Holmium Laser Endourethrotomy for the Treatment of Long-Segment Urethral Strictures: A Retrospective Study of 190 Patients

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Purpose: Long-segment urethral strictures (LSUS) are refractory to urethrotomy and urethroplasty. Holmium laser urethrotomy has shown favorable therapeutic outcomes in short-segment urethral stricture. We therefore evaluated the therapeutic effectiveness and safety of holmium laser endourethrotomy in the treatment of LSUS.

Materials and Methods: Holmium laser endourethrotomy was used to treat 190 consecutive male patients with LSUS. A urethrocystoscopic poking maneuver incorporating holmium laser ablation was used to eliminate the urethral strictures completely. Maximum flow rate (Qmax) on retrograde uroflowmetry, International Prostate Symptom Score (IPSS) and the Expanded Prostate Cancer Index Composite (EPIC) quality of life (QoL) index were assessed at baseline and at 1-, 3- and 6-months postoperatively.

Results: Holmium laser urethrotomy was successfully completed in all 190 patients. The mean operation time was 25 ± 17.8 min (range, 6-69 min). No significant intraoperative complications occurred, except that 23 patients (12.1%) experienced controllable scrotal and penile edema. None of these LSUS patients experienced recurrent strictures during a follow-up period of 6-36 months. From baseline to 6 months postoperatively, the mean Qmax increased significantly, from 1.4 ± 2.7 mL/sec to 19.7 ± 4.1 mL/sec ($P < .001$); mean IPSS decreased significantly, from 31.3 ± 7.2 points to 9.3 ± 3.1 points ($P < .001$); and mean QoL score showed significant improvement, from 5.7 ± 1.6 points to 1.8 ± 0.4 points ($P < .001$).

Conclusion: Holmium laser endourethrotomy with the poking maneuver is a therapeutically effective and minimally invasive treatment for LSUS.

Keywords: lasers; therapeutic use; treatment outcome; urethral stricture; surgery.

INTRODUCTION

Long-segment urethral stricture (LSUS) is defined as a narrowing of a urethra longer than 1 cm.[1] Etiologically, LSUS is due primarily to urinary tract trauma, surgery or infection. The symptoms and signs of LSUS vary in severity and manifest primarily as dysuria, urinary retention, urinary incontinence, and urinary obstruction. As a refractory urologic condition, LSUS usually requires surgical intervention, consisting of urethrotomy and urethroplasty.[1] Many surgical methods have been used to treat urethral strictures, with the choice of method depending primarily on the location and length of the stricture as well as on the experience of the urologist.[1] Current urological surgical techniques include visual internal urethrotomy,[2] one- or two-stage urethroplasty with skin flap[3] or mucosal onlay[4] and temporary or permanent urethral stenting.[5] Treatment outcomes, however, have been unsatisfactory due to high rates of iatrogenic urogenital injuries, urinary calculosis, urinary fistula, septic infection, and stricture recurrence.[6] These morbidities and complications are more likely to occur in patients with a history of previous urethrotomy and/or urethroplasty.[7]

Endourethrotomy with the holmium laser is an endourologic technique incorporating laser ablation for the management of urological stricture diseases.[8] This treatment is minimally invasive, with similar or even superior effectiveness and safety compared with conventional urethrotomy and urethroplasty.[9] Compared with other ablation methods, such as cold-knife and electrical resection, laser incision can efficiently eliminate scarred tissues through vaporization but with minimal thermal damage to adjacent urogenital tissues. The major benefit of laser ablation is small extent of scarring following urethrotomy.[10] Although this technique has rarely been used to treat complicating LSUS, we have utilized it to treat this condition since 2001, obtaining good treatment outcomes. We have retrospectively assessed the effectiveness and safety of endourethrotomy with holmium laser ablation in 208 males with complicating LSUS at our institution. To our knowledge, this report is the first to describe the use of laser endourethrotomy to treat LSUS.

