

Original Article

Comparison of holmium laser combined ureteroscopy and cold knife urethrotomy in treatment of simple urethral stricture: a 5 year follow-up study

Jiangang Chen, Lin Qian, Bing Zheng, Ming Lu

Department of Urology, The First People's Hospital of Nantong, Nantong, China

Received May 21, 2018; Accepted August 1, 2018; Epub December 15, 2018; Published December 30, 2018

Abstract: Objective: The objective of this study was to compare long-term efficacy and recurrence of holmium laser method and cold knife urethrotomy in treatment of simple urethral stricture. Methods: This prospective study included a total of 46 male adult patients with simple urethral stricture who went to our hospital during January 2010 to December 2011. All patients were randomly divided into a holmium laser group with 24 cases and a cold knife group with 22 cases. Etiology of strictures, stricture location, the maximum flow rate (Q_{max}), International Prostate Symptom Score (IPSS), Quality of Life Index (QoL), surgery time, intraoperative bleeding, hospitalization duration, and complications were recorded. Q_{max} , IPSS and QoL scores, and recurrence were measured for both short- and long-term efficacy, at 1 month, 3 months, 6 months, and for long-term at each year during the 5 year follow-up. Results: The results show that the surgery time of holmium laser group was significantly longer than the cold knife group. However intraoperative bleeding was significantly lower in the holmium laser group compared with the cold knife group. The Q_{max} values were significantly higher in holmium laser group compared with the cold knife group within 1 year follow-up. However after 2 years no significant difference was observed. In short-term follow-up, IPSS and QoL scores, and recurrent conditions seemed to be better in the holmium laser group, but no significant difference was shown in long-term follow-up. Conclusion: Holmium laser treatment had better short-term efficacy and lower recurrence rates than cold knife technique, but their long-term efficacy and recurrence conditions were similar.

Keywords: Holmium laser, cold knife urethrotomy, simple urethral stricture, long-term follow-up

Introduction

Urethral stricture, a common urinary tract disorder, is a disease with a long history, reported since ancient times [1, 2]. Among the causes of urethral stricture, the most common cause is trauma and secondary to surgical instrumentation, such as urethral catheterization, transurethral resection, and surgery for hypospadias [3, 4]. Other cases include idiopathic urethral stricture and failed hypospadias repair [5, 6]. It is estimated that about 0.6% people suffered from urethral stricture in developed countries and in developing countries the prevalence may be higher [7].

The main treatment methods for urethral stricture are surgery, including endoscopic procedures to open surgical interventions, like urethral dilation and visual internal urethrotomy, which can transiently improve urinary flow [8].

Among the methods, internal urethrotomy, and endoscopic urethrotomy are widely used, using a cold-knife technique to incise urethral strictures, often leading to unsatisfactory results with recurrent rates ranging from 35% to 60% [9]. In recent decades, the development of holmium: yttrium-aluminum-garnet laser (Ho: YAG) give a seemingly better way for treatment of urethral stricture [10]. It has been reported to be minimally invasive, as well as more effective and safe than traditional surgeries in some studies [11]. However, to the best of our knowledge, long-term efficacy and recurrence conditions for holmium laser treatments have been rarely reported.

In the present study, we aimed to compare the efficacy and safety, as well as long-term conditions between holmium laser combined ureteroscopy and cold knife urethrotomy in treatment of simple urethral stricture. This study

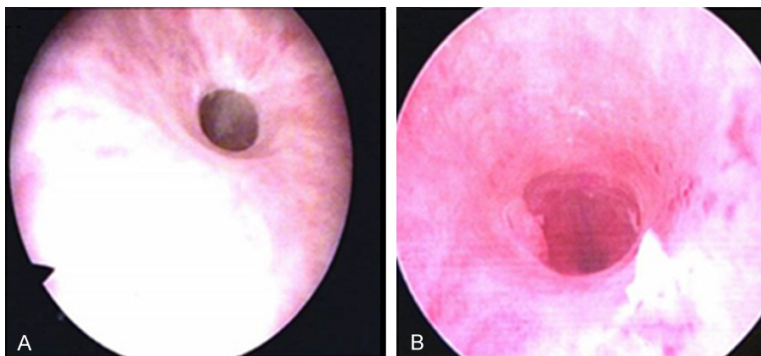


Figure 1. Images (A) before and (B) after laser urethrotomy.

may give more clinical evidence toward efficacy, safety, and long-term prognosis for holmium laser treatment in urethral stricture.

