Staged Flexible Ureteroscopic Holmium Laser Lithotripsy versus Microchannel Percutaneous Nephrolithotomy for 2-4 cm Kidney Stones: A Randomized Controlled Clinical Trial Postprint

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Abstract

Objective To compare the efficacy and safety of staged flexible ureteroscopy with holmium laser lithotripsy (FURS) versus mini-percutaneous nephrolithotomy (m-PCNL) for the treatment of 2-4 cm renal calculi.

Methods Seventy patients with renal calculi admitted to our hospital from January 2013 to December 2015 who met the inclusion criteria were enrolled and randomly assigned to Group A (staged FURS) or Group B (m-PCNL) using a computer-generated program, with 35 patients in each group. The total treatment duration, total postoperative hospital stay, total treatment cost, treatment success rate, postoperative hemoglobin decline, and complication rate were compared between the two groups.

Results Regarding clinical efficacy, the treatment success rates were 100% in both Group A and Group B, with no statistically significant difference between the groups ($P>0.05$). However, the complete stone clearance rate was 65.71% in Group A and 94.29% in Group B, which was significantly lower in Group A ($P<0.01$). The rate of clinically insignificant residual fragments was 34.29% in Group A and 5.71% in Group B, which was significantly higher in Group A ($P<0.01$). In terms of treatment safety, the perioperative hemoglobin decline was 3.37±1.56 g/L in Group A and 11.93±2.24 g/L in Group B, which was significantly lower in Group A ($P<0.01$). The complication rate was 6.25% in Group A and 9.37% in Group B, with no statistically significant difference between the groups ($P>0.05$). Minor complications included one case of fever in Group A and two cases of self-limiting hematuria in Group B. Major complications included one case of ureteral steinstrasse in Group A and one case of blood transfusion in Group B. The total treatment duration for the two procedures was 4.06±1.11 weeks in Group A and 1.26±0.47 weeks in Group B, which

was significantly longer in Group A (P<0.01). The total postoperative hospital stay was 3.66±1.29 days in Group A and 5.13±0.43 days in Group B, with no statistically significant difference between the groups (P>0.05). Regarding total treatment cost, Group A incurred 54,291.00±6,149.00 yuan compared with 23,482.00±2,317.00 yuan in Group B, which was significantly higher in Group A (P<0.01).

Conclusion FURS demonstrates favorable efficacy and safety for 2-4 cm renal calculi. Staged procedures are essential to improve the complete stone clearance rate for larger stone burdens. Advanced technical equipment and extensive surgical experience are critical to successful treatment.

Full Text

Abstract

Objective: To compare the efficacy and safety of staged retrograde flexible ureteroscopic lithotripsy (FURS) and miniaturized percutaneous nephrolithotomy (m-PCNL) for treatment of renal stones of 2–4 cm in diameter. **Methods**: This randomized controlled trial enrolled 70 patients with renal stones meeting inclusion criteria admitted to our hospital between January 2013 and December 2015. Patients were randomly assigned using a computer program to Group A (staged FURS) or Group B (m-PCNL), with 35 cases in each group. Total treatment time, total postoperative hospital stay, total treatment cost, treatment success rate, postoperative hemoglobin decline, and complication rates were compared between the two groups. **Results**: Both groups achieved 100% treatment success rates with no statistically significant difference (P>0.05). However, the complete stone-free rate in Group A was 65.71%, significantly lower than Group B' s 94.29% (P<0.01). The rate of clinically insignificant residual fragments was 34.29% in Group A, significantly higher than Group B' s 5.71% (P<0.01). In terms of safety, hemoglobin decline was 3.37±1.56 g/L in Group A versus 11.93±2.24 g/L in Group B, with Group A showing significantly less decline (P<0.01). Complication rates were 6.25% in Group A and 9.37% in Group B, with no statistically significant difference (P>0.05). Minor complications included one case of fever in Group A and two cases of self-limiting hematuria in Group B. Major complications included one case of ureteral steinstrasse in Group A and one blood transfusion in Group B. Total treatment time was 4.06±1.11 weeks in Group A, significantly longer than Group B' s 1.26±0.47 weeks (P<0.01). Total postoperative hospital stay was 3.66±1.29 days in Group A versus 5.13±0.43 days in Group B, with no statistically significant difference (P>0.05). Total treatment cost was ¥54,291.00±6,149.00 in Group A, significantly higher than Group B' s ¥23,482.00±2,317.00 (P<0.01). **Conclusion**: FURS demonstrates good efficacy and safety for 2–4 cm renal stones, with staged procedures necessary to improve complete stone-free rates for larger stone burdens. Advanced equipment and extensive surgical experience are critical for successful treatment.

