Urethral diverticulum carcinoma in females—a case series and review of the English and Japanese literature

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Abstract: The aims of our study were to describe our case series of three urethral diverticulum carcinomas (UDC) in women and to review the literature on UDC in females to determine patient characteristics, presenting symptoms and outcomes along with optimal investigations and treatment modalities. A literature search was performed utilizing Medline, EMBASE and the Cochrane library for all papers including case reports on UDC in women published to date. The results along with those of our three cases are detailed. A total of 126 cases of UDC in women have been reported; 75% adenocarcinoma (Adenoca), 15% transitional cell carcinoma (TCC) and 10% squamous cell carcinoma (SCC). Median age at presentation was 53 years (range, 14–81 years). The commonest presenting symptoms were bleeding and retention. Cystoscopy, MRI and trans-urethral biopsy were the commonest methods of diagnosis. Treatment was radiotherapy +/- chemotherapy alone in 21%, local excision +/- radiotherapy in 44%, urethrectomy in 3% and anterior exenteration +/- radiotherapy in 32%. At last follow-up 63% were alive and well, 10% were alive with recurrent cancer and 25% had died from their disease. UDC is rare in women. It is predominantly adenocarcinoma. There is no established treatment and survival is at best moderate. An international registry and consensus on management is needed if this is to be improved.

Keywords: Urethral diverticulum carcinoma (UDC); urethral diverticulum (UD); carcinoma

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Introduction

Urethral diverticulum carcinoma (UDC) in women is extremely rare with only 123 cases previously reported (Table 1). Relatively little is known about UDC in women. We detail three additional cases of UDC in women and review the literature on the subject to more clearly define patient characteristics, presenting symptoms, diagnostics, treatments and outcomes to determine optimal management strategies.

Methods

We performed a literature search using the keywords; urethral diverticulum, cancer, carcinoma, tumour and malignancy. Databases searched were Medline, EMBASE and the Cochrane library. The data collected included patient demographics, presenting symptoms, diagnostic investigations, treatment modality and outcome at last follow-up in terms of disease free survival, recurrence and mortality. Ethnicity was determined according to the Office
**Table 1** Signs and symptoms of female urethral diverticulum cancer

| Author                          | Age (years) | Race | Symptom 1 | Symptom 2 | Duration (months) | Histology |
|--------------------------------|-------------|------|-----------|-----------|------------------|-----------|
| Allen and Nelson, 1978 (1)     | 68          | –    | Bleeding  | –         | –                | Adenoca   |
|                                | 69          | –    | Bleeding  | –         | –                | Adenoca   |
| Awakura et al., 2003 (2)       | 75          | A    | Bleeding  | Retention | 7                | Adenoca   |
| Bracken et al., 1976 (3)       | –           | –    | –         | –         | –                | TCC       |
| Brown et al., 1956 (4)         | 40          | C    | Bleeding  | –         | –                | Adenoca   |
| Carneiro Neto et al., 1973 (5) | –           | H    | –         | –         | –                | Not known |
| Catalano et al., 1992 (6)      | –           | –    | –         | –         | –                | TCC       |
| Cea et al., 1977 (7)           | 48          | C    | Bleeding  | –         | 2                | Adenoca   |
|                                | 53          | C    | Bleeding  | –         | –                | Adenoca   |
| Christofferson, 1974 (8)       | –           | –    | –         | –         | –                | Adenoca   |
| Clayton et al., 1992 (9)       | 63          | B    | Urgency   | Mass      | –                | SCC       |
|                                | 44          | B    | Bleeding  | –         | 18               | SCC       |
|                                | 35          | B    | Bleeding  | UTIs      | –                | SCC       |
|                                | 44          | B    | Pain      | –         | –                | Adenoca   |
|                                | 47          | B    | Bleeding  | –         | –                | SCC       |
|                                | 67          | B    | Bleeding  | –         | –                | Adenoca   |
| Collado et al., 2000 (10)      | 65          | –    | Bleeding  | –         | –                | Adenoca   |
| Cruz-Ruiz et al., 2010 (11)    | –           | H    | –         | –         | –                | Adenoca   |
| Davis et al., 2003 (12)        | 58          | –    | UTIs      | –         | –                | Adenoca   |
| Davis et al., 1999 (13)        | 48          | –    | UTIs      | –         | –                | Adenoca   |
|                               | 48          | –    | Bleeding  | –         | –                | Adenoca   |
| Prudente de Toledo et al., 1978 (14) | 65          | C    | Urgency   | –         | –                | TCC       |
| Dodson et al., 1995 (15)       | –           | –    | –         | –         | –                | Adenoca   |
| Evans et al., 1981 (16)        | 47          | B    | Bleeding  | –         | –                | Adenoca   |
| Faulkner et al., 1959 (17)     | 57          | –    | Bleeding  | –         | –                | TCC       |
| Geisler et al., 1998 (18)      | 70          | –    | –         | –         | –                | Adenoca   |
| Ghoniem et al., 2004 (19)      | 71          | –    | Retention | Mass      | –                | Adenoca   |
| Godec et al., 1984 (20)        | 52          | C    | Dysuria   | –         | 2                | Adenoca   |
| Gonzalez et al., 1985 (21)     | 70          | C    | Bleeding  | –         | –                | Adenoca   |
|                                | 14          | C    | Urgency   | –         | –                | Adenoca   |
|                                | 27          | C    | Mass      | –         | –                | Adenoca   |
|                                | 37          | C    | Bleeding  | –         | –                | TCC       |
|                                | 40          | H    | Bleeding  | Dyspareunia| 5                | TCC       |
|                                | 48          | C    | Retention | –         | –                | SCC       |
|                                | 36          | C    | Mass      | –         | –                | SCC       |
| Author                        | Age (years) | Race | Symptom 1     | Symptom 2    | Duration (months) | Histology |
|-------------------------------|-------------|------|---------------|--------------|------------------|-----------|
| Graf et al., 1962 (22)       | 65          | C    | Frequency     | –            | –                | TCC       |
| Ha et al., 2010 (23)         | 60          | A    | –             | Bleeding     | 36               | Adenoca   |
| Hamilton et al., 1951 (24)   | 53          | –    | Bleeding      | –            | –                | Adenoca   |
| Hickey et al., 2000 (25)     | 50          | –    | UTI           | Bleeding     | –                | Adenoca   |
| Hinman et al., 1960 (26)     | 40          | –    | Bleeding      | –            | –                | Adenoca   |
|                            | 44          | –    | Bleeding      | –            | –                | TCC       |
| Hruby et al., 2000 (27)      | –           | –    | –             | –            | –                | Adenoca   |
| Huvos et al., 1969 (28)      | 58          | B    | Mass          | –            | –                | SCC       |
| Jensen et al., 1981 (29)     | –           | –    | –             | –            | –                | Adenoca   |
| Jimenez de Leon et al., 1989 (30) | –     | H    | Bleeding      | –            | –                | Adenoca   |
| Kanno et al., 2002 (31)      | 81          | A    | Bleeding      | –            | –                | Adenoca   |
| Kasahara et al., 2017 (32)   | 48          | A    | Voiding dysfunction | –     | 5                | Adenoca   |
| Kato et al., 1998 (33)       | 71          | A    | Frequency     | Dysuria      | 1                | Adenoca   |
| Klotz et al., 1974 (34)      | 67          | C    | Bleeding      | –            | –                | Adenoca   |
| Lang et al., 2008 (35)       | 54          | C    | Dysuria       | Frequency    | 72               | Adenoca   |
| Manning et al., 2012 (36)    | 56          | –    | UI            | Dysuria      | 60               | TCC       |
| Murayama et al., 1978 (37)   | 42          | A    | Pain          | –            | –                | Adenoca   |
| Marshall et al., 1977 (38)   | 64          | –    | Ulcer         | –            | 12               | Adenoca   |
|                            | 72          | –    | Bleeding      | –            | 12               | TCC       |
| McLoughlin, 1975 (39)        | 51          | B    | UTI           | –            | –                | TCC       |
| Melnick and Birdsall, 1960 (40)| 50    | –    | Bleeding      | –            | –                | TCC       |
| Nakamura et al., 1995 (41)   | 50          | A    | –             | –            | –                | Adenoca   |
| Nakatsuka et al., 2012 (42)  | 42          | A    | Bleeding      | Pain         | 3                | Adenoca   |
| Ney et al., 1971 (43)        | 59          | –    | Retention     | –            | –                | Adenoca   |
| Noguchi and Ida, 1983 (44)   | 58          | A    | Dysuria       | –            | –                | Adenoca   |
| Okubo et al., 1996 (45)      | 44          | A    | Bleeding      | Retention    | 3                | Adenoca   |
| Oliva and Young, 1996 (46)   | –           | –    | –             | –            | –                | Adenoca   |

