Efficacy of Flexible Ureteroscopy Lithotripsy and Percutaneous Nephrolithotomy in the Treatment of Patients with Kidney Stones and Their Impact on Inflammatory Response and Renal Function

Ann. Ital. Chir., 2024 95, 2: 220–226
https://doi.org/10.62713/aic.3175

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Background: Kidney stones are one of the most common benign diseases in urology. As technology updates and iterates, more minimally invasive and laparoscopic surgeries with higher safety performance appear. This paper explores the effectiveness of retrograde intrarenal surgery (RIRS) and percutaneous nephrolithotomy (PCNL) in treating kidney stones, focusing on their effects on inflammatory responses and renal function.

Methods: We conducted a retrospective analysis of 200 patients with kidney stones treated in our hospital between June 2019 and June 2023. 100 patients who underwent RIRS were included in the RIRS group. Another 100 patients who underwent PCNL treatment were included in the PCNL group. The intraoperative blood loss, operation duration, and hospitalization time of the two groups of patients were recorded and compared. The enzyme-linked immunosorbent assay (ELISA) was used to detect the levels of inflammatory factors in the serum of the two groups of patients: [serum amyloid A (SAA), interleukin-6 (IL-6) and high-sensitivity C-reactive protein (CRP)] and renal function index [blood urea nitrogen (BUN), creatinine (Scr) and serum cystatin (Cys-c)]. The two groups of patients were recorded separately: Postoperative complications and stone-free rate.

Results: Operation duration was longer for the RIRS group than the PCNL group, which exhibited significantly less intraoperative blood loss and shorter hospital stays ($p < 0.05$). Before surgery, there was no statistically significant difference in the serum levels of SAA, IL-6, and CRP between the two groups of patients ($p > 0.05$). On the first day after surgery, the serum SAA levels in both groups were lower than before surgery, IL-6 and CRP levels were higher than before surgery, and the serum levels of SAA, IL-6, and CRP in the RIRS group were significantly lower than those in the PCNL group. The difference was statistically significant ($p < 0.05$). Before surgery, there was no statistically significant difference in the serum BUN, Scr, and Cys-c levels between the two groups of patients ($p > 0.05$). On the first day after surgery, the serum BUN, Scr, and Cys-c levels of the two groups of patients were significantly higher than those before surgery. The serum BUN, Scr, and Cys-c levels of the RIRS group were significantly lower than those of the PCNL group, and the difference was statistically significant ($p < 0.05$). Both surgical methods have sound stone-clearing effects regarding long-term stone clearance rates 1 month and 3 months after surgery ($p > 0.05$). PCNL had a better stone clearance rate on the 2nd postoperative day ($p < 0.05$). The incidence of postoperative complications in the RIRS group was significantly lower than that in the PCNL group, and the difference was statistically significant ($p < 0.05$).

Conclusion: For kidney stones $\leq$2 cm, PCNL showed higher stone clearance rates on the second postoperative day. However, RIRS and PCNL demonstrated adequate long-term stone clearance at 1 and 3 months post-surgery. Both surgical methods are safe and effective, and RIRS is safer than PCNL. Compared with PCNL, RIRS is a new method of kidney stone operation, which has less trauma to the patient's body and fewer complications after the operation, speeding up the recovery process of the patient.

Keywords: flexible ureteroscopy lithotripsy; percutaneous nephrolithotomy; inflammatory response; renal function; clinical efficacy

Introduction

Kidney stones are one of the most common benign diseases in urology. As the quality of life improves, long-term high-protein and high-sugar diets are risk factors for stone formation [1, 2]. The incidence of kidney stones has increased linearly in recent years [3]. The incidence of urinary system diseases currently ranks first in the country [4]. There are noticeable regional differences, with the southern region being significantly higher than other regions in our country [5]. Open surgery was the most essential treatment method for kidney stones in the past [6], with a high stone removal rate. The surgery is performed under direct vision and is relatively safe, which can effectively reduce the risk of kidney tear or significant blood vessel damage caused by percutaneous puncture [7]. However, open surgery often leads to tissue adhesion and changes in the structure of the renal pelvis and calyces. The recovery time after surgery is long, and it is difficult to perform a sec-

