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The Complex Challenge of Urosymphyseal Fistula and Pubic Osteomyelitis in Prostate Cancer Survivors

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Abstract

Background and objective: Urosymphyseal fistula (UF) and pubic osteomyelitis (PO) are rare and often poorly recognized long-term complications of treatment for localized prostate cancer. Our aim was to describe UF/PO in prostate cancer survivors.
Methods: We performed a retrospective review of 26 patients treated for UF/PO after localized prostate cancer treatment at University Hospitals Leuven (1996–2021). We analyzed data for demographic characteristics, history, urethral manipulations (UMs), diagnostic and therapeutic approaches, microbiology, and treatment success.
Key findings and limitations: Before diagnosis, 80.8% of the patients had undergone RP, 88.5% received radiotherapy, and 84.6% had at least one UM. The median time from radiotherapy (RT), the last UM, and the first symptoms to diagnosis were 102 mo, 4 mo, and 43 d, respectively. Treatment included cystectomy (n = 19), bladder-sparing interventions (n = 5), and conservative treatment (n = 2). Pubic debridement was required in 21 patients. All cystectomy patients had a history of RT. Imaging-detected UF led to cystectomy in 94.1% of cases. Full conservative treatment succeeded only in non-irradiated patients. Bone cultures were positive in 95% of cases and discordant with urine cultures in 82.4%. Reinterventions and severe complications affected 56.5% of patients; all were UF/PO-free after up to four treatment attempts. Our study is limited by the small sample size, retrospective nature, and possible information and referral bias.
Conclusions and clinical implications: UF/PO can occur years after local prostate cancer treatment. Risk factors include RT and UMs. Conservative treatment rarely succeeds, particularly in irradiated patients with persistent UF. Most patients require multidisciplinary treatment involving cystectomy and pubic debridement. A perioperative bone culture to guide postoperative antibiotic treatment is crucial because of discordance with urine cultures. Postoperative complications are common, often requiring reintervention. Caution with UMs is advised after pelvic RT.
Patient summary: We looked at data for patients with a rare complication that can occur after treatment for localized prostate cancer that involves a small tunnel

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between the lower urinary tract and the pubic bone, and infection in the pubic bone. Diagnosis occurred years after pelvic radiotherapy and shortly after a procedure performed through the urethra, typically surgery for narrowing of the urethra. Most patients needed removal of their bladder and surgical cleaning of the pubic bone, followed by long-term antibiotics. The bacteria found in bone were often different from those found in the patient's urine, which is important in guiding antibiotic treatment after surgery.

1. Introduction

Prostate cancer is the second most common solid malignancy among men [1]. Cure or prolonged survival is expected after treatment for localized prostate cancer [2]. Consequently, management of treatment complications represents a major challenge in current urology practice [2,3]. Urosymphyseal fistula (UF) and pubic osteomyelitis (PO) are rare and often poorly recognized long-term complications [4–6]. A fistula between the urinary tract and pubic bone may be a predetermining factor in infectious problems, such as PO and abscesses [4]. Symptoms often include severe pelvic or groin pain, urinary tract infection (UTI), and infectious problems secondary to fistula or abscess formation [4,7]. Owing to its rarity, UF diagnosis is frequently delayed [5]. Furthermore, limited retrospective outcome data are available, and no standard-of-care workup or treatment algorithm is available. To the best of our knowledge, only 13 case series have been published to date, reporting on between five and 36 patients with UF/PO after prostate cancer treatment [2–14].

Here, we report tertiary care experience with this complex disease entity at University Hospitals Leuven, with a focus on demographics, history, urethral manipulations (UMs), diagnostic methods, therapeutic approaches, microbiology, and treatment success. We also propose a treatment algorithm.

2. Patients and methods

2.1. Study design

Ethics committee approval was granted (Supplementary Figure 1) and a single-center retrospective study was performed for men treated for UF/PO following treatment for localized prostate cancer in the urology department of University Hospitals Leuven (01/1996-12/2021). Diagnosis relied on clinical features, imaging, and cystoscopy. Imaging included computed tomography (CT), magnetic resonance imaging (MRI), cystography, and/or nuclear imaging (eg, single-photon emission CT-CT, fluorodeoxyglucose [FDG] positron emission tomography [PET]/CT, or a leukocyte scan), as illustrated in Supplementary Figure 2. UF was defined as a fistula between the lower urinary tract and the pubic symphysis/bone, adductor canal, or thigh on imaging [8,11]. PO was characterized by high signal intensity on T2 images and low signal intensity on T1 images of the area around the pubic symphysis and pubic rami, with or without regional myositis on MRI [15]. On CT, signs of PO included destruction of the pubic symphysis or bony cortex, an inflammatory soft-tissue mass, and stranding around the bone. Electronic patient files were queried using the search terms: "symphysitis", "osteitis pubis", "osteomyelitis", "rectus abscess", and "adductor abscess", which identified 26 patients meeting the inclusion criteria who were selected for analysis.