Table 1 (continued)
Table 1 (continued)

| Author                        | Age (years) | Race | Symptom 1   | Symptom 2     | Duration (months) | Histology |
|-------------------------------|-------------|------|-------------|---------------|------------------|-----------|
| Patanephan et al., 1983 (47)  | 74          | C    | Retention   | UTIs          | –                | Adenoca   |
|                               | 58          | B    | Mass        | –             | 18               | Adenoca   |
| Rajan et al., 1993 (48)       | 31          | B    | Dyspareunia | –             | –                | Adenoca   |
|                               | 47          | B    | Bleeding    | –             | –                | Adenoca   |
|                               | 65          | H    | Bleeding    | –             | –                | Adenoca   |
|                               | 52          | B    | Mass        | –             | –                | Adenoca   |
| Reheis et al., 1981 (49)      | 61          | C    | Bleeding    | –             | –                | Adenoca   |
| Rhamy et al., 1973 (50)       | 61          | C    | –           | –             | –                | TCC       |
|                               | 72          | B    | Bleeding    | –             | –                | Adenoca   |
| Rosenfeld and Frachtman, 1964 (51) | 52    | B    | Mass        | Dyspareunia   | 10               | TCC       |
| Roth, 1955 (52)               | 40          | B    | Bleeding    | –             | –                | TCC       |
| Salvador Alvarez et al., 2011 (53) | 57    | H    | Retention   | Pyrexia       | –                | Adenoca   |
| Scantling et al., 2013 (54)   | 47          | B    | UTI         | Bleeding      | –                | Adenoca   |
| Schilleru et al., 1984 (55)   | –           | –    | –           | –             | –                | Adenoca   |
| Schnoy and Leistenschneider, 1982 (56) | 39 | C    | –           | –             | –                | Adenoca   |
| Seballos and Rich, 1995 (57)  | 58          | –    | Bleeding    | –             | 3                | Adenoca   |
| Sekowska and Golajewski, 1961 (58) | –    | –    | –           | –             | –                | Adenoca   |
| Shalev et al., 2002 (59)      | 38          | –    | UTIs        | Urgency       | –                | SCC       |
| Sheahan and Vega Vega, 2013 (60) | 54     | –    | Bleeding    | Voiding dysfunc | 12               | Adenoca   |
| Srinivas and Dow, 1983 (61)   | 52          | –    | Dysuria     | –             | –                | TCC       |
| Tanabe et al., 1982 (62)      | 50          | C    | Mass        | Bleeding      | 2                | Adenoca   |
| Tesluk, 1981 (63)             | 46          | –    | Frequency   | Urgency       | –                | Adenoca   |
|                               | 46          | –    | Frequency   | Bleeding      | 2                | Adenoca   |
|                               | 62          | –    | Retention   | –             | –                | Adenoca   |
| Thomas and McGuire, 1991 (64) | –           | –    | –           | –             | –                | Adenoca   |
| Thomas et al., 2008 (65)      | Average 45  | –    | UI          | UTIs          | –                | Adenoca   |
|                               | –           | –    | UI          | UTIs          | –                | Adenoca   |
|                               | –           | –    | UTIs        | UTIs          | –                | Adenoca   |
|                               | –           | –    | Pain        | UTIs          | –                | Adenoca   |
|                               | –           | –    | –           | UTIs          | –                | Adenoca   |
| Thompson and Bivings, 1962 (66) | 65   | C    | Mass        | –             | –                | TCC       |
|                               | 46          | C    | Mass        | –             | –                | SCC       |
| Tines et al., 1982 (67)       | 56          | B    | Bleeding    | –             | –                | Adenoca   |
|                               | 71          | B    | Bleeding    | –             | –                | Adenoca   |
Table 1 (continued)

| Author                        | Age (years) | Race | Symptom 1 | Symptom 2         | Duration (months) | Histology |
|-------------------------------|-------------|------|-----------|-------------------|-------------------|-----------|
| Torres and Quattlebaum, 1972 (68) | 53          | C    | Pain      | Dysuria           | 3                 | Adenoca   |
| Uesaka et al., 2011 (69)      | 49          | A    | Asymptomatic – detected on smear | –                 | –                 | Adenoca   |
| von Pechmann et al., 2003 (70) | 69          | –    | UI        | Voiding dysfunction | –                 | Adenoca   |
| Washino et al., 2007 (71)     | 49          | A    | Dysuria   | Bleeding          | –                 | Adenoca   |
| Weng et al., 2013 (72)        | 65          | A    | Bleeding  | Frequency         | 6                 | Adenoca   |
| Wheeler et al., 1992 (73)     | 56          | C    | Bleeding  | Dyspareunia       | 5                 | Adenoca   |
| Wishard and Nourse, 1952 (74) | 39          | C    | Retention | –                 | –                 | TCC       |
| Wishard et al., 1960 (75)     | 54          | C    | Bleeding  | –                 | –                 | Adenoca   |
| Wishard et al., 1963 (76)     | 43          | –    | Bleeding  | –                 | –                 | SCC       |
| Yamigawa et al., 1988 (77)    | 54          | A    | Dysuria   | –                 | 3                 | Adenoca   |
| Young et al., 2007 (78)       | 41          | –    | Dysuria   | UTI               | 24                | SCC       |
| UCLH, 2018                    | 52          | B    | UTIs      | Dysuria           | 18                | Adenoca   |
|                              | 55          | B    | UTIs      | Dysuria           | 20                | Adenoca   |
|                              | 38          | Ar   | Pain      | Dysuria           | 24                | Adenoca   |

A, Asian; Ar, Arabic; B, Black; C, Caucasian; H, Hispanic; Adenoca, adenocarcinoma.

of National Statistics recommendations (79). For our own case series, we retrospectively reviewed patient records to glean symptoms at presentation, diagnostic modalities utilised, pathological stage and grade and management. Written informed consents were obtained from the patients for publication of their cases and any accompanying images.

**Case presentations**

**Case 1**

A 38-year-old Arabic female presented with an 18-month history of a palpable vaginal lump, dysuria, dyspareunia, urinary dribble, mixed urinary incontinence (UI), urinary tract infections (UTIs) and pain during urination. Per vaginal examination revealed a palpable hard and indurated mass.

Trans urethral (TUR) biopsy performed prior to referral revealed inflammation only. Pre-operative pelvic magnetic resonance imaging (MRI) showed a circumferential complex urethral diverticulum (UD) and videourodynamics (VUDS) indicated the presence of both idiopathic detrusor overactivity (IDO) and bladder outflow obstruction (BOO).

Initial management was excision of the UD with a modified Martius labial fat pad flap (MFP). Histological examination demonstrated a G3 adenocarcinoma of the UD with positive vaginal and proximal margins. She was counseled regarding all treatment and reconstructive options and went on to have a radical cystourethrectomy, pelvic lymph node dissection and ileal conduit formation 4 weeks after preliminary diverticulum excision. Formal histological analysis revealed a pT3N0M0 G3 adenocarcinoma. She remains under surveillance and is alive with a solitary lung recurrence at 72 months post diverticulectomy.

**Case 2**

A 55-year-old black female presented with a 9-month history of dysuria, urethral pain and poor flow. Clinical examination revealed a palpable non-tender vaginal mass. MRI pelvis showed a circumferential loculated complex UD and VUDS indicated the presence of BOO. Transvaginal biopsy indicated inflammation only.

