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# Endoureterotomy for Ureteral Stricture: A Retrospective Study of Holmium Versus Thulium Lasers

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**Background:** To compare the results of endoureterotomy for benign ureteral strictures by using holmium: yttrium-aluminum-garnet (Ho:YAG) and thulium lasers.

**Methods:** A total of 25 patients (15 men and 10 women, mean age: 49.16 years) underwent endoureterotomy with either Ho:YAG or thulium lasers for benign ureteral strictures (13 proximal, 3 middle, and 9 distal), using semirigid ureteroscopy and a 365-$\mu$m fiber (Ho-YAG laser) at 1.2 J/pulse and 10 Hz, or a 300-$\mu$m fiber (thulium laser) at 8W to 15W. Following incision, a 7-Fr double-J ureteral stent was left for 4 to 6 weeks. Thereafter, patients were followed-up using ultrasonography and/or intravenous urography at 3- to 6-month intervals.

**Results:** Success was defined as the absence of symptoms, plus radiographic resolution of obstructions, as assessed by diuretic renography and/or intravenous urography. With a mean follow-up of 43 months, success was achieved in 10 (52.6%) of 19 patients treated with Ho:YAG laser and in 5 (83.3%) of 6 patients treated with thulium laser. A total of 10 patients developed recurrent strictures and were considered to have treatment failures. Stricture length and the severity of hydronephrosis were correlated with successful outcome. Sex, etiology, side, and stricture location did not predict outcome.

**Conclusions:** Although endoureterotomies using Ho:YAG and thulium lasers had equal efficacy, our analysis revealed that a patient with longer stricture length or severe hydronephrosis is more suitable to receive thulium laser. This general laser procedure is recommended as a safe therapeutic option for the initial management of patients presenting with benign ureteral strictures because it is less invasive.

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A ureteral stricture is characterized by narrowing of the ureteral lumen, causing functional obstruction. The most common form of ureteral stricture is ureteropelvic junction (UPJ) obstruction, characterized by congenital or acquired narrowing at the level of the UPJ. Apart from UPJ obstruction, the most common causes of ureteral stricture are related to acquired and iatrogenic factors. Recent advances in endoscopy have allowed urologists to inspect the entire urinary tract directly through the urethra.[1] However, such wide application of endoscopy has led to an increased frequency of iatrogenic ureteral strictures. Development of small diameter ureteroscopy led to a reduction in ureteral stricture rate. However, endourologic and gynecologic (GYN) procedures are still the most common causes of ureteral injuries, which can subsequently lead to benign ureteral strictures.[2]

By the end of the 20th century, the holmium:yttrium-aluminum-garnet (Ho:YAG) laser had become an established method for the treatment of urinary tract diseases, including stones and ureteral strictures. Compared with open surgery for ureteral stricture, this minimally invasive laser procedure is associated with a shorter hospital stay, lower costs of treatment, and lower morbidity.[3] Over recent years, the thulium laser has begun to play an important role in urologic surgery. Indeed, a previous study reported successful endoscopic procedures for relieving ureteral strictures by using thulium laser.[4] However, to our knowledge, there has yet to be a comparative study of the use of these 2 lasers. In this retrospective study, we report our experience of using Ho:YAG and thulium lasers during endoureterotomy to treat ureteral strictures.

## METHODS

### *Patients*

Between 2002 and 2008, a total of 25 patients presenting with benign ureteral strictures underwent endoureterotomy using the Ho:YAG laser (19 patients) and thulium laser (6 patients) at the Tri-Service General Hospital. The patient cohort consisted of 15 men and 10 women, with a mean age of 49.16 years (range: 20–79 years). Stricture was caused by a stone scar in 22 patients, and ureteral injuries caused by thermal damage during hysterectomy for uterine myoma in 3 patients all of location at lower third of ureter. These cases of ureteral stricture were regarded as "benign."

