

Comparison of Holmium Laser versus Cold Knife Treatment in Patients with Urethral Strictures

Immad Ud Din, Zeeshan Nasir, Muhammad Farrukh Naveed, Ahmad Sajjad Habibi, Syed Ahmad Farooqi, Asra Aleem

ABSTRACT:

Objective: The goal of this study is to assess the efficacy of optical internal urethrotomy, which uses a holmium laser in comparison to a cold knife, in treating short-segment urethral strictures in our local setting.

Study design & Settings: Randomized controlled trial (ClinicalTrials.gov Identifier: NCT07505316) at the Department of Urology, Kidney Center- Bahawal Victoria Hospital, Bahawalpur.

Methods: Males aged 18 to 70 years with short segment urethral strictures (length <2 cm), planned to undergo internal urethrotomy were included. Patients with multiple or recurrent strictures, active urinary tract infections, complete urethral obliteration on urethroscopy, with pan-anterior strictures, posterior stenosis, failed prior interventions, were not included. Patients were randomly divided into group A (cold-knife) and group B (holmium laser) through lottery method using sealed opaque envelopes. Post procedure uroflowmetry was performed after 30 days and assessor was not aware of procedures performed

Findings: The mean Qmax of the holmium laser group was 18.9 +/- 3.5 ml/sec 30 days after surgery, as compared to the cold-knife group (14.8 +/- 3.2 ml/sec). This was found to be very statistically significant ($p < 0.001$), which indicated that the cold-knife method did not significantly enhance the urine flow rate compared to holmium laser urethrotomy.

Conclusion: In individuals with short-segment urethral strictures, cold-knife and holmium laser urethrotomy both significantly increase urine flow, but the traditional method of holmium laser urethrotomy has a significantly higher post-operative Qmax.

Keywords: urethral stricture, holmium laser, urethrotomy

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INTRODUCTION:

Urethral stricture, one of the earliest known urologic conditions, is still prevalent and challenging to cure.¹ It is a common disease, having high morbidity rate, in industrialized countries, the stricture has estimated incidence of 0.6% and in the underdeveloped world, it might be higher due to depth, location and length of scarring of the stricture. In the last few decades there has been the development of various modalities of treatment of urethral strictures including the least invasive endoscopic procedures up to the most complicated forms of reconstruction including urethroplasty. One of the most widely used and common initial treatments is direct vision internal urethrotomy (DVIU) especially on short-segment strictures. DVIU is associated with incising the stricture with the help of endoscopies to expand the lumen constriction and facilitate urinary flow. Different methods have been used to do this incision such as cold-knife urethrotomy, electrocautery and laser based procedures.^{2,3}

Urethrotomy of the cold-knife technique is a common and practiced technique owing to its simplicity, low cost and ease of availability. It entails mechanical abrasion of the fibrotic part usually at the 12 o'clock location to re-establish urethral patency.⁴ Although this method does not cause any

thermal damage to the surrounding tissues, it can be accompanied by mechanical trauma and an increased chance of recurrence because of the incomplete incision, or subsequent fibrosis. Electrocautery, on the other hand, has the benefit of providing hemostasis but has the potential of causing thermal damage, which can also be the cause of additional tissue damage and recurrence of strictures.⁵

Over the past few years, laser technology has received more and more interest in the field of urology as it is very precise and also has a better safety profile. One of the most used modalities that have been adopted to treat urethral strictures among the available laser systems is the Holmium:YAG (Ho:YAG) laser.⁶ The holmium laser has a number of benefits, such as a high level of accuracy when cutting the tissue, very low penetration depth and casualty thermal damage. Their characteristics make them especially suitable in the delicate endourological procedures. The laser can also be used to spot-vaporize and incise fibrotic tissue, which might result in better recovery and a lower recurrence rate.⁷

Various laser systems, such as carbon dioxide (CO₂), argon, neodymium-doped yttrium aluminum garnet (Nd:YAG) and holmium lasers have been considered in urethrotomy. Nevertheless, Ho:YAG laser has proven to be more effective and safe on several studies and has become commonplace in contemporary endourology. Its high degree of tissue penetration together with the fact that it is able to produce high-energy pulses enables a good cut through strictures without damaging structures. This has created the increasing interest in its application as a desirable modality against traditional methods.⁸