She proceeded to excision of the UD with MFP interposition. Histological examination revealed pT2 G3 adenocarcinoma of the UD with negative margins. Formal staging with CT chest, abdomen and pelvis and bone scan indicated her to be N0M0. She was counseled regarding
all treatment options and declined any further therapy. She died from metastatic adenocarcinoma 22 months following her diverticulectomy.

Case 3

A 52-year-old black female presented with an 8-month history of dysuria, dyspareunia, UTIs and urethral pain. On clinical examination she had a palpable vaginal mass.

She underwent simple excision of her UD at her local hospital and was referred when histological review revealed a pT3 G2 adenocarcinoma with positive urethral margins. Post excision MRI performed at our centre indicated partial excision of a circumferential complex UD. Additional staging with CT chest, abdomen and pelvis and bone scan indicated that she was N0M0. After full counseling regarding treatment options she elected to undergo radical urethrectomy, bladder neck closure with MFP interposition, pelvic lymph node dissection and formation of Mitrofanoff channel. Histological examination of the excised specimen confirmed pT3N0 G2 adenocarcinoma. She remains alive and disease free at 21 months post diverticulectomy.

Epidemiology

Primary urethral carcinoma in females is extremely rare, accounting for only 0.02% of genitourinary tract malignancies (2-6). Squamous cell carcinoma (SCC) predominates, accounting for 70% of urethral carcinoma, followed by urothelial (20%) and then clear cell adenocarcinoma (CCA) (10%) (1,3,78,80,81).

UDC represents just 5% of all female urethral carcinoma or 0.001% of female genitourinary tract malignancies (81,82). Unlike in primary urethral carcinoma, adenocarcinoma is the commonest type of UDC, accounting for 75% of UDC (Tables 1-4). Transitional cell carcinoma (TCC) (15%) is the next most common and SCC the least common (10%) (9,16,42,59). The first patient with UDC was reported by Hamilton in 1951 (24), and since then only 124 cases (including the 3 in this current series) have been reported in the world literature.

Female urethral diverticula are in themselves rare entities—affecting between 0.02–6% of the female population (83,84). First described in 1805, they are benign, localized, epithelium-lined urethral outpouchings (85,86). Histologically, they are difficult to distinguish from paraurethral cysts. Their lining is composed of squamous epithelial cells in 42%, columnar epithelial cells in 32%, a combination of both squamous and columnar cells in 18% and cuboidal cells alone in 14% (87). The majority of diverticula (77%) show signs of inflammation, and ulceration is often present (87).

Rarely, diverticula are congenital, arising from embryonic Gartner duct remnants, persistence of Mullerian rest cells or the faulty union of primordial folds (88). The majority of diverticula are acquired; arising from rupture of chronically obstructed and infected periurethral glands into the lumen of the urethra (89,90). Risk factors for the development of urethral diverticula are: recurrent infection of the periurethral glands, vaginal birth trauma and previous vaginal or urethral surgery (91-95).

Pathogenesis

There are 3 theories regarding the origin of UDC (15,81,94). The first is that they arise from periurethral gland changes occurring due to persistent/continued infection and obstruction to drainage (20,21,61). The second theory suggests a metaplastic origin with neoplastic squamous, glandular or TCC development resulting from chronic inflammation and urethritis glandularis (65). The final theory is that the malignant change originates in retained Gartner or mesonephric duct remnants (78,96).

Many UDC are considered to originate from the paraurethral duct, which may be homologous to the prostate gland because it is prostate-specific antigen (PSA) positive in some cases (33,42,97). Ogihara and Kato suggested that the adenocarcinomas that arise from urethral diverticula are either CEA-positive columnar and/or mucin-producing and originate from the proximal portion of the paraurethral duct, or are PSA positive clear cell-type arising from the distal part of the paraurethral duct (96).

Occasionally premalignant lesions such as villous adenomas, intestinal metaplasia and high-grade dysplasia may arise (9,65). There are very occasional instances of benign tumour, such as leiomyoma and nephrogenic adenoma (9,65).

Age and race

The median age at presentation of UDC is 53 years (range, 14–81 years). There may be a higher incidence in the black population, possibly related to the higher incidence of UD amongst black women (9,21) although this is disputed (25).
| Author                  | Location | Diagnostics | Findings                      | Histology |
|-------------------------|----------|-------------|-------------------------------|-----------|
| Allen and Nelson, 1978 (1) | Proximal; UK | –           | –                             | –         |
| Awakura et al., 2003 (2)  | Proximal | Cytology    | Malignant cells               | Adenoca   |
|                         |          | Cystoscopy  | Mass in diverticulum          |           |
|                         |          | Urethrogram | Filling defect                |           |
|                         |          | MRI         | Urethral mass                 |           |
|                         |          | TUR biopsy  | Adenoca                       |           |
|                         |          |             | OE                            | Anterior vaginal wall mass |
| Bracken et al., 1976 (3) | Proximal | –           | –                             | TCC       |
| Brown et al., 1956 (4)   | Distal   | –           | –                             | Adenoca   |
| Carneiro Neto et al., 1973 (5) | UK   | –           | –                             | UK        |
| Catalano et al., 1992 (6) | UK       | –           | –                             | TCC       |
| Cea et al., 1977 (7)     | Middle   | –           | –                             | Adenoca   |
|                         | Proximal | –           | –                             | Adenoca   |
| Christofferson, 1974 (8) | UK       | –           | –                             | Adenoca   |
| Clayton et al., 1992 (9) | Middle   | OE          | Anterior vaginal wall mass    | SCC       |
|                         | Middle   | Cystoscopy  | Tumour in diverticulum        | SCC       |
|                         |           | OE          | Anterior vaginal wall mass    |           |
|                         | TUR Biopsy |           | SCC                           |           |
|                         | Proximal | OE          | Anterior vaginal wall mass    | SCC       |
|                         | Middle   | OE          | Anterior vaginal wall mass    | Adenoca   |
|                         | Middle   | OE          | Anterior vaginal wall mass    | SCC       |
|                         | Proximal | OE          | Anterior vaginal wall mass    | Adenoca   |
| Collado et al., 2000 (10)| UK       | USS         | Mass in urethra               | Adenoca   |
|                         |          | Urethrogram | Intravesical cavity           |           |
|                         |          | Cystoscopy  | Diverticulum in urethra       |           |
|                         |          | CT          | Mass in anterior vaginal wall |           |
|                         | TV Biopsy |           | Adenoca                       |           |
|                         |          | OE          | Anterior vaginal wall mass    |           |
| Cruz-Ruiz et al., 2010 (11) | UK   | –           | –                             | Adenoca   |
| Davis et al., 2003 (12)  | UK       | CT          | Mass in urethra               | Adenoca   |
|                         | TV biopsy |           | SCC                           |           |
|                         |          | OE          | Anterior vaginal wall mass    |           |
| Davis et al., 1999 (13)  | Distal   | –           | –                             | Adenoca   |
|                         | UK       | –           | –                             | Adenoca   |
Table 2 (continued)

