

## Etiology and Treatment of Urethral Stricture Disease in Developing Countries: A Single-center Experience of 299 Cases

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### Abstract

We aimed to evaluate the etiology and treatment of urethral stricture disease in China. A total of 299 patients suffering urethral stricture disease (the mean age is  $53.71 \pm 17.63$  years old, ranging from 3 to 94 years old) between January 2008 and December 2014 were analyzed retrospectively. Patient's stricture sites, stricture length, stricture causes and postoperative complications were recorded. The main pathogenesis of patients younger than 45 years old was pelvic fracture, followed by straddle injury and hypospadias. In contrast, the most prevalent pathogenesis of older patients (45 or older) was transurethral resection (TUR), followed by pelvic fracture and straddle injury. The average operating time was  $53.16 \pm 40.65$ min in direct vision internal urethrotomy (DVIU),  $113.69 \pm 38.73$ min in end-to-end urethroplasty, and  $124.67 \pm 79.75$ min in substitution urethroplasty. No severe complication was observed. The frequency of perioperative complications was as follows, postoperative fever in 19.68% (38/193), urine exudation in 0.52% (1/193), and pain in 9.33% (18/193). Our data indicated that the most prevalent pathogenesis of urethral stricture was trauma in a second-tier city-Anhui, China. DVIU was effective and safe treatment for short stricture.

**Keyword:** Urethral Stricture; Etiology; DVIU

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### Introduction

Urethral stricture disease refers to the anterior urethral disease, fibrosis of the urethral mucosa and spongiosum [1]. Urethritis was the most important pathogenesis of stricture before [2]. Due to the effective prevention and treatment of the sexually transmitted diseases, the incidence of post-inflammatory stricture has decreased significantly. In today's developed countries, idiopathic and iatrogenic causes such as prostatectomy, TUR, urethral catheterization, and cystoscopy are important aetiological factors for urethral stricture

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disease. Urethral strictures are common but difficult disease, and its treatment remains controversial. For short stricture, direct vision internal urethrotomy (DVIU) shows a favorable response and nearly half of the patients have been cured. This research aims to investigate the etiology and treatment of urethral stricture disease in Chinese second-tier city.

### Materials and Methods

This study retrospectively analyzed 299 patients suffering urethral stricture disease (the mean age is  $53.71 \pm 17.63$  years old, ranging from 3 to 94 years old) between January 2008 and December 2014 in the First Affiliated Hospital of Anhui Medical University. All patients underwent preoperative retrograde urethra gram to evaluate the stricture site, stricture length and severity. Patients who underwent urological procedures (DVIU, Balloon dilation, End-to-end urethroplast and Substitution urethroplast), were placed with the urethral catheter postoperatively. The etiology of the groups was statistically analyzed by a chi-square test,  $p < 0.05$  considered statistically significant by SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). The data were presented as mean  $\pm$  standard deviation.

### Results

A total of 299 patients successfully completed our study protocol during the 7 years from 2008 to 2014. Their average age was  $53.71 \pm 17.63$  years old, and the age ranged from 3 to 94 years old. 213 (71.24%) patients were equal to or greater than 45 years old (Table 1). The main pathogenesis of patients younger than 45 years was pelvic fracture, followed by straddle injury and hypospadias. In contract, the most prevalent pathogenesis of older patients (45 or older) was TUR, followed by pelvic fracture and straddle injury. Pelvic fracture and straddle injury were significantly common in both the younger group and the older group. Meantime, TUR and prostatectomy were more prevalent in the older group ( $P < 0.0001$ ).

