Review

A brief review on anterior urethral strictures

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Abstract The treatment of urethral strictures remains a challenging field in urology even though there are a variety of procedures to treat it at present, as no one approach is superior over another. This paper reviewed the surgical options for the management of different sites and types of anterior urethral stricture, providing a brief discussion of the controversies regarding this issue and suggesting possible future advancements. Among the existing procedures, simple dilation and direct vision internal urethrotomy are more commonly used for short urethral strictures (<1 cm, soft and no previous intervention). Currently, urethroplasty using buccal mucosa or penile skin is the most widely adopted clinical techniques and have proved successful. Nonetheless, complications such as donor site morbidity remain problem. Tissue engineering techniques are considered as a promising solution for urethral reconstruction, but require further investigation, as does stem cell therapy.

1. Introduction

Urethral stricture is a common and challenging disease in urology. Currently, there are numerous surgical procedures to treat this disease. However, the diversity of treatment modalities reflects the scarcity of an optimal technique [1].

The male urethra can be divided into two parts, the posterior urethra which consists of the membranous and prostatic urethra, and the anterior urethra which includes bulbar and the penile urethra. The bulbar urethra is enclosed by the bulbospongiosus muscle and the penile urethra runs from the distal margin of the bulbospongiosus to the fossa navicularis and external meatus.

Considering the variety of surgical treatment modalities, urologists must be up-to-date with the use of different

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surgical techniques to deal with various conditions. The purpose of this article is to overview the current management of anterior urethral stricture, providing a brief discussion of the controversies regarding this issue and possible future advancements.

2. Etiology

Urethral stricture in developed countries mainly involves the anterior urethra, in particular the bulbar tract, which accounts for 46.9% [2]. In addition, 30% occur in the penile urethra, and the remainder in a combination of the two and panurethra. The reasons for stricture also vary by site. Basically, the anterior urethral strictures are caused by the following:

(1) Iatrogenic injuries are the most common reason for anterior urethral stricture [3]. In recent years, the rapid development of diagnosis and clinical techniques has resulted in more urological procedures performed in the clinic, leading to an increase in the incidence of iatrogenic injuries. Among the iatrogenic cases, catheterization appeared to be the most frequent cause, followed by hypospadias repair and transurethral surgery [2]. Mostly, stenotic segment caused by iatrogenic injury often involves the penile urethra and meatus, which may occur as a result of ischemia after urological endoscopic procedures, cardiovascular surgery or a long-term placement of an indwelling catheter.

(2) Idiopathic strictures occur more commonly in the bulbar urethra and are more frequent in younger versus older patients (48% *vs.* 23%) [4]. For younger patients, strictures may arise from unrecognized childhood trauma or a congenital anomaly in urethral development [5]. By contrast, decreased tissue blood supply and ischemia have been proposed as a possible mechanism in the older patients [6].

(3) Traumatic scarring after blunt straddle injury causes urethral stricture in the bulbar tract involving the spongiosum tissue. The blunt perineal trauma compresses the urethra against the pubic symphysis [7], causing urethral in continuity, local bleeding and urinary extravasation, giving rise to inflammation and scarring.

(4) Inflammatory stricture refers to a post infectious inflammatory reaction where the urethral lumen is narrowed [3]. This etiology is more common in undeveloped countries. In developed countries, lichen sclerosus is a more frequent cause of inflammatory strictures and often involves panurethra.

Other causes of anterior strictures such as infection, tumor, and prostatectomy only account for minor proportion.

3. Diagnosis and preoperative assessment

Before clinical treatment, a precise diagnosis and preoperative evaluation of anterior urethra stricture are necessary. While the American Urological Association symptom index captures the most common voiding complaint of men with urethral stricture, including lower urinary tract symptoms (LUTS) or acute urinary retention (AUR), 22.3% of patients have different presenting complaints [8]. The most common symptoms include spraying of urinary stream, dysuria or no symptoms. For men with lichen sclerosus, obstructive symptoms are more common. Sexual dysfunction was also reported, most commonly in patients with failed hypospadias repair and lichen sclerosus [9]. A validated, accurate methodology for diagnosis is needed to fully capture the presenting comprehensive voiding symptoms and other complaints of men with urethral stricture disease.