2.2. Data collection and statistics

Demographic, tumor, and disease-specific data were collected, including presenting symptoms, UMs, and potential precipitating factors. We evaluated intervals between tumor treatment, UMs, symptom onset, and treatment. Initial measures to stabilize the disease were assessed: antibiotic treatment, abscess drainage, catheter placement, and/or admission to the intensive care unit (ICU). Diagnostic modalities and their results, as well as treatment approaches, were assessed, including conservative treatment, cystectomy, bladder-sparing surgery, and/or pubic debridement. Results for urine, abscess, and bone cultures were collected. Any discordance between urine and bone cultures was categorized. We defined strict concordance as matching of all species between urine and bone culture results, whereas flexible concordance was defined as matching of at least one species [4]. For strict discordant results, at least one species was not identical between the urine and bone cultures. Antibiotic treatment, perioperative and postoperative parameters, complications, and outcomes were evaluated. Primary outcome parameters were fistula-free and osteomyelitis-free status, which were defined as no confirmed fistula or PO on imaging. UF/PO recurrence was defined on the basis of the combination of symptoms and imaging findings. Fistula recurrence was defined as a connection between the pubic bone and urethra or other anatomic structures on imaging. Descriptive statistics were used, with results for continuous variables reported as the median and interquartile range (IQR) for nonparametric data, and as the mean and standard deviation (SD) for parametric data. Results for categorical variables are presented as the frequency and percentage. All data were rounded to one decimal place.

3. Results

We identified 26 patients treated for UF/PO at University Hospitals Leuven. All cases occurred between 2006 and

2022, with 80.8% occurring after 2013. The majority (n = 20; 76.9%) were referred to our institution and were older, comorbid patients. Most patients (n = 14; 53.8%) initially had high-risk prostate cancer. The majority (n = 20; 76.9%) underwent multimodal cancer treatment; 23 patients received some form of radiotherapy (RT), 21 underwent radical prostatectomy (RP), and three had salvage high-intensity focused ultrasound (HIFU; Table 1 and Supplementary Fig. 3). The median time from primary treatment to diagnosis of UF/PO diagnosis was 106 mo (IQR 7–182) for those who underwent RP and 102 mo (IQR 33.8–149.8) for those who received RT.

All patients presented with symptoms of pubic pain, and most also experienced groin pain or gait problems (17, 65.4%). Infectious symptoms included UTI (eight, 30.8%), fever (four, 15.4%), wound or skin infection (four, 15.4%), a swollen leg secondary to adductor abscesses (four, 15.4%), and fluid drainage from a cutaneous fistula (two, 7.7%). The median time from first symptoms to UF/PO diagnosis was 43 d (IQR 15.2–122).

UMs were identified as precipitating factors in 20 patients (76.9%), comprising endoscopic instrumentation in 18 (69.2%) and manipulations related to a sling or artificial sphincter in two (7.7%). Cystoscopy, internal urethrotomy, and dilation were the most common UMs performed. Of five patients who underwent UMs for persistent bleeding, three had transurethral coagulation and two underwent transurethral resection of bladder tumor with tissue sent for pathology. Pathology results revealed local recurrence of prostate cancer in one patient and carcinoma in situ of the bladder in the other. The median time from the first and last UM to UF/PO diagnosis was 42 mo (IQR 16.5–79) and 4 mo (IQR 3–6), respectively. UMs were not the cause in six patients, of whom three were diagnosed shortly after RP. Table 1 lists the patient characteristics.

Table 1 – Demographic data and precipitating factors

Variable	Result
Patient demographics and comorbidities	
Median age at UF/PO diagnosis, yr (IQR)	74 (67.2–76.8)
Median American Society of Anesthesiologists score (IQR)	3 (2–3)
American Society of Anesthesiologists score, n (%)	
1	1 (3.8)
2	9 (34.6)
3	13 (50)
4	3 (11.5)
Median Charlson comorbidity index (IQR)	4.5 (3–5.8)
Charlson comorbidity index ≥5, n (%)	13 (50)
Median body mass index, kg/m^2 (IQR)	25.1 (23.8–26.5)
Diabetes, n (%)	4 (15.4)
History of smoking, n (%)	14 (53.8)
Urethral manipulations	
UM before UF/PO diagnosis, n (%)	22 (84.6)
Cystoscopy	18
Internal urethrotomy	11
Urethral dilatation	10
TURP	7
Transurethral coagulation	3
TURB	2
Clean intermittent self-catheterization	3
Artificial urinary sphincter placement	3
Cystolithotripsy	2
Male sling placement	2
Median number of UMs before UF/PO diagnosis, n (IQR)	2 (2–4.5)
1 UM (n)	1
2 UMs (n)	8
3 UMs (n)	5
>3 UMs (n)	8
Precipitating event for UF/PO	
Related to UMs, n/N (%)	20/26 (76.9)
Endoscopic instrumentation	18/26 (69.2)
Internal urethrotomy/anastomotic stricture dilation	11
Bladder neck incision/TURP	4
Radiation cystitis with hematuria: clot retention with TURB	2
Cystolithotripsy	1
Non-endoscopic instrumentation	2
Removal of infected artificial urinary sphincter + SPC	1
Tightening of Reemex male sling	1
Not related to UMs, n/N (%)	6/26 (23.1)
Persisting enterovesicopubic fistula	1
Leakage after primary RP	1
Leakage after salvage RP	1
RP with perioperative difficulties (adhesions + mesh)	1
Reason unclear	2

IQR = interquartile range, ASA = American Society of Anesthesiologists; UM = urethral manipulation; TURB = transurethral resection of the bladder; TURP = transurethral resection of the prostate; RP = radical prostatectomy; SPC = suprapubic catheter; UF/PO = urosymphyseal fistula/pubic osteomyelitis.

