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Original Article

Holmium laser lithotripsy reduces complications and relieves postoperative pain in elderly patients with urinary calculi

Qi Liu, Xiaoxiang Guo, Jun Li

Department of Urology, Zhumadian Central Hospital, Zhumadian 463000, Henan, China

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Abstract: Objective: To investigate the effectiveness of ureteroscopic holmium laser lithotripsy (HLL) and pneumatic lithotripsy (PL) in elderly patients with ureteral calculi. Methods: In this retrospective study, clinical data of 220 elderly patients with urinary calculi hospitalized in Zhumadian Central Hospital from March 2018 to December 2019 were analyzed. Among the 220, 104 patients were treated with PL (PL group) and the other 116 were treated with HLL (HLL group). The two groups of patients were compared regarding surgical conditions, postoperative complications, physiologic stress response, pain level, and restoration of cognitive and renal function. Results: Compared with the PL group, the HLL group had significantly shorter surgical duration, earlier time to first ambulation, shorter hospital stay, lower intraoperative bleeding, and higher stone-free rate. No significant differences were observed between two groups in complications. The norepinephrine (NE), cortisol (COR) and C-reactive protein (CRP) levels were all reduced postsurgically, but those in the HLL group were lower than those for PL. The VAS and MMSE scores in the HLL group were lower than those in the PL group at 6, 12, 36 and 48 hours after surgery. The blood urea nitrogen (BUN) and serum creatinine (SCr) levels decreased after surgery, and the decrease was greater in the HLL group. The WHOQOL-BREF scores in HLL group were higher than those of the PL group ($P<0.05$). Conclusion: Ureteroscopic HLL was shownhighly effective in promoting postoperative rehabilitation and reducing postoperative complications, pain, and physiological stress response, as well as crushing stones, with little impact on cognitive function.

Keywords: Elderly patients, ureteral calculi, holmium laser lithotripsy, pneumatic lithotripsy

Introduction

Urolithiasis is a common disease of the urinary system that stimulates the formation of stones in any part of the kidney, bladder, ureter and urethra. Over the past few decades, the prevalence of urolithiasis has been increasing worldwide [1]. The most common type of urolithiasis is are manifested by dysuria, hematuria, abdominal/lumbar pain and renal colic, which can trigger hydronephrosis, and even renal failure and uremia if left untreated, thus seriously compromising the health of patients [2, 3]. If conservative or pharmacological treatment fails, surgery is the best choice to treat ureteral calculi [4]. However, the traditional open surgery is highly traumatic, with severe postoperative pain and complications, which is not conducive to the recovery of patients and has great limitations [5]. The development of new medical technology has given rise to the gradual replacement of traditional open surgery by minimally invasive surgery with less trauma, less pain, and faster recovery [6].

Pneumatic lithotripsy (PL) and holmium laser lithotripsy (HLL) are the primary minimally invasive procedures for ureteral calculi. PL crushes stones by impaction, and later rinses the crushed stones out of the body. There is no extra heat production in the treatment process, and the endoscope causes less damage. However, shock-wave effects produced during the lithotripsy are likely to trigger stone displacement. Moreover, the large size of the crushed stones hinders the smooth progress of subsequent treatment [7, 8]. HLL combined with holmium laser coagulation and CO_2 laser

cutting can achieve the effect of vaporization, electrocoagulation, and cutting, with an instantaneous power of up to 10 kW, which could break stones of various compositions and densities [9]. There is no uniform standard for selection of surgical procedures. A study indicates HLL and PL are both effective and safe to treat ureteral calculi, but PL is less cost-effective [10, 11]. Also, another report suggests that HLL should be promoted with shorter surgical duration and higher stone-free rate [12].

Thus, in the present study, ureteroscopic HLL and PL were compared in terms of lithotripsy outcome, postoperative recovery, stress response, complications, and postoperative pain, so as to provide a basis for the selection of surgical approach for elderly patients with ureteral calculi.