Methods and materials

Patients and treatment

This prospective study included a total of 46 male adult patients (age from 18 to 59) with simple urethral stricture who went to our hospital during January 2010 to December 2011. All patients were diagnosed as simple urethral stricture by symptom scores, clinical history, uroflowmetry, and retrograde urethrography. All patients were primary diagnosed. Following patients were excluded: patients with recurrent urethral stricture, patients with diverticulum, multiple level urethral strictures, patients who had a fractured pelvis with urethral disruption. The present study was approved by the Ethic Committee of First People's Hospital of Nantong City. Informed consent was obtained from all patients.

All patients were randomly divided into 2 groups with different surgery strategies using computer random grouping. A total of 24 cases were in the holmium laser group and 22 cases were in the old knife group. For surgery treatment methods, all patients were treated with a third-generation cephalosporin antibiotic 2 days before surgery. For the holmium laser group, briefly, after general anesthesia all patients were placed in the bladder lithotomy position. A F9.8 Wolf ureteroscopy (WolfTM, Knittlingen, Germany) was initially inserted to the distal end of urethral stricture under continuous low pressure irrigation of normal saline. Then a guide wire was inserted through the urethral orifice to the urinary bladder. Then a 400 μ m laser fiber (VersaPulse® PowerSuite™ 100 W, Lumenis

Co. USA) was used to incise the scar tissues with setting of 1.0~2.0 J, frequency 10~20 Hz, at positions of 12, 9, and 3-o'clock. For patients with small narrow ring and ureteroscopy could not pass, the guide wire was first inserted into the urinary bladder and F8 ~ F16 renal fascia dilator was used to expand the narrow ring.

For the cold knife group, after general anesthesia at the bladder lithotomy position, F9.8 Wolf ureteroscopy was initially inserted to the distal end of urethral stricture under continuous low pressure irrigation of normal saline. Then a F4 ureteral catheter was inserted, and the scar tissues were radially incised at positions of 12, 4 and 8-o'clock using cold knife. The incision was gradually made until to the bladder under ureteroscopy and increasing the cutting depth was made from the distal end to the proximal end until the narrow ring at the junction of scar tissues and normal tissues was completely released.

After surgery, patients were maintained on intravenous broad-spectrum antibiotics for one week. A F20 double or triple-lumen urethral catheter could be indwelled according to the stricture degree, which remained for 4-6 postoperative weeks and was then removed. All patients underwent routine bladder continuous irrigation for 4-6 postoperative weeks.

Data collection and evaluation criterion

Etiology of strictures was collected before surgery. Stricture location and strictures length were identified during direct visualization with optical urethrotome. Uroflowmetry, the maximum flow rate (Q_{max}), International Prostate Symptom Score (IPSS) and Quality of Life Index (QoL) were measured and recorded before and after surgery. Surgery time, intraoperative bleeding, hospitalization duration, and complications were also recorded. Q_{max} , IPSS and QoL scores, and recurrence were measured for both short- and long-term efficacy, short term at 1 month, 3 months, 6 months, long-term at each year during the 5 year follow-up. Successful surgery was defined as $Q_{max} \geq 15$ mL and IPSS ≤ 12 , and micturition distance without requiring urethral dilation within 3 months after surgery.

Long-term efficacy of holmium laser in urethral

Table 1. Basic clinical information for all patients

Variable	Holmium laser, n=24	Cold knife, n=22
Mean age, years	42.8±8.1 (18~56)	44.6±9.0 (21~59)
Etiology of strictures, n (%)		
Traumatic	12 (50.0)	11 (50.0)
Inflammatory	3 (12.5)	2 (9.1)
Iatrogenic		
Transurethral resection of the bladder	3 (12.5)	2 (9.1)
Electrosurgical resection of the prostate	2 (8.3)	2 (9.1)
Improper irrigation of the bladder	1 (4.2)	2 (9.1)
Cystoscopy injury	2 (8.3)	1 (4.5)
Unknown cause	1 (4.2)	2 (9.1)
Strictures length, cm (range)	1.5±0.6 (0.2~2.0)	1.6±0.5 (0.3~2.1)
Stricture location		
Anterior urethra	15 (62.5)	13 (59.1)
Posterior urethra	9 (37.5)	9 (40.9)
Q _{max} , mL/s	5.8±1.6 (2~10)	6.0±1.8 (2~11)
IPSS	23.5±2.6 (18~30)	24.0±2.8 (17~30)
QoL	5.0±1.0 (4~6)	4.9±0.8 (4~6)

