African Journal of Urology

ORIGINAL RESEARCH Open Access

Stone-free rate after semirigid ureteroscopy with holmium laser lithotripsy versus laparoscopic ureterolithotomy for upper ureteral calculi: a multicenter study

Ahmed Issam Ali[1], Ali M. Abdel-Karim[2], Ahmed A. Abd El Latif[3], Amr Eldakhakhny[4], Ehab M. Galal[1], Ahmed Z. Anwar[1], Mamdouh M. El-Hawy[1], Tarek K. H. Fathelbab[1], Mohamed S. Elbadry[1], Mostafa S. Elsharkawy[1] and Ehab R. Tawfiek[1*]

Abstract

Background: Different treatment options were used to treat upper ureteral calculi. The aim of our study is to compare the stone-free rate and postoperative outcomes between semirigid ureteroscope with holmium laser lithotripsy and laparoscopic ureterolithotomy for the management of large solitary upper ureteral stones. Sixty-seven patients with a solitary upper ureteral stone who had LU or semirigid ureteroscopy in the period between January 2014 and March 2017 were included in our study. Out of the sixty-seven patients, 37 patients had semirigid ureteroscopy and holmium laser lithotripsy (Group A) and 30 patients had laparoscopic ureterolithotomy (Group B). Both groups were compared regarding operative time, intraoperative complications, need for auxiliary procedures, hospital stays, postoperative complications and stone-free rate.

Results: The mean stone size was 1.84 ± 0.12 cm in Group A and 1.79 ± 0.17 cm in Group B, *P* value = 0.2. The mean operative time was 61.5 ± 3.5 min in Group A and 63 ± 4.2 min in Group B, *P* value = 0.13. Stone migration was recorded in five cases (14%) in Group A while no cases in Group B had stone migration. Flexible ureteroscope was used as an auxiliary measure in five patients (14%) in Group A at the same session. No auxiliary measures were used in the LU group.

Conclusion: The stone-free rates after semirigid URS and laser lithotripsy are comparable to those following LU, especially when flexible URS is used to manage migrating stone fragments at the same session.

Keywords: Ureteroscopy, Laparoscopy, Lithotripsy, Laser, Upper ureter, Stone, Free rate

1 Background

Different treatment options are available for the management of upper ureteral calculi including medical expulsive therapy, shock wave lithotripsy (SWL), laparoscopic ureterolithotomy, ureteroscopy and open ureterolithotomy [1]. Medical expulsive therapy using alpha blockers (i.e., alfuzosin, tamsulosin) or calcium channel blockers (i.e., nifedipine) has been used to treat patients with ureteral stones [2, 3]; however, a multicenter, randomized, placebo-controlled trial has demonstrated different outcomes and questioned the efficacy of medical expulsive therapy for the treatment of ureteral calculi [4]. Different surgical options can be offered to patients with upper ureteral stones that are refractory to medical treatment and to patients with large upper ureteral stones. The EAU and AUA have recommended shock wave lithotripsy (SWL) or ureteroscopic lithotripsy as a first line of treatment. Nevertheless, percutaneous nephrolithotripsy (PCNL) and laparoscopic ureterolithotomy (LU) may

*Correspondence: Ehabr1966@yahoo.com
[1] Department of Urology, School of Medicine, Minia University Hospital, Minia University, Minia 61111, Egypt
Full list of author information is available at the end of the article

be suitable options [1, 5–7]. The management of upper ureteral large stones is still controversial. Ureteroscopic lithotripsy is a minimally invasive technique for the management of upper ureteral stones; however, its efficacy decreases in large upper ureteral stones [8].

Laparoscopic ureterolithotomy (LU) has been used for large upper ureteral stones. Although it is more invasive, it gives a chance of complete stone clearance in a single session [9]. The aim of our study is to compare the stone-free rate and postoperative outcomes between semirigid ureteroscopy with holmium laser lithotripsy and laparoscopic ureterolithotomy for the management of large upper ureteral stones.

