



Review Article

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Pathophysiology and Management of Long-term Complications After Transvaginal Urethral Diverticulectomy

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Female urethral diverticulum (UD) is a rare and benign condition that presents as an epithelium-lined outpouching of the urethra. It has various symptoms, of which incontinence in the form of postmicturition dribble is the most common. The gold standard for the diagnosis of UD is magnetic resonance imaging, and the treatment of choice is transvaginal diverticulectomy. Despite the high success rate of transvaginal diverticulectomy, postoperative complications such as *de novo* stress urinary incontinence (SUI), recurrence, urethrovaginal fistula, recurrent urinary tract infections, newly-onset urgency, and urethral stricture can occur. *De novo* SUI is thought to result from weakening of the anatomical support of the urethra and bladder neck or damage to the urethral sphincter mechanism during diverticulectomy. It can be managed conservatively or may require surgical treatment such as a pubovaginal sling, Burch colposuspension, or urethral bulking agent injection. Concomitant SUI can be managed by concurrent or staged anti-incontinence surgery. Recurrent UD may be a newly formed diverticulum or the result of a remnant diverticulum from the previous diverticulectomy. In cases of recurrent UD requiring surgical repair, placing a rectus fascia pubovaginal sling may be an effective method to improve the surgical outcome. Urethrovaginal fistula is a rare, but devastating complication after urethral diverticulectomy; applying a Martius flap during fistula repair may improve the likelihood of a successful result. Malignancies in UD are rarely reported, and anterior pelvic exenteration is the recommended management in such cases.

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INTRODUCTION

Female urethral diverticulum (UD) presents as a localized epithelium-lined outpouching of the urethra located between the periurethral fibromuscular layer and anterior vaginal wall. Histopathologically, most UD cases are reported to have a benign nature, although some cases are identified as malignancies that require further management. Since the clinical presentation of UD is diverse and nonspecific, a high index of suspicion is the

first step in the diagnostic evaluation to promptly treat the disease and avoid complications resulting from delayed management. Several conservative treatment methods such as endoscopic or open incision and drainage or marsupialization are available for UD, however, transvaginal surgical excision of UD has been described as the most definitive option for the disease in the literature. Despite the high success rate of urethral diverticulectomy, postoperative complications such as recurrence of UD, *de novo* stress urinary incontinence (SUI), lower urinary

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tract symptoms (LUTS), recurrent urinary tract infections (UTIs), and urethrovaginal fistula are concerning problems for both clinicians and patients. The present review aims to summarize the postoperative complications following surgical diverticulectomy and their management.

EPIDEMIOLOGY AND ETIOLOGY OF URETHRAL DIVERTICULUM

Female UD is a rare disease, the prevalence of which ranges from 1% to 6% worldwide [1,2]. Although most UD patients present in their 30s and 40s, several studies have reported that the disease can be found in all age groups [3,4]. Since the symptoms of UD are nonspecific, it is often misdiagnosed as other conditions such as incontinence, recurrent UTI, and LUTS, delaying the proper management of the disease. UD is incidentally found in up to 1.4% of women who are evaluated for urinary incontinence and in more than 80% of patients who present with periurethral masses [5,6].

The etiology of UD remains unclear; however, most cases are thought to be acquired rather than congenital. It is widely accepted that the development of UD begins from chronic obstruction of the periurethral glands, which causes dilatation of the gland lumen. When an abscess is formed due to repeated infection and inflammation of the obstructed gland, the abscess may rupture toward the urethral lumen with the formation of an ostium, which finally becomes a UD [7,8]. This process is demonstrated by the location of UD, which is consistent with that of periurethral glands, as well as the presence of fibrosis and inflammation in pathology examinations of excised UD specimens [9]. Obstetric trauma and iatrogenic injuries from urethral procedures, such as urinary incontinence surgery, are also possible etiologies for the development of UD [10-12].

CLINICAL PRESENTATION AND DIAGNOSIS OF URETHRAL DIVERTICULUM

The classic triad of presentation regarding UD is reported as the “3 D’s”: dysuria, dyspareunia, and a dribble of urine after micturition [13]. However, these 3 symptoms are not always present in many patients with UD, and co-occur in only about 20% of all cases [13]. The symptoms of most women with UD are vague, causing misdiagnosis; therefore, clinicians must have a high index of suspicion, especially in women with persistent LUTS without a definite corresponding disease [14]. The com-

mon symptoms of UD include dysuria, dyspareunia, postmicturition dribble, frequency, urgency, localized pain, recurrent UTIs, anterior vaginal discomfort, vaginal mass, hematuria, and urethral discharge. In particular, incontinence in the form of postmicturition dribble is the most common symptom, and is found in 60%–70% of cases [15].