Keywords: renal calculus; mini-percutaneous nephrolithotomy; flexible ureteroscopy; safety; efficacy; randomized controlled trial

Introduction

Flexible ureteroscopic holmium laser lithotripsy (FURS) offers advantages including minimal invasiveness, safety, rapid recovery, and repeatability [1-2], and has been recommended by European stone treatment guidelines as first-line therapy for renal stones under 2 cm [3]. It also demonstrates favorable outcomes for select patients with stones over 2 cm who are unsuitable for percutaneous nephrolithotomy (PCNL) [4-5]. However, limitations including lower fragmentation efficiency, poor durability of equipment, and the need for staged procedures in some patients [6-7] have generated ongoing controversy regarding its routine application for stones larger than 2 cm [8-10]. This clinical controlled study was designed to evaluate the efficacy and safety of staged FURS versus microchannel PCNL (m-PCNL) for 2–4 cm renal stones, aiming to explore the clinical value of staged FURS in this patient population.

Methods

Study Design and Participants

Inclusion Criteria: (1) Single renal stones 2–4 cm in diameter; (2) Age 18–65 years, regardless of gender; (3) Signed informed consent.

Exclusion Criteria: (1) Age <18 or >65 years; (2) Prior PCNL treatment; (3) Known ureteral stricture, severe malformation, or renal anatomical abnormalities; (4) Concurrent severe urinary tract infection or pyonephrosis, severe hydronephrosis, or coagulation disorders; (5) Severe cardiac disease or pulmonary insufficiency precluding surgery; (6) Multiple renal stones.

Randomization: Patients were allocated in a 1:1 ratio to staged FURS (Group A) or m-PCNL (Group B) using a computer program.

Allocation Concealment: Third-party allocation concealment was employed. The computer program and patient allocation were managed by designated personnel. Treating physicians remained unaware of group assignments before randomization.

Blinding: Due to the need to inform patients about treatment methods and the requirement for surgeons to know the procedure type in advance, patient and operator blinding was not feasible. However, data processing, analysis, and outcome assessment were performed blinded to treatment allocation.

Study Population: Patients were recruited from the urology department of the Second Affiliated Hospital of Fujian Medical University. Stone diameter and volume were confirmed via dual-source CT scan. From January 1, 2013 to December 30, 2015, 92 patients met inclusion criteria, with 70 ultimately providing informed consent (35 in FURS Group A, 35 in m-PCNL Group B). Baseline

characteristics including age, gender, BMI, stone diameter, stone volume, and stone CT values showed no statistically significant differences between groups ($P>0.05$), ensuring comparability .

Sample Size Calculation: Based on previous research data [11], with average hemoglobin decline of 5.5% in m-PCNL versus 1.5% in FURS, a significance level of 0.05 and power of 90% required a minimum of 30 patients per group. This study enrolled 70 patients, randomly assigned via computer program.

Ethical Approval: This study was approved by the Ethics Committee of the Second Affiliated Hospital of Fujian Medical University, complying with the Declaration of Helsinki and local regulations. All participants provided informed consent for both surgical procedures and research participation.

Surgical Procedures

All treatments were performed by two surgeons with >100 cases of experience each in FURS and m-PCNL. All patients received combined intravenous-inhalation anesthesia.

FURS Group (Group A): Patients were placed in lithotomy position. A Fr8.0/9.8 Wolf rigid ureteroscope was inserted retrograde to the ureteropelvic junction, and a 0.035-inch zebra guidewire was advanced into the collecting system. The operating table was adjusted to 15° Trendelenburg position. Under fluoroscopy, a Fr12/14 ureteral access sheath (Cook, American) was placed over the guidewire to 1 cm below the ureteropelvic junction. After removing the inner core and guidewire, a flexible ureteroscope (Olympus P5, Olympus, Japan) was introduced. Following confirmation of proper sheath position without perforation, the renal pelvis was entered and stone location identified. Holmium laser lithotripsy (LUMENIS Versa Pulse Power Suite 100W, Coherent, American) was performed using a 200 m fiber with power settings of 10–30 W (0.6–1.0 J/20–30 Hz). Manual saline irrigation maintained visualization. Stones were fragmented to 1–2 mm pieces, with larger fragments extracted using a 1.9Fr basket (Zero Tip™; Boston Scientific Microvasive). Stone analysis was routinely performed. Single procedure duration was approximately 60 minutes, targeting residual stone volume of 1/3–1/2 of original size. A Fr5 double-J stent was placed postoperatively. KUB was performed on postoperative day 1; patients were discharged 1–2 days later if no complications occurred. The second FURS session was performed 2 weeks later using identical technique. Treatment success was evaluated by KUB at 1 month, after which the double-J stent was removed.

