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Original Article

Effectiveness and safety of retrograde intrarenal surgery (RIRS) vs. percutaneous nephrolithotomy (PCNL) in the treatment of isolated kidney stones

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Abstract: Objective: To compare the effectiveness and safety of retrograde intrarenal surgery (RIRS) and percutaneous nephrolithotomy (PCNL) in the treatment of isolated kidney stones. Methods: A retrospective analysis was performed on 99 patients with isolated kidney stones treated in our hospital. Patients were divided into a flexible cystoscope group (FCG, n=48, receiving RIRS) and a nephoscopy group (NG, n=51, receiving PCNL) according to the operation methods. The two groups were compared in terms of the operative time, intraoperative bleeding, length of hospitalization, time to bowel function recovery, cost of hospitalization, one-session stone clearance, postoperative incidence of massive hemorrhage, postoperative 1-year recurrence rate, and levels of hemoglobin, urinary kidney injury molecule-1 (Kim-1), cysteine protease inhibitor C (Cys-C), interleukin (IL)-6, IL-10, cortisol (Cor), white blood cells (WBC) and C-reactive protein (CRP). Results: The two groups exhibited significant differences in operation time, intraoperative bleeding, hospital stay, time to bowel function recovery and medical costs ($P < 0.05$). The NG had a single session stone clearance rate of 88.24% and a total stone clearance rate of 98.04%, which were higher than 70.83% and 83.33%, respectively, in the FCG ($P < 0.05$). The incidence of postoperative hemorrhage in the NG was 15.69%, which was higher than 2.08% in the FCG ($P < 0.05$). The postoperative 1-year recurrence rate was 9.80% in the NG and 6.25% in the FCG ($P > 0.05$). The hemoglobin level of the NG was lower than that of the FCG at 1 day after surgery, and the decrease in the NG were greater than that in the FCG ($P < 0.05$). The levels of Kim-1 in the NG were higher than those in the FCG at 48 h postoperatively. The levels of Cys-C in the NG were lower than those in the FCG at 12 h, 24 h, 48 h and 72 h postoperatively ($P < 0.05$). The NG showed higher levels of IL-6, Cor, WBC and CRP, and lower level of IL-10 as compared with the FCG at 6 h, 12 h, 24 h, 48 h, and 72 h postoperatively ($P < 0.05$). The levels of IL-10 in both groups at different time points after surgery were higher than those before surgery, and the levels of IL-6, Cor, WBC and CRP in both groups at 6 h, 12 h, 24 h, and 48 h after surgery were higher than those before surgery ($P < 0.05$), whereas there was no significant difference in IL-6, Cor, WBC and CRP at 72 h after surgery as compared with those before surgery ($P > 0.05$). Conclusion: Both RIRS and PCNL were effective in the treatment of isolated kidney stones, so the surgical methods should be specifically selected in clinical practice according to individual patient conditions.

Keywords: Isolated kidney, kidney stone, surgical treatment, flexible ureteroscopic lithotripsy, percutaneous nephrolithotomy, safety

Introduction

An isolated kidney refers to a person who has only one available kidney, which may be caused by congenital renal agenesis or acquired disease [1]. Due to the loss of the compensatory function of the contralateral kidney, an isolated kidney is more prone to kidney stones than non-isolated kidneys, resulting in a higher concentration of stone components flowing locally through the isolated kidney [2].

Stones in isolated kidneys can induce urinary obstructions earlier than stones in non-isolated kidneys, and if not treated timely and effectively, they will increase the possibility of renal insufficiency and urinary tract infection, or even renal failure in severe cases, which directly threatens the life of patients [3]. The primary goals of the treatment for isolated kidney stones are to preserve renal function and reduce complications. Percutaneous nephrolithotomy (PCNL) is a common option for complex renal stones and large stones, showing a high stone clearance rate [4]. Retrograde intrarenal surgery (RIRS) has been reported to be an effective treatment for renal and ureteral stones < 2 cm, with fewer complications and more effective preservation of renal parenchymal function compared to PCNL [5].

However, both PCNL and RIRS have their own shortcomings. There is a higher risk of bleeding and sepsis as well as a higher incidence of requiring massive transfusion and embolization in patients with isolated kidneys who underwent PCNL compared to patients with non-isolated kidneys [6]. The stone clearance rate of RIRS is negatively correlated with the size of stones, with stones > 2 cm in diameter requiring multiple sessions of treatment and prolonged duration of treatment [7]. Therefore, both PCNL and RIRS have their own advantages and shortcomings, and there is no unified conclusion as to which method is more effective in the treatment of isolated kidney stones. In this study, 99 patients treated in our hospital were recruited for a comparative analysis.