The length of each ureteral stricture was measured by intravenous urography (IVU), retrograde pyelography, or during ureteroscopy. The severity of hydronephrosis was measured by abdominal sonography. For all cases, we also performed computed tomography (CT) scans with contrast, and urine cytology, in order to exclude the existence of congenital aberrant vessels, acquired fibrotic bands and mass lesion.

Written informed consent to publish the original article was provided by the patient, and the consent procedure was approved by the Ethics Committee of Tri-Service General Hospital.

### *Surgical Technique*

All procedures were performed with the patient in a lithotomy position under spinal anesthesia. Ureteral stricture location and length were typically evaluated by retrograde pyelography, after which a 0.035-inch guidewire was passed through the stricture segment, if possible. Then, the 7.8-Fr semi-rigid ureteroscopes (430 mm, Olympus) were inserted to the level of the stricture and the position was confirmed by fluoroscopy and direct visualization.

The Ho:YAG laser, operated at a wavelength of 2100 nm, with an output of 1.2 J/pulse at a rate of 10 Hz and was delivered via a 360-μm end-firing fiber. The wavelength of the thulium laser was 2013 nm, and the power was initially set to approximately 8W and gradually increased to 15W if necessary. The fiber was extended 2 to 3 mm beyond the tip of the ureteroscope and placed in direct contact with the tissue to be incised. A full-thickness incision, extending into the periureteral fat, was made and then extended 3 to 5 mm above and below the lesion. An incision was made laterally for strictures in the proximal and mid-ureter, and medially for strictures in the distal ureter, to avoid injury to vascular structures. After completing the incision, a 7-Fr double-J ureteral stent was inserted and left for 4–6 weeks. Thereafter, patients were followed-up with ultrasonography and/or IVU at 3- to 6-month intervals.

### *Statistical Analysis*

In this study, success was defined as the absence of symptoms, plus radiographic resolution of obstruc-

*Table 1 Patient clinical characteristics and operative results*

| | Total N = 25 | Holmium laser N = 19 | Thulium laser N = 6 | *P* value |
|---|---|---|---|---|
| Hydronephrosis before surgery | | | | 0.535 |
| Mild, n (%) | 10 (40.0) | 8 (42.1) | 2 (33.3) | |
| Moderate, n (%) | 8 (32.0) | 5 (26.3) | 3 (50.0) | |
| Severe, n (%) | 7 (28.0) | 6 (31.6) | 1 (16.7) | |
| Sex | | | | 0.702 |
| Female, n (%) | 10 (40.0) | 11 (57.9) | 4 (66.7) | |
| Male, n (%) | 15 (60.0) | 8 (42.1) | 2 (33.3) | |
| Stricture reason | | | | 0.687 |
| GYN surgery, n (%) | 3 (12.0) | 2 (10.5) | 1 (16.7) | |
| Stone, n (%) | 22 (88.0) | 17 (89.5) | 5 (83.3) | |
| Side | | | | 0.566 |
| Left, n (%) | 10 (40.0) | 7 (36.8) | 3 (50.0) | |
| Right, n (%) | 15 (60.0) | 12 (63.2) | 3 (50.0) | |
| Age | 49.16 (14.6) | 51.47 (14.6) | 41.83 (12.89) | 0.163 |

tions as assessed by diuretic renography and/or IVU. Statistical analysis was performed using standard statistical software (SPSS 15.0, SPSS Institute, Chicago, Illinois).

The interval to the last clinical or radiographic follow-up in successfully treated patients, and the interval to failure, were considered as the checkpoint and endpoint, respectively, for the construction of a Kaplan-Meier curve. Differences in stricture length in successful and failed operations were analyzed with the Wilcoxon two-sample test, with a value of $P < 0.05$ considered statistically significant.