2 Methods

We reviewed our records in the period between January 2014 and March 2017; sixty-seven patients with solitary upper ureteral stone who had LU or semirigid ureteroscopy and holmium laser lithotripsy were included in our study. All procedures in the four centers were performed by well-trained surgeons with equivalent surgical experiences.

The mean stone size was 1.82 ± 0.15 cm (range 1.5:2 cm). All stones were located at the upper ureteral segment. Out of 67 patients, 37 patients had semirigid ureteroscopy and holmium laser lithotripsy (Group A) and 30 patients had laparoscopic ureterolithotomy. We excluded patients with stones smaller than 1.5 cm and bigger than 2 cm, previous open abdominal surgery, bleeding disorders, current UTI, respiratory illness, pregnancy, patients with one functioning kidney, fever > 37.2 and leukocytosis > 12.000 per microliter.

All patients were subjected to history taking and clinical examination, urinalysis and urine culture, renal function test, liver function test, coagulation profile, serum calcium, serum phosphate and serum uric acid, 24H urinalysis for calcium, phosphate and uric acid, renal ultrasound, KUB and noncontrast CT scan.

In Group A, all patients received general anesthesia. Cystoscopy and retrograde pyelogram were performed first, and then 6/7.5 semirigid ureteroscope was introduced through the ureteric orifice. Using follow-the-wire technique, a sensor guide wire was introduced till the level of the stone [10]. Under direct vision, the sensor guide wire was advanced to pass the stone all the way up to the kidney. Semirigid ureteroscope allowed steadiness during stone manipulation and subsequently allowed controlled movement to pass the wire beyond the stone without pushing the stone back to the kidney. Through the whole procedure, the fluid irrigation force was limited to a degree sufficient to see the stone without any pushing force (Fig. 1).

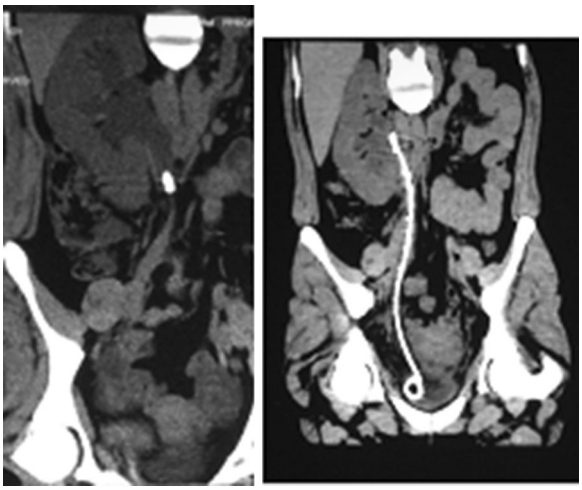

Fig. 1 Forty-year-old male patient presented with right upper ureteral stone (1.7 cm). Stone disintegration was performed using semirigid URS and laser lithotripsy. JJ stent was placed at the end of the procedure

Semirigid ureteroscope allowed passing the edema below the stone that may present in some cases and subsequently passing the guide wire under direct vision up to the kidney. The ureteroscope was withdrawn and reintroduced all the way to the stone. Holmium laser was used with setting of 0.5 J/20 Hz, and laser fiber size 270 was introduced through the scope. Laser dusting technique was used to minimize stone retropulsion. In case of stone migration to the kidney, flexible ureterorenoscopy with holmium laser lithotripsy was used for stone disintegration. A ureteral stent was left at the end of the procedure and was removed after 2 weeks (Fig. 2).

Group B included patients who underwent laparoscopic ureterolithotomy. All patients received general anesthesia, and the patient was placed in lithotomy position. Diagnostic cystoscopy and retrograde pyelogram at the side of the stone were performed followed by introduction of sensor wire up to the lower border of the stone. Open-end ureteral catheter was introduced over the wire till the lower end of the stone. After that, the patient was repositioned into the modified flank position, 10 mm camera port was placed through the umbilicus and 10 mm port was placed midway between the umbilicus and anterior superior iliac spine. A 5 mm port was placed at the lumber region on the mid-clavicular line. A 5 mm harmonic shear [Ethicon Endo-Surgery (Johnson & Johnson) GEN 11] was used to dissect and reflect the colon.