	Age (%)		Total	P
	Younger than 45	45 or older		
TUR	0	61 (28.64)	61 (20.40)	
Cystoscopy	4 (4.65)	11 (5.16)	15 (5.02)	Not significant
Cystostomy	2 (2.33)	2 (0.94)	4 (1.34)	Not significant
Hypospadias	8 (9.30)	0	8 (2.68)	<0.001
Pelvic fracture	26 (30.34)	52 (24.41)	78 (26.87)	Not significant
Penile fracture	4 (4.65)	0	4 (1.34)	0.009
Peritomy	3 (3.49)	2 (0.93)	5 (1.67)	Not significant
Prostatectomy	0	10 (4.69)	10 (3.34)	Not significant
Straddle injury	23 (26.74)	38 (17.84)	61 (20.40)	Not significant
Tumor	0	8 (3.76)	8 (2.68)	Not significant
Unknown	6 (6.98)	10 (4.69)	16 (5.35)	Not significant
Urethral Catheterization	6 (6.98)	2 (0.94)	8 (2.68)	0.014
Urethritis	4 (4.65)	17 (7.98)	21 (7.02)	Not significant
Total	86	213	299	

**Table 1:** The etiology in relation to the age.

TUR: transurethral resection

We identified a total of 14 pathogenesis of urethral stricture, including TUR, prostatectomy, cystoscopy and ureteroscope, cystostomy, urethral catheterization, hypospadias, peritomy, straddle injury, pelvic fracture, penile fracture, tumor, urethritis and unknown reasons. The most common pathogenesis of the 299 patients were follows: pelvic fracture accounting for 26.87%, straddle injury

accounting for 20.40% and TUR accounting for 20.40%. Moreover, the less common pathogenesis includes penile fracture in 1.34%, cystostomy in 1.34% and peritomy in 1.62%. In the anterior urethra, straddle injury was the most prevalent, followed by TUR. In the posterior urethra, pelvic fracture was the most common pathogenesis (Table 2). Overall, trauma (straddle injury, pelvic fracture and penile fracture) were the main pathogenesis of urethral stricture, accounting for 47.8%.

	Penile (%)	Bulbar (%)	Panurethral (%)	Posterior (%)	Total (%)
TUR	13 (30.23)	13 (12.26)	1 (20)	34 (23.45)	61 (20.40)
Prostatectomy	1 (2.32)	2 (1.89)	1 (20)	6 (4.14)	10 (3.34)
Cystoscopy and Ureteroscope	1 (2.32)	9 (8.49)	0	5 (3.45)	15 (5.02)
Cystostomy	0	1 (0.94)	0	3 (2.07)	4 (1.34)
Urethral Catheterization	1 (2.32)	4 (9.30)	0	3 (2.07)	8 (2.68)
Hypospadias	6 (13.95)	0	0	2 (1.38)	8 (2.68)
Peritomy	4 (9.30)	1 (0.94)	0	0	5 (1.62)
Straddle injury	0	59 (55.66)	0	2 (1.38)	61 (20.40)
Pelvic fracture	0	1 (0.94)	0	77 (53.10)	78 (26.87)
Penile fracture	4 (9.30)	0	0	0	4 (1.34)
Tumor	2 (4.65)	2 (1.89)	2 (40)	2 (1.38)	8 (2.68)
Urethritis	7 (16.28)	8 (7.55)	1 (20)	5 (3.45)	21 (7.02)
Unknown	4 (9.30)	6 (5.66)	0	6 (4.14)	16 (5.35)
Total	43	106	5	145	299

**Table 2:** Stricture Site and Etiology of Urethral Stricture Disease.

TUR: transurethral resection

The length of the patients’ urethra stricture ranged from 0.1cm to 6 cm, and the mean stricture length was 1.32 ± 0.91 cm (Table 3). The mean urethra length of patients treated by DVIU was 1.05 ± 0.59 cm shorter than those who underwent end-to-end urethroplast. Endoscopic operations (DVIU, Urethral dilatation and Balloon dilatation) were the most common treatment of urethral stricture, accounting for 79.26% (237/299), which were significantly more than end-to-end urethroplast and substitution urethroplast accounting for 6.35% (19/299). The most common treatment of the open urethral surgery especially for penile urethral stricture was meatotomy.

