Holmium: YAG Versus Cold Knife Internal Urethrotomy in the Management of Short Urethral Strictures: A Randomized Controlled Trial

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Abstract

Introduction: our study aimed to assess the safety and efficacy of Holmium: YAG laser internal urethrotomy compared to the cold knife internal urethrotomy.

Methods: Eighty adult male patients presented with a urethral stricture less than 1.5 cm were included in our study; they were randomly allocated into 2 groups representing Holmium and cold knife internal urethrotomy. A careful evaluation with ascending cystourethrogram and uroflowmetry were done on all patients, and they were followed up for 1 year with uroflowmetry.

Results: Each group included 40 patients sharing the same demographic data. The most common cause of a urethral stricture in both groups was iatrogenic injury. The mean operative time of the cold knife urethrotomy procedure was 10.98 ± 2.40 minutes compared to 15.43 ± 2.48 minutes in the holmium laser urethrotomy group with a highly significant difference. The results showed success rates of 90% and 80% for the holmium laser and cold knife internal urethrotomy groups respectively. The perioperative complication according to the Clavien-Dindo classification, showed no statistically significant difference in grade 1 and 2 complications. A recurrence rate with the need for redo surgery representing grade 3B complication was seen in 4 cases in the Holmium group compared to 8 cases in the cold knife group with a statistically significant difference.

Conclusion: Both Holmium Laser and cold knife internal urethrotomy are an effective surgical option for the treatment of a urethral stricture less than 1.5 cm with a promising outcome after 1-year follow-up with a better success rate using the Holmium laser.

Keywords: Holmium laser, Urethral stricture, Outflow obstruction, Internal urethrotomy, Uroflowmetry

Introduction

The urethral stricture is common urological morbidity affecting the voiding function and quality of life, where the severity of the symptomatology depends on the degree and length of the urethral stricture.¹ One of the most common causes for the urethral stricture was urethritis, especially following chronic infection over years rather than a single infection. However, with more endourological surgeries being done, iatrogenic urethral injury from instrumentation, urethral catheterization or thermal energy following an endourological procedure became the most common causes followed by idiopathic causes. Other traumatic causes induced urethral injury include pelvic fracture, straddle trauma to the perineum, previous urethral surgeries like hypospadias repair which may impact the overall prognosis.²⁻⁵

The management of the urethral stricture is planned according to the site and length of the stricture. The 2 main surgical interventions are endoscopic visual internal

urethrotomy and open urethral reconstruction.⁴ Cold knife endoscopic visual internal urethrotomy was first used by Sachse in 1971, and it is the most commonly used surgical treatment for a urethral stricture less than 2 cm in the posterior urethra. It has gained popularity for being safe, effective with an excellent outcome. VIU is a simple procedure with a short learning curve and associated with a low complication rate and a short hospital stay.⁵

Laser urethrotomy was first introduced in 1979. However, it failed to gain enough attention from surgeons at that time.^{7,8} Later, the holmium: YAG (Ho:YAG) laser started to gain attention in the management of a urethral stricture less than 1.5 cm as an effective alternative to the gold standard cold knife internal urethrotomy as it has shown a comparable outcome in both safety and efficacy.^{8,9}

The Ho:YAG laser provides ablation energy with adequate hemostasis that provides a clear field of vision during the procedure. In addition, it causes minimal

damage to the surrounding structure due to the minimal penetration depth of 0.4 mm.^{5,10} We aimed, through our study, to evaluate the efficacy and safety of the holmium laser application in the management of a urethral stricture in comparison to the standard cold knife internal urethrotomy.

Materials and Methods

Eight patients were included in our study, complaining of obstructive urinary symptoms secondary to a urethral stricture between March 2017 and December 2019. The patients were randomly allocated in our study into 2 equal groups with a ratio of 1:1 using a computer-based system after obtaining informed consent under the supervision of the local ethical committee. Group A represented the holmium laser internal urethrotomy while group B represented the Sachse cold knife internal urethrotomy. All adult male patients aged above 18 years with a urethral stricture measuring less than 1.5 cm were included in our study. A urethrogram study and uroflowmetry were done on all patients before surgery except for those with a suprapubic catheter. Pelviabdominal ultrasound was done to evaluate the presence of benign prostatic hyperplasia to exclude patients with enlarged prostate from our study. Those patients who had previously undergone surgical repair of the urethral stricture were excluded from our study. A careful evaluation was done to exclude patients with complete urethral lumen obstruction, multiple urethral strictures or balanitis xerotica obliterans. Any associated urinary tract infection (UTI) was treated properly before surgery.