| Author                      | Location | Diagnostics | Findings       | Histology |
|-----------------------------|----------|-------------|----------------|-----------|
| Prudente de Toledo et al., 1978 (14) | Proximal | VCUG        | Diverticulum   | TCC       |
|                             |          | IVU         | NAD            |           |
|                             |          | OE          | Anterior vaginal wall mass |           |
|                             |          | TUR biopsy  | TCC            |           |
| Dodson et al., 1995 (15)    | UK       | –           | –              | Adenoca   |
| Evans et al., 1981 (16)     | Middle   | –           | –              | Adenoca   |
| Faulkner et al., 1959 (17)  | Distal   | –           | –              | TCC       |
| Geisler et al., 1998 (18)   | Posterior| –           | –              | Adenoca   |
| Ghoniem et al., 2004 (19)   | UK       | MRI         | Mass in urethra| Adenoca   |
|                             |          | OE          | Anterior vaginal wall mass |           |
|                             |          | TV biopsy   | Adenoca        |           |
| Godec et al., 1984 (20)     | Middle   | –           | –              | Adenoca   |
| Gonzalez et al., 1985 (21)  | Anterior | –           | –              | Adenoca   |
|                             | Middle   | –           | –              | Adenoca   |
|                             | Distal   | –           | –              | Adenoca   |
|                             | Distal   | Cystoscopy  | Mass in diverticulum | TCC       |
|                             | Distal   | TUR biopsy  | TCC            |           |
|                             | Distal   | –           | –              | SCC       |
|                             | Middle   | –           | –              | SCC       |
| Graf et al., 1962 (22)      | Middle   | –           | –              | TCC       |
| Ha et al., 2010 (23)        | UK       | Cystoscopy  | Mass in diverticulum | Adenoca   |
|                             |          | Urethrogram | Urethral stricture |           |
|                             |          | MRI         | Urethral mass   |           |
|                             |          | OE          | Anterior vaginal wall mass |           |
| Hamilton et al., 1951 (24)  | Posterior| –           | –              | Adenoca   |
| Hickey et al., 2000 (25)    | Posterolateral | Cytology | Malignant cells | Adenoca   |
|                             |          | Cystoscopy  | Mass in diverticulum |           |
|                             |          | USS         | Mass in diverticulum |           |
|                             |          | OE          | Anterior vaginal wall mass |           |
|                             |          | TV biopsy   | Adenoca        |           |
| Hinman et al., 1960 (26)    | Middle   | –           | –              | Adenoca   |
|                             | Middle   | –           | –              | TCC       |
| Hruby et al., 2000 (27)     | UK       | –           | –              | Adenoca   |
|                             | UK       | –           | –              | Adenoca   |
Table 2 (continued)

| Author                | Location | Diagnostics | Findings                     | Histology |
|-----------------------|----------|-------------|------------------------------|-----------|
| Huvos et al., 1969 (28) | Proximal | OE          | Anterior vaginal wall mass   | SCC       |
| Jensen et al., 1981 (29) | UK       | –           | –                            | Adenoca   |
|                        | UK       | –           | –                            | Adenoca   |
| Jimenez de León et al., 1989 (30) | UK       | OE          | Anterior vaginal wall mass   | Adenoca   |
|                        |          | TUR biopsy  |                              |           |
| Kanno et al., 2002 (31) | UK       | MRI         | Urethral mass                | Adenoca   |
|                        |          | CT          | Urethral mass                |           |
|                        |          | OE          | Anterior vaginal wall mass   |           |
|                        |          | TV biopsy   | Adenoca                      |           |
| Kasahara et al., 2017 (32) | Proximal | MRI         | Urethral mass                | Adenoca   |
|                        |          | OE          | Anterior vaginal wall mass   |           |
|                        |          | TV biopsy   | Adenoca                      |           |
| Kato et al., 1998 (33) | UK       | Cytology    | Malignant cells              | Adenoca   |
|                        |          | Cystoscopy  | Mass in diverticulum         |           |
|                        |          | MRI         | Mass in diverticulum         |           |
|                        |          | OE          | Anterior vaginal wall mass   |           |
|                        |          | TUR biopsy  | Adenoca                      |           |
| Klotz et al., 1974 (34) | Middle   | –           | –                            | Adenoca   |
| Lang et al., 2008 (35) | UK       | MRI         | Mass in diverticulum         | Adenoca   |
|                        |          | OE          | Anterior vaginal wall mass   |           |
| Manning et al., 2012 (36) | UK       | Cytology    | NAD                          | TCC       |
|                        |          | MRI         | Diverticulum                 |           |
|                        |          | OE          | Anterior vaginal wall mass   |           |
| Murayama et al., 1978 (37) | Posterior | –           | –                            | Adenoca   |
| Marshall et al., 1977 (38) | Middle   | –           | –                            | Adenoca   |
| McLaughlin, 1975 (39) | Middle   | –           | –                            | TCC       |
| Melnick and Birdsall, 1960 (40) | Proximal | –           | –                            | TCC       |
| Nakamura et al., 1995 (41) | UK       | –           | –                            | Adenoca   |
| Nakatsuka et al., 2012 (42) | UK       | Cytology    | Adenoca                      |           |
|                        |          | MRI         | Mass entire urethra          |           |
|                        |          | Cystoscopy  | Mass in diverticulum         |           |
|                        |          | CT          | Mass entire urethra          |           |
|                        |          | TUR biopsy  | Adenoca                      |           |
| Ney et al., 1971 (43) | Proximal | –           | –                            | Adenoca   |
| Author                        | Location | Diagnostics | Findings                        | Histology |
|------------------------------|----------|-------------|---------------------------------|-----------|
| Noguchi and Ida, 1983 (44)   | UK       | OE          | Anterior vaginal wall mass      | Adenoca   |
| Okubo et al., 1996 (45)      | Proximal | Cytology    | Malignant cells                 | Adenoca   |
|                              |          | Cystoscopy  | Mass in diverticulum            |           |
|                              |          | OE          | Anterior vaginal wall mass      |           |
|                              |          | TUR biopsy  |                                 | Adenoca   |
| Oliva and Young, 1996 (46)   | UK       | –           | –                               | Adenoca   |
| Rajan et al., 1993 (48)      | Proximal | OE          | Anterior vaginal wall mass      | Adenoca   |
| Reheis et al., 1981 (49)     | Proximal | –           | –                               | Adenoca   |
| Rhamy et al., 1973 (50)      | UK       | –           | –                               | TCC       |
| Rosenfeld and Frachtman, 1964(51) | Proximal | Urethrogram | Diverticulum                    | TCC       |
|                              |          | OE          | Anterior vaginal wall mass      |           |
| Roth, 1955 (52)              | Proximal | –           | –                               | TCC       |
| Salvador Álvarez et al., 2011(53) | UK       | MRI         | Cystic mass between vagina and urethra | Adenoca   |
|                              |          | PET-CT      | High metabolic rate             |           |
|                              |          | Cystoscopy  | Mass in urethra                 |           |
|                              |          | OE          | Anterior vaginal wall mass      |           |
|                              |          | TUR biopsy  |                                 | Adenoca   |
| Author                          | Location | Diagnostics | Findings                        | Histology |
|--------------------------------|----------|-------------|---------------------------------|-----------|
| Scantling et al., 2013 (54)    | UK       | Cystoscopy  | Mass in diverticulum            | Adenoca   |
|                                |          | MRI         | Mass in diverticulum with enlarged LN |           |
|                                |          | CT          | As per MRI                      |           |
|                                |          | Bone scan   | NAD                             |           |
|                                |          | OE          | Anterior vaginal wall mass      |           |
| Schilleru et al., 1984 (55)    | UK       | –           | –                               | Adenoca   |
| Schnoy and Leistenschneider, 1982 (56) | Proximal | –           | –                               | Adenoca   |
| Seballos and Rich, 1995 (57)   | UK       | Cystoscopy  | Diverticulum                    | Adenoca   |
|                                |          | Urethrogram | Diverticulum                    |           |
|                                |          | OE          | Anterior vaginal wall mass      |           |
| Sekowska and Golajewski, 1961 (58) | UK       | –           | –                               | Adenoca   |
| Shalev et al., 2002 (59)       | UK       | Urinalysis  | Microhaematuria                 | SCC       |
|                                |          | IVU         | Diverticulum                    |           |
|                                |          | OE          | Anterior vaginal wall mass      |           |
| Sheahan and Vega Vega, 2013 (60) | UK       | USS         | Mass in urethra                 | Adenoca   |
|                                |          | MRI         | Mass in urethral diverticulum   |           |
|                                |          | Cytology    | Malignant cells                 |           |
|                                |          | Cystoscopy  | Mass in diverticulum            |           |
|                                |          | OE          | Anterior vaginal wall mass      |           |
|                                |          | TUR biopsy  | Adenoca                         |           |
|                                |          | TV biopsy   | Adenoca                         |           |
| Srinivas and Dow, 1983 (61)    | Middle   | –           | –                               | TCC       |
| Tanabe et al., 1982 (62)       | Proximal | –           | –                               | Adenoca   |
| Tesluk, 1981 (63)              | Proximal | –           | –                               | Adenoca   |
| Thomas and McGuire, 1991 (64)  | UK       | –           | –                               | Adenoca   |
| Thomas et al., 2008 (65)       | UK       | –           | –                               | Adenoca   |
|                                | UK       | –           | –                               | Adenoca   |
|                                | UK       | –           | –                               | Adenoca   |
|                                | UK       | –           | –                               | Adenoca   |
| Thompson and Bivings, 1962 (66)| UK       | –           | –                               | TCC       |
|                                | UK       | –           | –                               | SCC       |
| Author                        | Location | Diagnostics                  | Findings              | Histology |
|-------------------------------|----------|------------------------------|-----------------------|-----------|
| Tines et al., 1982 (67)       | Middle   | –                            | –                     | Adenoca   |
|                              | Middle   | –                            | –                     | Adenoca   |
| Torres and Quattlebaum, 1972 (68) | Middle | Cystoscopy; urethrogram      | Diverticulum, Adenoca |           |
| Uesaka et al., 2011 (69)      | Proximal | PET-CT                       | Proximal urethral uptake | Adenoca   |
|                              |          | Cystoscopy                   | Mass in diverticulum  |           |
|                              |          | MRI                          | Mass in diverticulum  |           |
|                              |          | OE                           | Anterior vaginal wall mass |           |
|                              |          | TUR Biopsy                   | Adenoca               |           |
| von Pechmann et al., 2003 (70) | Middle | Urinalysis                   | Microscopic haematuria | Adenoca   |
|                              |          | Cystoscopy                   | Diverticulum          |           |
|                              |          | Urethrogram                  | Urethral stricture    |           |
|                              |          | OE                           | Anterior vaginal wall mass |           |
|                              |          | TUR biopsy                   | Adenoca               |           |
| Washino et al., 2007 (71)     | UK       | Cytology                     | Malignant cells       | Adenoca   |
|                              |          | MRI                          | Mass in diverticulum  |           |
|                              |          | Cystoscopy                   | Mass in diverticulum  |           |
|                              |          | CT                           | Mass in diverticulum  |           |
|                              |          | OE                           | Anterior vaginal wall mass |           |
|                              |          | TUR biopsy                   | Adenoca               |           |
| Weng et al., 2013 (72)        | UK       | Cystoscopy                   | Mass in diverticulum  | Adenoca   |
|                              |          | IVU                          | NAD                   |           |
|                              |          | MRI                          | Mass anterior to vagina |           |
|                              |          | TUR biopsy                   | Adenoca               |           |
| Wheeler et al., 1992 (73)     | Proximal | Urinalysis                   | Microscopic haematuria | Adenoca   |
|                              |          | IVU                          | Filling defect bladder base |           |
|                              |          | Urethrogram                  | Mass in diverticulum  |           |
|                              |          | Cystoscopy                   | NAD                   |           |
|                              |          | OE                           | Anterior vaginal wall mass |           |
|                              |          | TV biopsy                    | No malignancy         |           |
|                              | Posterior| Urinalysis                   | Microscopic haematuria | Adenoca   |
|                              |          | IVU                          | Elevated bladder base |           |
|                              |          | Cystoscopy                   | Diverticulum          |           |
|                              |          | TUR biopsy                   | Mass in urethra       |           |
|                              |          |                              | Adenoca               |           |
Table 2 (continued)