Shaikh MI et al. used a sample of 130 patients with urethral strictures and randomly allocated the patients into two groups. Patients in Group A had an opening done with a cold knife, and patients in Group B had an opening done with a holmium laser. The mean peak flow rate of group A and B on the third day was 26.66 ± 3.69 ml/s and 28.72 ± 4.63 ml/s, respectively. On day 30, the maximum flow rates in groups A and B are 24.00 ± 3.44 ml/s and 20.84 ± 2.77 ml/s, respectively ($p=0.000$).⁹ Group A (holmium group, $n = 10$) and Group B (cold knife group, $n = 10$) each had internal urethrotomy using a holmium laser and a cold knife, respectively, in a study by Maged WA et al. At 3rd month follow-up, the holmium group experienced a greater post-operative drop in peak urinary flow rate compared to cold knife group.¹⁰

This study aims to determine the effectiveness of optical internal urethrotomy that can be performed on patients with short-segment urethral strictures in our local environment with the use of a holmium laser rather than a cold knife. According to the outcomes in terms of functionality, the research will contribute to the standardization of treatment methods of urethral stricture. The local study will enhance the availability of modern urologic care through the

encouragement of less invasive laser procedures in the government facilities. The study will help in informed decision making, enabling patients to understand treatment options and their expected outcomes based on evidence.

METHODOLOGY:

This randomized controlled trial (ClinicalTrials.gov Identifier: NCT07505316) was performed at the Department of Urology, Kidney Center- Bahawal Victoria Hospital, Bahawalpur (January 15 to April 14, 2026) under the authorization of the ethical review committees of the Quaid-e-Azam Medical College (QAMC). Sample size was calculated through OpenEpi online software using mean difference formula. Where, Peak flow rate in cold-knife = 24.00 ± 3.44 ml/s, Peak flow rate in Holmium laser = 20.84 ± 2.77 ml/s, Confidence level = 95% and Power of the study = 80%.⁹ Sample size = 30 in each group, Total sample size = 60. A non-probability consecutive sampling strategy was used to recruit the patients.

Males aged 18 to 70 years with short segment urethral strictures (length <2 cm), planned to undergo internal urethrotomy were included. Patients with multiple or recurring strictures, urethroscopic evidence of total urethral obliteration, pan-anterior strictures, posterior stenosis, attempted prior treatment or lichen sclerotic changes were excluded in the study. Some of the baseline variables noted included age, obesity, diabetes mellitus, hypertension, smoking, and the cause of the stricture (e.g., iatrogenic, post-infectious, and trauma). Confirmatory micturating cystourethrography (MCUG) was done on each patient by the radiology department. The consultant radiologist reported the site (bulbar, penile, or membranous) and the stricture length (mm) of the stricture. Also, uroflowmetry was carried out on the patients and peak urine flow (Q_{max} -ml/Sec) was recorded. Patients were randomly divided into group A (cold-knife) and group B (holmium laser) through lottery method using sealed opaque envelopes. In the cold-knife urethrotomy, a cystoscope was inserted through the urethra and a cold knife was used to incise the stricture at the 12 o'clock position to help increase the small lumen and a normal flow of urine. While in holmium laser urethrotomy procedure, a laser fiber was passed through a cystoscope, and precise incisions are made in the stricture, usually at the 12 o'clock position, to widen the lumen. Duration of procedure (minutes) was recorded in both the groups. Post-procedure 20Fr foley catheter was placed in all patients. All patients were discharged after 24–48 hours after the procedure, once they are stable. They are advised catheter care, antibiotic course completion, avoidance of heavy exercise and maintenance of good hydration. Post procedure uroflowmetry was performed after 30 days and assessor was not aware of procedures performed. All the data was recorded on proforma.

SPP version 25 was used for data analysis. Normality of numerical data was assessed through Shapiro-Wilk test.

Age, symptom duration, stricture length, and peak urinary flow (Qmax) were shown as mean and standard deviation (median and IQR if not normally distributed). Obesity, diabetes mellitus, hypertension, smoking and stricture etiology were presented as frequency and percentages. Post operative Qmax between the groups was compared through independent sample t-test (Mann Whitney U test if not normally distributed) and p-value <0.05 will be taken substantial. Data was stratified on age, Obesity, diabetes mellitus, hypertension, smoking and stricture etiology. Post stratification independent sample t-test (Mann Whitney U test if not normally distributed) was applied for comparing Qmax between both groups and p-value <0.05 was considered significant.