The diagnostic process varied among patients and required multiple imaging modalities in all but one case. Cumulative imaging demonstrated PO in 25 patients (96.1%), abscess in 17 (65.4%), and UF in 17 (65.4%). In four patients, PO was not confirmed on imaging before cystectomy. UFs commonly extended to the parasymphyseal (13/17) and adductor (seven of 17) compartments, and in rare cases to the prepubic (two of 17) or rectus (two of 17) compartment or cutaneously (two of 17). Abscesses were found in the Retzius space (ten of 17) and the adductor (nine of 17), prepubic (four of 17), and rectus (five of 17) compartments. Supplementary Table 1 provides additional details.

At diagnosis, stabilizing treatment varied. Almost all patients (92.3%) received immediate antibiotics. Three patients experienced critical bleeding due to radiation cystitis and required urgent cystectomy. In these patients, the diagnosis was made postoperatively because of simultaneous occurrence of abscesses and confirmation of PO after cystectomy.

The main treatments included cystectomy (19, 88.5%), bladder-sparing surgery (four, 19.2%), abscess drainage (one, 3.8%), and fully conservative treatment (two, 7.7%). Bladder-sparing surgery comprised pubic debridement (two); sling removal (one); and bladder-neck closure with a Mitrofanoff diversion, followed by pubic debridement and rectal amputation (one). In total, 21 patients underwent pubic debridement, of whom seven required at least one repeat pubic debridement. Most patients (15/26; 57.7%) underwent more than one intervention to resolve UF/PO. All patients were UF/PO-free after a maximum of four treatment attempts. Table 2 and Supplementary Figure 4 provide details on treatment and resolution rates.

An omental flap was used to fill the pubectomy defect in 13 patients. Four patients also underwent a rectal amputation. ICU admission was required preoperatively for three patients and postoperatively for six patients. After the main surgery, 13 patients (56.5%) underwent one or more reinterventions. Two patients had persistent pain, but neither had

Table 2 – Overview of treatment attempts and the overall healing rate

Intervention	Patients, *n/N* (%)				Overall
	1st attempt	2nd attempt	3rd attempt	4th attempt	healing rate
PD only	2/4	0/1	–	–	2/5 (40)
Cystectomy only (± abscess drainage)	0/2	1/1	–	–	1/3 (33.3)
Cystectomy + PD (+ rectal amputation)	5/8	4/5	0/1	2/2	11/16 (68.7)
PD after previous cystectomy or BNC	–	3/6	1/4	3/3	7/13 (53.8)
BNC + Mitrofanoff diversion	0/1	–	–	–	0/1 (0)
Rectal amputation after BNC + PD	–	–	–	1/1	1/1 (100)
Conservative	2/2	–	–	–	2/2 (100)
Conservative surgery [a]	2/9	0/2	0/2	–	2/13 (15.38)
Further intervention required	15/26 (57.7)	7/26 (26.9)	6/26 (23.1)	0/26 (0)	
UF/PO-free	11/26 (42.3)	19/26 (73.1)	20/26 (76.9)	26/26 (100)	

BNC = bladder neck closure; PD = pubic debridement
[a] Abscess drainage or sling removal.

evidence of persistent osteomyelitis. Table 3 and Supplementary Tables 4 and 5 provide details on complications.

Sixteen of 17 patients (94.1%) with proven UF on imaging needed cystectomy; the other patient underwent bladder-neck closure with a Mitrofanoff diversion, followed by pubic debridement and rectal amputation. The two conservatively treated patients had a history of RP only and no persistent fistula. The other patients who had bladder-sparing treatments had a mixed history.

Some 95% of the bone cultures available confirmed active osteomyelitis. Both urine and bone culture results were available for 17 patients, and showed strict discordance in 14 cases (82.5%) and flexible discordance in ten (58.8%). Among 19 patients with positive bone-culture results, 18 showed signs of PO on imaging. Facultative anaerobic bacteria were highly prevalent in bone and abscess cultures, with some cultures also yielding obligate anaerobes. Details on microbiology and antibiotics are listed in Table 4 and Supplementary Tables 6 and 7.

We developed a treatment algorithm on the basis of our findings, as shown in Figure 1.