Recurrence was defined as Q_{max} <15 mL and PVR >12, and urethral stricture confirmed by urethrography.

Statistical analysis

The measurement data are expressed by mean ± SD. Chi square test was used to compare the rates and Student *t*-test was used for comparison between two groups of continuous data. It was considered to be statistically significant when *P*-value was less than 0.05. All calculations were made using SPSS 22.0.

Results

Basic clinical characteristics for all patients

Clinical characteristics before and after surgery were analyzed (**Figure 1**). As shown in **Table 1**, among all patients, 19 cases were in the holmium laser group, with a mean age of 42.8±8.1 years, and 16 cases in the cold knife group with mean age of 44.6±9.0 years. Among all patients, 5 cases (3 in holmium laser group and 2 in cold knife group) were loss to follow-up during the long-term follow-up duration. In all cases, etiology of strictures was traumatic 23 (50.0%) cases; inflammatory 5 (10.9%) cases; iatrogenic 15 (32.6%) cases including Transurethral resection of the bladder 5 (10.9%) cases, electrosurgical resection of the prostate 4 (8.7%) cases, improper irrigation of the bladder

3 (6.5%) cases and cystoscopy injury 3 (6.5%) cases; and unknown cause 3 (6.5%) cases. Before surgery, the strictures length was 1.5±0.6 cm (0.2~2.0 cm) for the holmium laser group and 1.6±0.5 cm (0.3~2.1 cm) for the cold knife group; Q_{max} was 5.8±1.6 mL/s (2~10 mL/s) for the holmium laser group and 6.0±1.8 mL/s (2~11 mL/s) for the cold knife group; mean IPSS was 23.5±2.6 (18~30) for holmium laser group and 24.0±2.8 (17~30) for the cold knife group; mean QoL was 5.0±1.0 (4~6) for the holmium

laser group and 4.9±0.8 (4~6) for the cold knife group. No significant difference was found in the above characteristics.

Comparison of clinical outcomes and short term complications for all patients

For comparison of clinical outcomes and short term complications for different patients, surgery time, intraoperative bleeding, hospitalization duration, and complications during hospitalization were compared (**Table 2**). Results showed that the surgery time of the holmium laser group was significantly longer than the cold knife group, *P*<0.05. However intraoperative bleeding was significantly lower in the holmium laser group compared with the cold knife group, *P*<0.05, indicating smaller surgery injury for the holmium laser method. Hospitalization duration and complications during hospitalization showed no significant difference.

Comparison of short- and long-term postoperative efficacy and recurrence

At last we compared short- and long-term postoperative efficacy and recurrence for different surgery strategies. As shown in **Table 3**, the Q_{max} values were significantly higher in the holmium laser group compared with the cold knife group within 1 year follow-up, *P*<0.05. However after 2 years no significant difference was

Long-term efficacy of holmium laser in urethral

Table 2. Comparison of clinical outcomes and short term complications for all patients

	Holmium laser, n=24	Cold knife, n=22	P value
Surgery time, min	36.5±9.7	21.4±5.6	<0.05
Intraoperative bleeding, mL	18.7±5.4	30.2±7.8	<0.05
Hospitalization duration, d	3.6±0.8	3.7±1.0	0.647
Complications during hospitalization, n (%)			0.512
Extravasation of urine	1 (4.2)	2 (9.1)	
Uracratia	1 (4.2)	1 (4.5)	

Table 3. Comparison of short- and long-term postoperative efficacy and recurrence