The current standard is to use combined ascending and descending urethrograms to image the urethra, supplemented by urethroscopy when necessary [10]. However, one study suggested that independently reported retrograde urethrograms (RUGs), which are not usually performed by urologists, are not as accurate as reported by primary physicians. Consequently, such information should be used with caution for preoperative planning [11]. By contrast, urethroscopy allows urologists to directly view the length and ischemic condition, which is favorable to the evaluation of urethral narrowing and selection of treatment option. Ultrasonography of the anterior urethra is a reliable and valuable procedure to help select the optimal anterior urethral reconstructive approach [12].

4. Management of anterior urethral stricture

The purpose of management of urethral stricture is to restore the defect of the urethra continuity and to regain a patent urethra. Treatment options include simple dilation, urethrotomy, and a variety of urethral reconstructive techniques such as tissue engineering techniques. The choice of the treatment option must take all factors into consideration, such as the site, length, etiology of the strictures as well as any previous surgery. In addition, it is widely acknowledged that there is no one appropriate procedure for all stricture conditions [13].

5. Dilation

As one of the most common modalities used in clinic, urethral dilation is less invasive with minimal side effects, and appropriate for patients unwilling to undergo urethral surgery. A randomized study [14] compared dilation and direct vision internal urethrotomy (DVIU), showing no significance difference in the curative outcomes between the two modalities. However, due to the high recurrence rate of this procedure, urethral dilation is often performed as a palliative maneuver and most patients will require a further urethral repairing surgery [13].

6. DVIU

DVIU using a cold knife or laser remains the first-line therapy for short bulbar urethral stricture [15] (<1 cm, soft and no previous intervention). Although it is much less efficacious than urethroplasty, this modality can be justified by its simplicity of surgical procedure and relatively low

morbidity. Some studies using optical internal urethrotomy (OIU) with a laser have reported good results, and additional intralesional injection of triamcinolone, hyaluronidase and mitomycin may be favorable to avoid the reoccurrence of stricture. Various new articles on intralesional treatment of these strictures have shown good results [16,17].

Moreover, there is consensus that repeated DVIU for early recurrence has a far less curative effect than expected [18], thus, for patients with early stricture recurrence, reconstructive urethroplasty is likely to be a more appropriate choice rather than repeated DVIU.

7. End-to-end anastomotic repair

In the bulbar urethra, the choice of surgical techniques depends on the stricture length. Stricture excision and primary re-anastomosis are considered an appropriate procedure for short strictures within 2 cm. For strictures 3—5 cm or longer, augmented roof-strip anastomosis and substitution urethroplasty are recommended, respectively [19]. Eltahawy et al. [20] reported, with a mean follow-up of 50.2 months, a high success rate of up to 95% of primary end-to-end anastomosis in 168 patients with stricture length ranging from 0.5 to 4.5 cm (mean, 1.9 cm). However, some researchers suggested that this surgical procedure should be limited to strictures within 1 cm [21] as excision of a 1 cm urethral segment with opposing 1 cm proximal and distal spatulations results in a 2 cm urethral shortening, and excision of a longer urethral segment risks penile shortening or chordee.

In recent years, a novel approach without transecting the urethra was developed. Transecting the urethra allows complete removal of scarred tissue. In strictures after blunt perineal trauma and bulbar urethral injury, removal of the traumatic scarred tissues is mandatory, as not removing this tissue may lead to stricture recurrence over time [19]. However, this procedure may also cause vascular and neuronal damage to the urethra, thus leading to possible urinary and sexual dysfunction [22]. Andrich and Mundy [23] applied the non-transecting technique in 22 patients with a mean age of 34 years old. The range of follow-up was 6—21 months, and 16 of the patients had been followed up for at least 1 year. They achieved a 100% success rate, concluding that their non-transecting anastomotic bulbar urethroplasty technique was as good as the traditional anastomotic urethroplasty with less surgical trauma.

8. Tunic albuginea urethroplasty

For patients with unavailable autologous substitution tissue such as buccal mucosa, albuginea urethroplasty is also considered as a promising option or even as a primary approach with equivalent results. Sharma et al. [24] analyzed the results in 10 consecutive patients with a pan-anterior urethral stricture who underwent Monsieur's urethroplasty, demonstrating that Monsieur's tunica albuginea urethroplasty is an effective technique for the treatment of anterior urethral stricture, in particular, in those cases with unavailable buccal mucosa.