The ureter was identified, stone was located and a vertical ureterotomy over the stone was performed to extract the stone. A stone grasper was used to deliver the stone

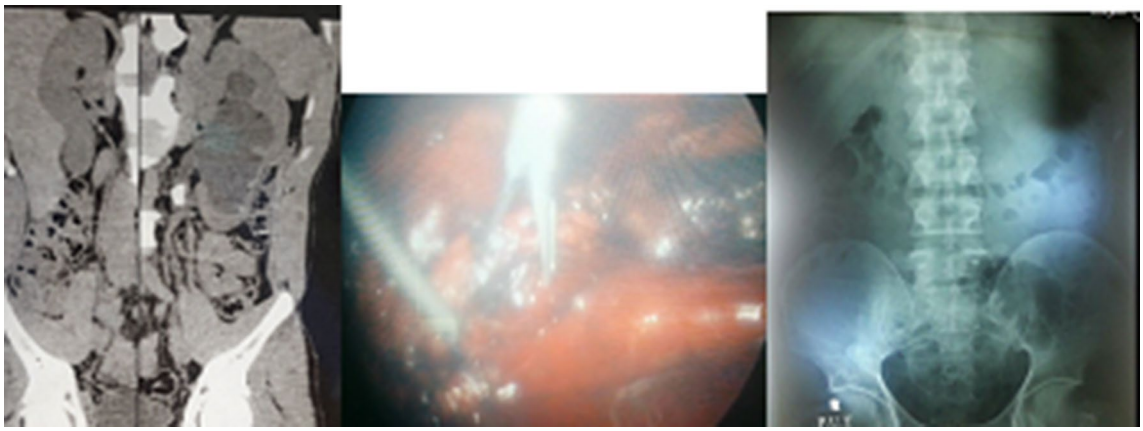

Fig. 2 Twenty-eight-year-old male patient presented with left upper ureteral stone (1.9 cm), Laparoscopic left ureterolithotomy was performed. KUB after JJ stent removal was stone free

through the ureterotomy. The sensor wire was advanced up to the kidney. A 4/0 Vicryl suture was used to close the ureterotomy. A small drain was introduced through the 10 mm port. The patient was then repositioned in lithotomy position, and a ureteral stent was then loaded over the wire. A Foley catheter was placed at the end of the procedure and was removed in POD 1.

Stone-free status was defined as absence of residual stones or the presence of residual stone fragments ≤ 4 mm in size on X-ray KUB performed up to 1 month after surgery [11].

Ureteral stents were removed after 2 weeks. In both groups, stones were sent for stone analysis. Postoperative follow-up included KUB/CT at 2 weeks postoperatively for both groups before ureteral stent removal to confirm stone clearance and absence of large residual stone fragments. (Fragment > 4 mm was considered residual stone.)

The need for any auxiliary measures either during the same session or at a different session was recorded in both groups.

3 Statistics

Data were analyzed using SPSS version 20.0 statistical software (SPSS Inc., Chicago, IL, USA). Chi-square test and Fisher exact were used to compare categorical variables. Mann–Whitney test was used to compare two groups. *P* value less than 0.05 was used as cutoff for significance.

4 Results

Of 115 patients who had solitary upper ureteral calculi, 67 patients met the inclusion criteria of our study. Of the 67 patients, 37 patients treated by semirigid ureteroscopy and laser lithotripsy were included in Group A and 30 patients treated by LU were included in Group B. The demographic data of our study included numbers of patients in each group, age, sex, stone location and stone size as shown in Table 1.

There was no significant difference between both groups regarding the operative time. The mean operative time was 61.5 ± 3.5 and 63.1 ± 4.2 min in both Groups A and B, respectively ($P = 0.13$). The number of auxiliary measures was significantly higher in Group A in comparison with Group B ($P = 0.02$).