## Results

Our study included 25 patients and their characteristics are summarized in Table 1. A total of 19 patients underwent Ho:YAG laser endoureterotomy and 6 patients underwent thulium laser endoureterotomy for benign ureteral strictures, 10 on the left ureter and 15 on the right. Surgery was dominated by the Ho:YAG laser (76%), and the degree of hydronephrosis prior to surgery was mainly "mild" (40%), followed by "moderate" (32%). Patients' sex was predominantly male (60%), and the main cause of stricture was stones (88%). The mean length of the strictures was 0.91 cm (range: 0.3–2.5 cm). Of the strictures, 13 were in the proximal ureter, 3 in the middle ureter, and 9 in the distal ureter. In all cases, direct endoscopic visualization of the incised area was possible. Blood loss was minimal, and the lasers provided excellent hemostasis, allowing a clear field of view throughout the procedure. No intraoperative complications were noted. As shown in Table 1, there was no significant difference between the 2 groups of patients treated with Ho:YAG laser and thulium laser ($P > 0.05$).

Endoureterotomy was successful in 9 of the 10 cases of mild hydronephrosis, in 5 of the 8 cases of moderate hydronephrosis, and in 1 of the 7 cases of severe hydronephrosis. There was a successful outcome in 8 of the 13 proximal ureteral strictures, in 1 of the 3 middle ureteral strictures, and in 6 of the 9 distal ureteral strictures. Of the 10 cases of failures, 9 underwent successful open ureteroureterostomy and 1 underwent simple nephrectomy due to renal scans showing reduced ipsilateral function (22.3%). Mean stricture length in the failed operations was 1.30 cm (range: 0.7–2.5 cm), compared with 0.65 cm in the successful operations (range: 0.3–2.0 cm).

The success rate of the Ho:YAG laser was 52.6%, compared with 83.3% for thulium laser. There was no statistically significant difference between the 2 laser methods in terms of success rate when compared by the Fisher's exact test ($P = 0.35$; Table 2).

Next, we used receiver operating characteristic curve (ROC) analysis to investigate how stricture length was related to success rate. As result, the area under the curve (AUC) for the Ho:YAG laser was 0.94, which was statistically significant ($P < 0.01$). Thus, stricture length can be used to predict the success of surgery with good precision. In contrast, the AUC for the thulium laser was 0.80, which was

*Table 2 Success rates of surgical modalities for urethral stricture*

| | Holmium laser | Thulium laser | *P* value |
|---|---|---|---|
| Success, n (%) | 10 (52.6) | 5 (83.3) | 0.35 |
| Failure, n (%) | 9 (47.4) | 1 (16.7) | |

*Table 3 Recommended stricture length by different surgical modality*

| Surgical method | Success if less than or equal to | Sensitivity | 1 - Specificity |
|---|---|---|---|
| Holmium laser | 0.55 | 0.8 | 0 |
| | 0.65 | 0.9 | 0 |
| | 0.75 | 0.9 | 0.22 |
| | 0.9 | 0.9 | 0.56 |
| Thulium laser | 0.900 | 0.400 | 0 |
| | 1.250 | 0.800 | 0 |
| | 1.750 | 0.800 | 1 |

Test result variable(s): stricture length.

*Table 4 The degree of hydronephrosis affect success rate of endoureterotomy*

| | Holmium laser | | | | Thulium laser | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Censored | | | | Censored | |
| Degree | Total, N | Events, N | N | Proportion | Total, N | Events, N | N | Proportion |
| Mild | 8 | 1 | 7 | 87.5% | 2 | 0 | 2 | 100.0% |
| Moderate | 5 | 3 | 2 | 40.0% | 3 | 0 | 3 | 100.0% |
| Severe | 6 | 5 | 1 | 16.7% | 1 | 1 | 0 | 0% |
| Overall | 19 | 9 | 10 | 52.6% | 6 | 1 | 5 | 83.3% |

not statistically significant ($P = 0.38$). Then, we attempted to identify the recommended stricture length. For the Ho:YAG laser, the recommended stricture length was 0.65 cm [maximizing (sensitivity + specificity)]; for the thulium laser, the recommended stricture length was 1.25 cm (Table 3).

