Flexible Ureteroscopic Lithotripsy Based on the Concept of Enhanced Recovery after Surgery: A Single-Centered Retrospective Study

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Purpose: To evaluate the efficacy of flexible ureteroscopic lithotripsy (FURSL) based on the concept of enhanced recovery after surgery (ERAS).

Materials and Methods: This study retrospectively analyzed 435 patients diagnosed with upper urinary calculi between 2017-2020 and categorized them into ERAS (ERAS management) and control groups (traditional management). The operative time, postoperative ambulation time, postoperative hospital stay, the total cost of hospitalization, postoperative complications, and stone removal rate between the two groups were subsequently compared.

Results: The FURSL procedure was successfully performed in 427 patients but failed in 4 patients of the ERAS group (n = 216) and 4 of the control group (n = 219). No postoperative complications occurred in either group except for fever and hematuria. There was no significant difference in postoperative fever and stone removal between the two groups (all $P > .05$). However, patients in the ERAS group had a shorter operative time, shorter postoperative ambulation time, less postoperative severe hematuria, shorter postoperative hospital stay, and lower total cost of hospitalization than those in the control group (all $P < .05$).

Conclusion: FURSL, based on the concept of ERAS, is safe and reliable for the treatment of upper urinary calculi, with rapid postoperative recovery and a low cost of hospitalization. It is worthy of clinical promotion.

Keywords: flexible ureteroscopy; lithotripsy; laser; upper urinary calculi; enhanced recovery after surgery; retrospective study

INTRODUCTION

Enhanced recovery after surgery (ERAS) was first advocated by Kehlet Henrik in colorectal surgery at the end of the last century.[(1)] The concept has become increasingly popular among surgical staff since then. According to existing evidence-based medical practice, ERAS uses multimodal strategies to optimize perioperative related treatments, reduce body stress response, and avoid complications. ERAS also adopts minimally invasive techniques to improve surgical safety and patient satisfaction to accelerate patients' recovery and shorten hospital stays.[(2)] Studies report that ERAS can reduce hospital stay by approximately 30%, thereby reducing medical costs without increasing the risk of postoperative complications and readmission rates.[(3-6)] Notably, the ERAS concept is relatively rare in urology despite its popularization in general surgery in recent years. In the same line, the awareness and application of ERAS by Chinese surgeons and patients is also under continuous improvement and development, with a need to update and change some traditional concepts.

Urinary calculi are common and frequently-occurring diseases amongst Chinese people. The overall prevalence of kidney stones is about 5.88% in China, with higher prevalences in the southern area of the Yangtze River.[(7)] In the past, surgical treatment of urolithiasis was mainly based on open surgery and was associated with a slow postoperative recovery process. In recent years, the rapid development of minimally invasive techniques in urology has enabled the removal of a vast majority of urinary stones through endoscopic surgery. Flexible ureteroscopic lithotripsy (FURSL) has been widely performed to treat upper urinary tract stones with reasonable safety and effectiveness. It is a typical representative of minimally invasive surgery in the urinary system and conforms to the core strategy of ERAS[(2,8)] Currently, there are only a few reports regarding applying ERAS in the perioperative period of FURSL.

We thus conducted a retrospective case-control study to evaluate the clinical effectiveness of ERAS during the perioperative period of FURSL.

MATERIALS AND METHODS

This study was approved by the Research Ethics Committee of The First Affiliated Hospital of Wannan Medical College. It was performed following the "Helsinki Declaration" and "International Bioethical Research Involving Human Ethical Guidelines." It included patients with upper urinary tract calculi treated using FURSL procedure between January 2017 and April 2020 at the department of urology, Wannan Medical College. All the patients underwent the preoperative examination, including B-mode ultrasonography (B-ultrasonography) scan, plain abdominal radiography for kidney-ure-

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Table 1. Summary of perioperative management measures