Materials and methods

Participants

In this retrospective study, clinical data of 220 elderly patients with urinary calculi hospitalized in Zhumadian Central Hospital from March 2018 to December 2019 were analyzed. Among them, 104 received PL (PL group) and the other 116 received HLL (HLL group). Inclusion criteria: patients with complete clinical data and imaging data; patients undergoing lithotripsy for the first time; patients aged from 60 to 80. Exclusion criteria: patients with contraindications to surgery; patients with severe dysfunction of vital organs such as heart, kidney and liver; patients with mental or cognitive impairment or inability to communicate; patients with severe hydronephrosis. Ethics approval was granted by the Medical Ethics Committee of Zhumadian Central Hospital, and all participants who agreed to participate in the present study (Ethics approval number: 2019 (review) 154 (approval)).

Surgical procedures

For the PL group: Preoperative preparation and anesthesia were the same as in HLL group. Instrument parameters: perfusion pressure, 100 mmHg; lithotripsy pressure, 0.4 MPa. The pneumatic lithotripter was started, and the impact rod was inserted into the affected side of ureter under the guidance of the catheter. The lithotripsy was carried out after the stone was lightly pressed against the ureteral wall, and a connection was formed with the air compression pump to ensure that the maximum lithotripsy diameter was ≤2 mm. For larger stones, lithotomy forceps were used to place stones in the patient's bladder to facilitate their discharge with urine. Double-J stents were routinely retained for postoperative drainage.

For the HLL group: After patients were positioned in the lithotomy position, spinal anesthesia or epidural anesthesia was selected as appropriate. After anesthesia, a guide wire was inserted into the opening of the diseased ureter, followed by the insertion of the ureteroscope into patients' bladder. Meanwhile, the bladder was carefully observed, and the water pressure was lowered after the stone was found. The guide wire was withdrawn and the optical fiber was inserted. The frequency and energy of the fiber varied depending on their condition, ranging from 11.0 to 20.0 Hz and from 1.4 to 2.0 J. Afterwards, the lithotripsy was started, and it was considered effective when the diameter of the broken stone was less than 2.0 mm. For those with a diameter above 2.0 mm, lithotomy forceps were used to facilitate the discharge of stones. If the patient experienced polyps during the operation, the polyps were resected first. Double-J stents were routinely retained for postoperative drainage.

Outcome measures

Surgical conditions were recorded, including the surgical duration, time to first ambulation, hospital stay, intraoperative bleeding and stone-free rate (CT examination of stone removal at one time, the presence of residual stones indicates unsuccessful clearance, and vice versa). The postoperative complications of infection, ureteral injury, hematuria, fever and ureteral stenosis were recorded.

Venous blood sampled from patients before and 1 d after surgery was centrifuged to obtain serum. Serum c-reactive protein (CRP) levels were quantified by ELISA (Shanghai MLBIO Co., Ltd., China, ml057570), and norepinephrine (NE) and cortisol (COR) levels were quantified by radioimmunoassay (RIA).

Table 1. Comparison of general data ([n (%)], x ± sd)

Group	PL group (n=104)	HLL group (n=116)	χ^2/t	P
BMI (kg/m^2)	22.67±2.78	22.82±3.02		
Age (years)	70.48±6.82	69.86±6.95		
Mean diameter of stones (cm)	1.67±0.45	1.77±0.49		
Course of disease (months)	6.15±3.86	6.84±4.03		
Gender			0.319	0.572
Male	68 (65.38)	80 (68.97)		
Female	36 (34.62)	36 (31.03)		
Location of stones			0.377	0.828
Left	37 (35.58)	38 (32.76)		
Right	41 (39.42)	45 (38.79)		
Bilateral	26 (25.00)	33 (28.45)		
Hypertension			0.421	0.517
Yes	23 (22.12)	30 (25.86)		
No	81 (77.88)	86 (74.14)		
Diabetes			0.335	0.562
Yes	20 (19.23)	26 (22.41)		
No	84 (80.77)	90 (77.59)		

A visual analogue scale (VAS) [13] was adopted to estimate the pain level of patients at 6, 12, 36, and 48 hours after surgery. The full score is 10 points, and a higher score indicates more severe pain. The cognitive function of patients was evaluated by a mini-mental state scale (MMSE) [14] with a full score of 30. Patients with less than 27 points showed cognitive impairment, and a lower score indicates higher degree of impairment.