The stone-free rates after 2 weeks in both groups were 100%. No significant difference was observed between both groups regarding postoperative complications. Postoperative UTI was detected in three cases in Group A (8.1%) and in one case in Group B (3.3%), UTI was treated by antibiotics according to urine culture and

Table 1 Demographic data

	Group A *N* = 37	Group B *N* = 30	*P* value
Sex			
Male	20 (54.1%)	17 (56.7%)	0.831 NS
Female	17 (45.9%)	13 (43.3%)	
Age			
Range	29–55	31–55	0.09 NS
Mean ± SD	39.4 ± 6.3	42.7 ± 7.2	
Median	39	42	
Location of stone			
Right side	16 (43.2%)	15 (50%)	0.581 NS
Left side	21 (56.8%)	15 (50%)	
Size of stone (cm)			
Range	1.5–2	1.5–2	0.240 NS
Mean ± SD	1.84 ± 0.12	1.79 ± 0.17	
Median	1.81	1.80	

sensitivity results and UTI was classified as grade II complication according to Clavien–Dindo classification. Macroscopic hematuria was detected in three cases in Group A (8.1%) and in one case in Group B (3.3%), macroscopic hematuria was classified as grade I complication according to Clavien–Dindo classification and was managed conservatively.

Stone migration was reported in five patients (14%) in Group A, for whom flexible ureteroscopy was used at the same session to disintegrate the migrated stones. No cases of stone migration were recorded in Group B (Table 2). Ureteric injury was not recorded in any case in Group A.

One case in the LU group was converted to open surgery due to extensive adhesions around the kidney and upper ureter; the patient had history of repeated episodes of acute pyelonephritis. No significant difference between both groups regarding stone composition was detected (Table 3).

Table 2 Operative data and postoperative complications

	Group A (37 patients)	Group B (30 patients)	*P* value
Operative time (min)			
Range	52–71	56–70	0.135 NS
Mean ± SD	61.5 ± 3.5	63.1 ± 4.2	
Median	62	63	
Hospital stay (days)			
1	30 (81.1%)	0 (0%)	< 0.001
2	6 (16.2%)	28 (93.3%)	
3	1 (2.7%)	2 (6.7gt %)	
Mean hospital stay	1.2 ± 0.47	2.07 ± 0.25	< 0.001
Stone migration			
Present	5 (13.5%)	0 (0%)	0.036
Absent	32 (86.5%)	30 (100%)	
Auxiliary			
Yes	5 (13.5%)	0 (0%)	0.036
No	32 (86.5%)	30 (100%)	
Free rate			
Free	37 (100%)	30 (100%)	1 NS
Residual	0 (0%)	0 (0%)	
UTI			
Present	3 (8.1%)	1 (3.3%)	0.412 NS
Absent	34 (91.9%)	29 (96.7%)	
Macroscopic hematuria			
Present	3 (8.1%)	1 (3.3%)	0.412 NS
Absent	34 (91.9%)	29 (96.7%)	
Urinary leakage	0 (0%)	0 (0%)	1 NS

Table 3 Stone composition

Stone composition	Group A (URS) *N* = 37	Group B (lap) *N* = 30	*P* value
Ca oxalate monohydrate	9 (24.3%)	4 (13.3%)	0.489 NS
Ca oxalate dehydrate	10 (27%)	8 (26.7%)	
Mixed stones	18 (48.6%)	18 (60%)	
Total	37 (100%)	30 (100%)	

Regarding hospital stay in both groups, mean hospital stay was 1.2 ± 0.47 and 2.07 ± 0.25 days in groups A and B, respectively ($P \leq 0.001$).

5 Discussion

Upper ureteral calculi management is always considered a point of debate. Stone size, intensity and duration of pain, presence of obstruction and availability of equipment are factors that determine which treatment line we select for the management of upper ureteral calculi. Different lines of treatment are available to treat upper ureteral stones like SWL, ureteroscopy and laparoscopic ureterolithotomy [12].