Next, we used survival analysis to distinguish the impact of each factor upon success rate. First, we analyzed whether the degree of preoperative hydronephrosis affected the success rate of surgery. Our results showed that the degree of preoperative hydronephrosis differed, and that the success rate differed significantly ($P < 0.01$); the success rate fell as the severity increased (Tables 4 and 5, Fig. 1). We used the same method for sex, side, and stricture cause. However, there were no significant differences in success rate for these factors (Figs. 2, 3, and 4).

Then, we separated the 2 different surgical methods in order to analyze the factors affecting success rate. The degree of preoperative hydronephrosis affected the success rate of surgery for the Ho:YAG laser ($P < 0.01$), but not for the thulium laser ($P = 0.114$; Table 4). Furthermore, sex, side, and stricture cause showed no significant differences in terms of success rate for the 2 different surgical modalities ($P > 0.05$). Next, we used age, side, degree of hydronephrosis, sex, and stricture cause as independent variables for Cox regression to analyze multiple variables and identify the main elements affecting success rate. The analysis showed that only the degree of preoperative hydronephrosis was a significant element: in severe cases, the hazard ratio (HR) was 44.34; in other words, the failure rate for severe patients was 44.34 times that of patients with mild preoperative hydronephrosis (Table 6). Finally, we used different surgical approaches as a factor for stratified Cox regression, to identify the common impact of factors in different surgical methods. This also showed that severe hydronephrosis was a significant factor, with a HR of 797.3 (Table 7).

## Discussion

Endourology is widely applied as a minimally invasive procedure in the urological field; the

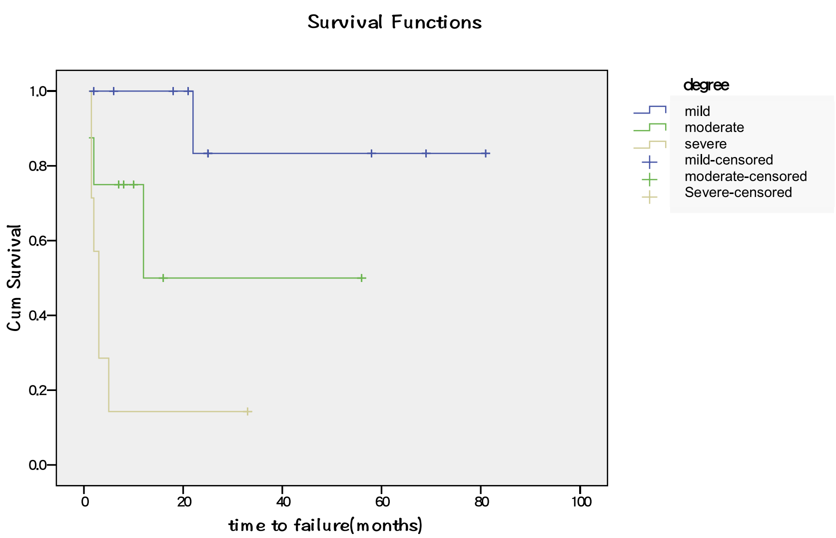


**Fig. 1** The degree of preoperative hydronephrosis differed, and that the success rate differed significantly ($P <$ 0.01); the success rate fell as the severity increased.