Materials and methods

Baseline data

A retrospective study was performed on 99 patients with isolated kidney stones treated in our hospital. Patients were divided into a flexible cystoscope group (FCG, n=48) and a nephoscopy group (NG, n=51) according to the operation methods. Inclusion criteria: patients with an isolated kidney combined with renal calculi; patients with unilateral renal agenesis as shown by urinary ultrasound; patients with no renal echo or renal images in the pelvic, abdominal or renal regions; patients with good tolerance to surgery; patients with normal preoperative cardiopulmonary and coagulation functions; patients with normal blood glucose level and blood pressure. This study was been approved by the Ethics Committee of Hangzhou Fuyang Hospital of Traditional Chinese Medicine (approval number 2019LSE-09). All study participants provided written informed consent prior to participating in the study. Exclusion criteria: patients aged < 18 years old; pregnant women; patients with systemic bleeding disorders; patients with severe cardiopulmonary dysfunction; patients with contraindications to surgery; patients with lower urinary tract stones, middle and lower ureteral stones, renal malignancy or hematological disorders.

Methods

The patients in the FCG were treated with RIRS under general anesthesia by tracheal intubation. In a lithotomy position, patients were given routine disinfection and draping. A guide wire (ST-32150, uroVision GmbH, Bad Aibling, Germany) was inserted into the ureteral opening of the affected side in a retrograde manner under ureteroscope (TYPE SS-3, Zhejiang Tiansong Medical Instrument Co., Ltd., Hangzhou, China) to complete placement. The F12 or F14 dilator ureteral access sheaths were advanced along the guide wire, and the F8 flexible ureteroscopy was also guided until encountering the stones. The energy of a holmium laser was set between 8 and 10 Hz. The stones were broken down into 0.1-0.2 cm stones by 200 μm a holmium laser fiber, then stone fragments were flushed out of the body by water pressure from a perfusion pump. F6 double J catheter and urinary catheter were routinely indwelled after surgery. The urinary catheter was removed 2-3 days after the surgery, and the stone clearance rate was determined by reexamination 1 week after the surgery.

The patients in the NG received PCNL under general anesthesia. The F6 ureter was inserted into the affected side in a retrograde manner under cystoscope. The distal end of the ureteral catheter and the catheter were fixed, and normal saline was injected through the ureteral catheter to dilate the renal pelvis appropriately. Prone position was adopted with soft pillow cushioned at the thoracoabdominal area. The middle and upper calyces of the affected side were punctured under ultrasound guidance. The guide wire was placed with the puncture needle. The skin and fascial layer was chosen and cut along the guide wire with a sharp knife. The puncture channel was expanded in sequence to F16 with the fascial dilator along the guide wire, and the ureteral access sheath of the dilator was indwelled. A short ureteroscope was placed into the calyces, renal pelvis and ureteropelvic junction to the upper ureter in order to determine the location of the stone. Holmium laser power was set to about 15 Hz, and the 500 μm holmium laser fiber was used to break down the stones. The stones were removed from the body by water pressure from a perfusion pump. F6 double J and F16 nephrostomy catheters were placed. The nephrostomy catheter and bladder catheter were removed according to the patient's condition after surgery, and the stone clearance rate was determined by reexamination within 1 week.

In both groups, if reexamination showed many remaining stones, the attending surgeon would decide whether a second treatment was needed.

Outcome measurements

Operative time: the time interval from the start of the procedure to the completion of sutures.

Intraoperative bleeding: the total volume of bleeding associated with the procedure during the surgery, measured by gravimetric method.

Length of hospitalization: the time interval from hospitalization to discharge.

Time to bowel function recovery: the time interval from the surgery until the patient had normal defecation and bowel movements as well as normal food intake.

Cost of hospitalization: the total cost from hospitalization to discharge.

One session stone clearance: the stones were completely cleared from the patient's body at the first treatment. Criteria for stone clearance [8]: no residual stones, or residual stones < 4 mm in diameter, without typical symptoms.

Total stone clearance rate: the sum of the stone clearance rate of all patients after the first course of treatment and the stone clearance rate of some patients after the second course of treatment.

Postoperative complications: postoperative hyperthermia, hemorrhage, pleural injury, pneumothorax and renal failure were recorded.

Recurrence rate: patients in both groups were followed up for 1 year after surgery, and recurrence rate during the follow-up period was compared.

Hemoglobin levels of the two groups were measured 1 day before surgery and 1 day after surgery, and the decrease in hemoglobin levels was compared between the two groups.

Renal function: serum neutrophil gelatinase-associated lipocalin (NGAL), cysteine protease inhibitor C (cystatin, Cys-C) and urinary kidney injury molecule-1 (Kim-1) levels were measured. Three mL of venous blood and 6 mL of urine were collected before and 6 h, 12 h, 24 h, 48 h, and 72 h after operation. All the samples were centrifuged, and the supernatant was retained to determine the levels of NGAL, Cys-C, and Kim-1 by enzyme-linked immunosorbent assay (ELISA). All kits were purchased from F. Hoffmann-La Roche & Co., (Lot No.: E-TSEL-H0003, E-EL-H3643C, E0785h). All operations were in strict accordance with kit instructions.