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ond surgery [8]. With the update and iteration of technology, more minimally invasive and laparoscopic surgeries with higher safety performance are emerging. There are various treatment methods for kidney stones, including traditional nephrolithotomy or pyelolithotomy, extracorporeal shock wave lithotripsy, percutaneous nephrolithotomy, and flexible ureteroscopic lithotripsy [9, 10]. Retrograde intrarenal surgery (RIRS) can access the kidney through the natural channels of the human body, ensuring minimal invasiveness, high efficiency, and a low incidence of postoperative complications [11, 12], which is its unique advantage. Percutaneous nephrolithotomy (PCNL) is often used to treat complex stones due to its accurate positioning and high clearance rate [13, 14]. Both RIRS and PCNL are optional surgical treatment options for kidney stones. However, both surgical options have their advantages and disadvantages. The final choice of surgical method to treat kidney stones needs to consider factors such as the specific location, size of the stone, and the financial situation of the patient's family to achieve better therapeutic effects. Based on previous research, this study applied RIRS and PCNL to treat patients with kidney stones, observed and analyzed the impact of two different surgical options on the inflammatory response and renal function of patients with kidney stones, and their clinical therapeutic effects. It aims to provide clinical treatment for kidney stones and serve as a reference material to improve clinical efficacy.

Materials and Methods

Research Subjects

From June 2019 to June 2023, we retrospectively analyzed 200 kidney stone patients treated at our hospital, dividing them into two groups: 100 underwent RIRS, and 100 underwent PCNL. The study received approval from the Medical Ethics Committee and was conducted after obtaining informed consent from patients or their family members (KY2022-069-B). This study was carried out in compliance with the Declaration of Helsinki.

Inclusion criteria: ① The diagnosis of kidney stones complies with the diagnostic criteria for kidney stones in the "Chinese Guidelines for Diagnosis and Treatment of Urology and Andrology Diseases: 2019 edition [15]". ② Patients with kidney stones $\leq$2 cm were diagnosed by urinary tract B-ultrasound and urinary tract CT. ③ Patients with indications for surgery and who have not undergone other surgeries within 6 months. ④ Patients whose preoperative routine tests and cardiopulmonary function tests meet the requirements for surgery and anesthesia and who have no contraindications to surgery. ⑤ Preoperative examination showed normal renal function, no renal malformation, and no history of renal trauma surgery. ⑥ The patient has clear consciousness, fully understands the study, and signs the informed consent form. Exclusion criteria: ① Patients with deformed urinary tract anatomy. ② Patients with abnormal function of important organs. ③ Patients with coagulation dysfunction. ④ Patients with tumors found in the preoperative examination. ⑤ Patients with incomplete information. ⑥ Psychiatric patients and patients with cognitive dysfunction.

Surgical Methods

In the RIRS procedure, patients were positioned and disinfected after tracheal intubation and anesthesia. A ureteroscope was used to navigate the bladder, followed by guidewire placement into the renal pelvis of the affected side under direct vision, and the scope was subsequently withdrawn. Insert the F13 flexible ureteroscope sheath into the ureteropelvic junction along the zebra guidewire, withdraw the guidewire, and then insert the flexible fiber ureteroscope. Explore the renal pelvis and each renal calyce, determine the location of the stone, and then advance the scope below the stone. Insert a 200 μm holmium laser fiber along the working channel of the soft mirror, and set the lithotripsy energy to 0.6–2.0 J and the frequency to 10–35 HZ. Start the lithotripsy operation to crush the target stones into powder (diameter $<$3 mm); for the small stones that are more hidden and some with larger residues, use a stone mesh basket to remove them individually. An F6 double J tube and an F16 urinary catheter were left in place after the operation was conducted. After the patient wakes up from anesthesia, they are transferred to the ward and given routine care.

For the PCNL group, the procedure followed tracheal intubation and anesthesia, with subsequent positioning and disinfection. A cystoscope facilitated ureteral catheter placement, and the F6 ureteral catheter on the affected side was intubated under the cystoscope, and the F16 urinary catheter was indwelled and then fixed. Change to a prone position and elevate the waist and abdomen on the affected side. B-ultrasound helped identify the stone's location and kidney hydrops, guiding the selection of an optimal puncture site, typically along the scapular to posterior axillary line, below the 12th rib, or within the 11th intercostal space. After the puncture is successful, withdraw the needle core. Make a 1 cm incision at the puncture point, place the zebra guidewire along the puncture channel in the renal calyces, put the fascia dilator on the zebra guidewire, and perform dilation at 8F for the first time, and increase it to 18F at the second. A nephoscope is inserted to observe the situation and understand the location and size of the stones. Use 550 μm holmium laser fiber for lithotripsy. The energy is set to 2.0 J, and the frequency is 20 Hz. The stones are pulverized and extracted through the working channel using suction. During the lithotripsy process, use isotonic saline for continuous perfusion and flushing. After the B-ultrasound examination, it was confirmed that no larger stones remained, and the optical fiber was removed. Pull out the ureteral catheter, leave the F6 double J tube in place, adjust the position of the double J tube, and withdraw the scope. An F16 nephros-