		DVIU	Balloon dilatation	Urethral dilatation	End-to-end urethroplast	Substitution urethroplast	cystostomy	meatotomy	Other treatments	Total
Stricture site	Penile	19	1	3	0	2	1	14	3	43
	Bulbar	66	14	6	9	0	5	0	6	106
	Posterior	107	16	4	7	1	4	0	6	145
	Panurethral	1	0	0	0	0	2	0	2	5
Stricture Length (cm)	1.05 ± 0.59	2.10 ± 0.77	1.02 ± 0.40	1.79 ± 0.76	3.43 ± 0.51	2.50 ± 2.07	1.08 ± 0.42	-	-	
Operation time (min)	53.16 ± 40.65	45.65 ± 31.74	11.54 ± 2.40	113.69 ± 38.73	124.67 ± 79.75	62.58 ± 42.35	43.79 ± 16.20	-	-	

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Postoperative Hospital stay (d)	4.51 ± 2.20	3.71 ± 2.93	2.00 ± 1.00	7.31 ± 4.29	7.67 ± 6.35	4.75 ± 3.28	4.07 ± 1.38	-	-	
Total	193	31	13	16	3	12	14	17	299	

**Table 3:** Treatment of Urethral Stricture Disease

DVIU: direct vision internal urethrotomy

Among the 243 patients who underwent operations (DVIU, Balloon dilation, end-to-end urethroplast and substitution urethroplast), the time to pull out the indwelling catheter is 2-6 weeks after the operation. The frequency of complications after DVIU was as follows, postoperative fever accounting for 19.68% (38/193), urine exudation accounting for 0.52% (1/193), and pain accounting for 9.33% (18/193). 103 cases after DVIU were followed up for 18–102 months (average 46.93 months). The operation was successfully completed in 93 (90.29%) cases. 80 patients (86%), 9 patients (9.68%) and 4 patients (4.30%) were treated by the first surgery, second operation and third surgery, respectively. Moreover, 66 (64%) patients accepted unobstructed micturition after treatment.

### Discussion

In this research, we found that pelvic fracture and straddle injury were the most common pathogenesis of urethral stricture among younger patients. The main pathogenesis of older patients was TUR, followed by pelvic fracture. Consistent with this research, recent studies [5] have shown that the most prevalent pathogenesis of patients greater than 45 years old was urethral instrumentation in China, but the most prevalent etiology pathogenesis of younger than 45 years old was hypospadias repair and catheterization. Considering our data’s collected from the second-tier city in China, economic condition, medical insurance and other issues explain why trauma counts much. In Western countries, the main pathogenesis of inflammatory strictures is lichen sclerosus. Nicolaas., et al. [3] confirmed that the pathogenesis of younger patients and elder patients varied considerably in developed countries. As for patients younger than 45 years, the most common pathogenesis includes idiopathy, hypospadias surgery and pelvic fracture. Nevertheless, the most common pathogenesis of patients greater than 45 years old was transurethral resection and idiopathy.

The pathogenesis of urethral stricture is significantly different between developing countries and developed countries. Xu., et al. [6] developed a large multi centre evaluation on the pathogenesis and management of male urethral stricture among 4764 men in China from 2005 to 2010. The results showed that the most frequent pathogenesis of urethral strictures was trauma which might be attributed to rapidly growing construction industry and increasing traffic accidents, followed by iatrogenic causes. Similarly, our results indicated that the main pathogenesis of urethral strictures was trauma and iatrogenic causes. According to the existing reports, the incidence of trauma ranges from 9.6 to 36.1% [7-9]. Moreover, many studies of the pathogenesis have been carried out in the West. The most common pathogenesis in developed countries was iatrogenic cause, mainly involving the anterior urethra, especially in the bulbar tract [7]. Nevertheless, according to American Urological Association Guideline, the main pathogenesis of urethral stricture is idiopathic in the current developed countries, followed by iatrogenic [4].

Benign prostatic hyperplasia is a common disease of aged men. Transurethral resection of the prostate (TURP) has been considered as the gold stand and treatment for decades [10]. The incidence of urethral stricture varies from 2% to 4.8% in the literature after the operation of benign prostatic hyperplasia [11-14]. This is mainly related to the size of the instrument and insufficient isolation by the lubricant. Anterior urethral stricture commonly occurs in external orifice stricture, which might be relevant with narrow external orifice, long term compression of instrument and injuries of indwelling catheterization. Posterior urethral stricture may be caused by the intraoperative injury of bladder neck during TUR. The research in this paper indicates that iatrogenic cause is the second ranked etiology. Moreover, we observed that TUR was significantly different among people in different age groups, and it was also the most prevalent pathogenesis for older patients.