9. Substitution urethroplasty

Substitution urethroplasty is commonly performed to deal with long or complex strictures. In carrying out this procedure, the substitution tissue must possess a thick epithelial layer, minimal donor site morbidities and be easy to procure [25]. Currently, alternative replacement tissues include scrotal skin [26], penile skin [27], bladder epithelium [28], colonic mucosa [29], and buccal and lingual mucosa [30]. Among all these tissues, genital skin and buccal mucosa are now most commonly used in the clinic and have met with success to some extent. Sharma et al. [31] compared lingual and buccal mucosa graft urethroplasty for anterior urethral stricture with respect to intraoperative, postoperative parameters and urethroplasty outcome. They showed that lingual mucosa graft urethroplasty provided outcomes equivalent to those of buccal mucosa graft urethroplasty, but postoperative morbidity and long-term change in speech made lingual mucosa a second choice for strictures >7 cm, and only for cases where a buccal mucosa graft was unavailable. In addition, there are some issues with substitution urethroplasty surgery which will be discussed later.

10. Flap *vs*. graft

This area is very controversial. In 2008, Barbagli et al. [32] reported their results of 375 patients who underwent one-staged bulbar urethroplasty using penile skin flap or oral mucosa graft,showing that the oral mucosa graft is superior to penile skin flap with a higher overall success rate (82.8% *vs*. 59.6%). However, another prospective randomized study compared the outcomes of buccal mucosa graft dorsal onlay and penile skin flap dorsal onlay urethroplasty, and revealed no significant difference between the success rate of the two modalities (89.9% *vs*. 85.6%) [33]. Consequently, it remains uncertain if buccal mucosa graft is superior to skin flap in curative outcomes, and the choice of substitution material is primarily based on the surgeon's preference and patients' conditions. Technically, the flap procedure is more complex. By contrast, substitution urethroplasty with buccal mucosa requires less extensive training and is associated with less morbidity [33]. Furthermore, due to the scarcity of clinical evidence of a large series of patients and adequate follow-up data, it is also questionable if the vascularized pedicled flap will perform better therapeutically.

In addition, for patients with lichen sclerosus, the use of oral mucosa is mandatory since lichen sclerosus is a skin disease and any skin that would be used for the repair is already or may become diseased [19].

In the case of crippled urethral stricture, techniques used include circumferential advancement of penile skin, dorsal transposition flap of preputial skin, distally based transposition flap of penile skin, and full-thickness skin graft [34].

11. Tubular graft *vs*. patch

Considering the tridimensional structure of the urethra, tubular graft was once regarded as a better choice for substitution urethra. Numerous studies were conducted

with this technique [35—37]. Venn and Mundy [36] performed one-stage urethroplasty using buccal mucosa for 39 patients (aged 23—59 years), 28 with a patch and 11 with tube grafts, and after a follow-up for 2—5 years, recurrent stricture (3%) occurred in only one patient in the group with a patch urethroplasty; However, five of the 11 patients in the tubular graft group (45.5%) had a recurrent stricture. Moreover, Andrich and Mundy [37] reviewed the results of urethroplasty using buccal mucosal graft in 128 patients and found the re-stricture rate was 11% for patch grafts and 45% for tube grafts. Generally, most of the studies revealed that tubular graft is not as good in curative outcomes as expected.

12. Ventral *vs.* lateral *vs.* dorsal onlay

As one-stage oral mucosa represents the most widespread method for the repair of bulbar urethral strictures due to its highly vascular spongiosum tissue, the location of the free graft on the dorsal or ventral or lateral urethral surface has become a contentious issue [19]. From 1997 to 2002, Barbagli et al. [38] repaired 50 bulbar urethral strictures using buccal mucosa grafts, with the graft placed on the ventral, dorsal and lateral bulbar urethral surface in 17, 27 and six cases, respectively. The mean follow-up was 42 months (range 12—76 months), and their results revealed that the placement of buccal mucosa grafts into the ventral, dorsal or lateral surface of the bulbar urethra showed the same success rates (83%—85%) and the outcome was not affected by the surgical technique. Furthermore, the curative outcomes are similar among these three procedures, and the ventral graft placement is considered technically easier, since it requires less urethral dissection and mobilization [39]. It is also suggested that the ventral graft is appropriate for non-traumatic urethral strictures located in the proximal bulbar urethra and the dorsal graft is preferred in patients with non-traumatic urethral strictures located in the distal bulbar urethra [40,41].