| Author                  | Location | Diagnostics | Findings                       | Histology |
|-------------------------|----------|-------------|--------------------------------|-----------|
| Wishard and Nourse, 1952 (74) | Proximal | –           | –                              | TCC       |
| Wishard et al., 1960 (75)   | Distal   | –           | –                              | Adenoca   |
| Wishard et al., 1963 (76)   | Proximal | –           | –                              | SCC       |
| Yamigawa et al., 1988 (77)  | Proximal | IVU         | Elevated bladder               | Adenoca   |
|                         |          | Cystoscopy  |                                |           |
|                         |          | TUR biopsy  |                                |           |
| Young et al., 2007 (78)    | Anterior | VCUG        | Diverticulum                   | SCC       |
|                         |          | Cystoscopy  |                                |           |
|                         |          | OE          | Anterior vaginal wall mass     |           |
| UCLH, 2018               | Proximal | Urinalysis  | Microhaematuria                | Adenoca   |
|                         |          | Proximal   | Anterior vaginal wall mass     |           |
|                         |          | MRI         | Suspicious diverticulum        | Adenoca   |
|                         |          | Cystoscopy  | Diverticulum                   |           |
|                         |          | TV biopsy   |                                | Negative  |
|                         |          | Proximal   | Anterior vaginal wall mass     |           |
|                         |          | MRI         | Suspicious diverticulum        | Adenoca   |
|                         |          | Cystoscopy  | Diverticulum                   |           |
|                         |          | OE          | Anterior vaginal wall mass     |           |
|                         |          | TUR biopsy  |                                | Negative  |

UK, unknown; TUR, transurethral resection; OE, on examination; TV, transvaginal; VCUG, voiding cystourethrogram; IVU, intravenous urogram; NAD, no abnormality detected.

Our latest review of the literature indicates that 38% of cases are in white women, 32% in black women, 22% in Asian women and 8% in Hispanic women (N=65). In our series of 100 women having UD excision 82% with benign UD were white whilst UDC was found in 2 black and 1 Asian female suggesting a preponderance of UDC in black and Asian women. The median age of presentation of women with benign diverticulum also tended to be younger than those with UD at 44 years (N=97). This contrasts with a median age at diagnosis of 53 in those with UDC (N=3) (98).

**Presentation**

There are no pathognomonic signs and symptoms of UDC. As can be seen in Table 1 UDC may present with signs and symptoms of UD—classically dysuria (13%), dyspareunia (7%) and/or post micturition dribble/UI (3%). UDC more commonly presents with urethral bleeding or hematuria in 55%, urethral obstruction/voiding dysfunction in 16%, urethral/introital mass in 13%, UTIs in 13% and localized pain in 6% (N=89). A painless mass of the anterior vaginal wall can be found on examination in the majority of patients (1,9,16,80,81,90,96). This mass may feel much like a benign diverticulum but is noted to be firm or hard in some cases.

Preoperative diagnosis of UDC remains difficult because of its nonspecific presentation. The differential diagnosis of a peri-urethral mass in women includes; UD, urethrocele and/or cystocele, vaginal inclusion cyst, Müllerian cyst, endometriosis, and urethral or vaginal carcinoma. (33,61,81,88,97).
| Author                        | Histology | Stage       | Grade |
|-------------------------------|-----------|-------------|-------|
| Allen and Nelson, 1978 (1)    | Adenoca   | T1          | –     |
| Awakura et al., 2003 (2)      | Adenoca   | T1          | –     |
| Bracken et al., 1976 (3)      | TCC       | T1          | –     |
| Brown et al., 1956 (4)        | Adenoca   | T2          | –     |
| Carneiro Neto et al., 1973 (5)| UK        | –           | –     |
| Catalano et al., 1992 (6)     | TCC       | –           | –     |
| Cea et al., 1977 (7)          | Adenoca   | T3N0M0      | –     |
| Christofferson, 1974 (8)      | Adenoca   | –           | –     |
| Clayton et al., 1992 (9)      | SCC       | T2          | –     |
|                  | SCC       | T3          | –     |
|                  | SCC       | T4N+M0      | G3    |
| Collado et al., 2000 (10)     | Adenoca   | T2N0MO      | –     |
| Cruz-Ruiz et al., 2010 (11)   | Adenoca   | –           | –     |
| Davis et al., 2003 (12)       | Adenoca   | T2N1M0      | –     |
| Davis et al., 1999 (13)       | Adenoca; Adenoca | – | – |
| Prudente de Toledo et al., 1978 (14) | TCC | T4 | – |
| Dodson et al., 1995 (15)      | Adenoca   | –           | –     |
| Evans et al., 1981 (16)       | Adenoca   | T2          | –     |
| Faulkner et al., 1959 (17)    | TCC       | T2          | G1    |
| Geisler et al., 1998 (18)     | Adenoca   | –           | –     |
| Ghoniem et al., 2004 (19)     | Adenoca   | –           | –     |
| Godec et al., 1984 (20)       | Adenoca   | T3N0M0      | G2    |
| Gonzalez et al., 1985 (21)    | Adenoca   | –           | G1    |
| Graf et al., 1962 (22)        | TCC       | T1          | G2    |
| Ha et al., 2010 (23)          | Adenoca   | T3N0M0      | –     |
| Hamilton et al., 1951 (24)    | Adenoca   | –           | –     |
| Hickey et al., 2000 (25)      | Adenoca   | –           | –     |