	ERAS group	Control group
Before surgery	Preoperative double-J stent indwelling 0-2 weeks	Preoperative double-J stent indwelling 2-4 weeks
	Individualized preoperative education using multimedia	Traditional preoperative education with paper materials
	Surgeons, nurses, and anesthetists formed a multidisciplinary team for preoperative visits	Surgeons, nurses or anesthetists performed preoperative visits respectively
	A list of rehabilitation plans	No
	No preoperative bowel preparation	No preoperative bowel preparation except for patients with constipation
	Normal oral solid nutrition until 6 hours before surgery	Normal oral solid nutrition until 10 hours before surgery
	Normal drinking water until 2 hours before surgery	Normal drinking water until 10 hours before surgery
	250-400 ml carbohydrate drinks for non-diabetic patients 2 hours before surgery	No
During surgery	Combining laryngeal mask ventilation with general anesthesia	Combining tracheal intubation with general anesthesia
	Selecting short-acting anesthetics as much as possible	No
	Strengthen monitoring of intraoperative body temperature	No
	Increasing the operating room temperature (24-26 ℃)	General operating room temperature (22-24 ℃)
	Warming intravenous fluids and surgical infusion fluids when ureteroscopy	No
	Goal-directed fluid therapy for intraoperative fluid administration	Standard intraoperative fluid regimen
	Using syringes for saline infusion of FURSL by the assistant with hands	An irrigation pump for saline infusion of FURSL
After surgery	Selecting non-opioids based on patients, postoperative analgesia needs	Not deliberately avoiding opioids for analgesia
	Drinking water 6 hours after surgery and then gradually resuming diet	Receiving oral intake after gastrointestinal function was recovered
	Mobilization out of bed 6 hours after surgery	Mobilization out of bed 12-24 hours after surgery
	Removing urinary catheter 12-24 hours after surgery	Removing urinary catheter 24-48 hours after surgery
Discharge and follow-up	Discharging based on the criteria, returning for KUB X-ray or CT scan 2 weeks later and removing double-J stent	Discharging based on the criteria, returning to KUB X-ray or CT scan 4 weeks later and removing double-J stent

Abbreviations: ERAS, enhanced recovery after surgery; FURSL, flexible ureteroscopic lithotripsy; KUB, kidney-ureter-bladder; CT, computed tomography

ter-bladder (KUB), computed tomography (CT) scan, or dual-source CT to confirm the diagnosis of urinary stones. Those with normal renal function were examined using intravenous pyelography (IVP). Magnetic resonance urography (MRU) or computed tomography urography (CTU) was performed if necessary.

Patients included in the study were those with kidney or upper ureteral calculi with stone diameter less than 30 millimeters, calculi with the unsatisfactory outcome of extracorporeal shockwave lithotripsy (SWL) or percutaneous nephrolithotomy (PCNL), and whose renal calculi were not suitable for PCNL because of obesity, scoliosis, or patient's wishes. Patients with other urinary diseases, such as excessive hydronephrosis, renal empyema, and severe urethral or ureteral stricture were excluded from the study.

The patients were categorized based on the management measures during the perioperative period of FURSL. The groups included the ERAS group comprising patients undergoing perioperative management based on the concept of ERAS and the control group comprising patients undergoing traditional perioperative management. Patients were divided into two groups based on the different responsible doctors. Physicians in one treatment team included their patients admitted to the outpatient clinic who required FURSL procedures into ERAS management, while physicians in the other treatment teams applied traditional management methods during the perioperative period of FURSL.