The data in this paper suggested that urethral strictures after hypospadias repair mostly occur among patients younger than 45 years old. Similarly, Zhou, *et al.* [5] Reported that urethral strictures after failed hypospadias repair generally locate at the distal penile urethra among Chinese adolescent. Moreover, it has been reported that the incidence of urethral stricture varies from 7% to 12% after hypospadias repair [15-19]. The presence of healthy tissue is vital to reoperative hypospadias [20]. We supposed that appropriate therapy of surgery, skilled surgeon and postoperative management are also key points for success. Boys have no memory of operation before 5 years old and early operation can decrease the cortical scar. Therefore, Jones, *et al.* [21] suggested that operation should be completed before 5 years old if possible. A long-term follow-up study of 275 patients more than 12 years old indicated that folks who underwent hypospadias repair in childhood were highly satisfied with their penile function and appearance [22].

### Treatment

Because of different treatment methods of urethral stricture, patients and physicians must have good knowledge of treatment goals and patients' preferences before the treatment. Generally, intermittent self-dilation is generally assumed as a simple and safe procedure which can avert complex surgical reconstruction but poor quality of life [23]. In short strictures, urethral dilation and direct visual internal urethrotomy have similar long-term treatment effects and the success rates range from 35 to 70% [24]. Moreover, urethral dilation has favorable therapeutic effect in the treatment of strictures less than 1 cm [25]. Dilation or internal urethrotomy may be applied in endoscopic treatment of urethral stricture. However, repeat dilation and internal urethrotomy will decrease the success rate of another endoscopic procedure and increase stricture complexity [26-27]. If self-catheterization was performed for longer than four months, recurrence rates of patients who underwent DVIU would decrease compared with the self-catheterization for less than three months [28].

Urethral dilatation and DVIU are widely used minimal invasive treatment. Open urethroplasty may have better long-term outcomes. Therefore, it is controversial to optimize out treatment for primary and recurrent urethral strictures. Hussmann and Rathbun [29] investigated the outcomes of direct vision urethrotomy for penile urethral strictures (< 1 cm) in the treatment of postoperative urethral stricture of hypospadias. They concluded that open urethral reconstruction should be considered when tubularized graft or flap urethroplasty was performed or urethral stricture recurred because of the poor long-term success and potential risk of urethral stricture progression. However, DVIU is recommended for short urethral stricture after onlay or dorsal plate urethroplasty. Holmium laser and cold knife urethrotomy DVIU have similar success rates and complication rates for bulbar urethral stricture ( $\leq 1.5$  cm) [30]. Mamdouh [31] put forward that open urethral reconstruction was recommended after unsuccessful posterior urethroplasty when urethral stricture is associated with marked fibrosis. In contrast, DVIU is recommended for patients with short or no fibrosis. In our study, we observed that 49 patients had fever, one patient had fluid extravasation, and 24 patients had pain. Furthermore, the recurrence of diseases is the most difficult complication.

Of course, this study has certain limitations. Firstly, it is a single-center study which results in biased results. Secondly, the study lacked sufficient long-term follow-up and flow rate data to estimate the outcomes of DVIU or other treatment, most patients were lost to follow-up. Thus, larger long-term follow-up sample data will be collected in our future study.

### Conclusion

This study indicated that the most common pathogenesis of urethral stricture was trauma. Meanwhile, patients with different ages had different pathogeneses. The most prevalent pathogeneses of elder patients and younger patients were TUR and pelvic fracture. There are various treatment methods of urethral stricture. For patients suffering short urethral stricture, DVIU was a safe treatment with few complications.

### Author contributions

This study indicated that the most common pathogenesis of urethral stricture was trauma. Meanwhile, patients with different ages had different pathogeneses. The most prevalent pathogeneses of elder patients and younger patients were TUR and pelvic fracture. There are various treatment methods of urethral stricture. For patients suffering short urethral stricture, DVIU was a safe treatment with few complications.

### Competing interests

All authors declare no competing interests.

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