All procedures were done by a single expert surgeon. The patients were placed in the lithotomy position under general or regional anesthesia. A 21 Fr cystoscope was used to evaluate the urethra, and a guidewire was passed to the urinary bladder. In the holmium laser group, a 365-micron laser fiber (end firing laser fiber) was used to deliver pulse energy of 1 joule with a frequency of 15 Hz and power of 15 watts generated from a Holmium laser device (Cyber Ho 35-watt, Quanta device, Milano, Italy).

The laser fiber was aimed at the 12 o'clock position of the urethral stricture using the end firing property of the laser fiber to incise the fibrotic tissue until an adequate lumen is opened with tissue ablation. In the other group, a rectangular cold knife was used in the endoscopic internal urethrotomy at the same site to incise the urethral stricture; this was followed by meatal dilatation of the urethra that was done only once in the intraoperative setting before urinary catheter insertion. A single dose of prophylactic antibiotic was given to all patients. A urethral catheter was kept in place for 7 days, and then it was removed in the outpatient clinic.

Our primary outcome measure was the improvement in the maximum flow rate (Qmax) in both techniques compared to the baseline and the other group at the same

time interval, while our secondary outcome measures included operative time, perioperative complication, recurrence of symptoms, and the need for redo surgery which was determined by patient complaints and a urethrogram to diagnose the recurrence of a urethral stricture.

Operative time was recorded from diagnostic urethroscopy until urethral catheter insertion. Perioperative complications like extravasation, bleeding, urinary tract infection, or erectile dysfunction were recorded. The patients were assessed at the interval of 3 months and 12 months after the procedure with uroflow to evaluate the voiding pattern. Cases with the recurrence of stricture that needed redo surgery were documented in both procedures. The success of the procedure was considered with a Qmax result of more than 15 m/s. urethrogram done was done for patients with symptoms recurrence or for those whom Qmax dropped below 15 m/s. No passive dilatation was done to our patients postoperatively.

Statistical Analysis

Data were analyzed using IBM SPSS version 23, and they were expressed as mean $\pm$ SD for quantitative parametric measures and both number and percentage for categorical data. A chi-square test was used to compare the qualitative data between groups. The comparison between two independent groups with quantitative data and parametric distribution was done by using an independent-samples *t* test. The comparison between two paired groups with quantitative data and parametric distribution was done by using a paired-samples *t* test. A *P* value < 0.05 was considered statistically significant and less than 0.01 was considered highly significant.

Results

Eighty patients were enrolled in our study as shown in Figure 1. There was no difference in the demographic data between both groups as shown in Table 1. The iatrogenic urethral stricture was the most common in both arms of our study with no statistical difference regarding etiology between both arms as shown in Table 1. A shorter operative time was recorded in the cold knife urethrotomy group with a mean operative time of 10.98 ± 2.4 minutes compared to 15.43 ± 2.48 minutes in the Holmium laser internal urethrotomy group with a highly significant difference (*P* value < 0.001).

The Qmax showed a statistically significant improvement in both groups in the 12-months follow-up period compared to the preoperative data in both groups (*P* value < 0.001) with no statistically significant difference between the groups in any time interval during our follow-up as shown in Table 2. The overall change in the Qmax in both groups is shown in Figure 2.

Regarding the peri-operative complication, there was no

Figure 1. consort flow chart

Figure 2: Uroflow curve

statistically significant difference between both groups as shown in Table 3. Regarding the recurrence rate and those patients who needed a redo surgery in our study, it was seen in 4 cases of group A compared to 8 cases in group B with no statistically significant difference between them (P value = 0.044). All patients with recurrence of stricture were reevaluated using a new urethrogram and they were scheduled for a redo-surgery.

Discussion

The urethral stricture is a common challenging urological problem dating from ancient times, causing obstructed voiding symptoms and affecting the quality of life (1). There are numerous causes for the urethral stricture, including urinary tract infection, straddle trauma, pelvic fracture, previous hypospadias repair (2).

Cold knife internal urethrotomy was first described by Sachse in 1971, and it is considered the gold standard procedure in the surgical management of a urethral stricture less than 2 cm in the posterior urethra (5). Variable results regarding the success rate have been published by many studies. However, the success rate reported by most of them was over 70% (11,12).