Renal function, serum creatinine (SCr), and urea nitrogen (BUN) were measured by an automated biochemical analyzer one day before surgery and one month after surgery.

A WHOQOL-BREF scale [15] was adopted to evaluate the quality of life (QoL) of patients one month after discharge. There are four domains in the scale, namely physical and psychological states, level of independence, social relationships. The total score of each domain is 100 points, and a higher score indicates better QoL.

Statistical analysis

SPSS 18.0 was used for statistical analysis, and GraphPad Prism 7 for graphing. Categorical data were compared by the chi-square test, and continuous data were compared by the independent samples t-test. Intra-group comparisons were conducted by the paired t-test, and the comparison among multiple time points were conducted by repeated measurement analysis of variance, expressed as F, and Bonferroni was used for post-hoc test. Significance was assumed at P<0.05.

Results

Comparison of general data

Patients in both groups were comparable in BMI, age, mean diameter of stones, course of disease, gender, location of stones, hypertension and diabetes (P>0.05) (**Table 1**).

Comparison of surgical conditions

Compared with the PL group, the HLL group had notably shorter surgical duration, earlier time to first ambulation, shorter hospital stay, lower intraoperative bleeding, and higher stone-free rate (P<0.05) (**Table 2**).

Comparison of postoperative complications

In the PL group, infection occurred in 3 patients (2.88%), ureteral injury in 4 (3.85%), hematuria in 5 (4.81%), and fever in 6 (5.77%) after surgery, showing a total incidence of 17.31%. In HLL group, there was 1 patient with infection (0.86%), 2 with ureteral injury (1.72%), 2 with hematuria (1.72%), and 4 with fever (3.45%), with a total incidence of 7.76%. No significant differences were observed in incidence of complications between the two groups (P>0.05) (**Table 3**).

Comparison of indicators of physiological stress and inflammatory response

We monitored indicators of physiological stress response and noticed that there was no significant difference in NE, COR, and CRP levels between the two groups before surgery (P>0.05). But the levels decreased in both

Table 2. Comparison of surgical conditions (x ± sd)

Group	PL group (n=104)	HLL group (n=116)	χ^2/t	P
Surgical duration (min)	41.05±5.45	30.85±4.76	14.817	<0.001
Intraoperative blood loss (mL)	60.68±10.08	47.32±9.84	9.939	<0.001
Time to first ambulation (h)	12.47±2.21	9.63±1.96	10.102	<0.001
Hospital stay (d)	4.89±0.92	3.98±0.68	8.398	<0.001
Stone-free rate (%)	81 (77.88)	104 (89.66)	5.679	0.017

Table 3. Incidence of complications [n (%)]

Group	PL (n=104)	HLL (n=116)	χ^2	P
Infection	3 (2.88)	1 (0.86)	1.257	0.262
Ureteral injury	4 (3.85)	2 (1.72)	0.931	0.335
Hematuria	5 (4.81)	2 (1.72)	1.693	0.193
Fever	6 (5.77)	4 (3.45)	0.681	0.409
Ureteral stenosis	1 (0.96)	5 (4.39)	2.383	0.123
Number of patients affected	18 (17.31)	14 (12.28)	1.097	0.295

groups postsurgically, and those of the HLL group were lower than those of the PL group (P<0.05) (**Figure 1**).

