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Review Article

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Urethral Stricture: Etiology, Pathogenesis, Diagnosis, and Management

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Abstract

A urethral stricture disease (USD), which is a restriction of the urethra brought on by scarring, effectively blocks the lower urinary system. By impairing the patient's capacity to pee, harming the entire urinary tract, and interfering with kidney function, this blockage can drastically diminish the patient's quality of life. Because of this, it is essential that urethral strictures, which can affect both men and women, are swiftly diagnosed and appropriately treated. Urethral stricture disease can be caused by iatrogenic injuries, due to idiopathic reasons, traumatic origin or due to inflammation. In this review we would like to throw the light on USD etiology, pathogenesis, diagnosis, and management.

KEYWORDS
Urethral stricture disease, Etiology, Diagnosis, Management

INTRODUCTION

The lower urinary system is effectively blocked by a urethral stricture, which is a constriction of the urethra brought on by scarring. The effects of this obstruction can significantly lower the patient's quality of life by disrupting their ability to urinate, as well as harm the entire urinary tract and affect their ability to function their kidneys. Therefore, it is crucial that urethral strictures, which can happen to both men and women (though they are far less common in women), are identified quickly and treated as needed. According to Tritschler *et al*. (2013), the prevalence in industrialized nations is predicted to be around 0.9%. In 0.6% of male patients, urethral stricture develops. It can be brought on by a number of factors, including mechanical and thermal injury, ischemia, and radiation (Santucci *et al*., 2007). Despite the variety of surgical techniques presently available, treating urethral stricture still poses a significant problem because no one treatment has been proven to be better than another (Peterson and Webster, 2004). Short (1 cm) urethral strictures have frequently been treated using urethral dilatation and direct visible internal urethrotomy. The gold standard surgical method for treating urethral stricture continues to be urethroplasty, either augmented (buccal mucosal graft or skin flap) or anastomotic, both of which have good success rates (83%–95%) (Barbagli *et al*., 2012). However, urethroplasty is a challenging treatment that relies on functional wound healing to be effective (Lumen *et al*., 2009).

Urethral stricture

The surgical anatomy of the urethra consists of posterior urethra, which comprises the membranous and prostatic urethra, and the anterior urethra, which includes the bulbar and penile urethra, are the two components of the male urethra. The bulbar urethra, which is surrounded by the bulbospongiosus muscle, and the penile urethra go from the bulbospongiosus distal boundary to the fossa navicularis and external meatus (Baskin *et al*., 1993).

A constriction of the urethra is known as urethral stricture disease (USD). The corpus spongiosum encased the urethral mucosa. From the meatus to the bulbar urethra, this blood-rich erectile tissue surrounds the urethra. The degree of fibrosis in the corpus spongiosum is closely related to the extent and severity of the stricture because the spongiosum supplies vascular supply to the urethra (Cavalcanti *et al*., 2007).

The two primary types of urethral strictures are anterior and posterior, which differ not only in location but also in underlying pathophysiology. In a retrospective analysis of all strictures reconstructed at a single institution, the vast majority (92.2%) were anterior, with the majority (46.9%) occurring in the bulbar urethra, followed by penile (30.5%) (Palminteri *et al*., 2013). The same author add that Stricture illness can have a significant impact on one's quality of life, leading to infections, bladder calculi, fistulas, sepsis, and renal failure.

Etiology of urethral stricture

Iatrogenic injuries

The most common cause of anterior urethral stricture is iatrogenic injury (Fenton *et al*., 2005). The rapid improvement of clinical and diagnosis techniques has led in an increase in the number of urological treatments performed in clinics in recent years, resulting in an increase in the prevalence of iatrogenic injuries. Catheterization revealed to be the most common source of iatrogenic cases, followed by hypospadias correction and transurethral surgery. The penile urethra and meatus are the most common stenotic segments induced by iatrogenic damage, which can occur as a result of ischemia after urological endoscopic op-

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erations, cardiovascular surgery, or a long-term installation of an indwelling catheter (Palminteri *et al*., 2013).

Idiopathic strictures

Idiopathic strictures affect the bulbar urethra more frequently than the urethra of elderly individuals (48 percent vs. 23 percent) (Smith, 2016). Strictures in younger patients can result from undetected childhood trauma or a congenital urethral abnormality (Latini *et al*., 2014). In older individuals, however, decreased tissue blood flow and ischemia have been hypothesized as a plausible explanation (Mundy and Andrich, 2011).

