Urethral Stricture: Etiology, Histopathology, Classification and Complications

Mohamed Mazen Elsheikh, Maged M. Ali, Mohamed M. H. Abdalla, Maarouf Aref

Urology Department, Faculty of Medicine, Zagazig University

Corresponding author: Mohamed Mazen Elsheikh

Email: drmohamedmazenuro@gmail.com

Abstract:

Urethral strictures are common and increasingly common in an ageing population. The treatment is controversial and particularly the relative roles of urethrotomy or urethral dilatation on the one hand and urethroplasty on the other. This review aims to provide a comprehensive overview of the subject including less commonly discussed issues such as the etiology and histopathology, classification and management of stricture disease.

Keywords: anterior urethra, review, urethral strictures, urethroplasty.

Tob Regul Sci. ™ 2023;9(1): 4772-4784
DOI: doi.org/10.18001/TRS.9.1.332

Introduction:

Urethral stricture is typically a fibrosis or inflammation of the epithelial tissue and corpus spongiosum that results in stenosis of the urethral lumen. As the urethral lumen progressively obstructs symptoms typically occur. Most symptoms of urethral stricture are thought to be directly related to this decrease in urethral caliber. (1)

Prevalence of Urethral Stricture:

The true modern prevalence of urethral stricture is unknown and can only be inferred from population-based data. It appears that the incidence of urethral stricture varies widely throughout the globe. In industrialized nations such as the United States the prevalence of urethral stricture has been reported to be approximately 0.9 % based on epidemiologic data in a Medicare population. (2)

In non-industrialized countries the incidence of urethral stricture is thought to be much higher. Furthermore even within the same country stricture prevalence may vary. Some epidemiologic data suggests that urethral stricture is more prevalent in urban centers (as opposed to more rural locations). As an example, in urban hospitals urethral stricture is 2.6 times more common than the community hospital setting. (3)

Interestingly the incidence of urethral stricture has declined in some nations. In the United States it was estimated that from 1992 to 2001 the diagnosis of urethral stricture in a Medicare population declined from 1.4 to 0.9 %. The exact reason for this decline is not known but may be related to better identification and treatment of sexually transmitted illness, a known risk factor for urethral stricture. (2) It is also unlikely that the true incidence of urethral stricture will be subject to further decline with the increasing application of energy-based technologies for treatment of common urologic conditions such as benign prostatic hyperplasia and prostate cancer. (4)

Although urethral stricture is not the most common urologic condition, it does represent a significant clinical entity in urology. In all likelihood the true prevalence of urethral stricture ranges from 1 to 9 strictures per 1,000 people. (1)

Risk Factors:

Several clinical and epidemiologic factors are associated with an increased likelihood of developing a urethral stricture. These risk factors include: advanced age, a history of sexually transmitted illness, lower socioeconomic status, African-American race, lichen sclerosus, and a history of prostate cancer treatment. (1)

It appears that the likelihood of being diagnosed with a urethral stricture increases with age. In a survey of Medicare patients in the United States, the incidence of urethral stricture was found to rise abruptly after the age of 55. (3)

Sexually transmitted illness is also a well-documented cause of urethral stricture. (5) Chronic inflammation from an unrecognized sexually transmitted illness results in an inflammatory urethral stricture. This is especially apparent in non-industrialized nations with up to 66 % of diagnosed urethral strictures related to sexually transmitted illness. (6).

There also appears to be an increased likelihood of developing a urethral stricture with declining socioeconomic status. This is particularly noticeable in non-industrialized nations with high rates of infectious and infammatory strictures. Some races, specifically African-American patients, have also shown increased rates of urethral stricture. Based on the Urologic Diseases in America data, African-Americans have a 2.3- fold higher incidence of urethral stricture compared to a similar Caucasian population. (3)

Lichen sclerosus (LS) is a chronic lymphocyte mediated skin disease with a predilection to the genitalia. Genital lichen sclerosus commonly involves the urethra in males, and it has been estimated that up to 47 % of patients with lichen sclerosus develop urethral stricture and lower urinary tract obstruction. Treatment of lichen sclerosus strictures may be challenging due to the inflammatory changes, dense fibrosis, poor tissue quality, and length of urethra involved. (7)