tomy tube was placed along the working channel, sutured, and fixed, followed by a drainage bag clamp for observation, and the operation was completed.

Surgical Indicators

We recorded both patient groups' intraoperative blood loss, operation duration, and hospitalization time. Intraoperative blood loss: expressed as the change in hemoglobin. The difference between preoperative hemoglobin and the hemoglobin level obtained from the first blood draw after completion of the operation was recorded as intraoperative blood loss. Operation duration: The time from when the patient starts anesthesia to when the operation is completed. Hospitalization time: the time from the first day after the operation to discharge (discharge must meet the following criteria: ① The patient has no obvious clinical symptoms after the operation; ② The patient has no residual large stones after the operation; ③ Normal result in blood routine, urine routine, and blood biochemistry).

Detection of Inflammatory Factor Levels

5 mL of fasting venous blood was taken into the ethylenediamine tetraacetic acid (EDTA) blood collection tube (K2/K3, Huanxi Medical, Shanghai, China) before treatment and in the morning of the first day after surgery. The centrifugation speed was 3000 r/min for 15 minutes, and the radius was 10 cm. The upper serum was taken. Enzyme-linked immunosorbent assay (ELISA) was used to measure levels of serum amyloid A (SAA) (RAB0420, Sigma-Aldrich, St. Louis, MO, USA), interleukin-6 (IL-6) (RAB0306, Sigma-Aldrich, St. Louis, MO, USA) and high-sensitivity C-reactive protein (CRP) (RAB0096, Sigma-Aldrich, St. Louis, MO, USA). The enzyme label (Epoch, BioTek Instruments Inc., Winooski, VT, USA) was used for detection. Strictly follow the kit instructions for testing.

Kidney Function Index Testing

Before treatment and one day after surgery, 5 mL of fasting venous blood was taken into the EDTA blood collection tube (K2/K3, Huanxi Medical, Shanghai, China). The centrifuged at a speed of 3000 r/min and a centrifugal radius of 10 cm for 15 minutes to separate the upper serum. A fully automatic biochemical analyzer (BS-350S, Nanjing Beden Medical Co., Ltd., Nanjing, China) was used to measure the blood urea nitrogen (BUN) (mlsh0416, Shanghai Enzyme-linked Biotechnology Co., Ltd., Shanghai, China), creatinine (Scr) (ml058645-1, Shanghai Enzyme-linked Biotechnology Co., Ltd., Shanghai, China) and serum cystatin (Cys-c) (ml058113-1, Shanghai Enzyme-linked Biotechnology Co., Ltd., Shanghai, China) levels of the two groups of patients. Among them, BUN uses the ultraviolet-glutamate dehydrogenase method, and Scr uses the sarcosine oxidase method. The testing was performed strictly follows the computer parameters and the kit instructions.

Stone-free Rate and Postoperative Complication Rate

The clearance rate of the two groups on the 1st day, 1 month, and 3 months after surgery was statistically analyzed, and CT examinations were performed. If no stone residue was found, or the diameter of the stone residue was $\leq$4 mm, the stone was determined to be cleared. The clinical manifestations are significantly improved, and the stone volume is reduced by >50%, achieving a clear state. If the stone volume is reduced by less than 30%, it is not cleared. Stone clearance rate (%) = (complete clearance + basic clearance) number of cases/total number of cases $\times$ 100%. Stone clearance rates of the two groups of patients were calculated and compared. The occurrence of postoperative complications, such as bleeding, fever, ureteral injury, urinary tract infection, etc., were recorded in the two groups of patients, and the incidence of postoperative complications in the two groups of patients was calculated.

Statistical Analysis

SPSS23.0 software (IBM Corp., Armonk, NY, USA) was used to analyze the obtained data statistically. The measurement data were tested for normality, normally distributed, and expressed as mean $\pm$ standard deviation ($\bar{x} \pm$ s). The independent sample *t*-test was used to compare the data. Count data are expressed as [n (%)], and the χ^2 test is used for data comparison. $p < 0.05$ means the difference is statistically significant.