Table 3 (continued)
Table 3 (continued)

| Author                        | Histology | Stage | Grade |
|-------------------------------|-----------|-------|-------|
| Hinman et al., 1960 (26)     | Adenoca   |       | –     |
|                               | TCC       | –     | G3    |
| Hruby et al., 2000 (27)       | Adenoca   | –     | –     |
| Huvos et al., 1969 (28)       | SCC       | T3N+  | G1    |
| Jensen et al., 1981 (29)      | Adenoca   | –     | –     |
| Jimenez de León et al., 1989 (30) | Adenoca | –     | –     |
| Kanno et al., 2002 (31)       | Adenoca   | –     | –     |
| Kasahara et al., 2017 (32)    | Adenoca   | T4N2  | –     |
| Kato et al., 1998 (33)        | Adenoca   | –     | –     |
| Klotz et al., 1974 (34)       | Adenoca   | T3    | G3    |
| Lang et al., 2008 (35)        | Adenoca   | T3    | –     |
| Manning et al., 2012 (36)     | TCC       | Tis   | G3    |
| Murayama et al., 1978 (37)    | Adenoca   | T3N0M0| –     |
| Marshall et al., 1977 (38)    | Adenoca   | T2    | G1    |
|                               | TCC       | T1    | –     |
| McLoughlin, 1975 (39)         | TCC       | –     | –     |
| Melnick and Birdsall, 1960 (40)| TCC   | –     | –     |
| Nakamura et al., 1995 (41)    | Adenoca   | –     | –     |
| Nakatsuoka et al., 2012 (42)  | Adenoca   | –     | –     |
| Ney et al., 1971 (43)         | Adenoca   | –     | –     |
| Noguchi and Ida, 1983 (44)    | Adenoca   | –     | –     |
| Okubo et al., 1996 (45)       | Adenoca   | –     | –     |
| Oliva and Young, 1996 (46)    | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |
|                               | Adenoca   | –     | –     |

Table 3 (continued)
Table 3 (continued)

| Author                          | Histology | Stage  | Grade |
|--------------------------------|-----------|--------|-------|
| Patanephan et al., 1983 (47)   | Adenoca   | –      | –     |
| Rajan et al., 1993 (48)        | Adenoca   | –      | –     |
| Reheis et al., 1981 (49)       | Adenoca   | T3     | G1    |
| Rajam et al., 1973 (50)        | TCC       | –      | –     |
| Reheis et al., 1973 (50)       | Adenoca   | –      | –     |
| Rajan et al., 1993 (48)        | Adenoca   | –      | –     |
| Reheis et al., 1981 (49)       | Adenoca   | T3     | G1    |
| Scantling et al., 2013 (54)    | Adenoca   | T3N0M0 | G2    |
| Schilleru et al., 1984 (55)    | Adenoca   | –      | –     |
| Schloy and Leistenschneider, 1982 (56) | Adenoca   | T2     | –     |
| Seballos and Rich, 1995 (57)   | Adenoca   | –      | –     |
| Sekowska and Golajewski, 1961 (58) | Adenoca   | –      | –     |
| Sheaf et al., 2002 (59)        | SCC       | –      | –     |
| Sheahan and Vega Vega, 2013 (60) | Adenoca  | T2N1M0 | G2    |
| Srinivas and Dow, 1983 (61)    | TCC       | T3     | G3    |
| Tanabe et al., 1982 (62)       | Adenoca   | T3N0M0 | G3    |
| Tesluk, 1981 (63)              | Adenoca   | T3     | G3    |
| Thomas and McGuire, 1991 (64)  | Adenoca   | –      | –     |
| Thomas et al., 2008 (65)       | Adenoca   | –      | –     |
| Thompson and Bivings, 1962 (66) | TCC       | T2     | –     |
| Tines et al., 1982 (67)        | Adenoca   | –      | –     |
| Torres and Quattlebaum, 1972 (68) | Adenoca  | T3N0M0 | –     |
Table 3 (continued)

| Author                  | Histology | Stage | Grade |
|-------------------------|-----------|-------|-------|
| Uesaka et al., 2011 (69)| Adenoca   | T2    | –     |
| von Pechmann et al., 2003 (70)| Adenoca | T3N2M0| –     |
| Washino et al., 2007 (71)| Adenoca  | T3    | –     |
| Weng et al., 2013 (72)  | Adenoca   | T4N0M0| G3    |
| Wheeler et al., 1992 (73)| Adenoca  | –     | –     |
| Wishard and Nourse, 1952 (74) | TCC    | T2    | G1    |
| Wishard et al., 1960 (75)   | Adenoca  | T2    | G1    |
| Wishard et al., 1963 (76)  | SCC      | T3    | G3    |
| Yamigawa et al., 1988 (77)| Adenoca  | –     | –     |
| Young et al., 2007 (78)   | SCC      | CIS   | –     |
| UCLH, 2018                | Adenoca  | T3N0M0| G2    |
|                         | Adenoca  | T3N0M0| G3    |
|                         | Adenoca  | T3N0M0| G3    |

TCC, transitional cell carcinoma; SCC, squamous cell carcinoma; Adenoca, adenocarcinoma; UK, unknown; CIS, carcinoma in situ.

**Diagnosis**

Diagnostic modalities used in the diagnosis and pre-operative planning of UDC are outlined in Table 2. Urine cytology may be a useful initial screening test and has been reported to be positive in 10/11 (91%) cases in which it was utilised (2,25,31,36,41,42,45,60,69,71,77,96,98). Imaging modalities that have been used to aid the diagnosis of UDC include ultrasound, intravenous urography, voiding cystourethrography, computed tomography (CT), MRI, and cystourethroscopy (2,9,25,31,36,41,45,60,69,71,77,80,96,98,99). The gold standard investigations to date appear to be a combination of gadolinium-enhanced MRI which can be used for diagnosis, staging and surveillance followed by transvaginal trucut or transurethral biopsies of the UD mass for definitive diagnosis. Case 2 above describes a 55-year-old lady with UD diagnosed on an initial MRI (Figure 1) with a follow up contrast enhanced study 2 months later (Figure 2). The differential diagnosis of increasing debris or thickening within the diverticulum includes infection and inflammatory change within the UD and biopsies may yield no evidence of malignancy as in 2/3 of our UDC cases. Cystoscopy was unhelpful in our cases but may play an important role in the pathological diagnosis and in localization of the tumor origin (1) with neoplasm in the diverticulum or urethra noted on cystoscopy in 23/29 (79%) cases in those series reporting its use (7,9,10,12,21,23,31,42,53,54,57,72,73,77,96,98,100).

A CT or an isotope bone scan may be used to assess for lymph node enlargement, distant tissue and bone metastasis (80). In our experience a T2 weighted thin slice post void pelvic MRI should be performed to diagnose the presence of a UD and if history, examination or MRI are suspicious for cancer an urgent urethral diverticulectomy should be performed as a definitive “excision biopsy”.

**Pathology**

**Macroscopically**

There is usually a mass within the diverticulum, which may be encroaching into the true urethral lumen or invading past the diverticulum walls into the surrounding paraurethral or paravaginal tissues (80).