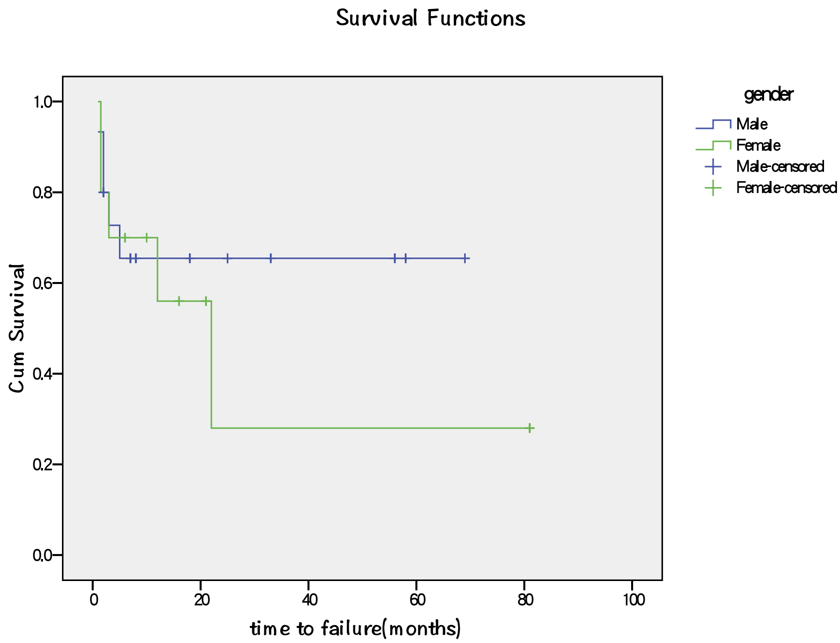


**Fig. 2** Sex is independent factor in success rate.

popularity of this technique is due to low morbidity, short hospitalization period, and the early restoration of preoperative activities.[5] However, the extensive application of the ureteroscope as an alternative to gynecological and general surgery soon became the main cause of ureteral stricture. The iatrogenic damage caused by ureteroscopy involves a variety of factors, including direct perforation, large-caliber ureteral instruments, thermal damage, and a lack of operator experience.[6] Ferraro *et al*[7] reported that the complication rate of ureteroscopy was markedly reduced when small caliber ureteroscopes were used, compared with those used in the late 1980s.

Traditionally, and prior to the emergence of minimally invasive methods, the most common methods for treating ureteral strictures were segmental resection and ureteral reimplantation. In 1983, Banner *et al*[8] reported the use of balloon dilatation for ureteral strictures. In the same year, Wickham[9] first reported the use of endoscopy in the treatment of obstructions at the ureteropelvic junction by using a cold-knife urethrotome to incise the ureteropelvic junction, using a percutaneous nephrostomy tract. The success rate of endoscopic ureteral incision using a cold knife or electrocautery was 57% to 100%.[10] Several clinical series have

