17.5%	23.7%	
Unknown	11.5%	12.5%	10.5%	
Any symptom (percentage)	59/75 (78.7%)	36/39 (92.3%)	23/36 (63.9%)	0.004
Urine leakage (percentage)	31/75 (41.3%)	22/39 (56.4%)	9/36 (25%)	0.006
Recurrent urinary tract infection (percentage)	18/74 (24.3%)	13/38 (34.2%)	5/36 (13.8%)	0.04
Median urethral diverticulum size in cm (IQR)	2 (1.3-2.6)	2.3 (1.3-2.8)	1.85 (1.2-2.2)	0.02

**Table 2.** Summary of histopathologic findings

Pathology	N (%)
Normal urothelial tissue	2 (5%)
Chronic inflammation	10 (25)
Acute inflammation	1 (2.5)
Acute and chronic inflammation	10 (25)
Squamous metaplasia	13 (32.5)
Nephrogenic adenoma	2 (5)
Invasive adenocarcinoma	1 (2.5)
Other	1 (2.5)

surgery), 6 (15%) developed de novo postoperative stress urinary incontinence, and 11 (28%) had other forms of postoperative voiding dysfunction.

Pathologic outcomes were reviewed. Among those patients who underwent surgery, 40 patients had an available pathology report. (see Table 2). One (3%) had findings consistent with invasive adenocarcinoma.

We analyzed the data to determine factors that were associated with the decision to undergo surgical resection. Bivariate associations between the outcome variable (surgery) and preoperative variables of interest (age, race, BMI, lower urinary tract symptoms, and size of diverticulum) were performed revealing statistically significant associations for the composite variable “lower urinary tract symptoms” ( $P = .004$ ) and size ( $P = .02$ ). In a logistic regression model adjusting for age, race, and BMI, the variable symptom (OR 14.3,  $P = .02$ ; 95% CI 1.44-142.8) remained statistically significant, while size (OR 1.7,  $P = .22$ ; 95% CI 0.72-3.99) did not.

## DISCUSSION

This study reports 78 cases of female UD collected retrospectively from 2009 to 2015 at a single institution. Several case series have been published in the literature, with similar findings compared to our cohort. Our study highlights an ethnically diverse population with information on pathology, an outcome not always reported in the larger case series.

In our series, we found a broad range of symptoms associated with presentation of UD, which extended beyond the classic triad of dysuria, dyspareunia, and postvoid dribbling. This finding is consistent with recent literature, with Ockrim et al reporting only 23% of their patients having presented with the classic triad.<sup>16</sup> Our series has even less, with no patients describing postvoid dribbling and only 3 describing both dysuria and dyspareunia. Other signs and symptoms described include recurrent UTIs, hematuria, pelvic pain, and urinary incontinence. The wide variety of presenting symptoms highlights the diagnostic challenge for clinicians when treating women with UD. Of note, 21% of patients were asymptomatic and were diagnosed either on exam or incidentally on pelvic imaging.

The imaging modality utilized in our patients was largely MRI. This reflects trends in clinical practice and recommendations in the literature where MRI has been described as the gold-standard imaging modality to evaluate for female UD.<sup>17</sup> We chose to utilize imaging results as

part of our inclusion criteria. For example, if a clinical report indicated the presence of a UD but no evidence was found on imaging, that case was not included in our final analysis. As such, our study relied heavily on imaging to confirm the diagnosis of UD.

Diverticular recurrence and postoperative complications were rare in our study. However, we state this cautiously given the retrospective nature of the study. Notably, another retrospective analysis in a cohort of 114 women who underwent surgical treatment for urethral diverticulum demonstrated that preoperative dysuria was the only variable found to be associated with recurrence (OR 4.4, CI 1.3-17.5) in a multivariable analysis.<sup>18</sup> However, this report, too, is limited by its retrospective design and lack of data on patient-reported outcomes

The rate of malignancy in the literature is between 3% and 6%.<sup>7,8</sup> We found a similar rate among our pathology specimens. Though we only had 1 patient with malignancy, our rate was 2.7%. This patient was a 46-year-old who presented with dysuria, recurrent UTI, urgency, and frequency. She did not have hematuria and was a non-smoker. The urethral diverticulum measured 3.2 cm in its greatest diameter on MRI. There are no widely recognized risk factors for urethral malignancy in patients with a urethral diverticulum. The fact that the rate could be as high as 1 in 17 for those with UD suggests surgical management is an appropriate choice even for the asymptomatic patient.

Factors associated with patients undergoing surgery have not been looked at in prior studies. In this study, we divided patients into 2 cohorts: those who underwent surgery and those who did not. We found that the presence of preoperative symptoms and urethral diverticulum size were significantly associated with undergoing surgery on bivariate analysis. However, on multivariate analysis, size was no longer significant, but preoperative symptoms remained statistically significant. Our findings suggest there is not a direct relationship between diverticula size and symptoms, and when surgery is chosen, the presence of symptoms is a significant determining factor. Given the small size of our cohort, we were unable to assess for the specific symptom(s) influencing this finding.