Comparison of postoperative pain

Evaluation of postoperative pain manifested that the VAS scores in the HLL group were lower than those in the PL group at 6, 12, 36 and 48 hours after surgery (P<0.05) (**Table 4**).

Comparison of postoperative cognitive function

Evaluation of postoperative cognitive function indicated that MMSE scores in the HLL group were lower than those in the PL group at 6, 12, 36 and 48 hours after surgery (P<0.05) (**Table 5**).

Comparison of indicators of renal function

There were no significant differences in BUN and Scr levels between the two groups before surgery (P>0.05); however, the levels decreased dramatically after surgery, with lower levels in the HLL group than in the PL group (P<0.05) (**Figure 2**).

Comparison of postoperative QoL

Assessment of the QoL of patients revealed that the scores of the WHOQOL-BREF scale of physical and psychological states, social relationships and independence level were notably higher in the HLL group than in the PL group (P<0.05) (**Table 6**).

Classic cases

The patient, a 43-year-old male, showed obvious white spots on the X-ray film before HLL treatment (**Figure 3A**). The patient was treated with HLL, and there was no residual stone 1 month after operation (**Figure 3B**).

Discussion

The present study proposed that compared to the PL group, the HLL group had significantly shorter surgical duration, earlier time to first ambulation, shorter hospital stay, lower intraoperative bleeding, and higher stone-free rate. This indicates that HLL is safe and effective in treating ureteral calculi in the elderly. The reason for this may be that PL primarily generates energy to impact stones through compressed gas to achieve stone clearance, which produces great mechanical thrust on the stones, easily displaces them and also damages surrounding tissues [7]; However, HLL relies on the photothermal effect of the holmium laser, a high-energy pulsed solid-state laser, and bubble cavitation, which does not mechanically push stones substantially and has more concentrated energy, thereby minimizing the displacement of stones and the damage of surrounding ureteral tissues with effective stone fragmentation [16, 17]. As a result, HLL allows a more efficient and safer lithotripsy. Nevertheless, there is evidence that HLL increases the risk of postoperative ureteral stenosis compared to PL [18]. The study recorded the occurrence of postoperative complications, and found that although the ureteral stenosis rate in HLL group was higher, no significant differences were found, and the overall complications were similar in both groups. Thus, we still believe that HLL is a safe way to treat ureteral calculi. Similar to our results, previous re-

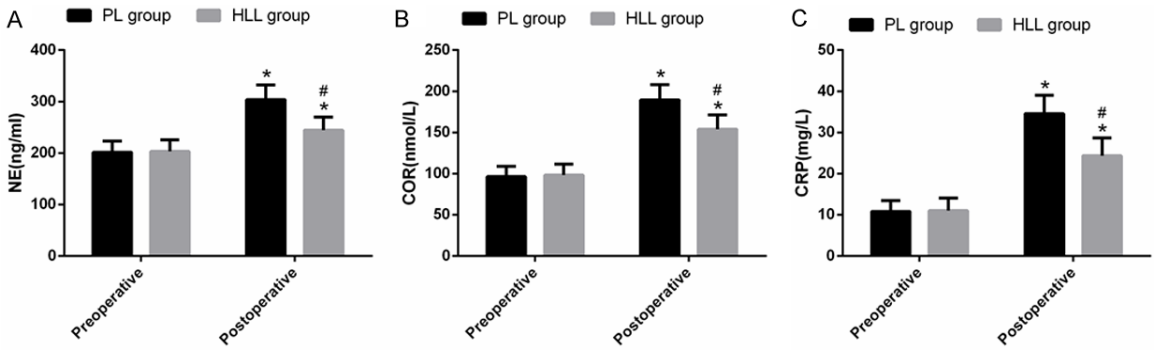

Figure 1. Comparison of indicators of physiological stress response. A. Comparison of NE levels before and after surgery. B. Comparison of COR levels before and after surgery. C. Comparison of CRP levels before and after surgery. Notes: before surgery *vs.* after surgery within the same group, *P<0.05; #P<0.05 vs. PL group after surgery.

