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TRAUMA AND RECONSTRUCTIVE UROLOGY

Comparison of cold-knife optical internal urethrotomy and holmium:YAG laser internal urethrotomy in bulbar urethral strictures

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Introduction To compare the results of cold-knife optical internal urethrotomy (OIU) and Holmium:YAG laser internal urethrotomy (HIU) in primary bulbar urethral strictures.

Material and methods A total of 63 patients diagnosed with primary bulbar urethral stricture between August 2014 and September 2015 were assigned to the OIU (n = 29) and HIU (n = 34) groups. The demographic variables, biochemistry panels, and preoperative and postoperative uroflowmetry results including the maximum flow rate (Qmax) and mean flow rate (Qmean) values, retrograde urethrography, and diagnostic flexible urethroscopy findings were recorded prospectively. Demographic features and preoperative values were not statistically different between groups ($p > 0.05$). Mean surgical times were 18.4 ±2.3 min for OIU and 21.9 ±3.8 min for HIU groups, which was statistically significant ($p < 0.05$). There was no significant difference in complication rates in both groups ($p = 0.618$).

Results Postoperative Qmax values were increased in both groups even though postoperative Qmax values were not significantly different between the two groups in the short- and long-term results at 3, 6, and 12 months ($p > 0.05$). There was no recurrence in the first 3 months in either group. The urethral stricture recurrence rate up to month 12 was not statistically significant for the OIU group (n = 6, 20.7%) as compared to the HIU group (n = 11, 32.4%; $p = 0.299$).
At follow-up, the SFR and IFR was 96% and 88% at 3-months, and 82% and 71% at 12-months, respectively ($p < 0.001$). While almost three-quarters of patients were stone and infection free at 12-months, the majority of those with stones recurrence also had recurrence of their UTI.

Conclusions HIU is an alternative method to OIU, and it has similar success rates in the treatment of short segment bulbar urethral strictures.

Key Words: urethral stricture ‹› holmium laser ‹› male urethra

INTRODUCTION

Urethral strictures are still among the most common reason for urology clinic admissions. In addition to their negative impact on quality of life (QoL), urethral strictures are also associated with further financial burden related to urinary tract infections, bladder stones, fistulas, sepsis and possibly renal insufficiency [1]. Minimally invasive surgical approaches are utilized efficiently and safely in the treatment of various disorders in urological practice. However, treatment options for urethral strictures have been limited both in number and level of success, as judged by the high recurrence rates. Treatment options for urethral strictures include self-catheterization, bougie dilation, balloon dilation, urethral stent placement, cold-knife optical internal urethrotomy (OIU), laser urethrotomy methods and open

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reconstructive urethroplasty, which is generally reserved for cases which did not benefit from endoscopic approaches [2]. OIU, described by Sachse in 1974, is still the preferred method due to the practical and minimally invasive nature of the procedure [3]. One of the alternative approaches is the correction of the stricture using laser energy, which was first used in urology in 1984 and established as a common method in internal urethrotomy since the nineties [4]. In the past, several prospective randomized clinical trials comparing OIU with Holmium:YAG laser internal urethrotomy (HIU) have been reported [4–9]. The aim of this prospective randomized study is to compare pre- and post-operative uroflowmetry results and operation characteristics of OIU and HIU in bulbar urethral strictures.