RESULTS:

The mean age of study patients in the cold-knife group (48.6 +10.2 years) and the holmium laser group (47.9 +9.8 years) did not differ significantly ($p = 0.78$). The median symptom duration of the cold-knife group was 14 (10-18) weeks and that of the holmium laser group was 15 (11-19) weeks ($p = 0.62$). The prevalence of comorbid conditions, obesity (33.3% vs. 36.7%), diabetes mellitus (30.0% vs. 26.7%), hypertension (36.7% vs. 33.3%) and smoking (43.3% vs. 40.0), did not differ statistically significant ($p > 0.05$) between the two groups. The median of stricture length in a cold-knife group was 12 (10-15) mm but in the holmium laser group, the length was 13 (10-16) mm ($p = 0.58$). Again, there was no notable difference ($p = 0.64$) between the mean of the cold-knife group 7.2 1.8 ml/sec and the holmium laser group 7.4 1.6 ml/sec of Qmax of the baseline. The results indicate that there was statistical similarity between the two groups at the baseline. Tables 1 and 2. The independent-samples t-test was applied to compare the peak urine flow rate (Qmax) of the two groups 30 days following surgery, the primary outcome of the study since the data were distributed normally. The mean Qmax of the holmium laser group was 18.9 +/- 3.5 ml/sec 30 days after surgery, as compared to the cold-knife group (14.8 +/- 3.2 ml/sec). This was found to be very statistically significant ($p < 0.001$), which indicated that the cold-knife method did not significantly enhance the urine flow rate significantly compared to holmium laser urethrotomy. In Table 3. Within-group analysis showed that the rate of urinary flow greatly improved in both treatment modalities. Qmax increased in cold-knife group to 14.8 ml/sec and in holmium laser group to 18.9 ml/sec after 30 days from baseline. Both improvements were also clinically significant but the holmium laser group had a greater improvement. Table 4 The mean procedure time in cold-knife group was 18.5 4.2 minutes and in the holmium laser group, it was 22.3 5.1 minutes. This was statistically significant ($p = 0.01$), indicating that the cold-knife method took a little bit less time to perform as compared to the holmium laser therapy. Stratified analysis has been performed in order to consider putative effect modifiers including age,

obesity, diabetes mellitus, hypertension, smoking status, and stricture aetiology. After the age stratification, the statistically significant differences ($p < 0.05$) in the mean values of Qmax were observed between the holmium laser and cold-knife groups across all age groups (18-40 years old, 41-55 years old, and 56-70 years old). It was also observed that the presence or absence of obesity, diabetes mellitus, hypertension, and smoking had significant post-operative Qmax values, according to the classification based on the existence of comorbid diseases ($p < 0.05$ in all cases). Moreover, the holmium laser treatment was more effective in each category stratified in terms of stricture origin, iatrogenic, post-infectious, and traumatic, where the statistically significant changes were observed in post-surgical Qmax ($p < 0.05$). The implication of these results is that the treatment effect was fixed and unresponsive to any underlying clinical variables or demographic factors about the patient. Table 5.

DISCUSSION:

The study findings indicate that cold-knife internal urethrotomy, as well as holmium laser urethrotomy, are equally effective in the enhancement of the urine flow in short-segment urethral stricture patients, though, the effects of holmium laser urethrotomy in this area were statistically better in terms of the post-operative Qmax at 30 days. These findings are in line with the existing guidelines which appreciate the shortcomings of long-term durability, but promote endoscopic therapy in certain short-term strictures.¹¹⁻¹³

The present study revealed that the mean postoperative Qmax of the group in which the operation was carried out with the help of the holmium laser was significantly higher than the mean postoperative Qmax of the group in which the same operation was done with the assistance of the cold-knife. The mean Qmax of the patients treated with the holmium laser was 18.9 +/-3.5 ml/sec as compared to 14.8 +/-3.2 ml/sec of the cold-knife group with a statistically significant p-value of less than 0.001. These results mean that the achievements of both techniques in relieving urethral obstruction are similar, but the extent to which holmium laser urethrotomy improved the degree of urinary flow was higher. The high-success of the holmium laser can be attributed to its capability to produce accurate incisions with minimal collateral tissue injuries. The holmium laser has the ability to wildly cut and incise fibrotic tissue with a restricted depth of penetration and a reduced spread of heat as compared to the cold knife, which relies on mechanical cutting and incision of fibrotic tissue with a limited depth of penetration and limited degree of thermal spread.

These findings correlate with the systematic review and meta-analysis by Chen et al.³, comparing laser urethrotomy with cold-knife urethrotomy in short-rule urethral strictures and found no significant differences in the overall functioning

Table 1: Demographic and Clinical Features (n = 60)

Variable	Group A (n=30)	Group B (n=30)	p-value
Age (years)	48.6 ± 10.2	47.9 ± 9.8	0.78
Symptom Duration (weeks)	14 (10–18)	15 (11–19)	0.62
Obesity, n (%)	10 (33.3%)	11 (36.7%)	0.79
Diabetes Mellitus, n (%)	9 (30.0%)	8 (26.7%)	0.77
Hypertension, n (%)	11 (36.7%)	10 (33.3%)	0.79
Smoking, n (%)	13 (43.3%)	12 (40.0%)	0.80
Stricture Length (mm)	12 (10–15)	13 (10–16)	0.58
Baseline Qmax (ml/sec)	7.2 ± 1.8	7.4 ± 1.6	0.64
Procedure Duration (minutes)	18.5 ± 4.2	22.3 ± 5.1	0.01