Table 4. Comparison of postoperative pain (Mean ± sd)

Group	PL (n=104)	HLL (n=116)	t	P
6 h after surgery	6.65±1.24	5.83±1.38	4.615	<0.001
12 h after surgery	5.27±1.33	4.37±1.49	4.704	<0.001
36 h after surgery	4.02±1.08	2.74±1.24	8.121	<0.001
48 h after surgery	2.57±0.94	1.73±0.89	6.806	<0.001

Table 5. Comparison of postoperative cognitive function (Mean ± sd)

Group	PL (n=104)	HLL (n=116)	t	P
6 h after surgery	22.29±2.46	24.56±2.59	6.646	<0.001
12 h after surgery	24.27±2.31	26.63±2.08	7.974	<0.001
36 h after surgery	26.63±1.68	27.45±1.45	3.885	0.001
48 h after surgery	27.85±1.34	28.54±1.08	4.223	<0.001

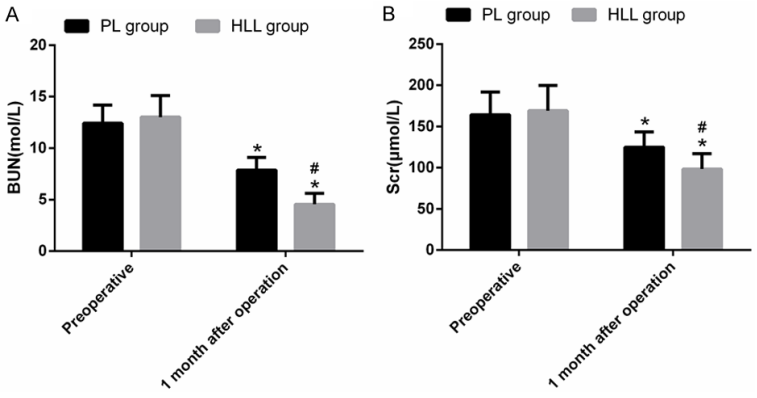

Figure 2. Comparison of indicators of renal function. A. Comparison of BUN levels before and after surgery. B. Comparison of Scr levels before and after surgery. Notes: before surgery vs. after surgery within the same group, *P<0.05; #P<0.05 vs. PL group after surgery.

ports also support that HLL is less harmful to patients than PL, with a higher stone-free rate [19, 20].

Ureteroscopic lithotripsy is one type of minimally invasive procedures, and prior research has focused on the effectiveness of surgical treatment, postoperative complications, and recurrence, with fewer reports on its overall effects on the organism. Clinical experience has shown that tissue trauma and pain perception activate the hypothalamus-pituitary-adrenal axis and sympathetic nervous system, triggering a stress response. Reducing perioperative stress response decreases potential complications, shortens hospital stay and accelerates the recovery of baseline functional status of patients [21, 22]. In this study, decreased levels of NE, COR and CRP were observed in both groups after surgery, but the decrease was greater in HLL group than in PL group. In addition, VAS scores in HLL group were lower than those in PL group at 6, 12, 36 and 48 h after surgery. This indicates that HLL induces a lower level of pain and a milder degree of stress response, which may be associated with the shallow tissue penetration and less damage to surrounding tissues of holmium laser. Although both ureteroscopic HLL and PL are minimally invasive, they can still cause damage to patients' tissues, thereby

Table 6. Comparison of postoperative QoL (Mean ± sd)

Group	PL (n=104)	HLL (n=116)	t	P
Physical state	72.47±8.59	78.21±10.35	4.447	<0.001
Physiological state	68.58±7.59	75.36±9.68	5.735	<0.001
Social relationships	81.54±7.92	84.64±8.46	2.796	0.006
Independence level	76.15±8.78	79.36±9.21	2.638	0.009