MATERIALS AND METHODS

Study Participants

We assessed 190 consecutive male patients, aged 10-65 years, diagnosed with LSUS (> 1.0 cm) on urethroscopy and/or urethrography and hospitalized for elective endourethrotomy with holmium laser between August 2001 and July 2011. Indications included a urethral stricture length > 1.0 cm; history of urethral stricture for more than 3 months; and undergoing urinary diversion 3 months prior to admission. Contraindications included active urinary tract infection; upper urinary tract stricture; being unable to complete outpatient follow-up of at least 6 months; or refusal to participate in this study. Chief patient complaints included narrow or interrupted urine stream, urinary incontinence, and progressively prolonged voiding time. The duration of LSUS ranged from 3 months to 7 years following the onset of stricture disease. During preoperative endoscopic examination in all patients, a 17.5-19.5 French (F) urethrocystoscope or an 8-10F urethral sound probe could not be advanced into the bladder; the stricture manifested as an oval-, radiating- or irregularly-shaped scarred obliteration. The urethral strictures ranged in size from 2.6 cm to 4.5 cm and were located in the pendulous urethra (n = 14, 7.4%), bulbous urethra (n = 142, 74.7%), and membranous urethra (n = 34, 17.9%). The causes of LSUS were determined to be trauma in 126 patients (66.3%), iatrogenic (instrumental or surgical) injury in 30 (15.8%), and urinary tract infection in 34 (17.9%). Of these 190 patients, 60 (31.6%) underwent suprapubic cystostomy due to complete or near complete urethral atresia, whereas 127 (66.8%) had a previous history of urethrotomy and/or urethroplasty. The study protocol was approved by the Institutional Review Board at The People's Liberation Army Kunmin General Hospital in accordance with the Declaration of Helsinki, and all patients provided written informed consent prior to surgery.

Endourethrotomy with Holmium Laser Ablation

All procedures were performed by a single surgeon (Q.L.), who had extensive experience with endourethrotomy for the treatment of simple urethral strictures and with holmium laser enucleation of the prostate. Patients were started on intravenous prophylactic fluoroquinolones, beginning two days prior to surgery. Following spinal anesthesia, each patient was placed in the lithotomy position. A 26F water-circulating lateral emission laser cystoscope (Olympus, Tokyo, Ja-

pan) equipped with a high-definition video monitoring and display system (Stryker, Kalamazoo, MI 49002, USA) was inserted into the urethra to visualize the urethral mucosae. If cystoscope insertion failed, urethrotomy was performed throughout the entire anterior urethra using an endourological cold-knife. Following clear visualization of the strictures, the cystoscope was used to poke the strictures and establish an artificial lumen.

A holmium laser optical-fiber knife (Coherent, Inc., Santa Clara, CA, USA), at a series of calibers (200 μm, 365 μm and 550 μm), was inserted through the endoscope working channel to completely eliminate the scarred tissues from the distal to the proximal direction. The power and frequency of the holmium laser emission were set at 2.5-30.0 W and 5.0-20.0 Hz, respectively. The scarred tissues were incised more frequently using cystoscopic poking than using laser ablation. Multiple incisions were made at the 0300, 0900 and 0600 counterclockwise positions for pendulous strictures and at the 1200, 0300 and 0900 clockwise positions for membranous strictures. In patients with complete urethral atresia or refractory urethral stricture, a metallic urethral sound was induced via the suprapubic cystostomy opening into the posterior urethra to guide the advance of cystoscope; the assistant's index finger was inserted into the rectum to assist the advance of the instrument into the bladder.

Postoperative Care and Follow-up

Patients were maintained on intravenous broad-spectrum antibiotics for one week after surgery and switched to oral medication for 4-6 weeks afterwards. The 18-24F double- or triple-lumen urethral catheter was allowed to remain for 4-6 postoperative weeks, and all patients underwent routine urethral dilation for 4-8 postoperative weeks. All patients were followed up at the outpatient clinic at 3 and 6 months after endourethrotomy. The main outcome measures were improvements from baseline in maximum flow rate (Qmax), International Prostate Symptom Score (IPSS), and quality of life (QoL) index. Treatment success was defined as complete or near complete restoration of a normal urinary stream and micturition distance without requiring urethral dilation within 6 months of urethrotomy.