**Microscopically**

Whilst only 10% of urethral cancers are adenocarcinoma, 30% of these originate from UD (1,3,78,80,81). Adenocarcinoma has two subtypes; clear cell and mucin
producing (33). The microscopic features of the CCA are similar to those of other CCA of the female genital tract and include; cells with abundant clear cytoplasm, some forms of pleomorphism, mitotic activity and a mostly flat shape. Focally, a hobnail appearance may be present. CCA of a UD may present patterns that are either tubule-cystic, papillary or diffuse (78). In a urine sample, the presence of malignant clear cells with the appearance of mirror balls is

| Author                        | Primary treatment                              | Survival in months | Outcome at last review       | Histology |
|-------------------------------|-----------------------------------------------|--------------------|------------------------------|-----------|
| Allen and Nelson, 1978 (1)    | Radiotherapy                                   | 48                 | Alive and well               | Adenoca   |
|                               | Radiotherapy                                   | 24                 | Alive and well               | Adenoca   |
| Awakura et al., 2003 (2)      | Chemotherapy + radiotherapy                    | 24                 | Alive and well               | Adenoca   |
| Bracken et al., 1976 (3)      | Radiotherapy                                   | 30                 | Died                         | TCC       |
| Brown et al., 1956 (4)        | Excision                                       | 30                 | Alive and well               | Adenoca   |
| Carneiro Neto et al., 1973 (5)| UK                                            | –                  | –                            | UK        |
| Catalano et al., 1992 (6)     | UK                                            | –                  | –                            | TCC       |
| Cea et al., 1977 (7)          | Excision + cystourethrectomy 12 m              | 24                 | Alive with recurrence        | Adenoca   |
|                              | Cystectomy                                     | 12                 | Alive and well               | Adenoca   |
| Christofferson, 1974 (8)      | UK                                            | –                  | –                            | Adenoca   |
| Clayton et al., 1992 (9)      | Excision                                       | 36                 | Died                         | SCC       |
|                              | Radiotherapy                                   | 30                 | Died                         | SCC       |
|                              | Excision                                       | 24                 | Died                         | SCC       |
|                              | Excision + radiotherapy                        | 12                 | Alive and well               | Adenoca   |
|                              | Excision + radiotherapy                        | 12                 | Died                         | SCC       |
|                              | Excision                                       | 18                 | Died                         | Adenoca   |
| Collado et al., 2000 (10)     | Cysto-urethrectomy + ileal conduit             | 16                 | Alive and well               | Adenoca   |
| Cruz-Ruiz et al., 2010 (11)   | UK                                            | –                  | –                            | Adenoca   |
| Davis et al., 2003 (12)       | Chemotherapy + radiotherapy + anterior         | 10                 | Alive and well               | Adenoca   |
|                              | exenteration + gracilis flap                   |                    |                              |           |
| Davis et al., 1999 (13)       | Excision                                       | –                  | –                            | Adenoca   |
|                              | Excision + vaginal wall reconstruction         | 39                 | Alive and well               | Adenoca   |
| Prudente de Toledo et al., 1978 (14) | Chemotherapy + radiotherapy + cysto-urethrectomy + ureterosigmoidostomy | 30 | Alive and well | TCC |
| Dodson et al., 1995 (15)      | UK                                            | –                  | –                            | Adenoca   |
| Evans et al., 1981 (16)       | Excision                                       | –                  | –                            | Adenoca   |
| Faulkner et al., 1959 (17)    | Radiotherapy                                   | 12                 | Alive and well               | TCC       |
| Geisler et al., 1998 (18)     | Cystourethrectomy                              | 3                  | Died                         | Adenoca   |
| Ghoniem et al., 2004 (19)     | Anterior exenteration + Florida pouch          | 12                 | Alive and well               | Adenoca   |
| Godec et al., 1984 (20)       | Cystourethrectomy                              | 12                 | Alive and well               | Adenoca   |

Table 4 (continued)
| Author | Primary treatment | Survival in months | Outcome at last review | Histology |
|--------|-------------------|--------------------|------------------------|-----------|
| Gonzalez et al., 1985 (21) | Radiotherapy | 60 | Alive and well | Adenoca |
| | Radiotherapy | 120 | Alive and well | Adenoca |
| | Excision | 12 | Died | Adenoca |
| | Radiotherapy | 30 | Died | TCC |
| | Radiotherapy | 12 | Alive and well | TCC |
| | Radiotherapy | 120 | Alive and well | SCC |
| | Radiotherapy | 12 | Died | SCC |
| Graf et al., 1962 (22) | Excision | 12 | Alive and well | TCC |
| Ha et al., 2010 (23) | Laparoscopic anterior exenteration | 6 | Alive and well | Adenoca |
| Hamilton et al., 1951 (24) | Excision | 18 | Alive with recurrence | Adenoca |
| Hickey et al., 2000 (25) | Excision and radiotherapy | 18 | Alive and well | Adenoca |
| Hinman et al., 1960 (26) | Excision | 48 | Alive and well | Adenoca |
| | Excision | 72 | Alive and well | TCC |
| Hruby et al., 2000 (27) | Excision + radiotherapy | – | – | Adenoca |
| Huvos et al., 1969 (28) | Radiotherapy | 12 | Died | SCC |
| Jensen et al., 1981 (29) | – | – | – | Adenoca |
| | – | – | – | Adenoca |
| Jimenez de León et al., 1989 (30) | Radical urethrectomy + pelvic and inguinal LN dissection + urethral reconstruction | – | – | Adenoca |
| Kanno et al., 2002 (31) | Urethrectomy + TAH + BSO + anterior vaginal wall excision | 8 | Alive and well | Adenoca |
| Kasahara et al., 2017 (32) | Anterior exenteration + pelvic LN dissection + chemotherapy | 5 | Alive and well | Adenoca |
| Kato et al., 1998 (33) | Anterior exenteration+ continent diversion | 12 | Alive and well | Adenoca |
| Klotz et al., 1974 (34) | Cystourethrectomy | – | – | Adenoca |
| Lang et al., 2008 (35) | Excision + radiotherapy | 18 | Alive and well | Adenoca |
| Manning et al., 2012 (36) | Excision | – | – | TCC |
| Murayama et al., 1978 (37) | Cystectomy | – | – | Adenoca |
| Marshall et al., 1977 (38) | Excision | 60 | Alive and well | Adenoca |
| | Excision | 12 | Alive and well | TCC |
| McLoughlin, 1975 (39) | Excision | 12 | Alive and well | TCC |
| Melnick, Birdsall, 1960 (40) | Radiotherapy | – | – | TCC |
| Nakamura et al., 1995 (41) | Excision | – | – | Adenoca |
| Nakatsuka et al., 2012 (42) | Cystourethrectomy + partial resection of vaginal wall | – | – | Adenoca |
Table 4 (continued)