The diagnosis and evaluation of UD can be initiated from a physical examination with a high index of suspicion for the disease. A palpable periurethral mass is found in more than half of UD patients [14], and UD is diagnosed in over 80% of women with periurethral masses UD [6]. Once there is a high suspicion of UD based on the physical examination, the diagnosis can be confirmed by cystourethroscopy and imaging modalities such as balloon positive-pressure urethrography, voiding cystourethrography, computed tomography, ultrasound, or magnetic resonance imaging (MRI). These imaging studies are useful to evaluate the size, location, shape, and complexity of UD, and can be a blueprint for planning the direction of treatment. Currently, the gold standard for the diagnosis of UD is MRI, which provides invaluable information on the anatomic and tissue status of UD for planning a surgical procedure [15-17].

TREATMENT OPTIONS

Conservative management can be used in a limited number of UD patients who are asymptomatic and in whom malignancies can be excluded. Such patients can be managed by observation with close follow-up [18]. Other conservative management techniques such as postmicturition digital compression, prophylactic antibiotics, and needle aspiration can also be performed in women with minimally bothersome symptoms of UD [19].

The current treatment of choice for women with UD is transvaginal excision of the diverticulum, which has been reported to be the most effective management of the disease, with high success and low complication rates. Transvaginal excision of the diverticulum via an inverted U or midline incision on the anterior vaginal wall, followed by 3-layer closure with or without the interposition of a Martius fat pad or a vaginal flap, has been reported to have a success rate of 83% to 97% [12,20,21].

Transurethral diverticulotomy can be another option to manage UD; in this technique, the diverticular sac is opened into the urethra by using a diathermy electrode. This method may relieve UD-related symptoms by ensuring the decompression and drainage of the diverticular sac into the urethra [22,23].

However, this is not a definitive treatment method because the diverticular sac remains in place and UD can recur at any time after the procedure. Therefore, transurethral diverticulotomy is preferred in patients with diverticular abscesses for incision and drainage before undergoing delayed surgical diverticulectomy. Vaginal marsupialization of the diverticulum can be a treatment option for UD located in the distal portion of the urethra. Although the procedure may be simple and minimally invasive, it is only appropriate in distal UDs because the urethral sphincter is likely to be injured when the procedure is performed in UDs that are proximally located, and such an injury is highly likely to cause urinary incontinence [24].

POSTOPERATIVE COMPLICATIONS OF TRANSVAGINAL URETHRAL DIVERTICULECTOMY

Surgical excision of UD is an effective treatment option that has been reported to have a high success rate of up to 97% [12,20, 21]. However, despite the high rate of success of transvaginal urethral diverticulectomy, there always exists a risk of potential postoperative complications that need to be reviewed with patients before treatment as part of the informed consent process. Complications that may occur specifically after urethral diverticulectomy include *de novo* SUI, recurrence of UD, urethro-

vaginal fistula, recurrent UTIs, new-onset urgency, and urethral stricture [15]. Although these complications may not be common, they may substantially impact patients' quality of life. Therefore, both surgeons and patients should always be aware of these complications. The incidence and management of long-term complications after the surgical excision of UD are summarized in Table 1.

De Novo SUI

Pathophysiology

De novo SUI has been reported to occur in 1.7% to 33% of patients who undergo transvaginal urethral diverticulectomy [13,25-34]. Although *de novo* SUI is one of the most common complications after urethral diverticulectomy, its pathophysiology remains unclear. However, the necessity of extensive suburethral dissection in a large diverticulum and a proximal location of the diverticulum are thought to be factors compromising the anatomical support of the urethra and bladder neck or the damaging urethral sphincter mechanism, which may cause postoperative *de novo* SUI. Denervation injury during urethral diverticulectomy or damage of the urethral musculature and bladder neck by inflammation and the diverticulum itself may also cause SUI [32]. These theories are supported by several studies reporting that there tended to be an increased risk for the development of *de novo* SUI in proximally located and/or

Table 1. The incidence and management of long-term complications after the surgical excision of urethral diverticulum

Postoperative complications	Incidence	Management
<i>De novo</i> stress urinary incontinence	1.7%–33%	Conservative management <ol style="list-style-type: none"> 1. Physical therapy 2. Continence pessary Surgical management <ol style="list-style-type: none"> 1. Pubovaginal sling 2. Burch colposuspension 3. Urethral bulking agent injection 4. Tension-free midurethral sling
Recurrent urethral diverticulum	2%–16%	<ol style="list-style-type: none"> 1. Observation 2. Secondary surgical excision of urethral diverticulum
Urethrovaginal fistula	0.9%–8.3%	<ol style="list-style-type: none"> 1. Observation 2. Surgical repair of fistula
Urethral stricture	0%–5.2%	<ol style="list-style-type: none"> 1. Simple urethral dilatation 2. Simple meatotomy 3. Vaginal wall flap urethroplasty

large size (>3 cm) and/or circumferential-shaped diverticula according to MRI [31,32,35-38]. Therefore, patients who are continent preoperatively should always be warned about the possibility of SUI after urethral diverticulectomy [18].