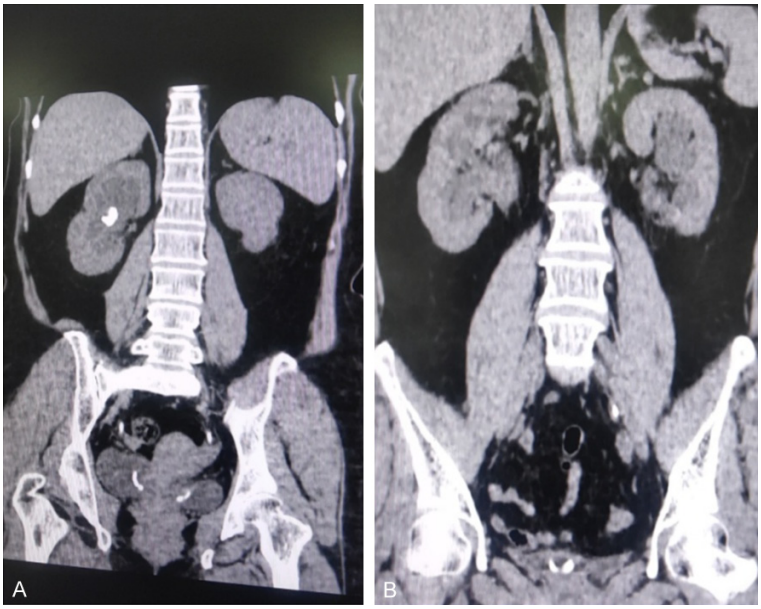

Figure 3. Image of a classic case. A. Male, 43 years old, right kidney stone (before treatment). B. Male, 43 years old, right kidney stone (after treatment).

inducing varying degrees of pain and affecting postoperative rehabilitation. Postoperative cognitive dysfunction (POCD) refers to prolonged cognitive abnormalities in patients (more common in the elderly) after surgery, manifesting as insanity, anxiety, personality changes and memory impairment, which adversely affects postoperative rehabilitation [23, 24]. The present study evaluated the influences of HLL and PL under ureteroscope on postoperative cognitive function of patients. With regard to VAS scores, we also found that the pain scores of patients in the HLL group were notably lower than those in the PL group, which was basically consistent with the research results of Li et al. [25]. Compared with their research, we further detected the changes of MMSE scores in HLL group after surgery and found that the scores in HLL group were lower than those in PL group at 6, 12, 36 and 48 hours after surgery. We speculated that this was mainly due to the shortened operation time of HLL compared with PL, which contributed to shorter anesthesia time and facilitated the recovery of postoperative cognitive function of patients. Surgical treatment will affect patients' renal function, so it is important to promote the restoration of renal function. Thus, indicators of renal function were measured. BUN and Scr levels were found to have decreased in both groups after surgery, with lower levels in HLL group than in PL group. Hence, HLL contributes to the restoration of renal function. Finally, assessment of the QoL of patients revealed that the scores on the WHOQOL-BREF scale of physical and psychological states, social relationships, and independence level were notably higher in HLL group than in PL group, indicating the superiority of ureteroscopic HLL over PL in the comprehensive treatment of ureteral calculi in the elderly.

There are several limitations in this study. First, lithotripsy operations were performed by different surgeons, likely to cause bias in our results. Second, the economic burden imposed by PL and HLL on patients was not analyzed. Finally, this study did not follow up patients for a long time, so further analysis is needed on whether these two schemes of treatment have any influence on postoperative recurrence.

In summary, ureteroscopic HLL is highly effective in promoting postoperative rehabilitation and reducing postoperative complications, pain, and physiological stress response, as well as crushing stones, with little impact on cognitive function.

Disclosure of conflict of interest

None.

Address correspondence to: Jun Li, Department of Urology, Zhumadian Central Hospital, No. 747 West

Section of Zhonghua Road, Zhumadian 463000, Henan, China. Tel: +86-15139636331; E-mail: lj163com2021@163.com

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