Female Urethral Diverticula: A Review of the Literature

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Abstract

Background: Female urethral diverticulum is a condition which is often overlooked and frequently misdiagnosed. It is hoped that as a result of greater awareness of female urethral diverticulum more timely diagnosis of the condition would be made which would result in early appropriate treatment.

Objective: The objective of this review is to summarize the presentation, investigation and management of female urethral diverticulum.

Result of the Literature Review: Urethral diverticula are more common than is currently being diagnosed. The presenting symptoms can be summarized as Dysuria, post-micturition Dribbling and Dyspareunia (‘the three Ds’). Patients may also present with other types of lower urinary tract symptoms. More than half of the cases of female urethral diverticula may be palpable on examination. With regard to investigation, traditional contrast studies are currently being replaced by advanced-imaging procedures including magnetic resonance imaging, and virtual computed tomography urethroscopy. These imaging modalities depict a much greater and better tissue definition; only few studies have directly compared the contrast-based investigative procedures, the various ultrasonography techniques, and cross sectional imaging modalities that are available. With regard to treatment small asymptomatic female urethral diverticula may not require treatment. There are three options of surgical treatment for urethral diverticulum and these include:

1. Trans-urethral incision of the urethral communication, thus transforming a narrow diverticulum into a wide-mouthed diverticulum.
2. Marsupialization of the diverticulum sac into the vagina by incising the urethro-vaginal septum.
3. Diverticulectomy with or without a reconstructive surgery.

Delay in the diagnosis of female urethral diverticulum can have a significant impact on a patient’s outcome. Patients with a delayed diagnosis (over 12 months) have been found to be at high risk of developing postoperative complications. More worryingly, high recurrence rate after surgery and early metastases is the unfortunate outcome of delayed diagnosis of diverticula-neoplasms.

Conclusions: Female urethral diverticulum is eminently treatable but there is little standardization of this condition. The greatest single improvement in the management of female urethral diverticulum would emanate from more widespread clinical awareness of the condition and its presentation and the fact that all available investigations when used as a result of increased awareness of the condition would lead to early diagnosis and appropriate early treatment. Delay in the diagnosis of female urethral diverticulum can have a significant impact on a patient’s outcome. Patients with a delayed diagnosis (over 12 months) have been found to be at high risk of developing postoperative complications. Therefore, by being more aware of urethral diverticulum as a differential diagnosis, clinicians may be able to reduce this delay and the complications that can occur with the condition.

Introduction

A urethral diverticulum can be described as an out-pouching of the urethra into the urethrovaginal potential space. Those with urethral diverticula are often misdiagnosed or there is a delay in diagnosis due to a lack of awareness amongst clinicians about the condition as well as due to its non-specific presentation. Urethral diverticula are more common in women than men and can often present in a urological or gynaecological setting. Complications of the condition include recurrent urinary tract infections, calculus and malignancy. The latter complication in particular, although uncommon, highlights the importance of clinicians including urethral diverticula in their differential diagnoses. Therefore, the aim of this review is to increase awareness of urethral diverticulum in females.
Literature Review of Urethral Diverticula in Females

Epidemiology

As females with urethral diverticula are often asymptomatic and the diagnosis is difficult, it is very likely the reported prevalence, estimated as 1 to 6% of women, is an under representation of those with the condition [1]. This number interestingly climbs to 16 to 40% in females with recurrent urinary tract infections [2]. Urethral diverticula are most common in women between 30 and 60 years old and are rare in children and neonates [3], [4], [5], [6]. In addition, surgery for urethral diverticula has been found to be higher in black women [7].

Anatomy and Aetiology

The urethra is lined by transitional cell epithelium at the bladder neck, becoming squamous epithelium as the external urethral meatus approaches. Paraurethral glands (glands of Skene) are most commonly located medially and posterolaterally along the mid and distal third of the urethra. These glands secrete mucous material which empties into the urethra via paraurethral ducts. There are a number of theories regarding the aetiology of urethral diverticula. The most prominent is that of an acquired origin, which is supported by the anatomy of the urogenital system. Urethral diverticula are most commonly found at the distal two thirds of the urethra, posterior-laterally, at the 3 and 9 o clock positions [8]. These are in very similar locations to the previously mentioned paraurethral glands. Therefore, it has been postulated that these paraurethral glands become obstructed and infected leading to the formation of a sub-urethral abscess. This subsequently ruptures into the urethral lumen creating the diverticulum [9]. Other theories include trauma, for example, from urethral and vaginal surgery. Childbirth trauma has also been suggested. However urethral diverticula are common in nulliparous women [6]. Congenital urethral diverticula are believed to be rare [10].