Treatment

Most cases of postoperative *de novo* SUI improve with time and are usually conservatively managed with physical therapy or continence pessary. However, up to 29% of the patients may require surgical treatment such as a pubovaginal sling, Burch colposuspension, or urethral bulking agent injection. Tension-free vaginal tape midurethral slings have also been reported to be a treatment option that can be successfully and safely placed [32]. Since synthetic midurethral slings can potentially increase the risk of diverticular recurrence, mesh erosion, and urethrovaginal fistula, some studies have suggested that slings should be contraindicated for managing *de novo* SUI after urethral diverticulectomy [30,39]. Therefore, surgeons should always warn patients of the possible risks following the placement of synthetic midurethral slings, and patients should weigh the advantages (e.g., minimal invasiveness, fast recovery, and less postoperative pain and voiding dysfunction) and disadvantages (mesh-related complications associated with prior urethral diverticulectomy) of midurethral slings before selecting a management option for *de novo* SUI [18].

Management of UD with concomitant SUI

Concomitant urinary incontinence is a common symptom reported by 10%–57% of UD patients [13,14,25,30]. Although some patients may count postvoid dribbling caused by the emptying of the diverticulum as incontinence, studies have reported that true concomitant SUI is found in up to approximately 50% of UD patients [25,40]. Since pre-existing SUI may disappear after surgical diverticulectomy in 50%–100% of patients [41], a urodynamic study should be performed before urethral diverticulectomy to decide whether concomitant anti-incontinence surgery is necessary to facilitate patient counseling regarding the treatment plan.

An important decision that should be made before urethral diverticulectomy in UD patients with SUI is whether to perform anti-incontinence surgery concurrently or to delay the procedure until the confirmation of persistent SUI postoperatively. Since SUI symptoms may disappear after urethral diverticulectomy in a certain number of patients, the decision of whether to perform concurrent anti-incontinence surgery is

ambiguous [32]. Once a surgeon decides to perform concurrent anti-incontinence surgery during urethral diverticulectomy, placement of an autologous pubovaginal sling is a feasible and safe option that offers a high cure rate (up to 88%–100%) for SUI [14,42-44]. The concurrent surgery may also have the advantage of preventing the need for a subsequent anti-incontinence procedure [16].

Bladder neck suspension has also been reported to be an effective procedure that could be performed during urethral diverticulectomy; according to Ganabathi et al. [25], 78% of SUI cases were reported to be cured in UD patients who underwent concurrent diverticulectomy and bladder neck suspension. However, since an autologous pubovaginal sling may act as another tissue layer and support, which may reinforce the diverticulum repair, it may be preferable in cases of suspected intrinsic sphincter deficiency due to urethral sphincter disruption from the diverticulum itself or the surgical resection [16,18].

Although sling placement at the time of diverticulectomy has shown a high cure rate of concomitant SUI, complications following concurrent surgery can also occur. Among patients who underwent urethral diverticulectomy with concurrent sling placement, wound infection was reported in 5%, diverticulum recurrence in 5%–14%, *de novo* detrusor overactivity in 5%–12%, and transient urinary retention requiring temporary postoperative urethral catheterization in 3%–62% [42-44]. Since synthetic slings have the risk of infection, urethral erosion, and fistula formation during diverticulectomy, they are avoided during diverticulectomy and are even contraindicated if the urethra is entered during surgery [16].