Traumatic scarring

After a blunt straddle injury, traumatic scarring induces urethral stricture in the bulbar tract, affecting the spongiosum tissue. The urethra is compressed against the pubic symphysis, resulting in urethral incontinence, local bleeding, and urine extravasation, as well as inflammation and scarring (Park and McAninch, 2004).

Inflammatory stricture

Inflammatory stricture is a narrowing of the urethral lumen caused by a post-infectious inflammatory reaction. This is a more common etiology in developing countries. Infection, tumors, and prostatectomy are just a small percentage of the causes of anterior strictures (Fenton *et al*., 2005).

Pathogenesis of urethral stricture

Urinary extravasation occurs as a result of small tears in this metaplastic tissue, causing a fibrotic reaction within the spongiosum. This fibrosis may be asymptomatic at the time of injury; nevertheless, over time, the fibrotic process can induce progressive narrowing of the urethral lumen, resulting in symptomatic obstructive voiding (Lindsay *et al*, 2014).

Changes in the extracellular matrix of urethral spongiosal tissue characterize urethral stricture pathophysiology (Cavalcanti *et al*., 2007), as seen on histologic examination of normal and strictured urethral tissue (Baskin *et al*., 1993).

Dense fibers interspersed with fibroblasts replace normal connective tissue, and the ratio of type III to type I collagen decreases (Baskin *et al*., 1993). In strictured urethral tissue, this alteration is accompanied by a decrease in the ratio of smooth muscle to collagen, as well as considerable changes in nitric oxide generation (Cavalcanti *et al*., 2004).

Spongiofibrosis is caused by anterior urethral strictures that form as a result of trauma or infection. The corpus spongiosum becomes fibrosed as a result of this process, resulting in a constricted urethral lumen. If the fibrosis is severe enough, it may also affect tissues outside of the corpus spongiosum. Posterior urethral stenosis is most commonly caused by an obliterative process that induces fibrosis of the posterior urethra, such as iatrogenic injuries from pelvic radiation or radical prostatectomy, or distraction injuries that occur following trauma, especially pelvic fractures. Rather than real strictures, these lesions are referred to as contractures or stenosis (Hampson *et al*., 2014).

Diagnosis and preoperative assessment of urethral stricture

A clear diagnosis and preoperative examination of anterior urethral stricture are required before clinical treatment. While the American Urological Association symptom score reflects the most prevalent voiding complaint of males with urethral stricture, such as lower urinary tract symptoms (LUTS) or acute urine retention (AUR), 22.3 percent of patients report with a variety of symptoms (Rourke and Hickle, 2012).

Spraying of the urine stream, dysuria, or no symptoms are the most prevalent signs. Patients with failed hypospadias correction were more likely to have sexual dysfunction (Nuss *et al*., 2012).

To fully capture the presenting comprehensive voiding symptoms and other complaints of men with urethral stricture illness, a validated, reliable diagnosis methodology is required. The current norm for imaging the urethra is to utilize a combination of ascending and descending urethrograms, complemented by urethroscopy as necessary (Chapple *et al*., 2014). Urethroscopy, on the other hand, allows urologists to see the length and ischemic condition of the urethra directly, which aids in the diagnosis of urethral narrowing and the selection of treatment options Ultrasonography of the anterior urethra is a safe and effective method of determining the best route for anterior urethral reconstruction (Buckley *et al*., 2012).

Management of urethral stricture

The goal of urethral stricture treatment is to correct the urethra's continuity defect and restore a patent urethra. Simple dilation, urethrotomy, and a range of urethral reconstructive methods, such as tissue engineering techniques, are all alternatives for treatment. The location, length, and genesis of the strictures, as well as any previous surgery, must all be considered when choosing a therapeutic approach. Furthermore, it is commonly known that no single technique is appropriate for all stricture conditions (Peterson and Webester, 2004).

Urethral dilation

The use of a balloon, filiform and followers, urethral sounds, or self-dilation with catheters are all options for urethral dilation. Overall, studies have found no difference between urethral dilation versus internal urethrotomy in terms of recurrence rates (Peterson and Webester, 2004; Buckley *et al*., 2012).

Although complications related with urethral dilation may be more likely to occur in patients who come with urine retention, rates of complications and failure at the time of the treatment do not differ significantly between dilation and internal urethrotomy (Peterson and Webester, 2004).

Direct Vision Internal Urethrotomy (DVIU)

A cold-knife transurethral incision is used to remove scar tissue, allowing the tissue to repair by secondary intention at a wider caliber and so increasing the size of the urethral lumen. Many studies have looked into the benefits of leaving a urethral catheter in place following urethrotomy, but no consensus has yet been reached on whether to leave the catheter in place and, if so, for how long (Sharma *et al*., 2013; Kumar *et al*., 2015).