Preoperative routine urine tests and urine culture were

Table 2. Baseline characteristics of the patients

Variables	ERAS group (n = 216)	Control group (n = 219)	*P* value	OR
Age in years, mean ± SD	50.38 ± 13.19	52.67 ± 12.62	.064[a]	
Gender, Male, n (%)	136 (63.0)	128 (58.4)	.335[b]	1.209
Stone location, n (%)			.483[b]	
Kidney	185 (85.6)	195 (89.0)		
Upper ureteral	14 (6.5)	9 (4.1)		
Kidney and upper ureteral	17 (7.9)	15 (6.9)		
Stone side, n (%)			.677[b]	
Left	99 (45.8)	109 (49.8)		
Right	106 (49.1)	101 (46.1)		
Bilateral	11 (5.1)	9 (4.1)		
Stone size (mm), M(IQR)	20 (5)	20 (5)	.272[a]	
Underlying diseases, Yes, n (%)	107 (49.5)	95 (43.4)	.198[b]	1.281
History of urolithiasis surgery, Yes, n (%)	18 (8.3)	26 (11.9)	.221[b]	.675
Type of flexible ureteroscope, n (%)			.514[b]	
Digital	86 (39.8)	77 (35.2)		
Modular	107 (49.5)	113 (51.6)		
Fiberoptic	23 (10.6)	29 (13.2)		

Abbreviations: ERAS, enhanced recovery after surgery; SD, standard deviation; OR, odd ratio; M, median; IQR, interquartile range.
[a] Continuous variables were compared by independent samples t-test or Mann-Whitney test.
[b] Categorical variables were compared by Pearson Chi-square test.

Table 3. Postoperative clinical outcomes

Variables	ERAS group (n = 212)	Control group (n = 215)	*P* value	OR
Operative time (min), M(IQR)	75 (50)	90 (50)	.003[a]	
Postoperative ambulation time (h), M(IQR)	10 (7)	22 (6)	< .001[a]	
Postoperative hospital stays (d), M(IQR)	2 (1)	3 (1)	< .001[a]	
Total cost of hospitalization (USD), M(IQR)	2709.6 (620.6)	2776.9 (873.1)	.015[a]	
Postoperative fever, n (%)			.579[b]	.887
Yes	57 (26.9)	63 (29.3)		
No	155 (73.1)	152 (70.7)		
Postoperative severe hematuria, n (%)			.015[b]	.477
Yes	18 (8.5)	35 (16.3)		
No	194 (91.5)	180 (83.7)		
Clavien-Dindo Classification, n (%)			.784[b]	1.163
Grade I	69(32.5)	89(41.4)		
Grade II	6(2.8)	9(4.2)		
Stone removal, n (%)			.541[b]	1.151
Complete	166 (78.3)	163 (75.8)		
Incomplete	46 (21.7)	52 (24.2)		

Abbreviations: ERAS, enhanced recovery after surgery; OR, odd ratio; M, median; IQR, interquartile range; USD, United States dollar (Converted from CNY at the exchange rate on July 6, 2020).
[a] Continuous variables were compared by Mann-Whitney test.
[b] Categorical variables were compared by Pearson Chi-square test.

done for patients in both groups. An anti-infective treatment was actively carried out if a patient was found to have obvious evidence of urinary tract infection (UTI), such as a positive urine culture or a negative urine culture but more than two urine tests showing increased leukocyte count. The treatment involved selecting sensitive antibiotics with the guidance of a drug susceptibility test or prescribing antibiotics empirically when urine culture was negative. The FURSL procedure was performed after significant improvement of the laboratory urinalysis results. Table 1 outlines the perioperative management measures of the two groups.

Patients were discharged when they agreed and had attained a normal temperature, started feeding on a normal diet, and had normal mobilization, with no urinary catheter, serious gross hematuria, severe flank or abdominal pain, and serious dysuria.

The main surgical instruments and accessory tools used included a flexible digital ureteroscope (URF-V, Olympus; Shinjuku-ku, Tokyo, Japan), modular flexible ureteroscope (PD-PS-0094, PolyDiagnost; Hallbergmoos, Freistaat Bayern, Germany), fiberoptic flexible ureteroscope (11278A1, Karl Storz; Tuttlingen, Baden-Württemberg, Germany), rigid ureteroscope (8/9.8F, Richard Wolf; Knittlingen, Baden-Württemberg, Germany), ureteral access sheath (12/14F, Cook; West Lafayette, Indiana, USA), holmium laser (PowerSuite 100W, Lumenis; Yokneam, HaZafon, Israel), and nitinol stone baskets (2.2F, Cook; West Lafayette, Indiana, USA).