MATERIAL AND METHODS

All patients diagnosed with primary bulbar stricture who underwent internal urethrotomy (IU) in our clinic between August 2014 and September 2015 were enrolled in the study. The local review board approved the study protocol. Patients with recurrent urethral strictures, a history of IU, abnormal ultrasound findings in the bladder (e.g. bladder tumor / calculi), suprapubic cystostomy, non-bulbar strictures and those with a stricture segment longer than 2 cm were excluded from the study. Urethral stricture was diagnosed with history, uroflowmetry, ultrasound, retrograde urethrography and diagnostic flexible urethroscopy performed under local anesthesia. Complete blood count, biochemistry panel and urinalysis was evaluated in all patients. Coagulation times were corrected in the patients with abnormal coagulation test results and urinary tract infections were duly treated with antibiotics and sterile urine was attained prior to the operation. The patients were randomly assigned to one of the two treatment groups, OIU (group 1) and HIU (group 2). All patients were evaluated with ultrasound, uroflowmetry, international prostate symptom score (IPSS), and QoL results preoperatively and at 3rd, 6th and 12th postoperative months. The procedure was accepted as successful when the patient did not complain of any persistent subjective and objective symptoms and the maximum flow rate (Qmax) was >12 ml/s. Diagnostic flexible urethroscopy was performed in patients with persistent subjective and objective voiding symptoms and/or with Qmax lower than 12 ml/s. If urethral strictures were detected by flexible cystoscopy, these were accepted as recurrent strictures.

All operations were performed in the lithotomy position. Prophylactic intravenous cefuroxime axetil 750 mg was administered with the induction of anesthesia. The guidewire (Boston Scientific, USA) was advanced to the urethra through the stricture with the help of a 7.5 French (Fr) Wolf ureterorenoscope (Richard Wolf, Knittlingen, Germany) in all patients before the intervention (Figures 1, 2). OIU was performed with a straight type urethrotomy knife inserted through a 21 Charrière Storz urethrotome (Karl Storz, Germany). Laser urethrotomy was performed with a Holmium:YAG laser litho fiber (LISA/