Presentation

Females with urethral diverticula may be asymptomatic or they can present with vague urogenital symptoms, thus contributing to the challenge of diagnosing the disorder. There are a variety of presentations in addition to the classic triad of dysuria (10 to 80%), dyspareunia (10 to 70%) and post-void dribbling (25%). These include frequency and urgency (40 to 100%), chronic or recurrent urinary tract infections (30 to 80%), stress or urge incontinence (4 to 70%) and haematuria (10 to 35%). Less frequent symptoms include urethral pain, pelvic or suprapubic pain, an anterior vaginal wall mass, purulent urethral discharge, urinary hesitancy and urinary retention [11], [12], [13]. Physical examination may reveal very little. On the other hand a mass on the posterior aspect of the urethra may be found. This may be tender and urine or purulent discharge may be expressed on palpation [2], [14]. Although uncommon, a hard mass should raise suspicion of a urethral diverticular neoplasm or calculus. Urethral neoplasms are more often adenocarcinomas. They appeared to be more prevalent in black people and in a study of patients who had surgery for urethral diverticulum 6% were found to have a malignancy [15], [16]. It has postulated that repeated injury to the diverticular wall leads to the re-proliferation that contributes to the development of neoplasms [17]. Calculus formation has been reported in up to 10% of cases [11]. Such calculi may form due to urinary stasis and salt deposition, however they are more commonly found to be migratory.

Differential Diagnosis

Differential diagnoses for periurethral masses include vaginal wall inclusion cyst, Skene's gland abscess, Gartner's duct cyst, ectopic ureterocele, periurethral fibrosis, urethrocele, vaginal leiomyoma, endometrioma and urethral or vaginal neoplasm [18]. In addition, urethral diverticulum should be considered in the differential diagnosis of patients who continue to re-present with the urogenital symptoms previously discussed.

Investigation

50 to 60% of urethral diverticula are diagnosed by physical examination therefore confirmation or further investigation is often necessary [6], [13]. Magnetic resonance imaging (MRI) is felt to be the most sensitive mode of imaging for the diagnosis of urethral diverticulum [19], [20], [21]. MRI offers higher resolution, providing detailed information regarding number, location, size, configuration, complications, and communication with the urethra of diverticula. In addition it has the ability to differentiate urethral pathology from anatomical variants and identify the presence of stones or neoplasms [22]. This modality of imaging therefore provides useful information for
surgical planning. Voiding-Computed-Tomography (CT) urethrography and virtual urethroscopy are further-imaging techniques, that provide high diagnostic accuracy. However, they may not always be available [23], [24]. If such imaging is not available, ultrasound is an alternative choice. [11][25, 26, 27, 28] The entire length of the urethra and surrounding tissues can be visualised in the absence of ionizing radiation, it can provide detailed information regarding the diverticulum and identify differential diagnoses. In addition, a study found ultrasound scan to be more sensitive than more traditionally used imaging such as cysstoposcopy and voiding cystourethrogram (VCUG).[26] Urethroscopy, balloon positive pressure urethrography, VCUG and retrograde positive pressure urethrography, although historically used, are no longer recommended for routine investigation of urethral diverticulum. VCU and retrograde positive pressure urethrography rely on contrast medium entering the lumen of the diverticulum therefore they are only effective if the opening is sufficiently patent. Hence they have a low sensitivity, VCUG more so than retrograde positive pressure urethrography [2], [29], [30].

Management

Patients with mild symptoms can be managed conservatively. This usually involves prophylactic antibiotics and monitoring. Digital decompression post voiding, periodic needle aspiration and urethral dilation has also been suggested. [31] However, these measures only provide symptomatic relief and do not target the underlying cause. There is also little documentation regarding the outcome of conservative management in urethral diverticulum. For symptomatic patients there are a number of surgical techniques that can be used. The approach chosen depends mainly on the location of the diverticulum along the urethra [2], [32]. If the middle or proximal third of the urethra is affected, the treatment of choice is urethral diverticulectomy. Transvaginal excision of the urethral diverticulum is considered definitive surgical treatment. [33] If the diverticulum is found at the distal third of the urethra, marsupialization into the vagina is an option. Marsupialization is avoided in the more proximal diverticulum as there is an increased risk of complications. Proximal incision of the urethra can lead to incontinence due to injury to urethral sphincters. Transurethral procedures have also been proposed [2], [34]. In order to reduce complications acute infection should be treated before surgery.