Patients undergoing treatment for prostate cancer are also at increased risk for developing urethral stricture. This risk is seen in patients undergoing radiation therapy or radical prostatectomy. **(8)**

Etiology of Urethral Stricture Disease

Most anterior urethral strictures in industrialized countries are due to blunt external perineal trauma (e.g., straddle injury) or instrumentation (e.g., traumatic catheter placement or removal, or transurethral surgery or endoscopy). **(9)** A recent meta-analysis of the literature shows that anterior strictures are idiopathic (33%), iatrogenic (33%), traumatic (19%) and inflammatory (15%)**(Table 1)(10).** The sites of stricture are Bulbar strictures (the most common) in 44-67 % of patients, penile strictures in 12-39 %, penobulbar in 6-28 %, external meatal or submeatal in 0-23 %, membranous in 0-20 %, and prostatic in 0-4%. **(9)**

Table (1) Meta-analysis of anterior urethral stricture etiology**. (10).**

	Cause				
Investigator	**Stricture**	**Idiopathic**	**Iatrogenic**	**Inflammatory**	**Traumatic**
Wessells and McAnich, 1996	40	5	12	13	10
Wessells et al, 1997	25	0	11	9	5
Andrich and Mundy, 2001	83	35	38	7	1
Santucci et al, 2002	168	64	24	12	68
Elliott et al, 2003	60	37	9	7	7
Andrich et a,l 2003	162	38	84	23	17
Fenton et al, 2005	194	65	63	38	28
Total(%);included only bulbar strictures	732	244(33)	241(33)	109(15)	136(19)

A. Inflammatory stricture:

Urethral strictures due to gonococcal urethritis, are very uncommon today. In the previous century or in some undeveloped countries, more than 90 % of strictures are inflammatory and commonly involve the bulbar and pendulous urethra. **(9)**

Gonococcal urethral strictures occur because of abscesses that are formed in the paraurethral glands of Littre **(Figure 1).** The abscess then affects the surrounding corpus spongiosum and heals by fibrosis and scarring. The paraurethral glands are more numerous in the bulb, and it explains why

bulbar urethra is the site of most inflammatory strictures. **(Figure 2)**.The membranous and the penile urethras (except a short segment proximal to the meatus) lack glands, while the penoscrotal junction has a few, sparse and small glands. Proximal to urethral stricture, during high pressure micturition, infected urine accumulates under and extravasate into the corpus spongiosum and result in spongiofibrosis. As a result, a relatively short stricture can slowly progress proximally **(Figure 3).** Long tortuous strictures, complicated by fistulas, periurethral abscesses or tuberculous prostatitis, are associated in the developing countries with tuberculosis of the urethra **(9).**

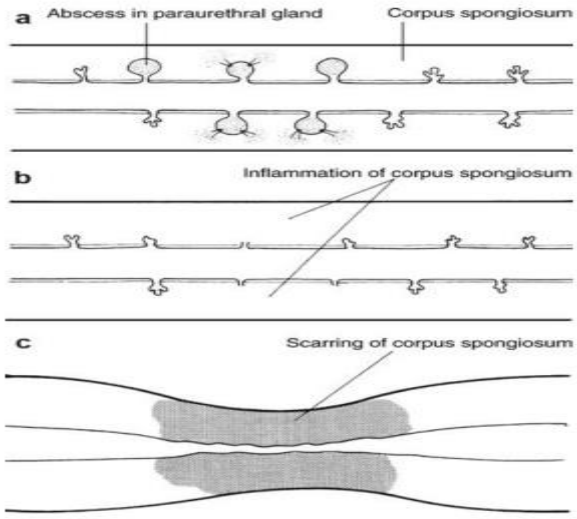

Figure 1 (a) Acute gonococcal inflammation of the paraurethral glands bursts out into the corpus spongiosum producing inflammation (b), which heals by scarring and, thus, (c) lumen stenosis and spongiofibrosis (**11**).