Statistical Analysis

All data were expressed as mean ± SD. Mean improvements from baseline in Qmax, IPSS, and QoL index were analyzed using one-sample Student's *t* tests. A *P* value less than .05 was considered statistically significant.

RESULTS

Following the incision of scarred tissues, the retrograde 26F lateral emission holmium laser cystoscopy could be successfully advanced through the strictured urethra into the bladder of all 190 patients. The mean operating time (the interval between the insertion and the withdrawal of the urethroscope) was 25 ± 17.8 min (range, 6-69 min). None of these patients experienced any intraoperative complications, such as massive urethral bleeding, rectal or corpus cavernosum penis injuries, urethral false passage, or urethral perforation. However, 23 patients (12.1%) experienced marked scrotal and penile edema suggesting urinary extravasation. These complications occurred mainly in the first 50 patients (11/50, 22.0%), but all of these complications resolved completely 2-3 days following symptomatic treatment, such as pressure dressing, scrotal elevation, and scrotal incision and drainage. During the postoperative period, none of these patients developed urinary tract infection, urethral fistula, false urethral passage, urinary incontinence, or erectile dysfunction. LSUS treatment with a single endourethrotomy using the holmium laser was determined to be successful in all 190 patients (100.0%), with all having a normal urinary stream and micturition distance.

The follow-up period ranged from 6-36 months (mean, 14.1 ± 7.2 months). No patient was lost to follow-up within the first six months. None of these patients experienced any types of recurrent strictures; therefore, none required second-look instrumental, endoscopic or surgical interventions during follow-up. The improvements from baseline in main outcome measures are shown in Figure 2. At baseline, the Qmax on uroflowmetry was 1.4 ± 2.7 mL/sec (range, 0.0-5.3 mL/sec), increasing to 23.2 ± 6.5 mL/sec following the removal of the urethral catheter ($P < .001$), to 21.4 ± 3.2 mL/sec after 3 months ($P < .001$), and to 19.7 ± 4.1 mL/sec after 6 months ($P < .001$). The IPSS, which has a maximum of 35 points,(11) was 31.3 ± 7.2 points (severely symptomatic) at baseline, decreasing to 10.4 ± 3.1 points after catheter removal ($P < .001$), to 8.8 ± 2.3 points after 3 months ($P < .001$),

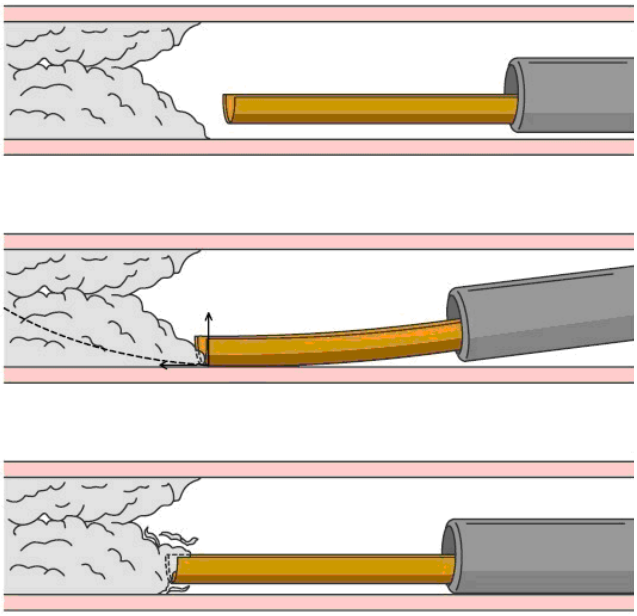

Figure 1. Schematic diagram of endourethrotomy using the poking technique: A) the urethrocystoscope or ureteroscope is advanced in proximity to the stricture; B) the scarred tissues are poked contralaterally to the normal mucosal tissue; and C) the advancement of urethrocystoscope is oriented to parallel the median plane.

and to 9.5 ± 1.8 points after 6 months ($P < .001$). The mean Expanded Prostate Cancer Index Composite (EPIC)[12] QoL index, which was 5.7 ± 1.6 points at the baseline, showed similar improvements, to 2.4 ± 1.1 points after catheter removal ($P < .001$), 1.8 ± 0.9 points after 3 months ($P < .001$), and 1.6 ± 0.7 points after 6 months ($P < .001$).