Table 3 – Postoperative complications among surgically treated patients (*n* = 23)

Postoperative complications	
Clavien-Dindo grade ≥3 complications after 30 d, n (%)	10 (43.5)
Clavien-Dindo grade ≥3 complications after 90 d, *n* (%)	13 (56.5)
Grade 3a	2 (8.7)
Radiographic abscess drainage	
Excision abdominal scar (local anesthesia)	
Grade 3b	4 (17.4)
Surgical abscess drainage	1
Operative debridement of the leg	1
Ablation for atrioventricular nodal re-entry tachycardia	1
Operative closure of the abdomen after evisceration	1
Grade 4a	5 (21.7)
ICU for postoperative hemorrhage and kidney failure	1
ICU for postoperative hypotension	1
ICU for sepsis	2
ICU for respiratory failure after aspiration pneumonia	1
Grade 4b	1 (4.3)
ICU for multiorgan failure	1
Grade 5	1 (4.3)
Died on day 88, reason unclear	1
Reintervention after main treatment (*n*)	
Pubic bone debridement	7
Laparotomy because of bleeding	1
Closure of the abdomen because of evisceration/ eventration	2
Ureteral reimplantation	1
Intersphincteric proctectomy, colostomy, pubic drainage (rectopubic fistula)	1
Plate and screw osteosynthesis	1
Removal of osteosynthesis material	1
Mainz pouch revision	1
Vacuum-assisted closure	2
Median length of hospital stay, d (interquartile range)	34.5 (23.5–48.8)
Median follow-up, mo (interquartile range)	36 (21–68)

ICU = intensive care unit.

4. Discussion

Our study represents a comprehensive analysis of tertiary care for patients with UF/PO after prostate cancer treatment for a substantial cohort and provides insights into both conservative and surgically managed cases. Our results confirm the rarity of this condition, while highlighting its increasing recognition over the past decade. The high referral rate underscores the limited experience with UF/PO.

Most patients had a history of prior pelvic RT and recent UMs, most commonly for anastomotic strictures. This suggests that UMs serve as a precipitating factor and confirms earlier studies reporting RT history in 68–100% and UMs in 59–100% of patients [2–14]. Notably, 11.5% of patients in our study received salvage HIFU, a known risk factor for severe genitourinary toxicity [16].

The pathophysiology of UF/PO is multifactorial and often stepwise. First, interruption of the urethral mucosal lining creates an entry point for microorganisms before invasion of deeper tissues. In RT-exposed patients, these tissues are particularly vulnerable because of chronic ischemia, radiofibrosis, and bone demineralization, which facilitate the spread of infection [4,11]. We observed high prevalence of (facultative) anaerobic bacterial growth in bone and abscess cultures. In an ischemic environment following RT, these bacteria can switch to anaerobic behavior, which facilitates their proliferation. On imaging, this becomes evident as the frequent presence of gas within abscesses and fistulous tracts. Furthermore, the compromised microvascular environment impairs both antibiotic delivery and immune responses, allowing infection to persist and spread. As the infection advances, it can result in sinus formation, osteomyelitis, and involvement of the surrounding tissues,

Table 4 – Culture results and antibiotics

Parameter	Result
Blood culture, *n* (%)	12 (46.2)
Positive	2 (16.7)
Negative	10 (83.3)
Facultative anaerobic bacteria	2 (16.7)
Urine cultures, *n* (%)	22 (84.6)
Positive	22 (100)
Single species	13 (59.1)
Multiple species	9 (40.9)
Negative	0 (0)
Obligate anaerobic bacteria	0 (0.0)
Facultative anaerobic bacteria	17 (77.3)
Obligate aerobic bacteria	2 (9.1)
Yeast	2 (9.1)
Polymicrobial growth (unspecified)	2 (9.1)
Abscess culture, *n* (%)	17 (65.4)
Positive	17 (100)
Single species	5 (29.4)
Multiple species	12 (70.6)
Negative	0 (0)
Obligate anaerobic bacteria	3 (17.6)
Facultative anaerobic bacteria	14 (82.4)
Obligate aerobic bacteria	3 (17.6)
Yeast	4 (23.5)
Polymicrobial growth (unspecified)	1 (5.9)
Bone culture, *n* (%)	20 (76.9)
Positive	19 (95.0)
Single species	9 (45.0)
Multiple species	10 (50.0)
Negative	1 (5.0)
Obligate anaerobic bacteria	2 (10.0)
Facultative anaerobic bacteria	14 (70.0)
Obligate aerobic bacteria	4 (20.0)
Yeast	4 (20.0)
Antimicrobial therapy	
Antibiotic therapy, *n* (%)	26 (100)
Antifungal therapy, *n* (%)	6 (23.1)
Median duration of postoperative antimicrobial therapy, d (interquartile range)	46 (42–67)
Median duration of antibiotic/antifungal therapy in total, d (interquartile range)	61 (43.5–96)
Multiple antibiotics, *n* (%)	24 (92.3)
Patients receiving antibiotic treatment before bone collection for culture, *n* (%)	16 (80)
Antibiotic switch based on bone culture results, *n* (%)	10 (50)
Antimicrobials most frequently used, *n* (%)	
Quinolone	12 (46.2)
Vancomycin	11 (42.3)
Amoxicillin-clavulanic acid	9 (34.6)
Piperacillin-tazobactam	9 (34.6)
Clindamycin	7 (26.9)
Third-generation cephalosporin	7 (26.9)
Metronidazole	6 (23.1)
Fluconazole	6 (23.1)

including fistula formation extending to the rectus abdominis or adductor fascia, and occasionally to the skin. This pathological progression mirrors the clinical spectrum observed in our case series, ranging from early-stage disease to severe cases characterized by extensive abscesses and fistulas penetrating the adductor and rectus compartment, with some breaking through the skin. Given the destructive nature of these infections, it is unsurprising that conservative antibiotic therapy alone often proves inadequate, with invasive measures required for source control. Interestingly, some patients presenting shortly after RP exhibited a milder disease course.