The medical expulsive therapy is suitable for stone less than 5 mm [13]. SWL can also be used for the treatment of upper ureteral calculi. SWL is a safe, noninvasive technique and can be performed as an outpatient procedure. [14]. SWL has a high success rate for upper ureteral stone that is less than 1 cm, and stone larger than 1 cm may require more than one session of SWL [15]. Ureteroscopy is an attractive modality used to treat upper ureteral stones; it is less invasive and has a high stone clearance rate. Ureteroscopy with holmium laser lithotripsy can be used for the management of stones larger than 1 cm. The main disadvantages of semirigid ureteroscopy and holmium laser lithotripsy are a higher retreatment rate for larger stones and stone up-migration [16, 17].

Laparoscopic ureterolithotomy is another treatment modality that can be used for the removal of large upper ureteral stone. LU can be done through a retroperitoneal or transperitoneal approach [18–22]. The LU allows complete stone removal in one sitting [19].

In 1992, Raboy et al. [23] performed the first transperitoneal laparoscopic ureterolithotomy. Neto et al. [24] reported a success rate of 93% for laparoscopic ureterolithotomy in comparison with SWL and semirigid ureteroscopy with laser lithotripsy (35%, 62%, respectively). Fang et al. [8] in his comparative study between LU and ureteroscopic holmium laser lithotripsy concluded that LU has a higher stone-free rate in comparison with ureteroscopy and laser lithotripsy. Ko et al. [25] recorded a higher stone-free rate after a single session in LU in comparison with rigid

ureteroscopy (93% vs 68%). Anup Kumar et al. [26] reported that for stone larger than 2 cm located at upper ureteral segment, LU is a better option for cure with lower complication and retreatment rates. Tugcu et al. compared LU and ureteroscopy for upper ureteral stone > 15 mm, and Tugcu et al. [27] found that the success rate was higher in the LU group (100% vs. 87%).

Different studies suggested that LU provides a higher stone-free rate than ureteroscopy and laser lithotripsy in the management of large upper ureteral stones [28]. In our study, there is no significant difference between both groups regarding the stone-free rate, especially when flexible ureterorenoscopy was used to manage migrating stone fragments at the same session after semirigid ureteroscope. In the ureteroscopy group, different precautions were followed to minimize stone retropulsion like usage of low and intermittent flow of irrigating fluid, patients were placed in a mild degree of anti-Trendelenburg position during the procedure and stone dusting technique was used as much as possible to minimize stone retropulsion. A shorter hospital stay was observed in the ureteroscopy group in comparison with the LU group.

The need for auxiliary measures was not needed for any case in the LU group while it was recorded in five patients in (14%) in the ureteroscopy and laser lithotripsy group ($P = 0.02$). The need for second session was not recorded for any patient in both groups. A conversion to open surgery was recorded for one case in the LU group, secondary to extensive adhesions around the kidney and upper ureter. Anup et al. did not report any auxiliary measures used in the LU group, but he reported 13 cases in the ureteroscopy group in whom auxiliary measures were used ($P = 0.001$) [26]. In our study, the operative time and hospital stay were longer in LU group in comparison with the ureteroscopy group with no significant difference between both groups ($P = 0.184$). There is no significant difference between both groups regarding early postoperative complications like UTI and hematuria.

Three patients in ureteroscopy group developed UTI controlled by antibiotics. No cases developed urosepsis in ureteroscopy group. We assume that using a low-pressure irrigation flow during the procedure reduces the incidence of septicemia in ureteroscopy group.

Unfortunately, we were not able to compare the cost-effectiveness between the two groups. However, our study showed that semirigid ureteroscope with laser lithotripsy is an effective technique to treat large upper ureteral stones with a low rate of stone migration that requires usage of flexible ureterorenoscopy. In our technique, the use of flexible ureterorenoscopy was limited to migrated stones only, which in turn decreases the frequency of usage of an expensive instrument (flexible ureterorenoscopy) and reduces the overall cost of the procedure.

6 Study limitations

Our study is a retrospective study that is subjected to selection bias and recall bias. Further prospective studies with prolonged follow-up periods are recommended to emphasize our study results and conclusion.