Internal urethrotomy success rates depending on the patient, the length of follow-up, and the methods used to determine success and recurrence. Long-term success rates are expected to be between 20 and 30% (Barbagli *et al*., 2012).

Urethral stents

It's also been looked into using urethral stents after dilation or an internal urethrotomy. Temporary stents, such as the Span-

ner® stent (SRS Medical, USA), must be replaced every 3–12 months, depending on the type of stent, and are better for men who have a posterior urethral obstruction. Permanent urethral stents, such as the Urolume® (Endo Health Solutions, USA) and Memotherm® (Bard, Germany), are inserted into the bulbar urethra and incorporated into the urethral wall (McKenzie and Badlani, 2011).

However, due to limited use and high rates of problems such as perineal pain, stent migration, stent obstruction (due to tissue hyperplasia or stone encrustation), incontinence, and infection, these stents have been mostly abandoned and, in some countries, removed from the market (Hsiao *et al*., 2003).

Novel management trials in animal studies

To assess the collagenase Clostridium histolyticum (CCH) therapy impact in a rat model of urethral fibrosis. Five sets of 30 male Sprague-Dawley rats (300-350 g each) were created. In order to induce urethral fibrosis, 10 g of transforming growth factor beta 1 was injected into the rat urethra in the other 4 groups in addition to normal saline in the sham group. The rats received different dosages of CCH or vehicles two weeks after receiving an injection of transforming growth factor beta 1. At 4 weeks after receiving the CCH or vehicle injection, the rats were killed. A sample of urethral tissue was taken for histological and molecular examinations. Western blot analysis was used to assess the amounts of type I and type III collagen. When urethral fibrosis was compared to the sham group, there was urethral fibrosis and a significantly higher expression of collagen types I and III (P.05). When compared to the treatment control group, the high-dose CCH treatment groups' urethral injection of CCH significantly reduced urethral fibrosis and the expressions of collagen types I and III (P<0.01). Their findings showed that CCH injections had a positive effect in a rat model of urethral fibrosis. These results call for additional research because they point to a potential therapeutic function for CCH in people with urethral strictures (Sangkum *et al*., 2015). In a rat model of urethral fibrosis, they examined the therapeutic potential of adipose tissue-derived stem cells (ADSCs). As a result, three groups of 18 male Sprague-Dawley rats (300–350 g) were created: (1) sham (10 g TGF-1) injection); (2) urethral fibrosis group (10 g TGF-1) injection; and (3) ADSCs group (10 g TGF-1 injection plus 2 105 ADSCs). Rat inguinal fat pads were used to collect rat ADSCs. Two weeks following urethral injection, all test animals were put to sleep. Rat urethral tissue was taken after the animals were put to sleep for histological analysis. The amount of type I and type III collagen was measured using Western blot analysis. The obtained data showed that TGF-1 injection significantly raised collagen type I and III expression and caused urethral fibrosis (P< 0.05). When compared to the urethral fibrosis group, the ADSCs group showed a significantly lower level of submucosal fibrosis and collagen type I and III expression (p 0.05). By injecting ADSCs, TGF-1-induced fibrotic alterations were reduced. They came to the conclusion that local injection of ADSCs significantly reduced collagen types I and III in a rat model of urethral fibrosis. These results imply that ADSC injection may reduce the development of scars and maybe act as an adjuvant therapy to improve the efficacy of the main therapy for urethral stricture disease (Sangkum *et al*., 2016). Besides, Wang *et al*. (2023) redesigned the structure and material of the conventional ureteral stent in order to reduce ureteral stent complications. The biodegradable mesh ureteral stent replaced the conventional nondegradable Double-J form tubular ureteral stent. The USD animals had their ureters fitted with a modified mesh ureteral stent and a Double-J ureteral stent, respectively. According to the findings of the gross morphology, serology, urinalysis, histology, microstructure, and other tests, the modified mesh ureteral stent supports the ureter well and has no adverse effects on the human uroepithelial cells' ability to proliferate, migrate, or undergo apoptosis. After being implanted for three to five months, the mesh ureteral stent can gradually biodegrade without the need for additional surgery to remove it, which could ease ureter obstruction. The modified mesh ureteral stent had less encrustation and a lower rate of urinary tract infection than the Double-J ureteral stent. It is anticipated to be a different treatment strategy for USD.

CONCLUSION

Urethral stricture can significantly lower quality of life of the patients by disrupting their ability to urinate, harm the entire urinary tract and affect their ability to function their kidneys. Several methods of managements were developed; however, more approaches are requested to reduce the adverse effects of current management methods.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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