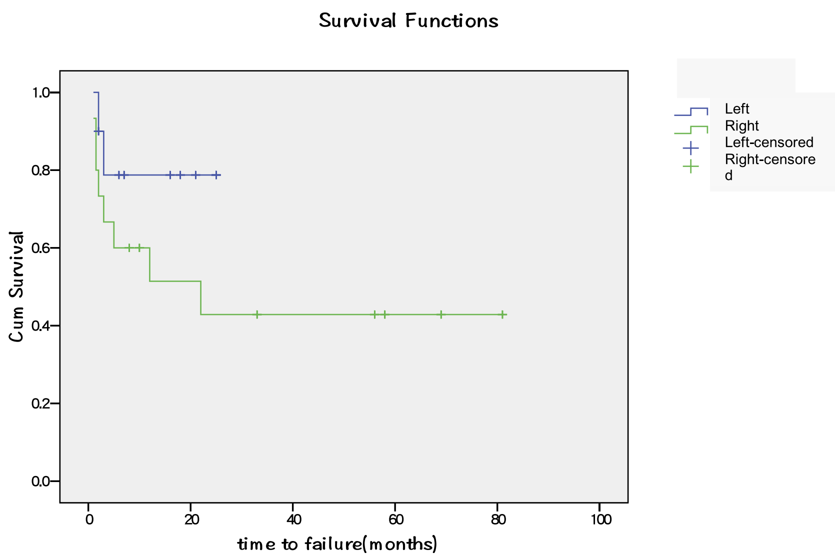


**Fig. 3** Side is independent factor in success rate.

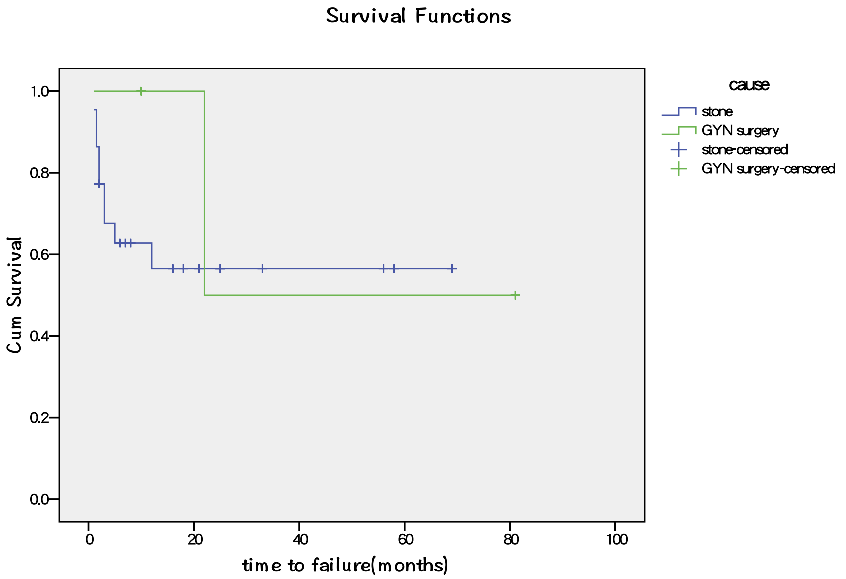


**Fig. 4** Stricture cause is independent factor in success rate.

further documented the efficacy of balloon dilation for benign ureteral strictures to range from 48% to 82%.[11,12] However, to date, there has been no standard treatment for ureteral strictures.

The ideal energy for endoureterotomy should be able to supply a full-thickness incision of a stricture segment, but not cause significant damage to the surrounding tissues. In addition, the energy source should be able to fit into flexible and semirigid ureteroscopes and provide a hemostatic incision with a clear field of view during surgery. We believe that direct visualization during use of ureteroscope is necessary; consequently, mounting evidence indicates that use of the Ho:YAG or thulium laser for endoureterotomy is preferred for hemostatic incision.

The long-term follow-up success rate for Ho:YAG laser endoureterotomy has been reported to be 68.4%,[12] while that for the thulium laser is 75%.[4] Predictors for a successful outcome include non-ischemic strictures, short strictures and those of recent origin (<6 months).[2] Use of the Ho:YAG laser in 19 patients with benign ureteral strictures led to a success rate of 52.6% (10 out of 19 patients), while the thulium laser showed a success rate of 83.3% (5 out of 6 patients) at a mean follow-up of 43 months. However, there was no statistically significant difference between the 2 laser methods in terms of success rate ($P = 0.35$); thus, no single method can yield a superior success rate.

Our analysis showed that stricture length was correlated with successful outcome. Cases of a stricture of less than 0.65 cm tended to show better success rates with the Ho:YAG laser ($P = 0.001$), while strictures of approximately 1.25 cm showed better success rates with the thulium laser ($P < 0.01$). The recommended stricture length for the thulium laser was nearly twice that of the Ho:YAG laser, and short

*Table 5 Overall comparisons*

| | $X^2$ | DF | P value |
|---|---|---|---|
| Holmium laser log rank (Mantel-Cox) | 8.453 | 1 | 0.004 |
| Thulium laser log rank (Mantel-Cox) | 2.500 | 1 | 0.114 |

DF, degree of freedom.