m-PCNL Group (Group B): Patients were placed in lithotomy position, and a Fr5 ureteral catheter was inserted to the renal pelvis via a Fr8.0/9.8 Wolf rigid ureteroscope. Position was changed to prone, and the puncture site was identified under ultrasound guidance. An 18G puncture needle entered the target calyx, the stylet was removed, and a zebra guidewire was placed. Skin and subcutaneous tissue were incised 1 cm, the needle sheath removed, and serial

dilation to Fr18 performed before advancing the working sheath. A nephroscope (Fr8.5/11.5) was inserted, and lithotripsy performed using holmium laser or pneumatic ballistic energy. Larger fragments were flushed out or grasped with forceps. All calyces were inspected for residual stones. A Fr5 double-J stent and Fr14 nephrostomy tube were placed. KUB was performed on postoperative day 1; if significant residual stones (>4 mm) remained, second-stage m-PCNL was performed 2–3 weeks later via the same tract. If no significant residual stones were present, the nephrostomy tube was removed at 3–7 days and the double-J stent at 2 weeks.

Outcome Measures

Primary Outcomes: (1) Treatment success rate: percentage of patients with complete stone clearance or clinically insignificant residual fragments (<4 mm) on KUB at 1 month postoperatively [12]; (2) Complication rate: percentage of patients with complications graded using the modified Clavien-Dindo classification system [13-14]. Minor complications were defined as self-limiting events requiring minimal supportive care or Clavien-Dindo Grade I, such as self-limiting hematuria, antibiotic-treated urinary infection, or analgesic-requiring pain. Major complications were defined as events requiring surgical intervention, intensive monitoring, or Clavien-Dindo Grade II or higher, including ureteral steinstrasse, ureteral perforation, subcapsular or perinephric hematoma, or severe hemorrhage requiring transfusion or renal artery embolization [15].

Secondary Outcomes: (1) Total treatment cost: sum of hospitalization, outpatient follow-up, auxiliary therapy (ESWL), and emergency treatment expenses; (2) Total treatment time: interval from initial hospitalization to final discharge; (3) Total postoperative hospital stay: cumulative days from postoperative day 1 to discharge (summed for staged procedures); (4) Mean hemoglobin decline: difference between preoperative and postoperative day 1 hemoglobin values.

Statistical Analysis

Data entry and statistical analysis were performed using SPSS 17.0. Continuous variables were expressed as mean±standard deviation and compared using independent samples t-tests; skewed data were analyzed using Wilcoxon rank-sum tests. Categorical data were expressed as percentages and compared using ^{2} tests. $P<0.05$ was considered statistically significant.

Results

Baseline characteristics showed no statistically significant differences between groups ($P>0.05$,). All patients completed surgical treatment without conversion to open surgery. Postoperative hemoglobin decline was 3.37±1.56 g/L in Group A versus 11.93±2.24 g/L in Group B, with significantly less decline in Group A ($P<0.01$). All Group A patients underwent two procedures, with total treatment

time of 4.06±1.11 weeks, compared to single procedures in Group B with total treatment time of 1.26±0.47 weeks (P<0.01). Total postoperative hospital stay was 3.66±1.29 days in Group A versus 5.13±0.43 days in Group B, with no significant difference (P>0.05). Total treatment cost was ¥54,291.00±6,149.00 in Group A, significantly higher than Group B' s ¥23,482.00±2,317.00 (P<0.01,).

Treatment success rates were 100% in both groups (P=1.0). However, complete stone-free rate was 65.71% in Group A versus 94.29% in Group B (P<0.01). Clinically insignificant residual fragment rate was 34.29% in Group A versus 5.71% in Group B (P<0.01,).

Complication rates were 6.25% in Group A and 9.37% in Group B (P>0.05). Group A experienced one minor complication (fever, 38.3°C) managed successfully with physical cooling and antibiotics (moxifloxacin 0.4 g/d) for 2 days, and one major complication (ureteral steinstrasse) with Clavien-Dindo Grade II classification. This steinstrasse measured <2 cm with fragments <4 mm, causing mild flank discomfort without infection, and resolved with conservative management and KUB confirmation of complete passage at 1 week. Group B experienced two cases of gross hematuria lasting >48 hours without significant hemoglobin decline (Clavien-Dindo Grade I) and one case requiring transfusion for hemoglobin drop to 86 g/L with perinephric hematoma (Clavien-Dindo Grade II), managed with 4 units packed red blood cells and hemostatic agents (Bangting, 1 U/d) for 3 days until hematuria resolved.