All FURSL procedures were performed by senior urologists. The patients were placed on the operating table in the lithotomy-Trendelenburg position after general anesthesia, followed by removal of a preoperative double-J stent using a rigid ureteroscope and retrograde placement of a 0.035-inch guidewire to guide the ureteral access sheath. A flexible ureteroscope was then inserted along the sheath to explore the renal pelvis and calyxes for stones. Fragmenting of the stones was subsequently conducted under a holmium laser with a 200-μm fiber at an energy of 0.8-1.2 J and frequency of 15-20 Hz. A nitinol stone basket was inserted at the end of the lithotripsy to grab larger fragments for analyzing stone composition. The final step was indwelling a 5-6F double-J stent and 16-18F catheter.

Patients' baseline characteristics including age, gender, stone location (kidney or upper ureteral), stone side, stone size (maximum diameter), underlying diseases (e.g., hypertension, diabetes mellitus, gout, chronic kidney disease), history of urinary stone, and type of flexible ureteroscope were collected for patients in both groups. Postoperative clinical data, including operative time, ambulation time, hospital stay, the total cost of hospitalization, complications, and stone removal rate of patients in both groups, were subsequently recorded for group comparisons.

Operative time refers to the time from rigid ureteroscope insertion to double-J stent placement. The main complications included postoperative fever and hemorrhage. Fever was defined as the axillary temperature higher than 37.3 ℃. It was further divided into low-grade fever (37.3-38.0 ℃), moderate fever (38.1-39.0 ℃), and high-grade fever (≥ 39.1 ℃). A patient was deemed to have severe postoperative hematuria if the gross hematuria lasted more than 24 hours after surgery,

Table 4. Distribution of the patients with postoperative fever.

Variables	ERAS group (n = 57)	Control group (n = 63)	*P* value
Postoperative fever, n (%)			.220[a]
Low-grade	42 (73.7)	38 (60.3)	
Moderate	13 (22.8)	19 (30.2)	
High-grade	2 (3.5)	6 (9.5)	

Abbreviations: ERAS, enhanced recovery after surgery.
a Categorical variables were compared by Pearson Chi-square test.

Table 5. Multivariate analysis of severe hematuria after FURSL in patients.

Variables	*P* value	OR	95% CI
ERAS management	.039	.343	.124- .946
Age	.000	1.143	1.098-1.190
Gender	.057	.185	.033-1.048
Underlying diseases	.009	7.103	1.616-31.226
History of urolithiasis surgery	.237	2.157	.604-7.709
Operative time	.000	1.022	1.010-1.035

Abbreviations: ERAS, enhanced recovery after surgery; OR, odd ratio; CI, confidence interval.

combined with blood clot formation, or the hemoglobin value continued to decrease. Complete removal of stones was evaluated using KUB X-ray or CT scan 2-4 weeks after surgery. Small residual stones or fragments smaller than 4mm diameter did not require surgical intervention.

Data were analyzed using SPSS version 22.0 (IBM, USA) to compare the baseline characteristics and postoperative clinical data between the two groups. Continuous data were expressed as means ± SD or median (interquartile range), while categorical data were expressed as percentages. Two-sided independent sample t-test, Mann-Whitney test and Chi-squared tests were performed to compare the means and percentage frequencies of the two groups. The significance threshold was set at $P < 0.05$.

RESULTS

This study enrolled 435 patients who gave informed consent. However, 8 patients, 4 from the ERAS group and 4 from the control group, were withdrawn because of failure of the FURSL procedure. Among the 4 in the ERAS group, 1 had a flexible ureteroscope and was unable to pass the ureteral stricture, 1 had a stricture of the renal calyx neck, 1 had no calculi after flexible ureteroscopy, and 1 had lower calyceal calculus whose treatment was changed to SWL because of the restricted angle for FURSL. Among the other 4 in the control group, 1 had no stones after flexible ureteroscopy, 1 had lower calyceal calculus whose treatment changed to PCNL owing to the angle limitation, and 2 had a hard texture of stones whose treatment changed to PCNL. The remaining 427 patients completed the trial and were assigned to two groups: 212 patients in the ERAS group and 215 patients in the control group.