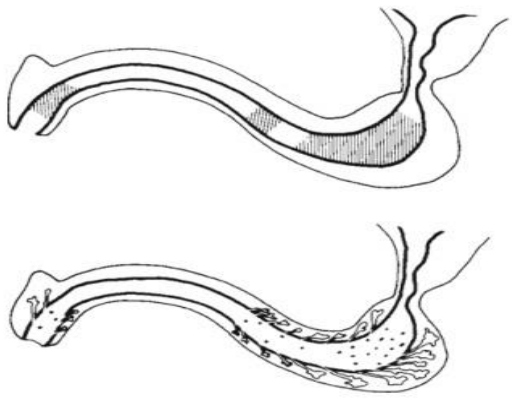

Figure 2 Paraurethral glands are most numerous in the distal pendulous and in the mid/proximal bulb. Inflammatory strictures commonly occur in the same location as the higher concentration of paraurethral glands (**12**).

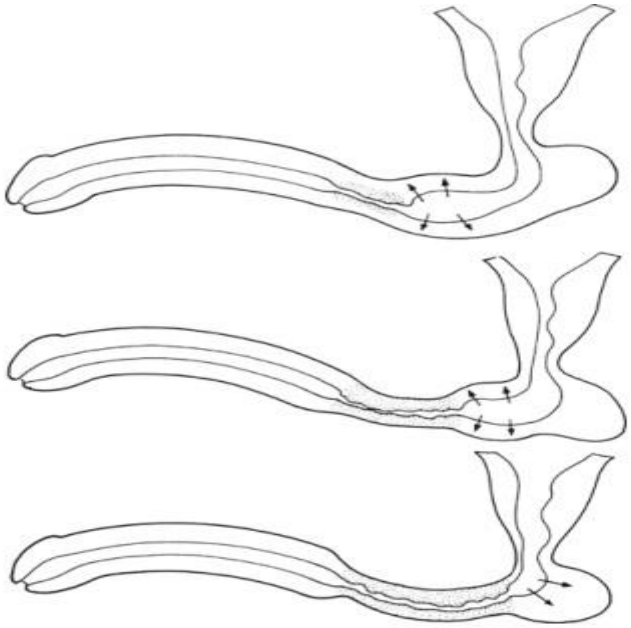

Figure 3 Inflammatory stricture tends to "creep up" the urethra as infected urine is forced into the corpus spongiosum upstream of a stricture **(11).**

The most common cause for inflammatory strictures In Western countries today is lichen sclerosus (LS), which begins by affecting only the glans, meatus, and preputial skin. Meatal stenosis can lead to high pressure voiding and cause inflammation or infection of the periurethral glands leading to panurethral stricture disease **(13).**

B. Traumaic stricture:

The most common cause of urethral strictures is the external trauma. Trauma can occur in the form of nonpenetrating, penetrating, avulsion or amputation injuries. Although iatrogenic trauma to the urethra still occurs, it occurs less frequently than in the past because of the development of small endoscopes and the limitation of indications for cystoscopy in the juvenile male. **(14)**

Nonpenetrating Injuries:

Nonpenetrating injures to the genitalia can occur in the form of result from blunt trauma, contusion, or penile fracture involving corpus spongiosum and urethra that causes severe damage of the internal structures without disruption of the skin.

Once a straddle trauma to the perineum or scrotum occurs or the penis is injured, a urethral injury should be suspected. **(14)**

Penetrating Urethral Injuries:

Penetrating injuries to the penis usually involve the urethra. Their management depends on the source of the trauma as low velocity injuries (e.g. sharp laceration, or laceration via a low-velocity

projectile) require exploration, irrigation, removal of foreign material and anatomical repair, while in high-velocity injuiries, suprapubic diversion and delayed reconstruction may be required. **(14)**

C. Iatrogenic stricture

Such strictures are mostly resulted from transurethral resection (41 %), prolonged catheterization (36.5 %), cystoscopy (12.7 %), prior hypospadias repair (6.3 %) and radical prostatectomy surgery (3.2 %). Such strictures are the result of an ischemic insult from the traumatic passage of large instruments into the urethra during transurethral surgery or by prolonged catheterization (particularly when a larger catheter is used). Thus, when catheterization is needed for short duration, a 16-Fr catheter is recommended for adults, while for prolonged duration, an SP tube is often placed. **(9)**