DISCUSSION

The goal of urethral stricture treatment is to reconstruct the anatomical continuity and patency of the urethra without significantly impairing urogenital functions.[16] Urethrotomy and urethroplasty are thought to be the definitive treatment modalities for urethral strictures; the latter is more frequently used in patients with LSUS due to the high recurrence rate following urethrotomy alone.[13] However, urethroplasty incorporating a skin graft/flap or mucosal onlay has been associated with technical complications, including patch graft failure, urinary tract infection, hair growth and urinary stone formation.[14,15] Therefore, urethrotomy with an end-to-end anastomosis is still recommended as the first-line treatment option of choice in patient with LSUS.[16]

Conventional open urethrotomy is regarded as massively invasive in male patients and has been associated with high risks of urinary fistula and erectile dysfunction.[17] Endourethrotomy, also called endoscopic urethrotomy, is a minimally invasive urological technique.[18] that has shown therapeutic benefits, including good technical reproducibility, precise incision of the scarred tissue, minimal intraoperative bleeding, accelerated postoperative recovery, and, importantly, controlled tissue scarring following wound healing.[19] In this technique, a retrograde urethral incision is performed using a guidewire or ureteral catheter to pass through the stricture. This pass-through, however, is not always possible, especially in patients with LSUS or multiple strictures. In the absence of a guidewire, the retrograde incision using the urethrocystoscope is technically difficult and associated with urethral perforation. We have therefore modified the advancement technique of conventional urethrocystoscopy by combining it with a 'poking' maneuver. In the latter, the urethrocystoscope, or ureteroscope for a small-caliber urethra, is advanced in proximity to the stricture, and the scarred tissues are simultaneously poked, contralaterally to the normal mucosal tissue, to create a lumen-like passage. This maneuver is repeated until the normal mucosal lining appears upwards to the bladder. The endoscope is subsequently withdrawn to the distal end of the stricture to completely eliminate the scarred tissues. If the urethra exhibits complete obliteration, laser ablation is used to incise the scarred tissues through the predefined urethral passage, and the advancement-poking-advancement maneuver is again performed as above. This modified technique was successful in all 208 of our patients with complicating LSUS. The operation time was shorter than that of conventional endoscopic laser urethrotomy, while the short- and long-term safety outcomes were also favorable.

The use of this modified technique requires some expertise and experience with endourological procedures, such as holmium laser enucleation of the prostate. Our results suggest that prior experience with at least 20 patients undergoing endourethrotomy for the treatment of simple urethral strictures is required before performing holmium laser endourethrotomy with the poking maneuver for the treatment of long-segment urethral strictures. Moreover, some technical measures should be considered when using this endoscopic