Prevention of UF/PO primarily involves addressing the initial steps in its pathophysiology, and specifically avoiding disruption of the urethral continuity, minimizing deep-tissue trauma, and avoiding anastomotic leakage and manipulation of the periosteum during RP. We strongly recommend a cautious approach to transurethral treatments, particularly in patients with a history of pelvic RT. In the majority of cases, UMs arise in the context of urethral stricture disease, including strictures or sclerosis at the anastomotic site, high urethral strictures with bladder neck sclerosis, and sclerosis of the membranous urethra. Given the likely higher prevalence of urethral stricture disease following RP and RT, a minimally invasive approach is already common in clinical practice. For anastomotic stricture disease after RT, options need to be discussed with the patient, which may include accepting lower urinary tract symptoms, opting for cautious dilation, or considering placement of a suprapubic catheter. Furthermore, we advise administration of broad-spectrum antibiotic prophylaxis before any UM in this context, with patient counseling on the early symptoms of UF/PO. Extensive transurethral resection or Turner-Warwick procedures should be avoided whenever possible. While complete prevention of UF/PO may not be achievable, our findings are a call for action for a cautious approach.

Typical symptoms include severe pubic pain, possibly groin pain, gait difficulties, leg swelling, infection, and cutaneous fistulous drainage. The occurrence of these symptoms in a patient with a history of pelvic RT and UMs warrants further investigation. Diagnostic assessments rely on laboratory tests, imaging, and microbiology. Delayed symptom recognition has led to the use of multiple imaging modalities. Recognition of pathognomonic symptoms in a typical history could potentially lead to earlier definitive treatment after fewer investigations. While CT scans were commonly performed first because of widespread availability, nearly all patients underwent additional imaging. Pelvic MRI is the imaging of first choice, as it demonstrates and characterizes UF, abscesses, myositis in cases of adductor involvement, and bone edema, and provides the most accurate assessment of the extent of osteomyelitis [4,6,11,15]. If MRI is not available or is contraindicated, pelvic CT can serve as an alternative for detection of abscesses and features of advanced osteomyelitis. If these investigations are inconclusive for PO, an FDG PET/CT or leukocyte scan can be considered [17]. Voiding cystourethrography or CT cystography could help in clarifying the presence or extent of UF.

Initial stabilization consists of antibiotic therapy, catheter placement, and abscess drainage. Additional issues such as bleeding, radiation cystitis, and sepsis may necessitate urgent intervention. Most patients require additional surgery. A complete diagnostic workup is essential and should consider three critical factors: the presence of osteomyelitis, persistent UF, and RT history. PO often necessitates pubic bone debridement because of the inherent resistance of cartilage to antibiotics. Deep-tissue culture of the pubic bone is crucial in diagnosing osteomyelitis, consistent with the management of fracture-related infection (FRI) [18]. Preoperative percutaneous bone culture in osteomyelitis is an understudied topic; a low yield has been reported for bone-culture positivity (18–22%) and this strategy cannot be recommended as a standard approach [19,20]. If a fistula