| Author                        | Primary treatment                                      | Survival in months | Outcome at last review | Histology |
|-------------------------------|-------------------------------------------------------|--------------------|------------------------|-----------|
| Ney et al., 1971 (43)         | Radiotherapy                                          | 24                 | Alive and well         | Adenoca   |
| Noguchi and Ida, 1983 (44)   | Excision                                              | 9                  | Alive and well         | Adenoca   |
| Okubo et al., 1996 (45)       | Anterior exenteration + pelvic LN dissection + Indiana pouch + radiotherapy | 16                 | Alive and well         | Adenoca   |
| Oliva and Young, 1996 (46)    | –                                                      | –                  | –                      | Adenoca   |
| Patanephan et al., 1983 (47)  | –                                                      | –                  | –                      | Adenoca   |
| Rajan et al., 1993 (48)       | Radiotherapy + chemotherapy                           | 12                 | Died                   | Adenoca   |
|                               | Cystourethrectomy                                     | 29                 | Alive and well         | Adenoca   |
|                               | Cystourethrectomy                                     | 44                 | Alive and well         | Adenoca   |
| Reheis et al., 1981 (49)      | Cystourethrectomy                                     | 12                 | Alive and well         | Adenoca   |
| Rhamy et al., 1973 (50)       | Radiotherapy                                          | 72                 | Alive and well         | TCC       |
|                               | Radiotherapy                                          | 12                 | Alive and well         | Adenoca   |
| Rosenfeld and Frachtman, 1964 (51) | Excision                                                | 12                 | Died                   | TCC       |
| Roth, 1955 (52)               | Excision                                              | 24                 | Alive and well         | TCC       |
| Salvador Álvarez et al., 2011 (53) | Anterior exenteration                                 | –                  | –                      | Adenoca   |
| Scantling et al., 2013 (54)   | Robotic anterior exenteration + Indiana pouch          | 12                 | Alive and well         | Adenoca   |
| Schileru et al., 1984 (55)    | –                                                      | –                  | –                      | Adenoca   |
| Schnoy and Leistenschneider 1982 (56) | Cystourethrectomy                                    | 24                 | Alive and well         | Adenoca   |
| Seballos and Rich, 1995 (57)  | Excision                                              | –                  | –                      | Adenoca   |
| Sekowska and Golajewski, 1961 (58) | –                                                      | –                  | –                      | Adenoca   |
| Author                        | Primary treatment                                                                 | Survival in months | Outcome at last review | Histology |
|------------------------------|-----------------------------------------------------------------------------------|--------------------|------------------------|-----------|
| Shalev et al., 2002 (59)     | Excision                                                                         | 6                  | Alive with recurrence  | SCC       |
| Sheahan and Vega Vega, 2013 (60) | Anterior exenteration + pelvic LN dissection + ileal conduit                     | 12                 | Alive with recurrence  | Adenoca   |
| Srinivas and Dow, 1983 (61)  | Radiotherapy + cystourethrectomy                                                 | 4                  | Alive and well         | TCC       |
| Tanabe et al., 1982 (62)     | Radiotherapy                                                                      | 30                 | Alive and well         | Adenoca   |
| Tesluk, 1981 (63)            | Cystourethrectomy                                                                | 36                 | Died                   | Adenoca   |
|                              | Cystourethrectomy                                                                | –                  | –                      | Adenoca   |
|                              | Cystourethrectomy                                                                | 12                 | Alive and well         | Adenoca   |
| Thomas and McGuire, 1991 (64)| –                                                                                | –                  | –                      | Adenoca   |
| Thomas et al., 2008 (65)     | Anterior exenteration + ileal conduit                                            | 36                 | Died                   | Adenoca   |
|                              | Anterior exenteration + ileal conduit                                            | 11                 | Died                   | Adenoca   |
|                              | Anterior exenteration + ileal conduit                                            | –                  | –                      | Adenoca   |
|                              | Anterior exenteration + ileal conduit                                            | –                  | –                      | Adenoca   |
| Thompson and Blivings, 1962 (66)| Excision                                                                      | 12                 | Died                   | TCC       |
|                              | Radiotherapy                                                                     | 12                 | Died                   | SCC       |
| Tines et al., 1982 (67)      | Cystourethrectomy                                                                | –                  | –                      | Adenoca   |
|                              | Radiotherapy                                                                     | –                  | –                      | Adenoca   |
| Torres and Quattlebaum, 1972 (68) | Anterior pelvic exenteration with ureterosigmoidostomy and adjuvant radiotherapy | –                  | Alive and well         | Adenoca   |
| Uesaka et al., 2011 (69)     | Urethrectomy + cutaneous vescicostomy                                            | 5                  | Alive and well         | Adenoca   |
| von Pechmann et al., 2003 (70)| Cystourethrectomy + vaginectomy + partial vulvectomy + TAH + pelvic LN dissection + ileal conduit | 3                  | Alive with recurrence  | Adenoca   |
| Washino et al., 2007 (71)    | Excision                                                                         | 6                  | Alive with recurrence  | Adenoca   |
| Weng et al., 2013 (72)       | Urethrectomy + anterior exenteration + ileal conduit                             | 24                 | Alive and well         | Adenoca   |
| Wheeler et al., 1992 (73)    | Excision + radical cystourethrectomy                                            | 30                 | Alive and well         | Adenoca   |
|                              | Anterior exenteration + pelvic LN dissection                                     | 24                 | Alive and well         | Adenoca   |
| Wishard and Noursem 1952 (74)| Excision                                                                         | 96                 | Alive and well         | TCC       |
| Wishard et al., 1960 (75)    | Excision                                                                         | 12                 | Alive and well         | Adenoca   |
| Wishard et al., 1963 (76)    | Excision                                                                         | 24                 | Died                   | SCC       |
| Yamigawa et al., 1988 (77)   | Cystourethrectomy + pelvic LN dissection + ileal conduit                         | 17                 | Alive and well         | Adenoca   |
| Young et al., 2007 (78)      | Excision                                                                         | 24                 | Alive and well         | SCC       |
highly suggestive for CCA arising from UD (9,16,42).

TCC accounts for around 15% of UDC and is histologically the same as that originating in the bladder although with a tendency to be of a higher stage at diagnosis due to the absence of a muscle layer within a UD. SCC is the least common form of UDC. SCC may be associated with the presence of calculus in a UD; Clayton found this to be the case in 56% (9).

Staging

Staging of UDC is very difficult because of the location of the periurethral glands inside the periurethral space abutting the paravaginal fascia. The TNM staging system has been used in some cases (83). Most cancers are at an advanced stage at diagnosis because there is little muscle underlying them; 83% of UDC were T2 and above at time of presentation in the 54 patients in whom the stage was known at diagnosis (Table 3) (9,16,99). They also tend to be high grade with 73% grade 2 or 3 at presentation (N=40) (9,16,99).

Treatment

The mainstay of treatment is surgical with the options including:

(I) Urethral diverticulectomy alone or with adjuvant radiotherapy or chemotherapy (9,36,100);

(II) Urethrectomy +/− pelvic or inguinal lymph node dissection +/− adjuvant therapy (31,81);

(III) Anterior exenteration (excision of the urethra, bladder, anterior vaginal wall, uterus and pelvic lymph nodes) +/− inguinal lymph node dissection +/− adjuvant therapy (12,13,31,45,68);
(IV) Radiotherapy +/- adjuvant chemotherapy alone (1,3,9).

The results from the various treatment options are summarized in Table 4. Accepting the limited (generally < 2 years) length of follow-up in most series, simple urethral diverticulectomy appears to be curative in 55% of the 22 patients who underwent same in which follow up was specified with a further 14% alive with recurrence at a mean of 26 months follow-up (4,9,16,21,22,24,26,36,38,39,41,44, 51,52,57,59,66,71,74-76,78). Urethrectomy appears to be curative in 100% at a mean of 13 months follow up (N=3) (30,31,69).

 Occasionally cisplatinum-based chemotherapy alone and chemoradiotherapy has been used, without formal documentation of its effectiveness (3,80). Other chemotherapeutic agents utilized include 5-fluorouracil and leucovorin.

**Prognosis**

Patients with adenocarcinoma and TCC of a UD fare better than those with SCC. The % of patients alive with no evidence of disease (NED) at last follow-up is:

(I) 72% for those with adenocarcinoma (median

Figures 2 MRI study performed 2 months later. Axial (A) and sagittal (B) fast spin-echo T2-weighted sequences show the posterior fluid component (*) has reduced in size and now contains a fluid level (arrowhead) due to debris. The anterior intermediate signal (arrows) has significantly increased in size and displaces the urethra (U) posteriorly; (C,D) axial T1 spin-echo fast suppressed pre- (C) and post- (D) contrast sequences. The solid anterior component (arrows) is isointense on the pre-contrast sequence and shows heterogeneous enhancement on the post-contrast studies, confirming this is a solid tumour rather than simple debris.
(I) 72% for those with SCC (median 48 months) (N=12).

Conclusions

UDC is an extremely rare condition and presents a serious situation due to non-specific presentation and delayed diagnosis. UDC needs aggressive treatment as survival is at best moderate and is particularly poor for those with SCC. Optimal treatment remains to be determined but appears to be radical surgery. Consideration should be given to adjuvant radiotherapy +/- chemotherapy in patients with SCC or high-grade adenocarcinoma or TCC. An international registry and consensus on treatment would greatly aid the management of this problematic condition.

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Footnote

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