Iatrogenic strictures occur after trauma from faulty catheterization. The inflammatory response aggravated by the catheter material, or compressive ischemia causing avascular necrosis, especially with use of a large catheter. It is clear that materials have a role in degree of local tissue reactions and destruction (from best to worst: silicone, plastic, latex, and rubber). Additionally, instrumentation strictures occur at sites of greatest compression and ischemia, called, points of urethral fixation or lumen narrowness. (**Figure 4) (9)**

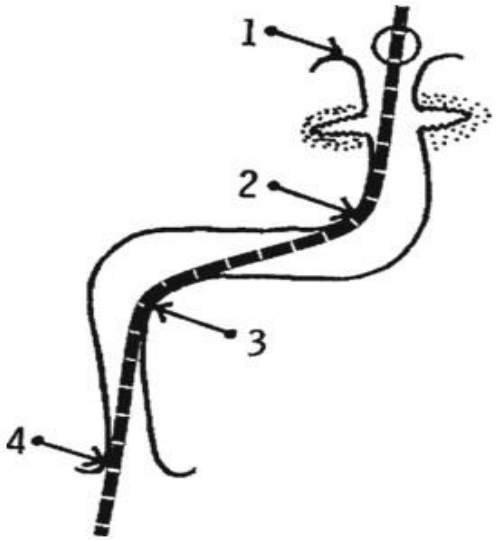

Figure 4 Locations of ischemic urethral strictures from instrumentation. (**15**) (1) Bladder neck, (2) membranous urethra, (3) penoscrotal junction, (4) fossa/meatus.

D. Idiopathic strictures:

Idiopathic strictures are short and common (up to 38 %). The cause of idiopathic strictures may be unrecognized perineal trauma in childhood. Baskin and McAninch noted that it may take years from the onset of the perineal trauma to development of a significant stricture **(16).**

Causes of strictures that involve the fossa navicularis are inflammatory (33–47 %) and iatrogenic (33–37 %) causes. In Fenton et al, mean stricture lengths in the anterior urethra were longest in the penile urethra (6.1 cm), shortest in the bulbar urethra (3.1 cm), and in the fossa navicularis (2.6 cm). So, the penile strictures almost need substitution urethroplasty, while bulbar strictures are often need anastomotic urethroplasty or an augmented anastomosis **(10).**

Histopathology of urethral stricture

The normal urethra is lined mostly by pseudostratified columnar epithelium. There is a connective tissue layer of the spongiosum beneath the basement membrane, which is rich in vascular sinusoids and smooth muscles. The connective tissue is composed mainly of fibroblasts and an extracellular matrix which contains collagen, proteoglycans, glycoproteins and elastic fibers. **(9)**

Urethral stricture is a fibrotic process with varying degrees of spongiofibrosis that results in decreased tissue compliance and decreased urethral lumen caliber. The most significant histologic changes of urethral strictures occur in the connective tissue. Finally Strictures are the consequence of epithelial damage and spongiofibrosis. **(9).**

In (1980) Scott and Foote (17) reported that, after trauma, the epithelium became ulcerated and covered with stratified columnar cells. It was noted that the stricture is rich in myofibroblasts and giant multinucleated giant cells. Both cells are responsible for collagen production and stricture formation.

In contrast**, Baskin et al**, **(16)** did not show an increase in collagen but showed a change in collagen subtype distribution, with predominance of type III collagen. The change in the ratio of type I to III collagen caused a decrease in urethral elasticity and compliance.

Etiology of stricture had no role in the content of smooth muscle or collagen in the corpus spongiosum. Increase in type II collagen was noted in the perilumen and type I in the spongiosum. Strictures also had fewer elastic fibers. Overall, urethral stricture is characterized by marked changes in the extracellular matrix. **(9)**

Urethral Stricture Classification

The stricture consists of dense collagen and fibroblasts and, therefore, contracts in all directions leading to shortening urethral length and narrowing luminal size. Strictures are usually asymptomatic until a lumen size below 16 Fr in caliber **(18).** In **(1983) Devine et al. (19)** recommended a urethral stricture classification based on the extent of spongiosal fibrosis **(Figure 5).**