Results

Comparison of General Information between the Two Groups of Patients

No significant differences were observed in gender, age, body mass index, stone diameter, and location between the two patient groups ($p > 0.05$), as detailed in Table 1.

Comparison of Surgical Indicators between the Two Groups of Patients

Surgical indices revealed longer operation times for RIRS than PCNL, whereas RIRS had significantly less intraoperative blood loss and shorter hospital stays. These differences were statistically significant ($p < 0.05$), as shown in Table 2.

Comparison of Inflammatory Factor Levels between the Two Groups of Patients

Before surgery, there was no statistically significant difference in the serum levels of SAA, IL-6, and CRP between the two groups of patients ($p > 0.05$). On the first day after surgery, the serum SAA levels in both groups were lower than before surgery, while IL-6 and CRP levels were higher than before surgery; one day after surgery, the serum levels of SAA, IL-6, and CRP in the RIRS group were significantly lower than those in the PCNL group ($p < 0.05$), see Table 3.

Table 1. Comparison of general information of the two groups of patients [$\bar{x} \pm$ s, n (%)].

Items	RIRS group (n = 100)	PCNL group (n = 100)	χ^2/t value	p value
Gender				
Male	56 (56%)	52 (52%)	0.322	0.570
Female	44 (44%)	48 (48%)		
Age (years)	47.50 ± 8.53	48.63 ± 9.28	0.896	0.371
BMI (kg/m^2)	22.36 ± 2.37	21.97 ± 2.28	1.186	0.237
Course of disease (years)	4.07 ± 1.05	4.15 ± 1.02	0.546	0.585
Stone diameter (mm)	15.54 ± 2.75	15.82 ± 3.05	0.682	0.496
Stone site				
Left	46 (46%)	44 (44%)	0.081	0.776
Right	54 (54%)	56 (56%)		

RIRS, retrograde intrarenal surgery; PCNL, percutaneous nephrolithotomy; BMI, body mass index.

Table 2. Comparison of surgical indicators between the two groups of patients ($\bar{x} \pm$ s).

Groups	Number of cases	Operation time (min)	Intraoperative blood loss (mL)	Length of stay (d)
RIRS group	100	75.82 ± 8.57	38.61 ± 5.24	3.84 ± 0.57
PCNL group	100	55.41 ± 6.26	52.32 ± 8.43	7.45 ± 0.48
t value		19.231	13.812	48.444
p value		<0.001	<0.001	<0.001

Comparison of Renal Function Index Levels between the Two Groups of Patients

Before surgery, there was no statistically significant difference in the serum BUN, Scr, and Cys-c levels between the two groups of patients ($p > 0.05$). On the first day after surgery, the serum BUN, Scr, and Cys-c levels of the two groups of patients were significantly higher than those before surgery; one day after surgery, the serum BUN, Scr, and Cys-c levels of the RIRS group were significantly lower than those of the PCNL group ($p < 0.05$), see Table 4.

Comparison of Stone Clearance Rates between the Two Groups of Patients

On the second postoperative day, the RIRS group's stone clearance rate was 73%, significantly lower than the PCNL group's 90% ($p < 0.05$). However, at 1 and 3 months post-surgery, the stone clearance rates between RIRS and PCNL groups showed no significant difference ($p > 0.05$), as detailed in Table 5.

Comparison of Postoperative Complication Rates between the Two Groups of Patients

Postoperative complication rates were significantly lower in the RIRS group compared to the PCNL group, with a statistically significant difference ($p < 0.05$), as shown in Table 6.