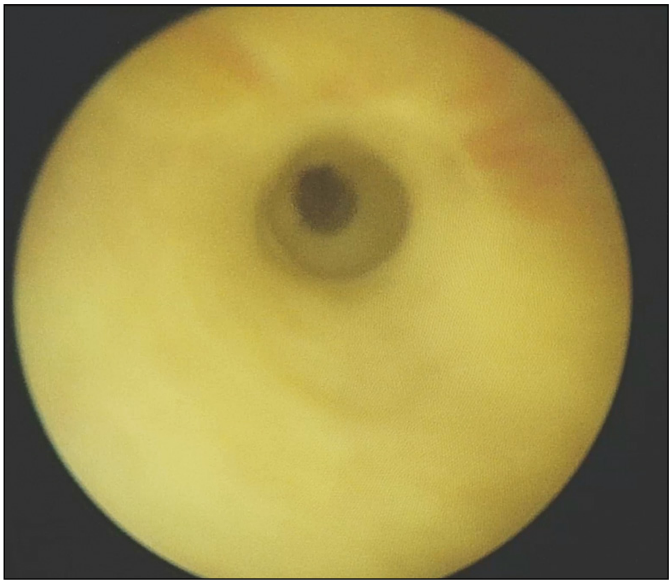

Figure 1. *Endoscopic appearance of short segment bulbar urethral stricture.*

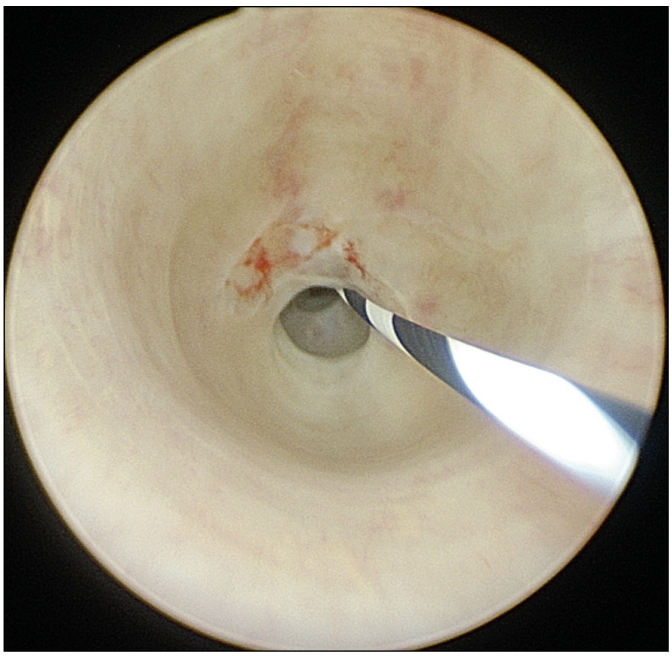

Figure 2. *Appearance of guidewire and urethral stricture segment.*

Sphinx 30) with the frequency set between 4–20 Hz, power set at 30 W and pulse energy of 0.5–4.0 J. Both interventions were aimed at the 12 o'clock position (Figures 3, 4). An 18 Fr foley urethral catheter was placed over the guidewire postoperatively and removed 3 days later. In patients with suspicion of stricture recurrence, a16 Fr flexible cystoscopy was performed (Karl Storz, Germany).

A total of 63 patients aged between 26 and 69 years (mean age ± standard deviation: 55.1 ±9.1 years) were included in the study. There was no significant difference between the mean ages of the treatment groups, which were 54.8 ±-9.5 years for OIU (n = 29) and 55.3 ±8.9 years for HIU (n = 34) ($p = 0.895$). Of the 63 patients, 59 (93.7%) were married, with 4 single patients in each treatment group. Urethral stricture was iatrogenic in 42 (66.7%) patients, secondary to trauma in 12 (19%), secondary to urethritis in 6 (9.5%), and idiopathic in 3 (4.8%) patients. There were no significant differences between the mean age, marital status and preoperative Qmax values between the two groups ($p < 0.05$ for all comparisons). The demographic features and etiology of the strictures are present in Table 1.

SPSS 22.0 program (SPSS Inc.; Chicago, IL, USA) was used in the analyzes. The distribution of the variables was measured by the Kolmogorov-Simirnov test. Mann-Whitney U test was used in the analysis of quantitative independent data. Chi-square test was used for the analysis of independent data and Fischer test was used when Chi-square test conditions were not met. Statistical significance was set at a p value of <0.05.

RESULTS

The OIU group and HIU group did not difference significantly ($p > 0.05$) in Qmax values for preop, postop 3 months, postop 6 months, or postop 12 months. Flexible urethroscopy was performed in 25 patients with objective voiding symptoms and/or Qmax<12 mL/s. Flexible urethroscopy detected recurrence in 6 (20.7%) patients in OIU group and 11 (32.4%) patients in HIU group ($p = 0.299$) who were symptomatic and had declining Qmax values at the 12th postoperative month (Table 2).

The mean operative time in HIU group, 21.9 ±3.8 min, was significantly longer as compared to OIU group (mean operative time 18.4 ±2.3 min) ($p < 0.05$) (Figure 5). Three patients in the OIU group experienced bleeding after the urethrotomy and one patient in the HIU group experienced urine extravasation postoperatively. All complications were managed conservatively.

Preoperative overall mean Qmax was 6.5 ±0.7 mL/sec, with no significant difference between the treatment groups (6.5 ±0.7 mL/sec for OIU group and 6.5 ±0.7 mL/sec for HIU group) ($p = 0.874$).