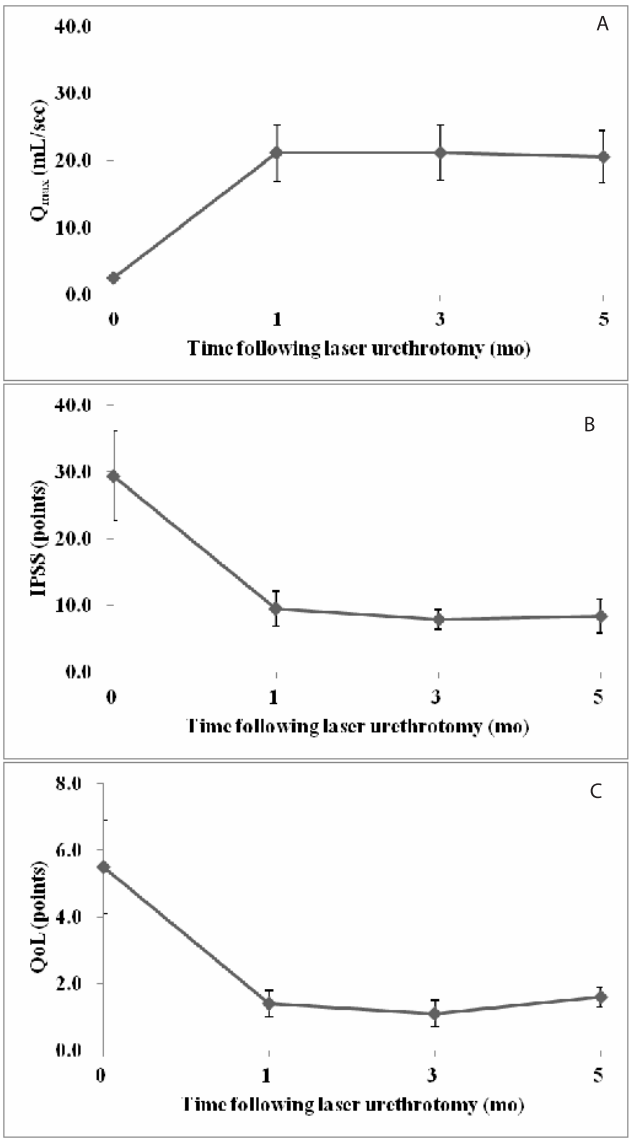

Figure 2. Figure 2. Improvements in maximum flow rate (A), International Prostate Symptom Score (B) and quality of life (C) in patients with long segment urethral strictures following holmium laser endourethrotomy.

maneuver. First, the operator should avoid poking normal mucosal tissues, while poking scarred tissues along their median line or along the interface between the scarred tissues and the normal mucosae. Even if iatrogenic injuries occur to the urethral mucosal lining, the urethral epithelia can proliferate and cover the wound with minimal squeal following the indwelling of the urethral catheter. Second, the urethrocystoscope should be advanced parallel to the median plane between the pubis and the rectum; this orientation is essential for surgical success and safety. Third, the urologist must be acquainted with advanced urogenital anatomy, including the urethral flexure, bulbous urethra, membranous urethra, external urethral sphincter, prostatic urethra, bladder neck and internal urethral orifice, as well as with neighboring structures, including the external urethral sphincter, pubis, rectum and pelvic vessels and nerves. Incidental damage to the external urethral sphincter and rectum are associated with high rates of urinary incontinence and rectal fistulae.[9]

Endourologic ablation methods include the cold-knife, electric resection, and laser incision. The cold-knife was the first ablation technology to be described.[18] This technique has a short patency time and a high recurrence rate, of up to 69% within 6 months of urethrotomy.[20] Our 'poking' maneuver was similar to the cold-knife but was more effective. Electrical resection can result in the complete elimination of scarred tissues and rapid urethral re-epithelialization via the electrothermal effect.[21] However, the resulting tissue coalization can cause fibrovascular proliferation, leading to high rates of stricture recurrence.

Several laser technologies have been widely used to treat urinary calculi, benign prostate hyperplasia, and urethral stricture.[8] The laser sources available for urologic practice include the neodymium,[22] argon,[23] thulium[10] and holmium[8] lasers. The holmium laser is a solid-state laser with a wavelength of 2140 mm and pulse-like emission. Tissue absorption of the holmium laser is nonselective but uniform, with a penetration depth of only 0.4 mm. The emission time is as short as 0.25 msec, with a transient power of up to 10 kW. The laser energy vaporizes its target, such as calculi and scars, in a very short time with minimal thermal release.[24] No tissue coalization or scarring occurs following laser ablation; vaporization, dissection and hemostasis can be achieved simultaneously, resulting in minimal intraoperative bleeding and allowing a precise incision in a clear operative field. No electric current or electric field emerges following holmium laser emission; and iatrogenic injuries, such as the formation of a false urethral passage and external urethral sphincter injury, do not occur incidentally due to the absence of the obturator nerve reflex. Our follow-up results indicate that holmium laser urethrotomy results in favorable therapeutic efficacy, as shown by the reduction in patient symptoms and improvements in urodynamics and overall life of qual-