This intervention is minimally invasive with less morbidity and hospital stay compared to open surgery. Additionally, it is safe with low rate of peri-operative complication, with a short learning curve and easy to be repeated. However, it is associated with a considerable recurrence rate of the urethral stricture. This high rate of recurrence cannot probably be explained, but it may be

Table 1. Age, Etiology, and Operative Time

		Laser Urethrotomy (Group A)	Cold Knife Urethrotomy (Group B)	P Value
		n = 40	n = 40	
Age	Mean $\pm$ SD	46.68 $\pm$ 13.19	47.58 $\pm$ 13.26	0.762
Etiology	Post traumatic (falling astride)	7 (17.5%)	7 (17.5%)	0.739
	Urinary tract infection	11 (27.5%)	11 (27.5%)	
	Iatrogenic (catheter induced)	19 (47.5%)	16 (40.0%)	
	Idiopathic	3 (7.5%)	6 (15.0%)	
Site of stricture	Bulbar	30	29	0.423
	Penile	7	6	
	Posterior urethra	3	5	
Operation time (min)	Mean $\pm$ SD	15.43 $\pm$ 2.48	10.98 $\pm$ 2.40	<0.001

Table 2. Uroflowmetry

Time of Qmax Assessment (mL/s)	Preoperative	3 Months	12 Months	P Value
Laser urethrotomy (group A)	3.58 $\pm$ 0.71	20.65 $\pm$ 1.82	19.88 $\pm$ 3.71	0.001
Cold knife urethrotomy (group B)	3.85 $\pm$ 0.98	19.15 $\pm$ 1.39	17.03 $\pm$ 4.42	<0.001
P value	0.845	0.203	0.559	

Table 3. Perioperative Complication

Clavien-Dindo Classification		Laser Urethrotomy (Group A)	Cold Knife Urethrotomy (Group B)	P Value	Study Population (N=80)
		n= 40	n= 40		
Grade 1 (deviation from the normal course without the need for pharmacological treatment or surgical interventions)	Bleeding per urethra	1 (2.5%)	2 (2.5%)	0.654	7 (8.75%)
	Penile extravasation	1 (2.5%)	3 (7.5%)	0.455	
Grade 2 (pharmacological management)	UTI	3 (7.5%)	1 (2.5%)	0.325	4 (5%)
Grade 3- B (Procedure under regional or general anesthesia)	Urethral stricture recurrence	4 (10 %)	8 (20%)	0.044	12 (15%)
Overall complication		9 (22.5%)	14 (27.5%)	0.721	23 (28.8%)

UTI, urinary tract infection; SUI, Stress urinary incontinence.

related to the urethral scar tissue and excess fibrosis with lateral contracture (13-15).

Laser urethrotomy was first introduced in 1979, and it has been shown to be effective in a short segment stricture less than 1.5 cm with a comparable outcome to the gold standard cold knife optical urethrotomy (8,16,17). The Ho:YAG laser has a penetration depth of 0.4 mm with adequate hemostasis, giving the advantage of ablation with less bleeding that allows a more clear field with minimal peripheral damage to the surrounding tissue (10). It remains controversial among different studies regarding the superiority of one technique over the other.

The etiology of the urethral stricture in our study was mainly an iatrogenic cause representing 43.75% of cases followed by the UTI induced urethral stricture with an incidence of 27.5%, then traumatic and idiopathic causes. Their results were consistent with the previous reports

where false catheterization or endoscopic instrumentation represented the most common causes in adult patients. (4,7,18)

Our study showed a shorter mean operative time of 10.98 $\pm$ 2.40 minutes in the cold knife group compared to a mean time of 15.43 $\pm$ 2.48 minutes in the laser group with a highly significant difference. However, the clinical significance was hard to achieve in 5 minutes. These results were comparable to a study that was done by Atak et al showing cold knife mean operative time of 7.44 min (range 5-10 min) and Holmium internal urethrotomy operative time of 8.4-16.4 minutes. Also, Singh et al reported a mean operative time in cold knife urethrotomy to be 7.44 minutes compared to 19.8 minutes in laser urethrotomy (7); this could be related to some technical demanding time of the laser fiber to ablate fibrous tissues, not just mechanical incision (19).

The success rate in our study was estimated by a Qmax of more than 15 mL/s in the uroflowmetry 12 months after the surgery in both groups. The mean Qmax in group A was 20.65 ± 1.82 mL/s compared to 19.15 ± 1.39 mL/s in group B with a highly significant difference compared to the preoperative values of both techniques with no statistical or clinical difference between both groups at the same follow-up period. The follow-up of our patients after 1 year revealed a decrease in the Qmax in both groups, where the mean Qmax in group A was 19.88 ± 3.71 mL/s compared to 17.03 ± 4.42 mL/s in group B.

The success rate in our study was 90% in group A compared to 80% in group B with a statistically significant difference. Previous studies that were done by [Mazo et al](#), [Dogra et al.](#) and [Lagerveld et al.](#) reported the superiority of the laser over cold knife urethrotomy in terms of uroflow improvement (7,8,16,17). Laser urethrotomy in our study showed a better visualization duration laser ablation because of the hemostatic effect that provided an accurate site of ablation with a meticulous depth of ablation and trimming of the edges with the vaporization of the scar tissue.