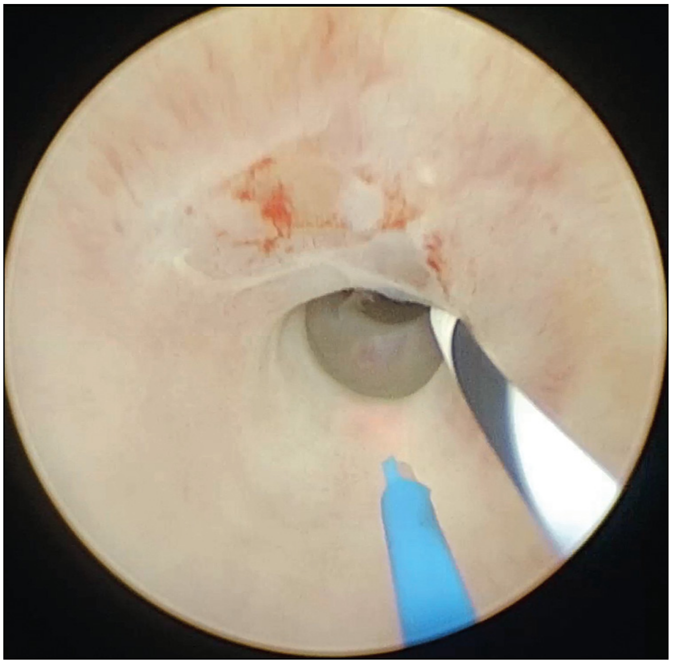

Figure 3. *Appearance of laser urethrotomy with a Holmium:YAG laser litho fiber at the 12 o'clock position.*

Figure 4. *Postoperative appearance of urethral lumen.*

DISCUSSION

Although blunt perineal trauma, urethral instrumentation, lichen sclerosis of atrophicus, sexually transmitted diseases and a history of urethral infec-

Table 1. *Patient's characteristics*

		Min–Max	Median	Mean ±s.d./n-%	
Age		26–69	57	55.1	± 9.1
Marital Status	Married			4	6.3%
	Single			59	93.7%
Etiology	Iatrogenic			42	66.7%
	Traumatic			12	19.0%
	Urethritis			6	9.5%
	Idiopathic			3	4.8%
Operation Time		15–30	19	20.3	± 3.6
Complication				4	6.3%
Qmax ml/sn					
Preoperative		5.1–7.9	6.4	6.5	± 0.7
3rd month		14.5–19.1	17.3	17.0	± 1.4
6th month		10.7–17.9	15.7	15.0	± 1.9
12nd month		8.9–15.9	13.9	13.3	± 2.1
Recurrence					
3rd month				0	0.0%
6th month				9	14.3%
12nd month				17	27.0%

tions are listed among the underlying reasons for urethral strictures, most cases observed in clinical practice are iatrogenic [10]. First detectable histological changes are squamous metaplasia of the pseudostratified epithelium into columnar cells, resulting in loss of fluid isolation and increase in permeability which leads to urine extravasation and fibrosis [11]. Major factors to be considered in treatment selection are etiology, stricture length, depth of scar and localization [12, 13]. The etiology of the patients in our study group was consistent with the previous reports, with the majority of the patients classified as iatrogenic (n= 42, 66.7%), while 12 patients (19%) had a stricture secondary to trauma, 6 patients (9.5%) related to a history of urethritis and 3 patients (4.8%) had an idiopathic cause. In addition, all strictures were localization in the bulbar urethra and had a short-segment bulbar urethral stricture (less than 2 cm).

Various alternative approaches have been proposed for urethral stricture treatment over the years and there is no consensus on the most successful method yet. Along with advances in laser technology, laser urethrotomy is widely used. Most common

Table 2. *Comparison of the preoperative and postoperative parameters*

		Group I			Group II			p	
		Mean ±s.d./n-%		Median	Mean ±s.d./n-%		Median		
Age		54.8	± 9.5	58.0	55.3	± 8.9	57.0	0.895	m
Marital Status	Married	2	6.9%		2	5.9%		0.869	χ^2
	Single	27	93.1%		32	94.1%			
Etiology	Iatrogenic	21	72.4%		21	61.8%			
	Traumatic	5	17.2%		7	20.6%			
	Urethritis	2	6.9%		4	11.8%			
	Idiopatic	1	3.4%		2	5.9%			
Operation Time		18.4	± 2.3	18.0	21.9	± 3.8	20.0	0.000	m
Complication		1	3.4%		3	8.8%		0.618	χ^2
Maximum Flow Rate mL/s									
Preoperative		6.5	± 0.7	6.4	6.5	± 0.7	6.4	0.874	m
3rd month		17.0	± 1.4	17.2	16.9	± 1.4	17.4	0.719	m
6th month		15.3	± 1.7	15.4	14.7	± 2.0	15.7	0.232	m
12nd month		13.7	± 2.0	14.1	13.0	± 2.1	13.8	0.159	m
Recurrence									
3rd month		0	0.0%		0	0.0%		–	χ^2
6th month		3	10.3%		6	17.6%		0.409	χ^2
12nd month		6	20.7%		11	32.4%		0.299	χ^2