Our study has several advantages. These data reflect a large ethnically and racially diverse population of women who sought care at an academic, urban medical center. Our series had a large number of women with asymptomatic UD and women with symptoms other than the classic triad. There are several limitations also. First, the utilization of billing and coding data to find cases relies upon accurate coding. Additionally, given the retrospective nature of our study, symptom reports were reliant on accurate and complete physician documentation. The retrospective nature of the research also provided limits in the longitudinal data, especially on the patients that were managed expectantly. As such, there were no standardized outcomes data. Another significant limitation is the lack of a standardized method to screen for recurrences or complications. Additionally, we did not control for surgeon

preferences. Though there were only 6 surgeons performing the procedures, we could not account for individual surgeon's tendencies in whether or not to operate on a urethral diverticulum.

Female UD has limited data regarding its diagnosis, treatment, pathology, and clinical outcomes. Clinicians must be aware that UD can present with a broad range of symptoms beyond the classic triad of dysuria, dribbling, and dyspareunia. Preoperative workup should include a history and physical exam and may include imaging. In our cohort, MRI was the most commonly used imaging modality. Though most frequently benign, clinicians must be aware of the possibility of a urethral malignancy.

Studying female UD is made difficult by the relatively limited prevalence of the disease. However, despite the challenges, further research is needed to more fully understand the condition. Currently, most published series are data from single institutions. A regional or national database, or at least a multi-institution study, of women with female UD could help further delineate the natural history and the efficacy of surgery. Additionally, studies controlling for surgeon preference could help define the role the surgeon's characteristics has in opting for surgery. These are a few examples of the types of research still necessary to further understand the optimal management of female UD.

**Acknowledgment.** The authors thank Stephanie Morgan for her help in querying and managing the database.

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## EDITORIAL COMMENT



We commend the attempts of the authors of “Female urethral diverticula: diagnosis, pathology, and surgical outcomes at an academic, urban medical center” for providing insight into their experience managing female urethral diverticula. The uncommon nature and unpredictable presentation of this condition indeed pose challenges to its formal, accurate study.

This study reiterates a lack of sensitivity or specificity of symptoms at presentation in predicting diagnosis—like many that have come before them.<sup>1–3</sup> Stating that no patient presented with textbook symptoms reaffirms that the trinity of dysuria, dribbling, and dyspareunia is more a relic of dogma than a reflection of clinical evidence. Moreover, we are reminded that the symptomatic patient is the one most likely to proceed with surgical intervention. In addition, the ethnic variability of the population, while not reflective of U.S. demographics, does corroborate findings that African Americans are more likely to be affected<sup>1</sup> and undergo surgical treatment<sup>4</sup> for urethral diverticula.

In fact, with regards to the pathology results presented, a 2.8% rate of adenocarcinoma is similar to the 6% quoted by Thomas et al<sup>5</sup> in a larger study population (n=90) with a similar demographic makeup (34% African American).

Unfortunately, this study fails to appropriately define and meet its primary objective. Its title reads “diagnosis, pathology, and surgical outcomes”. The abstract objective states “to describe the outcomes”, and the introduction throws in a “focus on factors influencing patient selection for [surgery].” Unfortunately, there is no information on what led to surgical management (or not). Many patients did not undergo surgery because they did not return, and while the median follow up was 7.5 months, it is unclear how many patients actually had adequate follow-up.

The authors rightfully concede that the study's retrospective nature leaves something to be desired. There is no consistency with follow-up information, and there are no standard, validated outcome measures. The only outcomes data provided are descriptive rates of complications, stress urinary incontinence, and recurrence that even the authors mention, given the study's limitations, should be taken with a grain of salt.

Thus, this study only echoes back what we already know about female urethral diverticula without building on top of it and ultimately adds little new information to the literature.

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<https://doi.org/10.1016/j.urology.2018.12.053>  
UROLOGY 128: 45–46, 2019. © 2019 Elsevier Inc.

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## AUTHOR REPLY



We agree that our findings confirm the lack of sensitivity and specificity of clinical symptoms associated with the diagnosis of female urethral diverticula. Our study supports the notion that no set of symptoms is truly pathognomonic for female urethral diverticula.

Additionally, our findings, though not unique, bolster the current literature as it pertains to the relationship between symptoms associated with urethral diverticula and the decision to proceed with surgical management.

Finally, the purpose of investigating and publishing our experience with female urethral diverticula was to share what we have learned by caring for patients at our institution, which largely serves a diverse and under-represented patient population. We recognize and have clearly acknowledged in the manuscript the limitations of our retrospective, observational study design. Furthermore, we hope this work encourages future research on the appropriate management of asymptomatic female urethral diverticula which remains an unsettled clinical scenario.

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<https://doi.org/10.1016/j.urology.2018.12.054>  
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