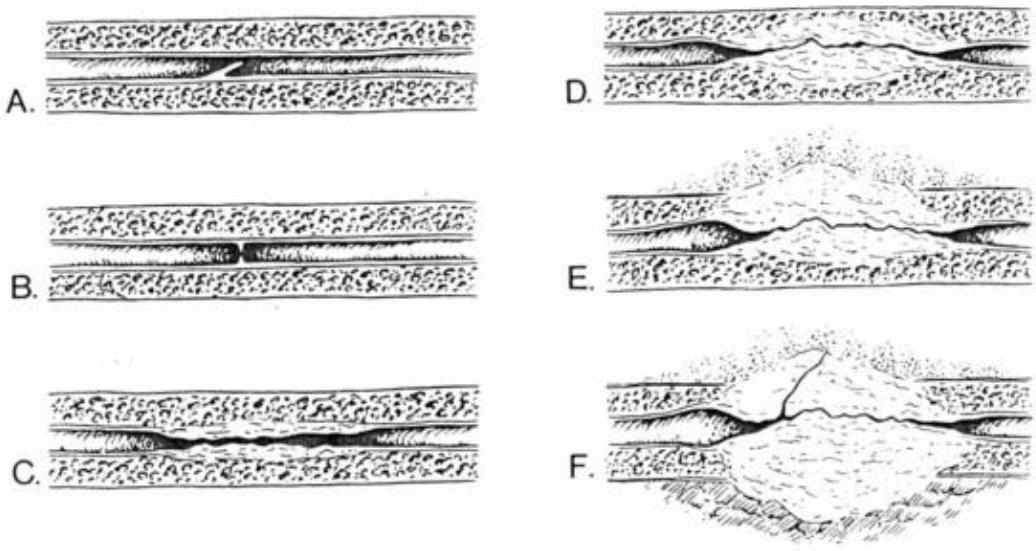

Figure 5 Devine classification of urethral stricture disease according to the anatomy of the stricture. (a) Stricture with no spongiofibrosis and an epithelial flap. (b) Epithelial scar with minimal spongiofibrosis. (c – e) Progressive spongiofibrosis. (f) Spongiofibrosis occupies the entire corpus spongiosum and potential fistula formation (**20**).

In **(1988) Jordan and Devine (21)** recommended a treatment algorithm (urethrotomy or surgery) according to the classification stage. For instance, for class D or greater (full thickness spongiosal fibrosis) open urethroplasty was recommended. The concept of treatment selection based on the extent of spongiosal fibrosis is sound; but, it is not practical clinically except there is a reliable noninvasive method to evaluate the degree of spongiofibrosis.

Conventional urethrography shows luminal narrowing only, not the character of the beneath spongiosal tissue. Physical examination for palpation of urethral induration and urethroscopy for evaluation of elasticity of the tissue and the color of the epithelium, can be helpful predictors for underlying fibrosis, but the reliability of such procedures is limited. Ultrasonography has promise as a modality for assessing fibrosis. The best prediction for fibrosis is the degree of lumen narrowing and the stricture length. The Longer and narrower strictures, the more spongiofibrosis is predicted. The recent introduction of ultrasound technology gives excellent images that help for better assessment of the length and location of stricture because the images look like an urethrography. The lack of blood flow on color Doppler may be of more value for prediction of spongiofibrosis. More spongiofibrosis is predicted with less blood flow. **(9).** In **(1988), McAninch (22)** first proposed a urethral stricture staging system based on sonographic appearance, ranging from normal to severe, according to the degree of lumen obstruction**.** But, ultrasonography is operator dependent, and clinical evaluation of strictures by this method is very subjective. Excessive compression with the probe during sonourethrography may result in a false narrowing of the urethral lumen. **(9)**

Later, **Chiou et al (23)** classified urethral strictures into five categories considering the length of the urethral stricture and the sonographic findings of spongiosal involvement: **I: Short** stricture (<2.5 cm) + minimal spongiofibrosis, **II: Short** stricture (<2.5 cm) + moderate spongiofibrosis (some normal spongiosal tissue in the periphery), **III: Short** stricture with extensive (full thickness) spongiofibrosis, **IV: Long**(>2.5 cm) or multiple strictures + moderate spongiofibrosis**, V: Long**(>2.5 cm) or multiple + extensive spongiofibrosis. **(Figure 6)**

Because they can be particularly challenging to successfully manage, strictures due to LS may deserve their own classification system. **(24)** recommended a classification system for Lichen Sclerosis according to degree of tissue affection. His proposal is as follows: In **stage 1** The foreskin only is affected by LS , in **stage 2** the foreskin, the coronal sulcus, and meatus are affected by LS while in **stage3** stricture of the fossa navicularis and anterior urethra up to pan-urethral stricture plus the affection of foreskin, glans, and external meatus. Lastly in **stage 4** premalignant or cancerous lesion is associated with LS.