Of note, there were no significant differences between patients in the ERAS and the control groups in age, gender, stone location, stone side, stone size, underlying diseases, history of urinary stone, and type of flexible ureteroscope ($P > .05$) (**Table 2**).

No postoperative complications occurred in either group except for fever and hematuria, with no significant differences in postoperative fever and stone removal between the two groups ($P > .05$) (**Table 3 and Table 4**). However, patients in the ERAS group had shorter operative time, shorter postoperative ambulation time, less postoperative severe hematuria, shorter postoperative hospital stay, and lower total cost of hospitalization than those in the control group ($P < .05$) (Table 3). Postoperative complications mainly included fever and severe hematuria, considered Grade Ⅰ or Grade Ⅱ according to the Clavien-Dindo Classification. Notably, the majority of the postoperative fever cases in both groups were low to moderate fever (**Table 4**). A patient in the control group having postoperative hematuria with repeated hemorrhage was finally cured using super-selective renal artery embolization for hemostasis.

In the multivariate logistic regression analysis, the ERAS management, age, underlying diseases, and operative time were independent risk factors for severe hematuria after FURSL in patients ($P < .05$) (**Table 5**).

DISCUSSION

The current proportion of minimally invasive surgery in the field of urology is more than 90% in many regional medical institutions, a phenomenon that is in line with the requirements of ERAS. Some studies report satisfactory outcomes of the ERAS program in laparoscopic radical prostatectomy, radical cystectomy, and laparoscopic radical nephrectomy.[5,9-12] However, there are only a few reports about ERAS application in ureteroscopy, especially a lack of specialist guidance similar to that in general surgery. In view of minimally invasive surgeries, ERAS has broad application prospects in the perioperative period of FURSL. This study evaluated the clinical application of ERAS in FURSL to explore the optimization and implementation of ERAS measures, which proved to be advantageous, especially for patients.

Hematuria is one of the most common complications after the FURSL procedure. Severe hematuria is often related to factors such as abnormal coagulation function related to the patient's age or underlying diseases, long operation time, and intraoperative renal injury. Our findings were also consistent with these observations. Compared with the traditional perioperative management measures, ERAS measures had significant advantages in shortening the operative time, decreasing postoperative hematuria, promoting recovery, and reducing hospital costs. In the ERAS group, an experienced assistant used a 50ml syringe for saline infusion by hands instead of an irrigation pump during the FURSL procedure, thus flexibly controlling the infusion speed and timing. Fluids infusion during ureteroscopy increases the hydrostatic pressure in the renal collecting system, causing harmful effects during the early term.[13] Notably, the irrigation pressure may substantially increase the intraoperative renal pelvic pressure.[14] Studies postulate that excessive intrarenal pressure may lead to serious infection, especially in patients with preoperative uncontrolled UTIs who are prone to urosepsis.[15-17] In addition, continuous high pressure in the renal pelvis may also lead to renal injury or hematoma.[18] The ureteral access sheath in place may drain most fluids to maintain low intrarenal pressure in the FURSL procedure.[19] Using intelligent pressure-controlled devices may also be beneficial for maintaining low pressure, increasing the hospital costs for patients.[20-21] In this study, the 12/14F ureteral access sheath achieved a great drainage effect. The excessive intrarenal pelvic pressure was effectively avoided in the ERAS group using inexpensive artificial irrigation in which the irrigant was timely adjusted for more suitable flow, thus enhancing the safety of surgery.

Studies postulate that ERAS intervention can alleviate the postoperative stress response in patients and accelerate their recovery.[22-24] Notably, this study came to a similar conclusion. The severity of postoperative hematuria in the ERAS group was lower than in the control group, attributed to a milder stress response. Despite patients ambulating out of bed earlier, the incidence of severe hematuria was not increased in the ERAS group, which may lead to less spending on medical interventions and shorter postoperative hospital stays. As a result of these two factors, although the difference in cost of surgery was limited, patients in the ERAS group had lower total hospitalization costs which improved their satisfaction.