[m]Mann-whitney u test / χ^2 Chi-square test (Fischer test)

laser types used for urethral stricture treatment are neodymium-doped yttrium aluminium garnet (Nd: YAG), argon, potassium titanyl phosphate (KTP), thilium and Holmium:YAG [14, 15]. In this study, we used; a Holmium:YAG laser with the frequency set between 4–20 Hz, power set at 30 W and pulse energy of 0.5–4.0 J.

OIU is a more practical and economical approach as compared to HIU regarding high recurrence rates and bleeding rates [6]. One of the advantages of laser urethrotomy over OIU is the scar tissue that remains after the incision which is very useful in haemostasis. Laser approach also provides a better visualization of the lesion but unfortunately, this method is not widely available due to relatively higher costs [16, 17].

Previous studies have reported contradicting results regarding the duration of the procedure for OIU and HIU. While Atak et al. [5] reported a significantly shorter mean operative time for HIU (16.4 ±8.04 min) compared to OIU (23.8 ±5.47 min), performing the OIU (7.44 min) took significantly shorter than performing the HIU (19.8 min) in the report by Jain et al. [8]. In our study, similar to the Jain et al. study, the duration of the operation was statistically longer in the HIU group than in the OIU group. The difference between these results may be related to technical difficulty and lack of experience for laser treatment.

The most widely accepted method for minimizing bleeding in IU is incising the scar tissue at the 12 o'clock position between the corpus cavernosum or wherever the scar tissue is more extensive. Kamp et al. compared the Holmium:YAG laser incisions at the 12 and 6 o'clock positions and could not detect a difference between the complication or bleeding rates between the groups [7]. In a series of 190 patients treated with HIU, surgery related complications were seen in 23 patients but it was noted that nearly half of the complications occurred in the first 50 procedures and all were resolved with conservative measures [6]. In another study, Jhanwar at al. reported a total complication rate of 14.6%. Insemblance to our study, they reported fever and urinary tract infection [9]. We performed all of the incisions at the 12 o'clock position and did not have major complications or cavernous body injury. Bleeding was detected in 3 patients in the OIU group and treated by perineal compression. Bleeding was not encountered in the HIU group. This condition may be explained by the fact that the Holmium:YAG laser can provide coagulation.

In a randomized clinical study reported by Atak et al., success rates at 12 months for HIU and OIU were 81% and 53%, respectively [5]. A meta-analysis of 44 articles comprising of 3230 patients reported the success rates in urethral strictures as 74.9% for laser and 68.5% for cold-knife urethrotomy [18]. In our study, the mean success rates for groups OIU and HIU were 79.3% and 67.6%, respectively. We did not detect any differences between the success rates in both groups at all follow ups. Our results can be accepted like a similar study which compared laser versus cold-knife urethrotomy under local anesthesia [9].