Surgical Outcomes

A review found excision of the diverticulum to have an overall symptomatic cure rate of 70% with a recurrence rate of 10 to 20%. [13] From the small number of reports published, marsupialization procedures have achieved essentially 100% symptomatic cure rate and have very minimal complications if limited to distal diverticula. Common post operative complications include recurrence of diverticulum (1 to 25%), urethrovaginal fistula (1 to 8%), stress incontinence (1 to 16%), urethral strictures (0 to 5%) and recurrent urinary tract infections (7 to 31%) [13], [14], [35]. A high recurrence rate is associated with delay in the diagnosis and treatment of female urethral diverticulum. [36], [37].

Discussion

Lee and Fynes [2] stated that appropriate investigations play a vital role in the diagnosis of urethral diverticula and these investigations should provide the surgeon with information in relation to the location, number, size, configuration and communication of the urethral diverticulum. The investigations should also be able to identify any associated malignancy or calculi. Golomb and associates [29] stated that it is equally as important to accurately diagnose large urethral diverticula, which would require extensive dissection, as it is to identify difficult-to-diagnose small or non-communicating urethral diverticula. Experiences gained by a number of authors regarding the investigation of female urethral diverticula are summarized as follows:

Urethroscopy:

Saito [38] stated that urethroscopy allows direct visual inspection of the urethra, and thus identification of the location of the position of the ostia; however, although frequently performed it quite often fails to be helpful, especially if the urethral diverticulum is collapsed and the ostium is not visible. Lee and Fynes [2] stated that urethroscopy is not of much use in assessing the size, or shape of the diverticulum, as well as the fact that any concurrent inflammation may further obscure the visualization.

Micturating cysto-urethrogram [Voiding cystourethrogram (VCUG)]

Lee and Fynes [2] stated that micturating cysto-urethrogram had been considered the investigation of choice for the identification of urethral diverticula with a sensitivity of 65%. However, Colomb and associates [29] are of the opinion that micturating cysto-urethrogram is equivocal and additional imaging
studies are usually necessary. The attached video illustrates a cysto-urethrogram which demonstrates a small urethral diverticulum.

**Double balloon urethrogram (DBU):**
Lang and Davis [39] stated that VCUG for some-time was considered the gold standard investigation, however, it has the potential for urethral injury and there is significant discomfort to the patient and additionally it is an invasive procedure which is associated with radiation. Fortunato and associates [31] found that DBU has the highest accuracy. Nevertheless, Neitlich and associates [40] reported that other studies have shown greater urethral diverticula detection with other modalities of investigation such as magnetic resonance imaging (MRI). Jacoby and associates [30] reported a prospective study which had compared DBU with VCUG in 32 patients with urethral diverticula. They reported that sensitivity which was confirmed by surgery of 100% with DBU and 44% with VCUG (P=0.002). They observed that the cases that were missed by VCUG were those of smaller urethral diverticula (12.4 mm compared with 24.2 mm; P=0.018).

**Urodynamics:**
Urodynamics is useful for the detection of any associated stress incontinence [13], [41], as well as any associated lower urinary tract obstruction [42]. Radiographic pictures that are taken during voiding when performing voiding cystourethrogram or video-urodynamic studies may show urethral diverticula as some urethral diverticula empty at the end of voiding and would be missed in the event of taking only filling and post-micturition films [43].

**Ultrasound scan:**
Siegel and associates [28] compared voiding cystourethrogram with the ensuing ultrasound scan techniques: trans-vaginal, endo-urethral, and trans-perineal. They reported that both modalities of investigation voiding cysto-urethrogram and ultrasound scan detected 13 out of 15 urethral diverticula. The ultrasound scan identified the neck of the diverticula in all detected cases but the voiding cystourethrogram identified the neck of the diverticulum in only 2 cases. In addition ultrasound scan was able to identify nearby disorders which included infected peri-urethral cysts and leiomyomas which were missed by voiding cystourethrogram.

**Magnetic Resonance Imaging:**
Various Magnetic Resonance Imaging techniques have been used in the investigation of the female urethra and these include endoluminal [21], endovaginal [44] endorectal [45] and external coils. Some of the advantages of magnetic resonance imaging include: accuracy of the diagnosis, the fact that patients do not require catheterization and are not required to void for the study, there is no radiation exposure involved and the procedure can be performed in three breath-hold sequences. [46].