Discussion

Advances in flexible ureteroscopic technology, auxiliary lithotripsy devices, and accumulated surgical experience have gradually expanded FURS indications, with increasing clinical application for 2–4 cm renal stones [16-17]. However, high-level evidence remains limited, and FURS selection often relies on surgeon experience and patient preference. This controlled study compared staged FURS and m-PCNL for 2–4 cm renal stones to evaluate the feasibility of staged FURS as first-line therapy.

Treatment success represents the primary outcome measure for stone treatment efficacy. To provide comprehensive evaluation, this study simultaneously assessed both complete stone-free (SF) and clinically insignificant residual fragment (CIRF) rates—a novel approach in domestic literature. Results demonstrated equivalent treatment success rates (100%) between staged FURS and m-PCNL, but significantly lower SF rates (65.71% vs 94.29%, P<0.01) and higher CIRF rates (34.29% vs 5.71%, P<0.01) with FURS. Ghani et al. [12] similarly reported SF rates of only 55–60% even with active basket extraction, consistent with our findings. This reflects FURS' s emphasis on fragmentation ("powderization") rather than complete extraction, contrasting with m-PCNL' s ability to remove fragments during the procedure. Fragment size determines postoperative passage success and timing. While various studies define clini-

cally insignificant fragments as <2, <3, or <4 mm, most adopt 4 mm as the threshold [12]. Rebuck et al. [18] followed FURS patients with <4 mm fragments for a mean 19 months, finding 20% required urological intervention, 60% remained asymptomatic, and 20% passed fragments spontaneously. Osman et al. [19] followed 75 PCNL patients with 5 mm fragments for a mean 36 months, identifying >3 mm fragments as an independent risk factor for stone growth, with >1/3 requiring secondary procedures. Our staged FURS group experienced one Clavien-Dindo Grade II steinstrasse case with fragments <4 cm, managed conservatively with complete resolution at 1 week. These findings suggest that while clinical efficacy appears comparable, FURS may carry higher risks of stone-related events and growth, warranting longer-term follow-up.

Complication rates objectively evaluate surgical safety. The modified Clavien-Dindo classification provides standardized, widely accepted severity grading increasingly applied to urological procedures [13-14]. This study' s application to both FURS and m-PCNL complications represents a novel domestic approach. Overall complication rates were similar between staged FURS (5.71%) and m-PCNL (9.37%). Zeng et al. [1] reported 14.4% complication rates in 466 FURS patients, with fever being most common (10.7%), increasing to 13.5% for 2–3 cm stones and 14.6% for 3–4 cm stones. Gao et al. [2] reported 6.06% fever rates in 99 patients with 2–4 cm stones. Our FURS group fever rate of 2.86% was notably lower, attributable to our staged treatment strategy with strict 60-minute procedure times. Zhong et al. [20] advocated strict time control for high stone burden (>2 cm) and infection stones, with staged procedures reducing systemic inflammatory response syndrome. Sugihara et al. [21] similarly identified >90 minute procedures as significantly increasing infection risk. Our results confirm that staged FURS with strict time limits effectively reduces postoperative infection.

Postoperative hemoglobin decline reflects overall blood loss and tissue injury [22]. Staged FURS demonstrated significantly less hemoglobin decline than m-PCNL (3.37 vs 11.93 g/L, P<0.01), attributable to FURS' s natural orifice approach avoiding renal parenchymal injury. The m-PCNL group required one transfusion for significant hemoglobin drop (Clavien-Dindo Grade II). These findings indicate staged FURS causes less surgical trauma, reducing severe hemorrhage risk and improving patient acceptance.

While single FURS procedures were limited to approximately 60 minutes, staged FURS patients recovered faster with shorter single-procedure hospital stays and higher acceptance. However, staged FURS disadvantages include longer total treatment time, need for two anesthetic sessions, and higher total costs. m-PCNL advantages include higher single-procedure success rates, simultaneous fragmentation and extraction, shorter treatment cycles, but disadvantages include greater surgical trauma, slower recovery, and higher potential risks of hemorrhage and infection.

Study limitations include small sample size, single-center design, lack of stratified analysis, and absence of long-term follow-up. The clinical value and gener-

alizability of staged FURS require confirmation through large-scale multicenter studies.

Conclusion

FURS demonstrates favorable efficacy and safety for 2–4 cm renal stones, with staged procedures necessary to improve complete stone-free rates for larger stone burdens. Advanced technical equipment and extensive surgical experience are essential for successful outcomes.

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Note: Figure translations are in progress. See original paper for figures.