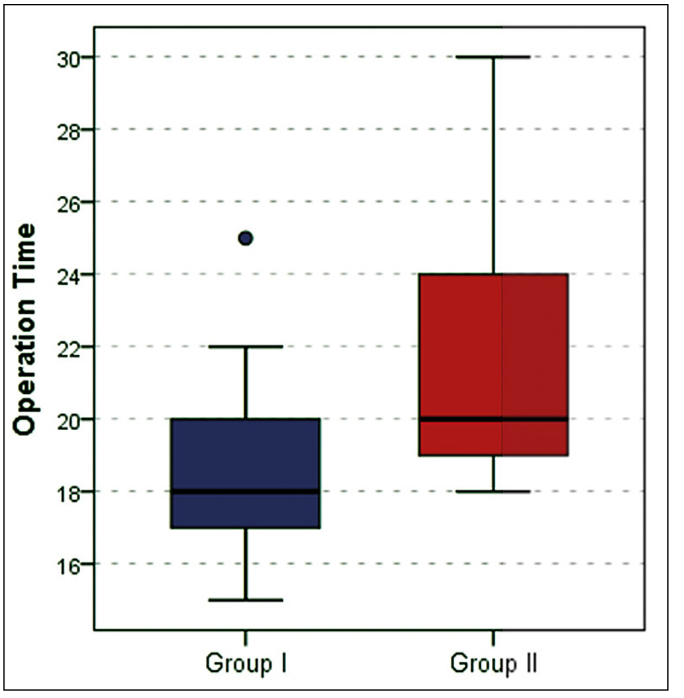

Figure 5. *Operation time of cold-knife optical internal urethrotomy and Holmium:YAG laser internal urethrotomy in both groups (p <0.05 and p <0.05, respectively).*

Repetitive endoscopic interventions in bulbar urethral strictures are related to increases in stricture segment length and complexity and delay in urethroplasty operations [19]. Endoscopic treatment of urethral strictures are associated with high recurrence rates, ranging between 30% and 80% [20], which led to numerous studies comparing the efficacy of various treatment approaches. Sachse et al. reported a recurrence rate of 23% in their case series [21]. Comparable recurrence rates are still reported up to this day in urethral stricture treatment. Pansadoro and Emiliozzi reported a recurrence rate of 58% following OIU in bulbar urethral strictures [22]. Recurrences usually occur within 3–12 months, as Naude and Heyns emphasize [23]. In another study, Heyns et al. reported that recurrences within the first 3 months were a poor prognostic factor [24]. In our study, there was no recurrence in the third month in both groups. When recurrence rates at 6 and 12 months were considered, recurrence was detected in 18 patients in both groups.

Another type of energy for IU is plasmakinetic. There are several studies in the literature about the treatment of urethral strictures with plasma kinetics [25, 26]. Until now, there is no clear criterion to assess success or failure after IU. Cecen at al. [25] and Ozcan at al. [26] deemed the intervention successful in their studies when the patient did not complain of any voiding difficulty and the Qmax was >12 mL/s. Other studies were accepted as successful if the patient did not report any voiding difficulty, and the Qmax was greater than 10 mL/sec [5, 9]. Tom at al. have reported that sensitivity of both Qmax and IPSS to detecting stricture recurrence is low. There is a need for tools with high sensitivity and specificity for urethral stricture recurrence follow-up [27, 28]. In this study, the procedure was accepted as successful when the patient did not complain of any persistent subjective and objective symptoms and the Qmax was >12 mL/s.

This study has several limitations. First, only short segment bulbar urethral strictures can be considered. Other limitations are that operations were performed by different surgeons and the lack of a questionnaire for assessment of urinary symptoms. High recurrence rates of urethral strictures following IU have incited the proposal of novel approaches for the treatment of this condition. Results with HIU have been encouraging so far but more improved approaches either with Holmium:YAG or other novel methods will be necessary to achieve higher success and lower recurrence rates.

CONCLUSIONS

Urethral strictures are associated with a high burden on the QoL and healthcare expenditures similar to other chronic disorders. Although various methods have been proposed, none of them were able to prevent recurrences definitively. Lack of a significant difference between recurrence rates and complication rates of HIU and OIU suggests that both are safe and effective treatment methods in bulbar urethral strictures. Larger studies encompassing cases with different characteristics may help to identify the variables that may favor or discourage the use of either method in future studies.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

Informed consent was obtained from all individual participants included in the study.

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