Regarding the recurrence of urethral stricture and the

need for a redo surgery, it was seen in 12 cases of our study population representing 15% of the whole population, 4 of them were in the laser group compared to 8 cases in the cold knife group. The success rate was enhanced by the proper treatment of the urinary tract as it could increase the success rate from 28% to 72%. (7)

A randomized clinical study reported by [Atak et al.](#) showed success rates of 81% and 53% at 12 months for holmium and cold knife urethrotomy respectively (19). [Yenice et al.](#) reported a mean success rate of 79.3% and 67.6% for cold knife and Holmium urethrotomy respectively (18). [Dutkiewicz and Wroblewski](#) indicated that no superiority was confirmed for the holmium laser over the classical cold knife internal urethrotomy at a 1-year follow-up (11).

[Karkan et al](#) reported a 73.2% success rate with Holmium urethrotomy in their clinical experience with 138 patients (20). Evaluation of previous studies is shown in [Table 4](#).

The reported incidence of perioperative complications varies greatly in different studies. Regarding our study, we documented our complications according to the Clavien-Dindo classification. As shown in [Table 3](#), the overall

Table 4. previous studies evaluated Holmium and cold knife VIU

Study	Type of studies	Number of patients	Arms of the study	Primary end point	Secondary end point	Success rate	complication	limitation
Dogra et al. 2002	Retrospective cohort	61	Singles (Holmium VIU)	Improved Qmax at 3 months > 15 ml/sec.	Operative time Durable success rate till 30 months	96 %	Recurrence of stricture in 2 cases	-Lack of comparative arm -Retrospective nature of the study
Singh et al. 2014	Randomized controlled trial	90	Cold knife versus VIU Holmium VIU	Improved Qmax at 3 months > 15 ml/sec	Operative time Postoperative complication	100% 86.7 %	Overall, 13.3% including urethral bleeding, postoperative pain, UTI, and recurrence in 6 cases	-Short duration of follow up.
Atak et al. 2011	Randomized controlled trial	30 patients 21 patients	cold knife VIU holmium VIU	Improved Qmax > 15 ml/sec	Durability regarding restenosis	81% 53 %	No reported complication	Heterogenous etiology and site of stricture
Dutkiewicz et al. 2011	Prospective clinical trial	50 patients	Cold knife VIU Holmium VIU	Improved Qmax	Post voiding residual Quality of life	The results obtained did not confirm a superiority based on Qmax improvement and QoL of one technique over the other at 1-year follow-up.	No reported complications	No assessment for success rate and restenosis in the study

Aboulela et al. 2018	Prospective clinical trial for holmium VIU compared to a historical control of cold knife VIU	42	Cold knife VIU Holmium VIU	Improved Qmax at 3 months > 15 ml/sec	Post-operative morbidity	47.6% 76.2%	No reported complications	-Short follow up -Retrospective analysis -Non randomization -Heterogenous etiology and site of stricture
Yenice et al. 2018	Randomized controlled trial	29 patients 34 patients	Cold knife VIU Holmium VIU	Improved Qmax	Recurrence rate Complications	79.3% 67.3%	3 cases of urethral bleeding in cold knife group 1 case of extravasation in holmium group	Small sample size
Karkan et al. 2019	Prospective single arm clinical trial	138	Holmium VIU	Improved Qmax	Recurrence rate Complications	73.2%	24 cases of intraoperative hematuria 9 cases of penile burning sensation	Lack of comparative group

VIU: Visualized internal urethrotomy, Qmax: maximum flow rate

complication rate in our study was 28.8% representing grades 1, 2 and 3B with no statistically significant difference. The complications of grades 1 and 2, including penile edema, bleeding per urethra or UTI, were treated conservatively. The recurrence rate with the need for redo surgery representing grade 3B complication was seen in 4 cases in the Holmium group compared to 8 cases in the cold knife group with a statistically significant difference (P value=0.044).

Both surgical techniques of laser and cold knife internal urethrotomy have the advantage to be repeated, but there is no clear evidence for the criteria for the repetition of the procedure (3). We recommend performing a multicentric comparative study between both techniques on a larger sample size with a longer period of follow-up and evaluating their effectiveness in the management of the urethral stricture.

From our study, both the Holmium Laser and cold knife internal urethrotomy are considered safe and effective in the management of a urethral stricture less than 1.5 cm with a promising outcome after a 1-year follow-up. Holmium laser internal urethrotomy was associated with a longer operative time with a better success rate compared to cold knife urethrotomy.

Ethical considerations

The study was approved by the Research Ethics Committee of Faculty of Medicine, Ain Shams University (FWA000017585), with ID: R55/2017. The study was conducted in accordance with the declaration of Helsinki. The study was registered on Clinicaltrial.gov with ID number: NCT04650347.

Consent for Participation

written consent was obtained from all patients before participation.

Conflict of Interests

Nothing to declare.

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