7 Conclusion

The stone-free rate following semirigid ureteroscope and laser lithotripsy of upper ureteral calculi (between 1.5:2 cm) is comparable to that following LU, especially when flexible ureteroscope is used to manage migrating stone fragments at the same session.

Abbreviations

LU: laparoscopic ureterolithotomy; URS: ureteroscopy; SWL: shock wave lithotripsy; EAU: European Association of Urology; AUA: American Urological Association; PCNL: percutaneous nephrolithotripsy; J: joule; Hz: hertz; ASIS: anterior superior iliac spine; POD: postoperative day; CT: computed tomography; KUB: kidney, ureter, bladder; UTI: urinary tract infection.

Acknowledgements

Not applicable.

Committee's reference number

Not applicable.

Authors' contributions

AIA conceived the idea performed the laparoscopic surgery and was involved in data collection, writing and doing statistics. AMA performed the laparoscopic surgery and reviewed the manuscript. AAA performed the surgery and was involved in data collection. AE performed the surgery and was involved in data collection. EMG helped in writing the manuscript. AZA did the statistical part and reviewed the paper. MME was involved in data collection and reviewed the paper. TKHF conceived the idea, reviewed the manuscript and was involved in data collection. MSE was involved in data collection. MSE reviewed the manuscript. ERT conceived the idea, did all the ureteroscopic procedures and reviewed the manuscript. All authors read and approved the final manuscript.

Funding

This study was not funded.

Availability of data and materials

All data and materials belonging to the manuscript are available.

Ethics approval and consent to participate

Our study is a retrospective study, and all procedures performed in our study participants were in accordance with the ethical standards of the National Research Committee and Faculty of Medicine Research Ethics Committee at Minia University, Minia, Egypt. A written informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details
[1] Department of Urology, School of Medicine, Minia University Hospital, Minia University, Minia 61111, Egypt. [2] Department of Urology, School of Medicine, Alexandria University Hospital, Alexandria University, Alexandria 61111, Egypt. [3] Department of Urology, School of Medicine, Beni-Suef University Hospital, Beni-Suef University, Beni Suef 61111, Egypt. [4] Department of Urology, School of Medicine, Benha University Hospital, Benha University, Benha 61111, Egypt.

Received: 17 October 2019 Accepted: 29 October 2019
Published online: 20 December 2019