13. One-staged *vs.* staged urethroplasty

One-staged urethroplasty using a buccal mucosa graft has been reported to achieve a high success rate. Nonetheless, when dealing with a more complex stricture or cases with adverse local conditions, a staged procedure is more commonly recommended [42]. Complex anterior urethral strictures include strictures simultaneously involving the penile and bulbar urethra (pan-urethral stricture) commonly caused by lichen sclerosus [43], and strictures in patients who had undergone repeated prior failed urethroplasties, frequently referred to as a failed hypospadias repair [44]. Furthermore, the length of the urethral stricture (greater than 4 cm), prior urethroplasty and failed endoscopic therapy were considered to be predictive factors of a failed urethroplasty [45]. Thus, in these patients, the one-staged technique may not be the most appropriate option due to the possible high risk of failure [46].

For cases with adverse local conditions, such as extensive scarring, fistula, infection and cancer, both Palminteri et al. [42] and Andrich et al. [47] recommended

a two-stage approach owing to its lower re-stricture rate than the one-stage urethroplasty in the penile urethra, despite the expense of a significantly higher revision rate. Furthermore, when the penile shaft is on the whole normal and the urethral plate, corpus spongiosum and dartos fascia are suitable for single-stage reconstruction, a single-stage procedure should be performed whenever possible to avoid patient discomfort and disability [43]. On the other hand, for strictures after hypospadias repair or where the penile skin, urethral plate and dartos fascia are not suitable for single-stage reconstruction, a two-stage urethroplasty is recommended [48,49].

14. Sexual morbidity after surgery

Among the side effects of urethral surgeries, sexual function, which consists of sexual drive, erectile function and ejaculatory function, is much concerned in patients' satisfaction [50], while few studies systemically introduced. Using the O'Leary's Brief Male Sexual Function Inventory (BMSFI), Erickson et al. [51] evaluated the sexual function of 52 men (aged 18—79 years) who underwent urethral reconstructive procedures for anterior urethral stricture disease before and after surgery. They reported that in general, sexual drive and erectile function did not show a decline after surgery. However, when the patients were further divided by age, the results revealed that the older men ($>$50 years old) might have a higher incidence of erectile dysfunction post-operation, but this morbidity might recover with time. Besides, for younger men ($<$40 years old), the ejaculatory function might improve significantly.

In addition, some factors, such as the size and location of the stricture, operation modalities and prior interventions may also influence patients' sexual function after surgery. Sharma et al. [52] argued that patients without prior interventions might have a better prognosis in ejaculation function and overall satisfaction. However, there is still some controversy regarding whether the size and location of the stricture and operation modalities impact on sexual morbidity [51—53].

15. Tissue-engineering urethroplasty

Despite the significant progress made by the current procedures, there are still major challenges in urethral reconstruction. The scarcity of sufficient substitution materials, donor morbidity and time-consuming harvesting has yet to be resolved. However, the advent of tissue engineering techniques may provide potential solutions. Through regenerative medicine, a tissue-engineered urethra can be constructed with a limited amount of material without harvesting a mass of autologous healthy tissue. Recent clinical trials conducted on animals have achieved satisfactory outcomes, but few human clinical trials have been performed.

The choice of scaffold plays a crucial role in tissue engineering. To date, acellular matrix such as acellular dermal matrix grafts and acellular porcine small intestinal submucosa (SIS) have been applied clinically due to their appropriate biomechanical properties [54,55]. De Filippo et al. [56]

compared the acellular and cell-seeded scaffold, and argued that the cell-seeded scaffold is a superior option in urethral reconstruction. In 2011, a major breakthrough was made when an observational clinical study reported that satisfactory therapeutic results were achieved in five patients (aged 10—14 years) using an urothelium-seeded scaffold. The median follow-up was 71 months (range 36—76 months) and no re-stricture occurred. Currently, stem cell therapy has been applied in urethral reconstruction [57,58], but more clinical data are required to fully evaluate its effects and potential hazards. Moreover, the mechanism of differentiation from stem cells to urothelium has not been fully elucidated.

16. Conclusion

During the last few decades, reconstructive surgeries of the anterior urethral stricture have been successful and are continually evolving. However, as yet, there is no one approach for urethral stricture that can be considered superior. Tissue engineering techniques may provide a promising solution for urethral reconstruction, but further investigation is required. Likewise, stem cell therapy may also be an option in the future.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgments

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