Discussion

The occurrence mechanism of kidney stones is relatively complex, and there is still no unified conclusion on its formation mechanism so far [16]. It is closely related to multiple factors such as genetics, dietary habits, remission, and metabolism [17, 18]. Among them, urine supersaturation promotes the formation of crystals, and the lack of inhibitory factors and the presence of a nuclear matrix are the main factors affecting stone formation [19]. The lesions of kidney stones are concentrated in the renal pelvis, renal calyces, and at the junction between the renal pelvis and the ureter. If not treated in time, it will cause complete or incomplete urinary tract obstruction, leading to complications such as hydronephrosis and urinary tract infection [20]. With the rapid development of laparoscopic technology, the development direction of kidney stone treatment methods is becoming more minimally invasive, efficient, and safe, allowing patients to return to everyday life in the shortest possible time [21]. With the continuous development of various minimally invasive techniques, kidney stone treatment's success rate has significantly improved in recent years. Different minimally invasive surgical techniques have distinct advantages and disadvantages, influenced by the particularity of the renal nodes' anatomical structure and spatial location. There are still some significant challenges in selecting surgical techniques [22]. Therefore, 200 patients with kidney stones in our hospital were studied, and the effects of two different surgical procedures, RIRS and PCNL, were observed on the surgical indicators, inflammatory response, and renal function of patients with kidney stones. This study aimed to explore their effectiveness in treating kidney stones.

In this study, the operation time of the RIRS group was significantly longer than that of the PCNL group, and the intraoperative blood loss and hospitalization time were considerably shorter than those of the PCNL group. PCNL had a better stone clearance rate on postoperative day 2. Both surgeries have good stone-clearing effects regarding

Table 3. Comparison of inflammatory factor levels between the two groups of patients ($\bar{x} \pm$ s).

Groups	Number of cases	SAA (mg/L)		IL-6 (pg/mL)		CRP (pg/mL)	
		Preoperative	1 day after surgery	Preoperative	1 day after surgery	Preoperative	1 day after surgery
RIRS group	100	11.64 ± 1.42	4.47 ± 0.45*	12.72 ± 2.11	21.56 ± 2.05*	7.46 ± 0.68	22.82 ± 2.13*
PCNL group	100	11.27 ± 1.49	5.63 ± 0.52*	13.16 ± 2.04	26.24 ± 2.46*	7.62 ± 0.71	27.51 ± 2.84*
t value		1.798	16.868	1.499	14.615	1.627	13.211
p value		0.074	<0.001	0.135	<0.001	0.105	<0.001

Note: Compared with patients in the same group before surgery, *$p < 0.05$. SAA, serum amyloid A; IL-6, interleukin-6; CRP, C-reactive protein.

Table 4. Comparison of renal function index levels between the two groups of patients ($\bar{x} \pm$ s).

Groups	Number of cases	BUN (mmol/L)		Scr (μmol/L)		Cys-c (mmol/L)	
		Preoperative	1 day after surgery	Preoperative	1 day after surgery	Preoperative	1 day after surgery
RIRS group	100	6.45 ± 0.67	8.54 ± 0.92*	86.46 ± 6.62	103.78 ± 10.68*	5.38 ± 0.62	7.46 ± 0.81*
PCNL group	100	6.56 ± 0.64	9.75 ± 1.03*	87.25 ± 6.43	114.08 ± 12.75*	5.42 ± 0.67	8.36 ± 0.95*
t value		1.187	8.761	0.856	6.193	0.438	7.209
p value		0.237	<0.001	0.393	<0.001	0.662	<0.001

Note: Compared with patients in the same group before surgery, *$p < 0.05$. BUN, blood urea nitrogen; Scr, creatinine; Cys-c, serum cystatin.

Table 5. Comparison of stone clearance rates between the two groups of patients [n (%)].

Groups	Number of cases	Day 2 after surgery	1 month after surgery	3 months after surgery
RIRS group	100	73 (73%)	86 (86%)	93 (93%)
PCNL group	100	90 (90%)	93 (93%)	96 (96%)
χ^2 value		9.584	2.607	0.866
p value		0.002	0.106	0.352

Table 6. Comparison of postoperative complication rates between the two groups of patients [n (%)].

Groups	Number of cases	Bleeding	Fever	Ureteral injury	Urinary tract infection	Complication rate
RIRS group	100	1 (1%)	1 (1%)	0 (0%)	1 (1%)	3 (3%)
PCNL group	100	6 (6%)	3 (3%)	2 (2%)	1 (1%)	11 (11%)
χ^2 value						4.916
p value						0.027