The potential risk of complications regarding the concurrent anti-incontinence procedure and the minimal patient bother [4,31] associated with mild SUI after urethral diverticulectomy have demonstrated that staged anti-incontinence surgery can be another feasible option for UD patients with concomitant SUI. Staged surgery can also avoid unnecessary anti-incontinence surgery for those who experience the disappearance of SUI symptoms after urethral diverticulectomy. In fact, a study in 2014 reported that concomitant SUI was resolved in 62% of UD patients after urethral diverticulectomy [4]. If concurrent SUI persists after diverticulectomy, secondary anti-incontinence procedures are usually performed about 6–8 months after the initial surgery [4,31,32]. Staged anti-incontinence surgery is required in approximately 4%–10% of patients after diverticulectomy [31,32,34], and the success rate reaches up to 100%, although 23% of these patients are reported to experi-

ence urinary retention [4]. Staged anti-incontinence surgery may also be required in patients with *de novo* SUI after diverticulectomy, especially in those who are expected to have preoperative SUI that is masked by the mass effect of UD. Such *de novo* SUI has been reported to occur in approximately 10%–33% of UD cases that are >3 cm and/or proximally located [4,29,31,32,34]. Because concurrent SUI can regress after diverticulectomy and performing a concomitant anti-incontinence procedure increases the operative time, which may lead to increased postoperative morbidity, surgeons who prefer delayed anti-incontinence surgery should consider delaying the urodynamic study until the patient complains of persistent SUI even after diverticulectomy is successfully performed. Currently, there is no consensus on whether to perform concomitant or staged anti-incontinence surgery in women who undergo urethral diverticulectomy. Thus, the severity of symptoms, urodynamic findings, and the patient's goals should be taken into account before deciding whether to perform concomitant anti-incontinence procedures with urethral diverticulectomy [16].

Recurrence of UD

The presence of UD after urethral diverticulectomy that is presumed to have been performed successfully may be a newly formed diverticulum or a result of recurrence. Studies have reported that UD had a recurrence rate of 2%–16% after urethral diverticulectomy, with a reoperation rate of 2%–13% [4,30,34,40,45]. The recurrence of UD, both symptomatic and asymptomatic, can easily be diagnosed by using transverse MRI [46]. A study conducted in 2011 [47] showed that among cases of recurrent UD diagnosed by MRI, 33% initially had a horseshoe-shaped diverticulum and 66% initially had a circumferential diverticulum. However, no recurrence after the excision of a simple diverticulum was reported using MRI in that study [47].

The recurrence of UD is thought to be caused by remnant diverticulum from an incomplete excision of the original UD, active infection of the diverticulectomy site, difficult dissection during diverticulectomy, inadequate or excessive suture line tension, residual dead space, or other technical factors [48]. Such causes likely reflect the complexity of UD, which has been identified to be one of the greatest risk factors of UD recurrence potentially requiring secondary surgical excision. UD is regarded as complex when it is proximally located, loculated, larger than 3 cm in diameter, associated with prior pelvic or vaginal surgery, or horseshoe-shaped or circumferentially enfolds the urethra on a transverse image, as well as if the case involves

multiple diverticula [35,36]. These features of complex UD have all been reported to be factors associated with recurrence except the loculated shape [32,35]. During repeated urethral diverticulectomy, placing a rectus fascia pubovaginal sling may be effective to reduce the risk of further recurrence [49].

A study published in 2011 [34] reported that 10.7% of 122 patients who underwent urethral diverticulectomy at a single institution during 12 years showed recurrence requiring repeat surgical excision. In this study, a large proportion (69.2%) of subjects with recurrence had undergone previous urethral or vaginal surgery, and proximal diverticula, multiple diverticula, and prior pelvic or vaginal surgery were identified as other risk factors for recurrence. According to a study in 2002 [29], a delayed diagnosis (>12 months) of the primary diverticulum, a diameter larger than 4 cm, incomplete excision of the diverticular wall, and lateral or horseshoe-shaped diverticula were reported as risk factors for UD recurrence, as well as other complications such as urethrovaginal fistula and *de novo* SUI.

Urethrovaginal Fistula

Urethrovaginal fistula is a devastating complication after urethral diverticulectomy; its incidence rate is reported to range from 0.9% to 8.3% [25]. This complication is thought to be correlated to infection of the excision site, overlapping suture lines during urethral diverticulectomy, tension on the repaired site caused by insufficient urethral tissue, insufficient flaps or grafts with poor vascularization, multiple previous urethral surgical procedures, and an inadequate quality of tissue applied on the repair site [16].

A urethral fistula may not require surgical repair if it is located at the distal portion of the urethra beyond the sphincteric mechanism, although it may cause splitting of the urinary stream or vaginal voiding. However, patients with a urethral fistula located proximally to the sphincter causing urinary incontinence may require surgical repair. Since sufficient wound healing of the previous diverticulectomy site and optimal status of tissue quality affects the success rate of fistula repair, the procedure is usually recommended to be attempted at least 3 months after urethral diverticulectomy [50]. Applying an adjunct tissue flap, such as a Martius flap, during closure to aid the fistula repair site may prevent further fistula recurrence. A Martius flap may also be useful during urethral diverticulectomy for preventing urethrovaginal fistula by providing a well-vascularized additional tissue layer during closure of the diverticulectomy site. Furthermore, a meticulous surgical technique, good

hemostasis, avoidance of contamination, preservation of a well-vascularized anterior vaginal wall flap, and a multilayered closure should be combined with a Martius flap to prevent urethrovaginal fistula after urethral diverticulectomy [51].