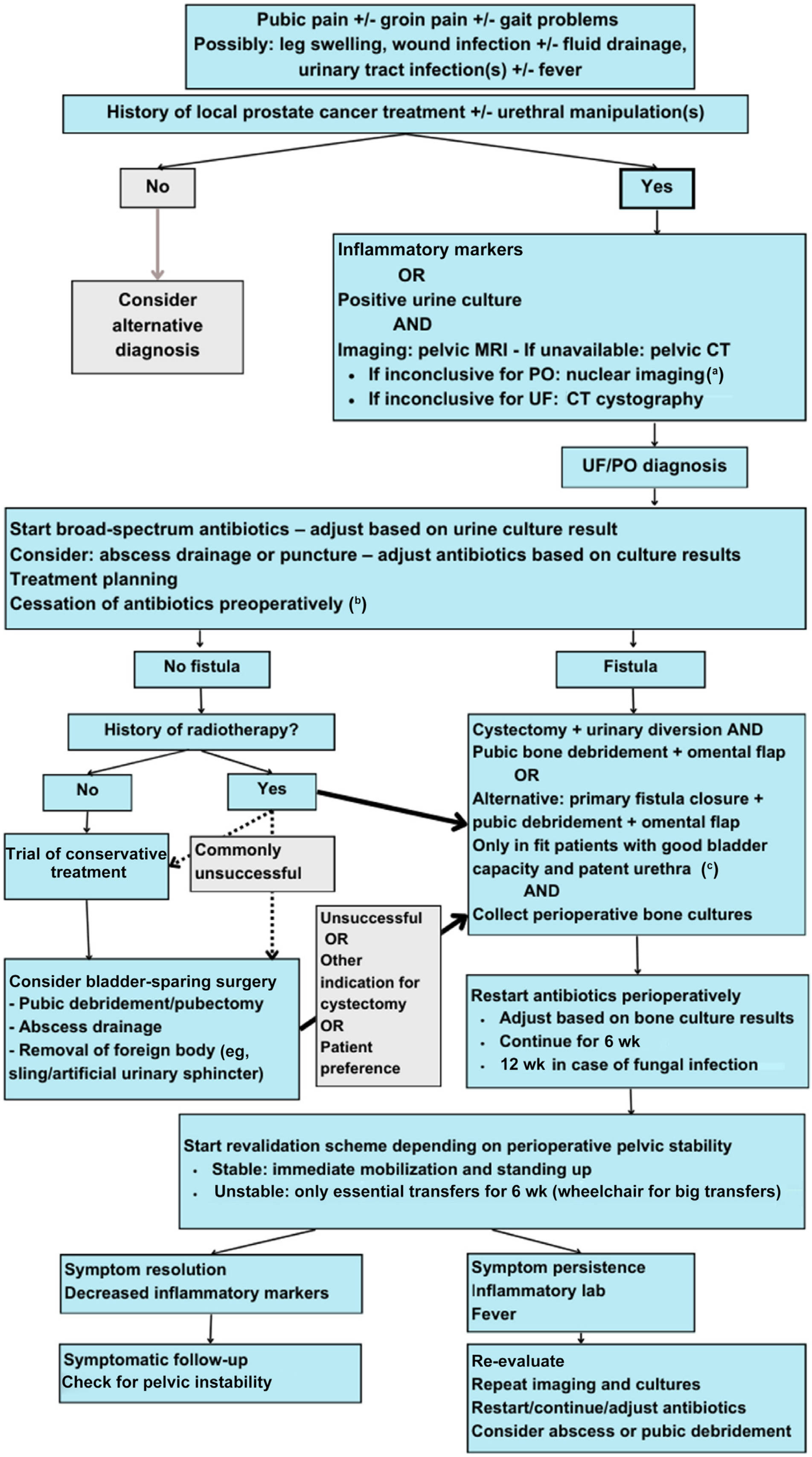

Fig. 1 – Proposed treatment algorithm. CT = computed tomography; MRI = magnetic resonance imaging; UF = urosymphyseal fistula; PO = pubic osteomyelitis. [a] Bone scan, positron emission tomography-CT, leukocyte scan. [b] Cessation of antibiotics ≥2 wk before surgery is indicated to reduce the chance of distorted bone-culture results. [c] Counsel the patient regarding functional outcomes and the risk of recurrence.

is present, cystectomy is often the only effective solution, as indicated by the 16/17 UF patients in our cohort who underwent cystectomy. RT can complicate the healing process and seems to have a negative impact on successful bladder-sparing treatment. The high reintervention rate highlights the importance of considering these three factors simultaneously. To avoid a prolonged disease course, cystectomy and/or pubic debridement should not be delayed if bladder-sparing interventions fail. The use of preoperative hyperbaric oxygen therapy (HBOT) as an adjunct to surgery for UF/PO has been described in the literature, but no definitive conclusions about its role in treating UF/PO have been established [3,13,14]. A systematic review of chronic osteomyelitis of various etiologies does suggest a potential beneficial effect of adjuvant HBOT following antibiotics and surgical debridement [21]. However, HBOT was not used in an attempt to resolve UF/PO in our patient cohort, and its additive role remains uncertain.

During pubic debridement, it is important to remove the pubic disc and cartilage, while preserving the anterior and inferior pubic ligaments. These ligaments are anchors for muscle origins and connect the pyramidalis and rectus abdominis muscles to the adductor muscles, providing important stability to the symphysis [22,23]. Preservation of the anterior musculotendinous attachment and the superior part of the pubic rami maintains the blood vessels, ensuring blood and antibiotic delivery to the pubis [22]. The use of flaps to fill the pubectomy defect, to separate the intestine from the pubic bone, and to promote vascularization, healing, and antibiotic delivery, is generally accepted [4,10]. Omental flaps were used in our cohort. Another option is a rectus abdominis flap [4,10].

Two studies reported the possibility of bladder-sparing fistula closure in 38.7–46.7% of cases but covered a different patient cohort involving slightly younger patients, all exposed to RT but to RP to a lesser extent [8,11]. Moreover, reconstruction is associated with a risk of incontinence and treatment failure, and requires adequate bladder capacity and urethral length [8]. The importance of cystectomy for source control was highlighted by Brändstedt et al [7], who reported high failure rates in cases of supravesical urinary diversion without cystectomy. Supplementary Table 8 lists details of previous studies.