**Virtual computed tomography urethroscopy:**
Computed tomography (CT) urethrography has the advantage of being non-invasive and can identify the anatomy and pathology of the extraluminal organs better than urethroscopy. Chou and associates [47] reported a case study in which a horseshoe-shaped diverticulum with a clearly identified orifice in the mid-urethra. The diverticulum was missed on urethroscopy and voiding cystourethrogram. Kim and associates [48] reported two cases with improved ability to detect the ostia compared with MRI.

**Treatment:**

**Non Surgical Treatment:**
Fortunato and associates [31] stated that there is no need or indication for surgical treatment in cases of asymptomatic urethral diverticula and patients with only mild symptoms. They recommended that these two groups of patients should be followed and treated symptomatically with antibiotics; and a high index of suspicion for carcinoma should be present in the event of development of any insidious signs.

**Surgical Treatment:**
Patients with symptoms related to their urethral diverticulum require treatment. Scarpero and associates [46] recommended that all cases of acute suppuration and inflammation should require pre-operative short course of antibiotics. Greenberg and associates [49] also recommended that in the case of presence of significant infection, incision and drainage may be required prior to formal surgery; in cases of urinary stress incontinence or an open bladder neck in association with urethral diverticulum a decision is required whether or not to perform concomitant sling surgery. Some authors [13], [41], [50], [51], have reported successful concomitant surgery. However, Patel and Chapple [32] tend to treat the urethral diverticulum initially and later on re-assess the appropriateness for sling insertion. Patel and Chapple [32] observed that in many instances there was no need for a sling procedure later. Aspera and associates [11] stated that there are three options of
surgical treatment for urethral diverticulum and these include:
1. Trans-urethral incision of the urethral communication, thus transforming a narrow diverticulum into a wide-mouthed diverticulum.
2. Marsupialization of the diverticulum sac into the vagina by incising the urethra-vaginal septum.
3. Diverticulectomy with or without a reconstructive surgery.

Patel and Chapple [32] stated that they have not found trans-urethral incision to be necessary. Instead of trans-urethral incision, they allow infected diverticula to settle with antibiotics. Patel and Chapple [32] stated that marsupialisation of a urethral diverticulum is one of the most common causes of the development of urethro-vaginal fistulae in view of the fact that diverticula usually extend through all layers of the urethra. Because of the aforementioned reasons, Patel and Chapple [32] have adopted their standard management plan to perform a diverticulectomy via the vaginal approach in the prone position, adopting a technique to that which was reported by Leach and associates [52].

Complications of trans-vaginal urethral diverticulectomy:
Porpiglia and associates [37] stipulated that the risk factors for the development of post-operative complications emanating from trans-vaginal urethral diverticulectomy include:
1. Delayed diagnosis (> 12 months),
2. Size (> 4 cm)
3. Complex configuration (e.g. horseshoe shape)

Patel and Chapple [32] stated that common complications arising from trans-vaginal diverticulectomy include: urinary incontinence, (1.7-16.1%), urethral-vaginal fistula (0.9 – 8.3%), urethral stricture (0-5.2%), recurrent urethral diverticula (1-25%), and recurrent urinary tract infections (0-31.3%). Aspera and associates [11] stated that the discovery of a urethral diverticulum pursuant to a presumably successful diverticulectomy may occur as a result of a new diverticulum, or, alternatively as a result of recurrence. They postulated that recurrence of a urethral diverticulum may be as result of incomplete excision, active infection, difficult dissection, inadequate or excessive suture line tension, residual dead space or due to other technical factors. Aspera and associates [11] stated that repeat diverticulectomy could be carried out if necessary.

Conclusions:
Urethral diverticula are more common than is currently being diagnosed. A recent study found that the mean time from onset of symptoms to diagnosis was 5.2 years.[14] This delay in diagnosis can have a significant impact on a patient's outcome. Patients with a delayed diagnosis (over 12 months) have been found to be at high risk of developing postoperative complications. More worryingly, high recurrence rate after surgery and early metastases is the unfortunate outcome of delayed diagnosis of diverticular neoplasms [15], [36], [37]. Therefore, by being more aware of urethral diverticulum as a differential diagnosis, clinicians may be able to reduce this delay and the complications that can occur with the condition.

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