*Table 6 Analyze multiple variables of success rate for ureteral stricture*

| | Frequency | (1) | (2) |
|---|---|---|---|
| Side | | | |
| 1 = left | 10 | 0 | |
| 2 = right | 15 | 1 | |
| Degree | | | |
| 1.00 = mild | 10 | 0 | 0 |
| 2.00 = moderate | 8 | 1 | 0 |
| 3.00 = severe | 7 | 0 | 1 |
| Sex | | | |
| 1.00 = Male | 15 | 0 | |
| 2.00 = Female | 10 | 1 | |
| Cause | | | |
| 1.00 = stone | 22 | 0 | |
| 2.00 = GYN surgery | 3 | 1 | |
| P value | | HR | |
| Degree: moderate | 0.17 | 6.29 | |
| Degree: severe | 0.03 | 44.34 | |
| Sex: female | 0.09 | 4.9 | |
| Side: right | 0.8 | 1.29 | |
| Cause: GYN surgery | 0.78 | 0.68 | |
| Age | 0.31 | 0.96 | |

Categorical variable codings.

*Table 7 Distinguish multiple variables affecting success rate between different surgical modality*

| | B | SE | Wald | DF | *P* value | HR | 95.0% CI for HR | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| Degree: moderate | 4.07 | 2.48 | 2.69 | 1 | 0.10 | 58.77 | 0.45 | 7654.45 |
| Degree: severe | 6.68 | 3.29 | 4.12 | 1 | 0.04 | 797.30 | 1.26 | 505847.0 |
| Sex: female | 1.34 | 0.90 | 2.18 | 1 | 0.14 | 3.81 | 0.65 | 22.40 |
| Side: right | –0.95 | 1.30 | 0.54 | 1 | 0.46 | 0.39 | 0.03 | 4.92 |
| Cause: GYN surgery | 1.85 | 2.40 | 0.60 | 1 | 0.44 | 6.38 | 0.06 | 699.04 |
| Age | –0.09 | 0.06 | 2.50 | 1 | 0.11 | 0.91 | 0.81 | 1.02 |

stricture length may be associated with a favorable outcome. In addition, our study showed that the degree of preoperative hydronephrosis was shown to affect the success rate of surgery using the Ho:YAG laser ($P < 0.01$), but not the thulium laser ($P = 0.114$). After further analysis, this association was only statistically significant when the degree of preoperative hydronephrosis was severe (HR = 44.34). Thus, severe preoperative hydronephrosis may predict a poor outcome for the two laser methods. However, age, sex, cause, side, and the location of strictures were not able to predict surgical outcome.

Interestingly, one previous study reported a different opinion to ours in terms of the location of stricture, in which the proximal and distal ureters were associated with the greatest chance of success.[14] However, in our study, only 3 patients had stricture of the middle third and showed no statistical difference in terms of success rate.

There is no standard duration of stenting following an endoureterotomy. Most authors agree in that there is a requirement for insertion of a stent following endoureterotomy; however, if the stent retention time is too long, inflammation can occur and may induce secondary stricture. The rational duration for the use of a stent is 6 weeks according to the findings of Davis,[15] who demonstrated that ureteral muscular regrowth occurred after 6 weeks. However, some authors have documented similar success rates with shorter stenting periods.[16] In our current cohort, stents were removed 4 to 6 weeks after surgery, depending upon the surgeon's judgement, and there was no significant difference detected in terms of success rate. Thus, due to the lack of randomized prospective studies, the duration of stenting remains controversial.

Our work has shown that endoureterotomy with Ho:YAG and thulium-lasers is a safe, less invasive, and effective modality for treating benign ureteral strictures. Furthermore, the degree of preoperative hydronephrosis and stricture length play an important role in the prognosis. Although endoureterotomy using Ho:YAG and thulium lasers were associated with equal efficacy in our present study, thulium laser is more suitable for patients with a longer stricture length or severe hydronephrosis. The recommended stricture length for thulium laser (1.25 cm) was nearly twice that for Ho:YAG laser (0.65 cm) and short stricture length may have led to favorable outcomes. However, the thulium laser is more expansive than the Ho:YAG laser; this factor will therefore influence the choice made by doctors and patients. Our study was based upon reviews of retrospective data and our patient numbers are small; these limitations should be considered when interpreting our conclusions. Larger randomized prospective studies, with longer follow-up periods, are now required to allow us to make a reliable assessment of efficacy and prove which laser system is superior.

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