References

1. Preminger GM, Tiselius HG, Assimos DG et al (2007) 2007 guideline for the management of ureteral calculi. J Urol 178(6):2418–2434
2. Campschroer T, Zhu Y, Duijvesz D et al (2014) Alpha-blockers as medical expulsive therapy for ureteral stones. Cochrane Database Syst Rev 4:Cd008 509
3. Dellabella M, Milanese G, Muzzonigro G (2005) Randomized trial of the efficacy of tamsulosin, nifedipine and phloroglucinol in medical expulsive therapy for distal ureteral calculi. J Urol 174(1):167–172
4. Pickard R, McClinton S, Starr K et al (2015) Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. Lancet 386(9991):341–349
5. Tiselius HG, Ackermann D, Alken P et al (2001) Guidelines on urolithiasis. Eur Urol 40(4):362–371
6. Bader MJ, Eisner B, Porpiglia F et al (2012) Contemporary management of ureteral stones. Eur Urol 61(4):764–772
7. Matlaga BR, Jansen JP, Meckley LM et al (2012) Treatment of ureteral and renal stones: a systematic review and meta-analysis of randomized, controlled trials. J Urol 188(1):130–137
8. Fang YQ, Qiu JG, Wang DJ et al (2012) Comparative study on ureteroscopic lithotripsy and laparoscopic ureterolithotomy for treatment of unilateral upper ureteral stones. Acta Cir Bras 27(3):266–270
9. El-Feel A, Abouel-Fettouh H, Abdel-Hakim AM (2007) Laparoscopic transperitoneal ureterolithotomy. J Endourol 21(1):50–54
10. Tawfief ER (2009) Ureteroscopy during pregnancy with follow-the-wire technique. Afr J Urol 15(4):245–249
11. Bhat A, Singh V, Bhat M et al (2019) Comparison of antegrade percutaneous versus retrograde ureteroscopic lithotripsy for upper ureteric calculus for stone clearance, morbidity, and complications. Indian J Urol 35(1):48–53. https://doi.org/10.4103/iju.iju_89_18
12. Nikoobakht MR, Emamzadeh A, Abedi AR et al (2007) Transureteral lithotripsy versus extracorporeal shock wave lithotripsy in management of upper ureteral calculi: a comparative study. Urol J 4(4):207–211
13. Morse RM, Resnick MI (1991) Ureteral calculi: natural history and treatment in an era of advanced technology. J Urol 145(2):263–265
14. Nabi G, Baldo O, Cartledge J et al (2003) The impact of the Dornier Compact Delta lithotriptor on the management of primary ureteric calculi. Eur Urol 44(4):482–486
15. Rabani SM, Moosavizadeh A (2012) Management of large proximal ureteral stones: a comparative clinical trial between transureteral lithotripsy (TUL) and shock wave lithotripsy (SWL). Nephrourol Mon 4(3):556–559
16. Lam JS, Greene TD, Gupta M (2002) Treatment of proximal ureteral calculi: holmium:YAG laser ureterolithotripsy versus extracorporeal shock wave lithotripsy. J Urol 167(5):1972–1976
17. Tawfick ER (2010) Treatment of large proximal ureteral stones: extra corporeal shock wave lithotripsy versus semi-rigid ureteroscope with lithoclast. Int Arch Med 3:3
18. Gaur DD, Trivedi S, Prabhudesai MR et al (1994) Retroperitoneal laparoscopic ureterolithotomy for multiple upper mid ureteral calculi. J Urol 151(4):1001–1002
19. Keeley FX, Gialas I, Pillai M et al (1999) Laparoscopic ureterolithotomy: the Edinburgh experience. BJU Int 84(7):765–769
20. Gaur DD (1993) Retroperitoneal endoscopic ureterolithotomy: our experience in 12 patients. J Endourol 7(6):501–503
21. Harewood LM, Webb DR, Pope AJ (1994) Laparoscopic ureterolithotomy: the results of an initial series, and an evaluation of its role in the management of ureteric calculi. Br J Urol 74(2):170–176
22. Nualyong C, Taweemonkongsap T (1999) Laparoscopic ureterolithotomy for upper ureteric calculi. J Med Assoc Thai 82(10):1028–1033
23. Raboy A, Ferzli GS, Ioffreda R et al (1992) Laparoscopic ureterolithotomy. Urology 39(3):223–225
24. Lopes Neto AC, Korkes F, Silva JL et al (2012) Prospective randomized study of treatment of large proximal ureteral stones: extracorporeal shock wave lithotripsy versus ureterolithotripsy versus laparoscopy. J Urol 187(1):164–168
25. Ko YH, Kang SG, Park JY et al (2011) Laparoscopic ureterolithotomy as a primary modality for large proximal ureteral calculi: comparison to rigid ureteroscopic pneumatic lithotripsy. J Laparoendosc Adv Surg Tech A 21(1):7–13
26. Kumar A, Vasudeva P, Nanda B et al (2015) A prospective randomized comparison between laparoscopic ureterolithotomy and semirigid ureteroscopy for upper ureteral stones > 2 cm: a single-center experience. J Endourol 29(11):1248–1252
27. Tugcu V, Resorlu B, Sahin S et al (2016) Flexible ureteroscopy versus retroperitoneal laparoscopic ureterolithotomy for the treatment of proximal ureteral stones > 15 mm: a single surgeon experience. Urol Int 96(1):77–82
28. Torricelli FCM, Monga M, Marchini GS et al (2016) Semi-rigid ureteroscopic lithotripsy versus laparoscopic ureterolithotomy for large upper ureteral stones: a meta analysis of randomized controlled trials. Int Braz J Urol 42:645–654

Publisher's Note