Other Complications

Other postoperative complications, such as urethral stricture, recurrent UTIs, dysuria, *de novo* urgency, and urethritis also have been reported. Urethral stricture has been reported to occur in 0%–5.2% of cases after urethral diverticulectomy [16, 30,40], and can be managed by simple urethral dilatation or surgical procedures such as simple meatotomy or vaginal wall flap urethroplasty. Most postoperative recurrent UTIs and dysuria cases persisted since before urethral diverticulectomy rather than occurring *de novo*; recurrent UTIs and dysuria were persistent up to 23% and 26% of patients, respectively [32,35], *De novo* urethritis rarely appears after urethral diverticulectomy and it is usually difficult to cure by any medical means. This condition may contribute to the formation of a new UD [35]. Antibiotics and analgesics may alleviate postoperative UTIs, dysuria, and urethritis, and anticholinergic agents or beta-3 agonists may be effective for *de novo* urgency.

MALIGNANCY IN DIVERTICULA

Underlying malignancy may be present in a rare subset of patients with UD. According to a study published in 2008 [52], 6% of female patients with UD presented invasive carcinoma in the pathology report. The majority of malignancy cases were classified as adenocarcinoma, while 1 case was clear cell carcinoma. Glandular dysplasia, intestinal metaplasia, and villous adenoma were also reported in a few patients, which are correlated to an increased risk of subsequent adenocarcinoma. Squamous cell and transitional cell carcinomas can also be rarely found in patients reported to have diverticular malignancies [53].

Diverticular malignancies may present with symptoms such as hematuria, urethral bleeding, dysuria, UTIs, and urinary obstruction [53]. On imaging, diverticular carcinoma can manifest as an irregular filling defect of the diverticulum or a mass within the diverticular lumen [52]. However, since MRI can miss the presence of diverticular carcinoma, and benign granulation tissue within diverticular space can be misdiagnosed as diverticular carcinoma, imaging studies may have low accuracy in diagnosing carcinoma [54,55]. Therefore, preoperative imaging of the UD should not be considered as a definitive diagnos-

tic method to predict the presence of diverticular malignancies, underscoring the importance of a pathologic study of the resected UD specimen.

A clear consensus regarding the management of urethral diverticular carcinoma does not yet exist due to its rarity and varied histology. Since there is a high risk of local recurrence and metastasis after only simple excision of UD that is revealed to be malignant, anterior pelvic exenteration with urinary diversion is usually recommended to manage diverticular carcinoma [52]. Adjuvant chemoradiation has also been suggested with anterior pelvic exenteration [53].

CONCLUSION

Complications following urethral diverticulectomy may be rare events; however, they greatly impact quality of life and require proper management. The most common postoperative complication is *de novo* SUI, which can be successfully managed by conservative treatment or surgical interventions such as a pubovaginal sling, Burch colposuspension, or urethral bulking agent injection. In contrast, concomitant SUI can be effectively managed by either concurrent or staged anti-incontinence surgery. The prevalence of recurrent UD depends on the location, size, and morphology of the original UD, and recurrence is thought to be caused by remnant UD, the condition of the surgical wound, and technical factors related to surgery. As management, placing a rectus fascia pubovaginal sling may be an effective method to reduce the risk of further recurrence of UD. Urethrovaginal fistula is a rare, but devastating complication after urethral diverticulectomy, and applying a Martius flap during fistula repair may improve the likelihood of a successful result. Urethral diverticular carcinoma is rarely reported after urethral diverticulectomy, and anterior pelvic exenteration with urinary diversion is usually recommended to manage the condition. Complications after urethral diverticulectomy have a substantial impact on patients' quality of life; therefore, patients should receive counseling with informed consent before surgery and proper management should be performed once a complication occurs.

AUTHOR CONTRIBUTION STATEMENT

- Conceptualization: HWK, JZL, DGS
- Formal analysis: HWK
- Funding acquisition: DGS

- Methodology: *HWK*
- Project administration: *DGS*
- Visualization: *HWK*
- Writing-original draft: *HWK*
- Writing-review & editing: *HWK, JZL, DGS*

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