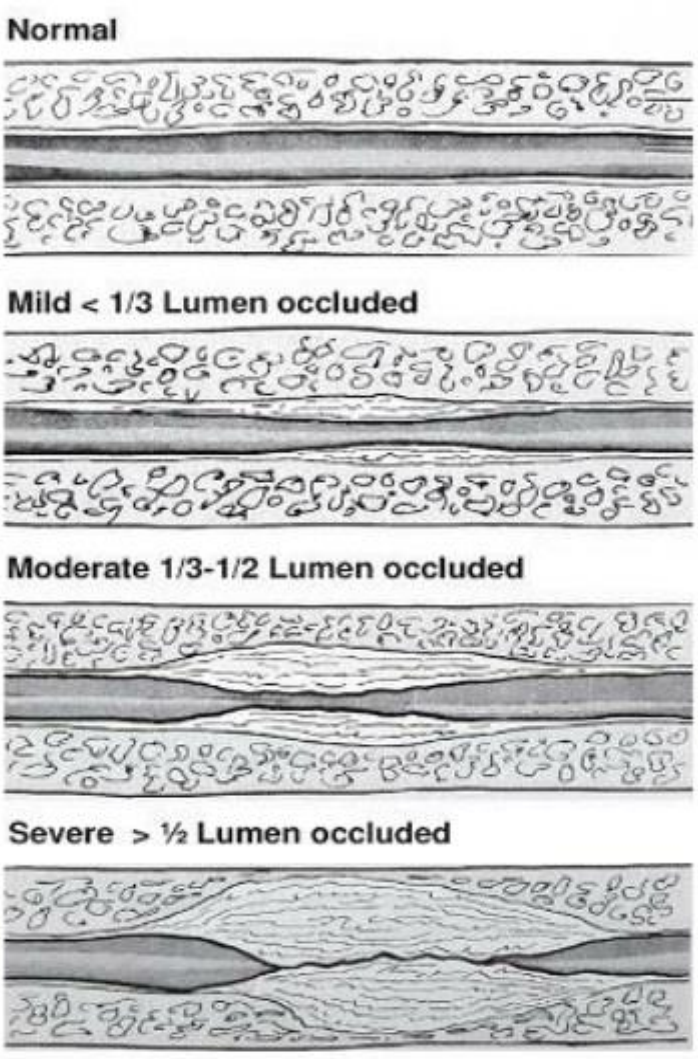

Figure 6 Ultrasound classification of the degree of urethral occlusion (**25**).

Clinical Presentation of urethral stricture

I- Signs and Symptoms of Urethral Stricture:

Clinical questioning can disclose multiple symptoms associated with urethral stricture. Typical symptoms include lower urinary tract symptoms (LUTS) (54%) such as weak urinary stream, straining to void, urinary hesitancy, incomplete emptying, nocturia, frequency, and urinary retention (29.8 %). Patients may also present with postvoid dribbling, urinary tract infection (6.1 %), epididymitis, genitourinary pain (2.9 %), hematuria (3.1 %), difficult catheterization (4.8 %), overflow incontinence, and ejaculatory dysfunction. Deviation or spraying of the urinary stream is usually found in patient with urethral meatus stricture. **(6).**

History of patients with urethral stricture may reveal presence of perineal or penile trauma, pelvic fracture, or a history of difficult urethral catheterization. Past medical history may reveal presence of medical problems which may have an effect on voiding function e.g. BPH, diabetes mellitus, or other neurological disorders, including chronic self-catheterization which usually has a harmful effect on the urethra. These clinical conditions can amplify symptoms due to a urethral stricture after that. **(Table 2) (26).**

Table (2) An analysis of the signs and symptoms of urethral stricture presenting in a first-world" cohort of 611 patients (**26**) .