	1 mon	3 mon	6 mon	1 y	2 y	3 y	4 y	5 y
Q_{max} , mL/s								
Holmium laser	17.2±4.1*	21.6±5.3*	20.8±4.2*	20.5±4.8*	18.7±5.9	19.3±6.0	19.8±5.4	19.5±5.7
Cold knife	15.3±3.8	18.2±5.1	17.8±4.0	17.3±4.1	18.9±5.4	19.0±5.0	19.9±5.1	19.6±5.4
IPSS								
Holmium laser	7.6±2.1*	5.9±1.8*	4.8±1.3*	5.1±1.8	5.3±1.6	5.3±1.5	5.1±1.7	5.1±1.5
Cold knife	9.2±2.9	7.0±2.0	6.1±1.7	5.5±1.9	5.1±1.7	4.9±1.1	5.0±1.8	5.1±1.3
QoL								
Holmium laser	2.0±0.4*	1.6±0.3	1.2±0.3	1.3±0.4	1.2±0.2	1.2±0.3	1.1±0.3	1.2±0.3
Cold knife	2.6±0.5	1.8±0.4	1.5±0.3	1.4±0.4	1.2±0.3	1.3±0.4	1.2±0.3	1.1±0.2
Recurrence, n (%)#								
Holmium laser	0 (0)*	0 (0)*	1 (4.2)*	3 (12.5)*	18 (75.0)	19 (79.2)	21 (87.5)	21 (87.5)
Cold knife	3 (13.6)	8 (36.4)	14 (63.6)	18 (81.8)	19 (86.3)	20 (90.9)	20 (90.9)	20 (90.9)

*P<0.05, compared with the Cold knife group; #All recurrence cases within the duration.

observed. Similar results were also found in IPSS and QoL scores, as well as recurrence. In short-term follow-up, IPSS and QoL scores, and recurrent conditions seemed to be better in the holmium laser group, but no significant difference was shown in long-term follow-up. These results suggested that the holmium laser method might give better short-term efficacy, but didn't improve the long-term efficacy and recurrence.

Discussion

Urethral stricture is a prevalent condition which can cause obstructive urinary symptoms. If not treated properly, urethral strictures can lead to obstructive uropathy, urinary tract infection and renal disease and finally threatening the patient's quality of life [12]. Currently, the main management of urethral strictures includes cold knife technique, electrical resection and endourethrotomy with the holmium laser [13]. It is considered that laser incision can efficiently remove scar tissues through vaporization with minimal thermal damage, thus it is more effective and safer compared with other ablation methods, such as cold-knife and electrical

resection. However despite development of treatment strategies, recurrence remains a big problem.

Several studies have already reported the efficacy and safety for the holmium laser method in treatment of urethral stricture. In a retrospective study, Liu et al. showed that holmium laser endourethrotomy was effective in a 6 months follow-up for the treatment of long-segment urethral strictures with significantly increased Q_{max} [14]. Shoukry et al. reported that holmium laser was also effective for urethral strictures in pediatrics with 37.9% recurrence rate after 6 months [15].

Despite these studies, few focused on comparison of long-term efficacy and recurrence for holmium laser and cold knife methods. In the present study, holmium laser treatment was shown for the first time to have better short-term efficacy and lower recurrence rates than the cold knife technique, but long-term efficacy and recurrence conditions were similar. Some related studies have been reported. Atak et al. studied difference between YAG laser urethrotomy and cold-knife technique, and found that

YAG laser could provide shorter operative time and lower recurrence rate compared with cold knife [16]. However in our study, operation time of holmium laser treatment was longer, but intraoperative bleeding was significantly lower, indicating smaller surgery injury for holmium laser method. The difference might be due to different study cases and operators. In a meta-analysis for comparison of holmium laser and cold knife, Torres et al. showed that laser urethrotomy has a lower recurrence rate at 6 and 12 months compared to cold knife urethrotomy [17]. However we are the first to show that the 2 methods' lower recurrence was similar.

In conclusion, a prospective study was performed to compare long-term efficacy and recurrence of the holmium laser method and cold knife urethrotomy in treatment of simple urethral stricture. Results show that holmium laser treatment has better short-term efficacy and lower recurrence rates than cold knife technique, but long-term efficacy and recurrence conditions were similar. This study may give more clinical evidence to efficacy, safety, and long-term prognosis for holmium laser treatment in urethral stricture.

Disclosure of conflict of interest

None.