Table 2: Distribution of Stricture Etiology and Location

Variable	Group A (n=30)	Group B (n=30)	p-value
Stricture Etiology			
Iatrogenic, n (%)	12 (40.0%)	11 (36.7%)	0.79
Post-infectious, n (%)	10 (33.3%)	11 (36.7%)	0.79
Traumatic, n (%)	8 (26.7%)	8 (26.7%)	1.00
Stricture Location			
Bulbar, n (%)	18 (60.0%)	19 (63.3%)	0.79
Penile, n (%)	8 (26.7%)	7 (23.3%)	0.76
Membranous, n (%)	4 (13.3%)	4 (13.3%)	1.00

Table 3: Comparison of Peak Urinary Flow Rate (Qmax)

Variable	Group A (n=30)	Group B (n=30)	Mean Difference	p-value
Baseline Qmax (ml/sec)	7.2 ± 1.8	7.4 ± 1.6	-0.2	0.64
Qmax at 30 Days (ml/sec)	14.8 ± 3.2	18.9 ± 3.5	-4.1	<0.001

Table 4: Within-Group Improvement in Qmax

Group	Baseline Qmax (ml/sec)	30-Day Qmax (ml/sec)	Mean Increase
Cold-knife Group	7.2 ± 1.8	14.8 ± 3.2	+7.6
Holmium Laser Group	7.4 ± 1.6	18.9 ± 3.5	+11.5

Table 5: Stratified Comparison of Post-operative Qmax (30 Days) Between Groups

Variable	Category	Cold-knife Qmax (Mean ± SD)	Holmium Laser Qmax (Mean ± SD)	p-value
Age	18–40 years	15.2 ± 3.1	19.5 ± 3.3	0.002
	41–55 years	14.6 ± 3.4	18.7 ± 3.6	0.001
	56–70 years	14.3 ± 3.0	18.4 ± 3.2	0.003
Obesity	Yes	14.2 ± 3.0	18.1 ± 3.2	0.004
	No	15.1 ± 3.3	19.2 ± 3.5	0.001
Diabetes Mellitus	Yes	14.0 ± 3.1	17.8 ± 3.3	0.005
	No	15.3 ± 3.4	19.4 ± 3.6	0.001
Hypertension	Yes	14.1 ± 3.0	18.0 ± 3.2	0.006
	No	15.0 ± 3.3	19.1 ± 3.5	0.002
Smoking	Yes	14.3 ± 3.1	18.2 ± 3.3	0.004
	No	15.2 ± 3.4	19.3 ± 3.6	0.001
Stricture Etiology	Iatrogenic	15.0 ± 3.2	19.1 ± 3.4	0.002
	Post-infectious	14.5 ± 3.1	18.6 ± 3.3	0.003
	Traumatic	14.7 ± 3.2	18.8 ± 3.4	0.002

outcomes and recurrence rates in both techniques. Likewise, Faizan et al.⁴ demonstrated that the safety and efficacy profiles of laser-assisted DVIU was better than the conventional cold-knife methods. The present research thus, adds to the current international evidence whereas it also provides local critical information based on a tertiary care center of a Pakistani based hospital. This regional evidence is especially significant since there could be significant disparities between high- and low-resource countries regarding treatment patterns, patient characteristics, healthcare infrastructure, and access to advanced equipment.

Indeed, VanDyke et al. discovered that drug-coated balloon technology had significantly higher results (77.8% vs. 23.6% vs. $p < 0.001$) than their standard endoscopic treatment, which provides a significant insight into the importance of technological advancements in the treatment of urethral strictures.¹⁴ The increased Qmax outcomes observed in this study are supported by high short term success rates of the contemporary minimally invasive procedures by Mahenthiran et al.¹⁵

The exact incision and less thermal destruction of the holmium laser urethrotomy that has a lower fibrosis and better recovery is the reason why it is advantageous in this study. This is in line with findings in systemic studies that prove the excellence of modern technology and adjuncts as compared to the traditional ones.^{16,17} Further, meta-analytical data also shows that minimally invasive methods are still in the development stage and that they have better functional outcomes compared to traditional methods.¹⁸