long-term stone clearance rates 1 month and 3 months after surgery. RIRS has the advantages of less intraoperative blood loss and shorter recovery time than PCNL. Flexible ureteroscopic lithotripsy is a more minimally invasive, safer, and more effective stone treatment method that has been rapidly developed recently. It has the advantage of a good stone-clearing rate in treating kidney stones [23]. RIRS uses an almost non-invasive surgical method to explore the collecting system without blind spots and has unique advantages in treating kidney stones in complex locations and with abnormal renal anatomy [24]. With the gradual reduction of the PCNL working channel in recent years, PCNL surgery has become safer. It is a preferred surgical procedure for treating staghorn and multiple renal stones [25]. Nevertheless, although PCNL is a minimally invasive treatment, puncturing and establishing a channel will cause unavoidable damage to the kidneys. A nephrostomy tube needs to be left in place after the operation to pay attention to whether there is bleeding, which can also play a role in compressing and stopping bleeding. At the same time, Bed rest is necessary because people with bleeding and organ damage need to stay in bed for a long time to restore body functions [26]. RIRS surgery is non-invasive and does not require the placement of a fistula tube, and the postoperative recovery is significantly faster. The indwelling urinary catheter can be removed, and the patient can be discharged within 1 to 4 days after the operation. Relevant studies have found that for urinary tract stones of the same size, flexible ureteroscope lithotripsy takes significantly longer than percutaneous nephrolithotomy, and this study also supports this view. This may be attributed to the thinness of the holmium laser used in RIRS and the relatively low lithotripsy efficiency compared to Electro Medical System (EMS) and pneumatic lithotripsy in the PCNL group. At the same time, the inner diameter of the flexible ureteroscope sheath is small. To facilitate stone removal, it is essential to powder the stones as much as possible, which takes a long time to complete the operation. In addition, we found that the incidence of postoperative complications in the RIRS group was significantly lower than that in the PCNL group. Therefore, it can be seen that when treating single kidney stones with a diameter of less than or equal

to 2 cm, compared with PCNL, RIRS has apparent advantages in intraoperative blood loss, postoperative complication rate, and postoperative recovery.

SAA is one of the classic cytokines that reflects inflammation in the body. SAA has been found to change expression levels significantly upon infection [27]. IL-6 is a cytokine, a type of interleukin. When the body is stimulated by trauma, infection, etc., the content of IL-6 in the serum will be affected and increase accordingly [28]. CRP is an acute response protein in the body [29]. Its concentration rises significantly when the body is stimulated by trauma, infection, etc., which can be used as an indicator to monitor and diagnose infection, and evaluate postoperative inflammatory response. SAA, IL-6, and CRP are selected as research indicators to reflect the body's inflammatory response level. In this study, one day after surgery, the serum SAA levels in both groups were lower than before surgery, while IL-6 and CRP levels were higher than before surgery. The serum levels of SAA, IL-6, and CRP in the RIRS group were significantly lower than in the PCNL group. At the same time, it was found that the serum BUN, Scr, and Cys-c levels of the two groups of patients one day after surgery were significantly higher than those before surgery, and the levels in the RIRS group were significantly lower than those in the PCNL group. It is suggested that RIRS has less impact on patients' inflammatory response and less damage to renal function. RIRS can use a flexible ureteroscope to detect difficult-to-treat stones outside the field of view of the nephroscope or parallel to the channel. It employs the natural channels of the human body and will not damage the normal body structure. It will have less interference with the renal parenchyma to improve the level of renal function indicators. During the PCNL operation, the renal calyces need to be punctured, and the channels expanded, which is highly invasive and requires perfusion during the operation. This will increase the burden on the renal pelvis, cause reflux of fluid in the pelvis, and result in a certain degree of damage to renal function.

Due to the small sample size of this study, the results have certain limitations and may have inevitable errors with the actual situation. This needs to be further verified after the sample size is expanded. Future research could benefit from a larger, prospective study design to validate these findings and comprehensively explore the long-term outcomes and patient satisfaction.

Conclusion

In summary, PCNL has a better stone clearance rate on postoperative day 2 when treating kidney stones $\leq$2 cm. Both surgeries have good stone-clearing effects regarding long-term stone clearance rates 1 month and 3 months after surgery. Both surgical methods are safe and effective, but RIRS is safer than PCNL. Compared with PCNL, RIRS is a new method of kidney stone operation, which has less trauma to the patient's body and fewer complications after the operation, speeding up the recovery process of the patient.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

JHW and YW designed the research study. JY and LX performed the research. JHW and JY provided help and advice on the ELISA experiments. YW and LX analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study received approval from the Medical Ethics Committee of Wujin Hospital of Traditional Chinese Medicine and was conducted after obtaining informed consent from patients or their family members (KY2022-069-B). This study was carried out in compliance with the Declaration of Helsinki.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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