Address correspondence to: Ming Lu, Department of Urology, The First People's Hospital of Nantong, 6 Beierxiang North Road, Nantong 226001, China. Tel: 86-513-85061251; E-mail: storz888@aliyun.com

References

- [1] Wessells H, Angermeier KW, Elliott S, Gonzalez CM, Kirkby E, Kodama R, Peterson AC, Reston J, Rourke K, Stoffel JT, Vanni AJ, Voelzke BB, Zhao L, Santucci RA. Male urethral stricture: AUA guideline. *J Urol* 2016; 197: 182.
- [2] Brandes SB, Morey AF. *Advanced male urethral and genital reconstructive surgery*: Springer New York; 2014.
- [3] Wessells H, Angermeier KW, Elliott S, Gonzalez CM, Kodama R, Peterson AC, Reston J, Rourke K, Stoffel JT, Vanni AJ, Voelzke BB, Zhao L, Santucci RA. Male urethral stricture: American urological association guideline. *J Urol* 2017; 197: 182.
- [4] Zhou SK, Zhang J, Sa YL, Jin SB, Xu YM, Fu Q, Lazzeri M. Etiology and management of male iatrogenic urethral stricture: retrospective analysis of 172 cases in a single medical center. *Urol Int* 2016; 97: 386-391.
- [5] Lazzeri M, Sansalone S, Guazzoni G, Barbagli G. Incidence, causes, and complications of urethral stricture disease. *European Urology Supplements* 2016; 15.
- [6] Kojovic V, Majstorovic M, Bizic M, Ducic S, Korac G, Djordjevic M. S127 hanged ventral buccal mucosa graft in the treatment of urethral stricture after failed hypospadias repair. *European Urology Supplements* 2009; 8: 649.
- [7] Santucci RA, Joyce GF, Wise M. Male urethral stricture disease. *J Urol* 2007; 177: 1667-74.
- [8] Zhao LC. Management of urethral strictures. *Urol Clin North Am* 2017; 44.
- [9] Kamp S, Knoll T, Osman MM, Köhrmann KU, Michel MS, Alken P. Low-power holmium: YAG laser urethrotomy for treatment of urethral strictures: functional outcome and quality of life. *J Endourol* 2006; 20: 38-41.
- [10] Hu WF, Li CL, Zhang HP, Li TT, Zeng XY. An experimental model of urethral stricture in rabbits using holmium laser under urethroscopic direct visualization. *Urol Int* 2014; 93: 108-12.
- [11] Dutkiewicz SA, Mariusz W. Comparison of treatment results between holmium laser endourethrotomy and optical internal urethrotomy for urethral stricture. *Int Urol Nephrol* 2012; 44: 717-24.
- [12] Mundy AR, Andrich DE. Urethral strictures. *BJU Int* 2011; 107: 6-26.
- [13] Hampson LA, Mcaninch JW, Breyer BN. Male urethral strictures and their management. *Nat Rev Urol* 2014; 11: 43-50.
- [14] Liu Q, Ma W, Li X, Zhang W, Cao W, Zhou Q, Duan J. Holmium laser endourethrotomy for the treatment of long-segment urethral strictures: a retrospective study of 190 patients. *Urol J* 2014; 11: 1264-70.
- [15] Shoukry AI, Abouela WN, Elsheemy MS, Shouman AM, Daw K, Hussein AA, Morsi H, Mohsen MA, Badawy H, Eissa M. Use of holmium laser for urethral strictures in pediatrics: a prospective study. *J Pediatr Urol* 2015; 12: 42, e1-e6.
- [16] Atak M, Tokgöz H, Akduman B, Erol B, Dönmez I, Hancı V, Türksöy O, Mungan NA. Low-power holmium: YAG laser urethrotomy for urethral stricture disease: comparison of outcomes with the cold-knife technique. *Kaohsiung J Med Sci* 2011; 27: 503-7.
- [17] Torres CL, Moreno Bencardino MC, Bravo-Balado A, Garc a Mayorga CA, Vargas MI, Fern n N. Evaluation of the efficacy and safety of laser versus cold knife urethrotomy in the management of patients with urethral strictures: a systematic review and meta-analysis of randomized clinical trials. *Urol Int* 2017; 99: 453-459.