In spite of these advantages, recurrence remains to be a serious problem in the management of urethral strictures. Endo et al. identified stricture length, past operations and low baseline Qmax as the most significant predictors of recurrence after internal urethrotomy.¹⁹ Hernandez-Hernandez et al. also proved that DVIU remains useful most of the time in short (less than 2 cm) primary bulbar strictures, and this fact confirms the inclusion criteria of the current study and explains the positive outcomes in the short term.²⁰ Also, Yadav et al. underlined that the recurrence rates remain high even after the initial recovery, which once again makes it clear that the selection of the patients can also be considered an important aspect.²¹

The stratified analysis of the current study revealed that holmium laser urethrotomy yielded superior Qmax outcomes in diverse age groups, co-morbidities and etiologies. However, Gul et al. concluded that comorbidity, like diabetes mellitus and hypertension are factors that are associated with an increased risk of recurrence after urethrotomy, meaning that patient factors might still influence the end outcomes despite the short-term success.²² Similarly, in a study by Garcia Fernandez et al., the authors also underlined the complex nature of urethral stricture recurrence by noting that the success rates are influenced by a number of factors.²³

The scope of endoscopic treatment is further compared with the reconstructive procedures. Although endoscopic techniques remain to be useful in some cases of short-segment stricture, Babelay et al. demonstrated that the outcomes of urethroplasty are superior compared to those of internal urethrotomy.²⁴ Also, Gilbert et al. have shown that other less invasive procedures such as balloon dilation could give the same output under certain clinical conditions.²⁵

This trial also showed a significant increase in Qmax in the cold-knife group, which showed that traditional urethrotomy remains a viable short term treatment. Its reduction in Qmax relative to the holmium laser group, however, suggests laser urethrotomy may be superior in providing better early functional outcomes. This observation is supported by recent studies that have revealed that improved techniques and complementary medicines would help to improve outcomes and reduce recidivism.^{16,17}

Additionally, the marginally longer working time of the holmium laser group is consistent with the previous studies that established that setting up of the equipment and precision-based techniques prolonged the time of the procedure. This is however acceptable given the improved clinical outcomes that are associated with laser urethrotomy.¹⁸

In general, the inferences made in the present research are quite consistent with the recent studies. The Qmax in holmium laser group is significantly higher after operation and this fact gives a credence to the growing number of studies leading to the fact that advanced minimal invasive procedures provide better functional outcome than standard ones. A success can be achieved in the long-term, though, it remains dependent on several variables, including patient comorbidities and stricture features. Questions of patient selection are therefore still needed in pursuit of the most favorable long-term outcomes despite the fact that holmium laser urethrotomy provides better short-term outcomes.

Limitations: In the interpretation of the findings, one should consider a large number of limitations of the present study. To begin with, the findings might not be as generalizable to a greater population because of the small sample ($n = 60$). Second, the brief 30-day follow up also hindered the measurement of long-term outcomes such as recurrence rates that are instrumental in the management of urethral strictures. Thirdly, the research was conducted in one place, which might decrease external validity and introduce an institutional bias. In addition, despite stratification, one could not adequately control the possible confounding factors such as variation in surgical technique, experience of the operator, and compliance of the patient to post-operative therapy. Also, the outcome cannot be extended to longer, more complex, or recurring strictures as the investigations involved studying of short-segment strictures. The objective assessment did not include subjective symptom ratings and quality-of-life measures, which might have provided a more

comprehensive measure of treatment outcomes, as it only included Qmax. Lastly, there could be measurement or observer bias since there was no blinding. These limitations mean that follow-up studies with more extended follow-up duration and bigger and multicenter studies will be required to triangulate the findings.

CONCLUSION:

Cold-knife and holmium laser urethrotomy also significantly enhance the flow of urine in patients with short-segment urethral strictures, although the conventional holmium laser urethrotomy is more successful in the short run, where there was a significantly higher post-operative Qmax. Nevertheless, it appears that the laser modality is more useful in terms of successful early functional improvement, even though its operating time is somewhat longer.

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Authors Contribution:

Immad Ud Din: Conception and Design, acquisition of data, analysis and interpretation of data, drafting and critical revision, final approval of the version to be published.

Zeeshan Nasir: Conception and Design, acquisition of data, analysis and interpretation of data, drafting and critical revision, final approval of the version to be published.

Muhammad Farrukh Naveed: Conception and Design, acquisition of data, analysis and interpretation of data, drafting and critical revision, final approval of the version to be published.

Ahmad Sajjad Habibi: Acquisition of data, drafting and final approval of the manuscript.

Syed Ahmad Farooqi: Acquisition of data, drafting and final approval of the manuscript.

Asra Aleem: Conception, acquisition of data, critical revision of the manuscript.

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