Some patients were referred late in the disease process following multiple treatment attempts and with advanced disease complexity, emphasizing the importance of prompt referral to an experienced center. However, despite adequate treatment, disease resolution is not guaranteed, with high recurrence rates and complications necessitating reintervention. Secondary pubic debridement was often required if omitted during cystectomy or in cases of recurrent osteomyelitis. Given the rarity of the disease, its complex pathogenesis, and often challenging disease course, management by a multidisciplinary team at a tertiary referral center should be pursued. Furthermore, centralization creates opportunities for gaining further insights.

With 95% bone-culture positivity, our results confirm the infective nature of the disease, in line with rates of 66.7–100% reported in the literature [2,5,8,13], Interestingly, we observed a high rate of strict discordance (82.5%) with urine cultures, consistent with the 94.5% discordance reported by Andrews et al [4]. By contrast, our flexible discordance rate (58.8%) is higher than the 37–40% reported by Anele et al [5] and Nosé et al [3]. Missing a pathogen can cause antimicrobial failure and relapse, underscoring the need for accurate perioperative bone cultures, treatment adjustments based on bone culture results, and consideration of polymicrobial growth [4]. However, inconsistencies between urine and bone cultures could possibly result from extensive empiric antimicrobial treatment and selection of multiresistant bacteria. Preoperative antibiotic discontinuation 2 wk before definitive surgery is recommended to ensure accurate intraoperative cultures [6].

In accordance with the standard of care for osteomyelitis and on the basis of our findings, a prolonged course of antibiotics (minimum 6 wk) is recommended and should be part of multidisciplinary team discussion, similar to treatment for FRI and prosthetic joint infection [18]. Given the considerable prevalence of yeast in bone cultures, empiric fungal therapy could be considered, with extended antifungal treatment of 12 wk for culture-proven yeast in PO [4,7].

Our study is limited by the small sample size, retrospective nature, and possible information and referral bias. The patient cohort may primarily reflect individuals with more advanced disease who required surgical intervention, with potential under-representation of those with milder symptoms managed conservatively, limiting the possibility to draw conclusions on prevalence. According to our results, the estimated prevalence would be 0.24%, as we identified six cases in the series of approximately 2500 RP procedures performed over 15 yr originally retrieved from our own center. The true prevalence is probably higher because of possible under-reporting of cases, especially those not referred to our center, and because of the lack of description of this condition in the literature. Another limitation is the narrow study population, consisting exclusively of men treated for localized prostate cancer, limiting the generalizability to other pelvic tumors.

Despite these limitations, our study provides important insights into this complex disease. The findings provide a comprehensive picture of UF/PO cases treated by a multidisciplinary team at a tertiary referral center, covering both surgical and conservative cases. Since treating physicians have access to a nationwide open patient file, we provide the most complete and detailed information available. Our study is the first to develop a detailed, stepwise treatment algorithm for this condition. Future research encompassing larger, multicenter patient cohorts could enhance data reliability and validate our treatment algorithm. Implementation of the algorithm could help in standardization and could facilitate insights into diagnosis and the outcomes of treatment strategies, ultimately optimizing patient care.

5. Conclusions

UF/PO can occur years after local prostate cancer treatment. Risk factors include RT and UMs. Conservative treatment rarely succeeds, with prior RT and persistent UF negatively affecting the success of bladder-sparing treatment. Most patients require multidisciplinary treatment involving cystectomy and pubic debridement. Perioperative bone cultures and adjustment of postoperative antibiotics according to the culture results are crucial because of discordance with urine cultures. Postoperative complications are common and often require repeat intervention. Early diagnosis and multidisciplinary treatment are crucial. Preventative measures include cautious use of UMs, particularly following pelvic RT, administration of broad-spectrum antibiotics before UM, and counseling patients on recognizing early symptoms of UF/PO if they undergo UM.

Author contributions: Laurien Smeyers had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Smeyers, Borremans, Joniau, Van der Aa, Herteleer.
Acquisition of data: Smeyers, Borremans, Joniau.
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2024.09.008.