This study affirms that the key to implementing ERAS measures during the perioperative period of FURSL is to change some traditional and backward medical concepts. A few medical staff, patients and their families are convinced of some traditional concepts, such as long-term fasting before surgery, preoperative bowel preparation, postoperative oral intake after the recovering of gastrointestinal function, lying without a pillow for 6 hours or more after surgery, rare mobilization out of bed, long-term indwelling catheter, excessive infusion, and antibiotic treatment, which are currently outdated in China. Of note, many traditional concepts lack the support of evidence-based medicine. For example, a catheter was retained for 3 days after ureteroscopic lithotripsy, while a double-J stent was indwelt for 4 weeks before FURSL during the early stages of endoscopic surgery. Such seemingly safe measures increase the risk of postoperative local infection, deep vein thrombosis, backache, and urination discomfort. In the study, we decided the time of removing urinary catheters according to the different intraoperative conditions and postoperative recovery of each case. The time in ERAS group was controlled within 12-24 hours, while the control group within 24-48 hours. The extubation time was not exactly the same for each patient in each group, but was within the above ranges. Similarly, we reduced the time to remove double-J stent from the traditional 4 weeks to 2 weeks postoperatively in the ERAS group.

It is also reported that an appropriate amount of carbohydrate drinks and shortening of the fasting time before surgery may alleviate the patients' thirst, hunger, nervousness, and other discomforts, thus having a positive effect on the patients during and after surgery.[10] A preoperative double-J stent in patients without ureteral stricture may inhibit the successful placement of the ureteral access sheath and complete removal of stones by FURSL.[25] We believe that preoperative bowel preparation is mainly suitable for colorectal surgery patients. An enema may cause complications, such as pain, bleeding, and infection, especially in patients with hemorrhoids or the elderly. We also believe that short-term placement of double-J stent or preparation without stent before FURSL procedure should be tried if the ureter is unobstructed by imaging suggestion or the patients have a history of ureteroscopy. There was no preoperative bowel preparation for patients in the ERAS group in this study. Those without diabetes mellitus had a carbohydrate drink (250-400 ml, 10% glucose injection) 2 hours before surgery. Preoperative placement of the stent for 0-2 weeks is a measure of ERAS. These measures significantly relieved the negative mood, particularly in patients who were waiting for surgery, and did not increase the postoperative gastrointestinal discomfort and complications. With the prolongation of the double-J stent intubation time, the patient will have obvious lower urinary tract symptoms after the FURSL procedure. In fact, 2 weeks of postoperative indwelling time of the double-J stent is sufficient for most patients, instead of the traditionally thought of 4 weeks. Discomfort caused by the stent and lower urinary tract symptoms associated with the stent was also reduced in the ERAS group.

Despite the invaluable findings, this study was limited by its retrospective nature. The standard ERAS program was altered to fit the colorectal surgery field. Some measures such as nutritionist participation, pain score, and multimodal analgesia were not strictly implemented. Data on intraoperative pelvic pressure were also missing, as the pelvic pressure was not monitored in most cases during the FURSL procedure. Future studies should focus on conducting prospective randomized controlled trials with an adequately optimized ERAS protocol for FURSL.

CONCLUSIONS

ERAS measures can shorten the operative time, accelerate postoperative recovery, and reduce the total hospital cost of patients with FURSL surgery. ERAS ameliorated the traditional measures regarding patients' diet, bowel preparation, anesthesia, and infusion in the perioperative period of FURSL and strengthened the communication with anesthetists, nurses, and other specialists that deal with comorbidities. Individualized ERAS measures can be developed and implemented to ensure rapid rehabilitation after surgery, as in this study. This study strongly suggests that FURSL, based on the concept of ERAS, is safe and reliable with excellent clinical results, highlighting the worth of the ERAS program. Nonetheless, future prospective randomized controlled studies should be conducted to evaluate whether an optimized ERAS protocol may improve outcomes.

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CONFLICT ON INTEREST

The authors report no conflict of interest.

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