ity. Holmium laser treatment is also associated with minimal invasiveness, less pain, and rapid postoperative recovery.[25] The elimination of scarred tissues using holmium laser treatment can be completed in either a radiating or an annular manner. This elimination is superior to that achieved with the cold-knife or electric resection, advantages attributed to the high degree of spatial and temporal coherence of the laser. Annular strictures are more common, and usually include a small-size cracked at their center. Laser incision should be started from the center, without requiring any guidance. However, the 0500, 0600 and 0700 o'clock positions cannot be used as the starting points for laser incision of irregularly-shaped strictures. Guidewire is usually needed to eliminate scarred tissues, with a metallic urethral sound used for patients who undergo cystostomy and treatment with a light source, urethral dilator, and ureteral catheter following the poking of scarred tissues. As an alternative to guidewire, optical fibers 200-550 μm in diameter can be advanced into a strictured urethra.

Most LSUS patients have a complex history of treatment with several types of urethral instrumentation and/or surgery. Stricture recurrence is the primary complication following urethrotomy, especially in patients with irregularly-shaped or valve-like residual scarring.[26] The complete elimination of scarred tissues is essential for the reconstruction of urethral continuity and patency. Caution is required during the process of laser urethrotomy to increase the treatment success rate and decrease the restenosis rate. The location, length and severity of strictures should be fully characterized, and a proper guidewire, metallic sound or optical fiber should be inserted to orientate the endoscopic maneuver and prevent the formation of false urethral pathways. In patients with anterior urethral strictures, massive incision of scarred tissues located at the 1200 o'clock position should be avoided to minimize the risk of urethral perforation or fistula. In patients with LSUS following prostate surgery, the external urethral sphincter should be protected to reduce the occurrence of urinary incontinence. Careful wound finishing is critical to minimize postoperative recurrent strictures, and fibrotic scarred tissues should be removed completely. False urethral passages in patients with posterior LSUS should be incised, allowing the passage to communicate with the posterior urethra and to expand the urethral lumen. Scarred tissue projecting into the urethral lumen should be incised thoroughly, but care should be taken to avoid incising the normal urethral mucosae to eliminate the formation of new strictures.

LSUS patients undergoing urethrotomy usually require postoperative urethral dilation. This benefits patients, by minimizing mucosal fibrosis while maximizing urethral re-epithelialization.[27] The duration of urethral catheter placement following holmium laser urethrotomy is relatively shorter, with the duration of catheter indwelling depending primarily on the length of the stricture. For example, catheter indwelling is not required for patients with strictures < 0.5 cm in length, whereas catheter placement should be maintained for one week in patients with 1-cm long and one or two weeks in patients with 1-2 cm long strictures. Following the removal of scarred tissues, mucosal re-epithelialization sufficient to cover the wound normally takes up to 4 weeks, suggesting that the urethral catheter be maintained for at least 4 weeks in patients with complicating LSUS. Most LSUS patients require prophylactic treatment with broad-spectrum antibiotics, as urinary tract infection is a risk factor for recurrent stricture. We have utilized these urethral catheter placement and antibiotic prophylaxis protocols in our patients with LSUS, with none of our patients experiencing stricture recurrence after mid- to long-term follow-up. Although the recurrence rate following holmium laser urethrotomy has been reported to be 18.7% in patients with short-segment urethral stricture, the recurrence rate in our LSUS patients following holmium laser endourethrotomy incorporating the poking maneuver was 0%.

CONCLUSIONS

Holmium endourethrotomy using the poking maneuver is a technically feasible and therapeutically effective urologic modality with minimal invasiveness for the treatment of LSUS. A long-term (>1 year) prospective, blinded, randomized, controlled study is currently ongoing at our institute to further evaluate the clinical usefulness and safety of holmium laser endourethrotomy for the treatment of LSUS.

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CONFLICT OF INTEREST

None declared.

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