References

[1] Gandaglia G, Leni R, Bray F, et al. Epidemiology and prevention of prostate cancer. Eur Urol Oncol 2021;4:877–92. https://doi.org/10.1016/j.euo.2021.09.006.
[2] Shapiro DD, Goodspeed DC, Bushman W. Urosymphyseal fistulas resulting from endoscopic treatment of radiation-induced posterior urethral strictures. Urology 2018;114:207–11. https://doi.org/10.1016/j.urology.2017.12.020.
[3] Nosé BD, Boysen WR, Kahokehr AA, et al. Extirpative cultures reveal infectious pubic bone osteomyelitis in prostate cancer survivors with urinary-pubic symphysis fistulae (UPF). Urology 2020;142:221–5. https://doi.org/10.1016/j.urology.2020.04.095.
[4] Andrews JR, Hebert KJ, Boswell TC, et al. Pubectomy and urinary reconstruction provides definitive treatment of urosymphyseal fistula following prostate cancer treatment. BJU Int 2021;128:460–7. https://doi.org/10.1111/bju.15333.
[5] Anele UA, Wood HM, Angermeier KW. Management of urosymphyseal fistula and pelvic osteomyelitis: a comprehensive institutional experience and improvements in pain control. Eur Urol Focus 2022;8:1110–6. https://doi.org/10.1016/j.euf.2021.08.008.
[6] Gupta S, Zura RD, Hendershot EF, Peterson AC. Pubic symphysis osteomyelitis in the prostate cancer survivor: clinical presentation, evaluation, and management. Urology 2015;85:684–90. https://doi.org/10.1016/j.urology.2014.11.020.
[7] Brändstedt J, Abrahamsson J, Baseckas G, et al. Urosymphyseal fistula after pelvic radiotherapy in a tertial referral centre – a rare entity with significant comorbidity requiring multidisciplinary management. Scand J Urol 2023;58:4–10. https://doi.org/10.2340/sju.v58.5765.
[8] Bugeja S, Andrich DE, Mundy AR. Fistulation into the pubic symphysis after treatment of prostate cancer: an important and surgically correctable complication. J Urol 2016;195:391–8. https://doi.org/10.1016/j.juro.2015.08.074.
[9] Inouye BM, Krischak MK, Krughoff K, Boysen WR, Peterson AC. Resection of pubic symphysis and cystectomy significantly improves short-term patient-reported physical functioning among patients with pubovesical fistula and pubic bone osteomyelitis. Urology 2022;167:218–23. https://doi.org/10.1016/j.urology.2022.05.009.
[10] Myers JB, Hernandez BS, McCormick B, et al. Comparison of urinary diversion in patients with prostatic fistula to those with localized radiation injury after prostate cancer. Urology 2023;183:256–63. https://doi.org/10.1016/j.urology.2023.11.006.
[11] Osterberg EC, Vanni AJ, Gaither TW, et al. Radiation-induced complex anterior urinary fistulation for prostate cancer: a retrospective multicenter study from the Trauma and Urologic Reconstruction Network of Surgeons (TURNS). World J Urol 2017;35:1037–43. https://doi.org/10.1007/s00345-016-1983-3.
[12] Matsushita K, Ginsburg L, Mian BM, et al. Pubovesical fistula: a rare complication after treatment of prostate cancer. Urology 2012;80:446–51. https://doi.org/10.1016/j.urology.2012.04.036.
[13] Kahokehr AA, Boysen WR, Schild MH, et al. Urinary pubic symphysis fistula leads to histopathologic osteomyelitis in prostate cancer survivors. Urology 2021;148:297–301. https://doi.org/10.1016/j.urology.2020.07.038.
[14] Lavien G, Chery G, Zaid UB, Peterson AC. Pubic bone resection provides objective pain control in the prostate cancer survivor with pubic bone osteomyelitis with an associated urinary tract to pubic symphysis fistula. Urology 2017;100:234–9. https://doi.org/10.1016/j.urology.2016.08.035.
[15] Sexton SJ, Lavien G, Said N, Eward W, Peterson AC, Gupta RT. Magnetic resonance imaging features of pubic symphysis urinary fistula with pubic bone osteomyelitis in the treated prostate cancer patient. Abdom Radiol 2019;44:1453–60. https://doi.org/10.1007/s00261-018-1827-2.
[16] Valle LF, Lehrer EJ, Markovic D, et al. A systematic review and meta-analysis of local salvage therapies after radiotherapy for prostate cancer (MASTER). Eur Urol 2021;80:280–92. https://doi.org/10.1016/j.eururo.2020.11.010.
[17] Cools J, Ghijselings S, Ruythooren F, et al. Advanced imaging shows extra-articular abscesses in two out of three adult patients with septic arthritis of the native hip joint. J Bone Jt Infect 2024;9:27–35. https://doi.org/10.5194/jbji-9-27-2024.

[18] Metsemakers WJ, Morgenstern M, Senneville E, et al. General treatment principles for fracture-related infection: recommendations from an international expert group. Arch Orthop Trauma Surg 2020;140:1013–27. https://doi.org/10.1007/s00402-019-03287-4.
[19] Yen C, Kaushik S, Desai SB. Image-guided percutaneous bone biopsy for pediatric osteomyelitis: correlating MRI findings, tissue pathology and culture, and effect on clinical management. Skeletal Radiol 2023;52:39–46. https://doi.org/10.1007/s00256-022-04131-4.
[20] Said N, Chalian M, Fox MG, Nacey NC. Percutaneous image-guided bone biopsy of osteomyelitis in the foot and pelvis has a low impact on guiding antibiotics management: a retrospective analysis of 60 bone biopsies. Skeletal Radiol 2019;48:1385–91. https://doi.org/10.1007/s00256-019-3152-4.
[21] Savvidou OD, Kaspiris A, Bolia IK, et al. Effectiveness of hyperbaric oxygen therapy for the management of chronic osteomyelitis: a systematic review of the literature. Orthopedics 2018;41:193–9. https://doi.org/10.3928/01477447-20180628-02.
[22] Becker I, Woodley SJ, Stringer MD. The adult human pubic symphysis: a systematic review. J Anat 2010;217:475–87.
[23] Pieroh P, Li ZL, Kawata S, et al. The topography and morphometrics of the pubic ligaments. Ann Anat 2021;236:151698. https://doi.org/10.1016/j.aanat.2021.151698.