Symptoms/sign	No. of patients	%
LUTS	332	54.3
Urinary retention	143	23.4
UTI	37	6.1
Difficult catheterization	29	4.8
Gross hematuria	19	3.1
Pain	18	2.9
Urethral abscess	14	2.3
Renal failure/hydronephrosis	8	1.3
Incontinence	6	1.0
Sexual dysfunction	5	0.8

II- Physical Examination:

Abdominal examination in may identify chronic urinary retention by palpation of a distended bladder and suprapubic percussion in patients with urethral stricture. Examination of the penile skin can reveal the presence of lichen sclerosus. Urethral meatus examination may reveal stenosis or complications of hypospadias. A urethrocutaneous fistula may be detected in some cases, particularly in patients who did previous urethral surgery or have history of prolonged lower urinary tract obstruction. Urethral palpation usually reveals thickening or induration which is related to the severity of periurethral fibrosis. Diffuse urethral induration often indicates severe spongiofibrosis, as in cases of lichen sclerosus, but if extensive should suspect the urethral carcinoma. Digital rectal examination (DRE) is performed in older males to detect the degree of prostatic enlargement and rule out other possible prostate pathology. **(1).**

III- Complications of Urethral Stricture:

Urethral stricture has adverse effects on voiding function and quality of life but minimally affect overall health status. Although common complications associated with urethral stricture are typically minor, such as, pain, urinary tract infection, urethral discharge, bladder calculi, prostatitis, epididymitis, urethral diverticulum, and urethrocutaneous fistula. Almost one-third of patients with urethral stricture will be complicated by acute urinary retention which needs urgent urologic intervention. In addition a significant proportion of patients with stricture present with a life threatening complications such as acute renal failure or urethral abscess directly related to urethral stricture occur in 4.1 and 3.3 % of patients, respectively. **(26)** Urethral stricture is a risk factor for necrotizing infection and Fournier's gangrene. **(Figure 7).** Prevalence of Fournier's gangrene increases in patients with urethral stricture when associated urinary extravasation. Additionally, urethral cancer is a rare but potentially devastating complication of urethral stricture. **(27).**

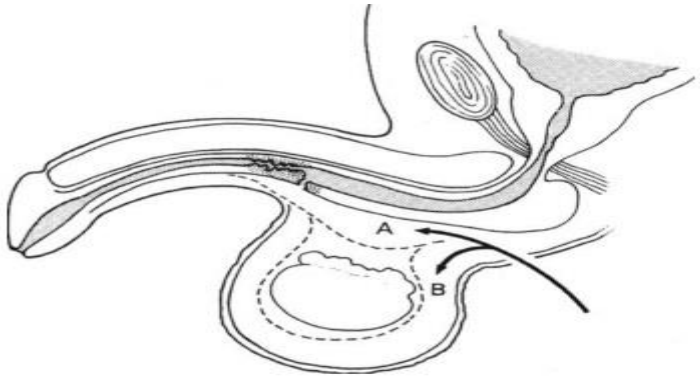

Figure 7 (A, B) Development of periurethral abscess and Fournier's gangrene secondary to urethral stricture. Urethral stricture with subsequent extravasation of urine into both compartments of Colle's fascia (**11**).

References:

1. **Rourke K, Brandes SB and Morey AF (2014):** Advanced Male Urethral and Genital Reconstructive Surgery, Current Clinical Urology, the Epidemiology, Clinical Presentation, and Economic Burden of Urethral Stricture. Doi: 10.1007/978-1-4614-7708-2_7, © Springer Science + Business Media New York.
2. **Anger JT, Scott VC, Sevilla C, et al (2011):** Patterns of management of urethral stricture disease in the Veterans Affairs system. Urology.78 (2): 454–8.
3. **Santucci RA, Joyce GF and Wise M (2003):** Male urethral stricture disease. J Urol. 177(5):1667–74.
4. **Taşçı AI, Ilbey YÖ, Luleci H, et al (2011):** 120-W Green Light laser photoselective vaporization of prostate for benign prostatic hyperplasia: midterm outcomes. Urology.78(1): 134–40.
5. **De Schryver A and Meheus A (1990):** Epidemiology of sexually transmitted diseases: the global picture. Bull World Health Organ. 1990; 68: 639 –54.
6. **Ogbonna BC (1998):** Managing many patients with a urethral stricture: a cost-benefit analysis of treatment options. Br J Urol. 81(5):741–4.
7. **Pugliese JM, Morey AF and Peterson AC (2007):** Lichen sclerosus: review of the literature and current recommendations for management. J Urol. 178(6):2268–76.
8. **Elliott SP, Meng MV, Elkin EP, et al (2007):** Ca PSURE Investigators. Incidence of urethral stricture after primary treatment for prostate cancer: data from CaPSURE. J Urol.178 (2):529–34.
9. **Elliot S, Brandes S and Morey AF (2014):** Advanced Male Urethral and Genital Reconstructive Surgery, Current Clinical Urology, Etiology, Histology, and Classification of Urethral Stricture Disease. Doi 10.1007/978-1-4614-7708-2_8, © Springer Science + Business Media.
10. **Fenton AS, Morey AF, Aviles R, et al (2005):** Anterior urethral strictures: etiology and characteristics. Urology. 65(6):1055–8.
11. **Blandy JP and Fowler C (1996):** Urethra and penis inflammation. In: Urology. Oxford: Blackwell Science; p. 477.
12. **Singh M and Blandy JP (1976):** The pathology of urethral stricture. J Urol. 115:673–6.
13. **Virasoro R, Jordan GH, Brandes SB, et al (2014):** Advanced Male Urethral and Genital Reconstructive Surgery, Current Clinical Urology, Lichen sclerosus. doi 10.1007/978-1-4614-7708-2_4, © Springer Science + Business Media New York.
14. **Schlossberg SM (2006):** Urethral Reconstructive Surgery: A Current Overview of the Treatment of Urethral Strictures: Etiology, Epidemiology, Pathophysiology, Classification, and Principles of Repair.
15. **Edwards LE, Lock R and Jones P (1983):** Post catheterization urethral strictures. A clinical and experimental study. Br J Urol. 55:53 – 6.
16. **Baskin LS and McAninch JW (1993):** Childhood urethral injuries: perspectives on outcome and treatment. Br J Urol. 72(2):241–6.

17. **Scott TM and Foote J (1980):** Early events in stricture formation in the guinea pig urethra. Urol Int.35: 334–9.
18. **Heyns CF, Brandes SB and Morey AF (2014):** Advanced Male Urethral and Genital Reconstructive Surgery, 41 Current Clinical Urology. doi 10.1007/978-1-4614-7708-2_28, © Springer Science + Business Media New York .
19. **Devine CJ, Devine PD, Felderman TP, et al.(1983**): Classification and standardization of urethral strictures. American Urological Association, 78th annual meeting. J Urol. 56:A325.
20. **Schlossberg SM and Jordan GH (2005):** Urethral stricture. In: Rakel RE, Bope ET, editors. Conn's current therapy. Amsterdam: Elsevier.
21. **Jordan GH and Devine PC (1988):** Management of urethral stricture disease. Clin Plast Surg.15: 493–505.
22. **McAninch JW, Laing FC and Jeffrey RJ (1988):** Sonourethrography in the evaluation of urethral stricture: a preliminary report. J Urol. 139:294–7.
23. **Chiou RK, Donovan IM, Anderson JC, et al (1998):** Color Doppler ultrasound assessment of urethral anatomy artery location: potential implications for technique of visual internal urethrotomy (OIU). J Urol. 159:796–9.
24. **Barbagli G, Palminteri E, Balò S, et al (2004):** Lichen sclerosus of the male genitalia and urethral stricture diseases. Urol Int. 73(1):1–5.
25. **Choiu RK, Anderson JC, Tran T, et al (1996):** Evaluation of urethral strictures and associated abnormalities using high resolution and color Doppler ultrasound. Urology. 47:102–7.
26. **Rourke KF and Hickle J (2013):** The clinical spectrum of the presenting signs and symptoms of anterior urethral stricture: analysis of a large contemporary cohort. J Urol.189 (5): A1.
27. **Atakan IH, Kaplan M, Kaya E, et al (2002):** A life- threatening infection: Fournier's gangrene. Int Urol Nephrol.34 (3):387–92.