Serum cytokines: five mL of venous blood was collected before and 6 h, 12 h, 24 h, 48 h, and 72 h after operation to detect the levels of interleukin-6 (IL-6), interleukin-10 (IL-10), cortisol (Cor), white blood cells (WBC), and C-reactive protein (CRP). After centrifugation at 3000 rpm for 10 min, the levels of IL-6 and IL-10 were determined by ELISA (all kits were purchased from F. Hoffmann-La Roche & Co., Lot No.: ELSHIL06, PI528), Cor level by radioimmunoassay, WBC level by automated hematocrit analyzer, and CRP level by immunoturbidimetric assay.

Statistical methods

Statistical analysis was performed with SPSS 23.0. Counting data were expressed as [n (%)] and examined by chi-squared test. Measurement data were expressed as (mean ± SD) and compared by t test. Multi-point comparisons were performed by ANVOA with post hoc F-test. Graphs were drawn with Graphpad Prism 8. $P < 0.05$ was considered statistically significant.

Results

Baseline data

There was no significant difference between the NG and the FCG in gender, mean age, mean body mass index, mean stone diameter, stone type, and causes of isolated kidney ($P > 0.05$) (**Table 1**).

Table 1. Comparison of Baseline data

Baseline data		NG (n=51)	FCG (n=48)	t/X^2	*P*
Sex	Male	47 (92.16)	45 (93.75)	0.096	0.757
	Female	4 (7.84)	3 (6.25)		
Age (years)		50.27±15.17	48.76±13.62	0.520	0.604
BMI (kg/m²)		22.58±1.82	22.61±1.86	0.081	0.936
Stone diameter (cm)		2.65±1.23	2.61±1.18	0.165	0.869
Stone type	Single	10 (19.61)	8 (16.67)	0.144	0.705
	Multiple	41 (80.39)	40 (83.33)		
Etiology of isolated kidney	Functional	40 (78.43)	37 (77.08)	1.086	0.381
	Anatomical	10 (19.61)	8 (16.67)		
	Transplanted kidney	1 (1.96)	3 (6.25)		

Note: NG: nephoscopy group; FCG: flexible cystoscope group; BMI: body mass index.

Surgical and postoperative conditions

The NG had shorter operation time, higher volume of intraoperative bleeding, longer hospital stay, longer recovery time of bowel function, and lower medical costs than the FCG, with statistically significant differences ($P < 0.05$) (**Figure 1**).

Stone clearance rate

The NG had 45 cases of successful clearance of stone removal at the first course of treatment, with a clearance rate of 88.24%, while the FCG had 34 cases of successful clearance at the first course of treatment, with a clearance rate of 70.83%. The successful clearance rate of stone removal at the first course of treatment in the NG was significantly higher than that in the FCG ($P < 0.05$). As for total clearance rate, the NG had 50 cases of successful clearance, accounting for 98.04%, which was significantly higher than 83.33% (40 cases) in the FCG ($P < 0.05$) (**Table 2**).

Post-operative complications

The incidence of postoperative hemorrhage was 15.69% in the NG, which was higher than 2.08% in the FCG ($P < 0.05$). The incidence of postoperative hyperthermia, pleural injury and pneumothorax in the NG was 5.88%, 7.84% and 3.92%, respectively, which were not statistically different from those in the FCG (4.17%, 4.17% and 0.00%, respectively) ($P > 0.05$) (**Table 3**).

Postoperative recurrence rate

The recurrence rates of the NG and the FCG were 9.80% and 6.25%, respectively. There was no significant difference in the postoperative recurrence rate between the two groups ($P > 0.05$) (**Table 4**).

Hemoglobin level

The preoperative and postoperative 1 day hemoglobin levels in the NG were (116.69±20.12) g/L and (110.15±18.76) g/L, respectively, and (117.21±20.36) g/L and (115.75±19.73) g/L in the FCG. The hemoglobin levels of the NG and the FCG were decreased by (6.54±1.36) g/L and (1.56±0.67) g/L, respectively. There was no significant difference in the preoperative hemoglobin levels between the two groups ($P > 0.05$), while the decrease of the hemoglobin level in the NG was significantly higher than that in the FCG at 1 day postoperatively ($P < 0.05$) (**Figure 2**).

Renal function

The preoperative levels of NGAL, Cys-C and Kim-1 showed no significant difference between the two groups ($P > 0.05$). The postoperative levels of NGAL, Cys-C, and Kim-1 levels at 6 h, 12 h, 24 h, 48 h and 72 h were increased and then decreased in both groups ($P < 0.05$). There was no statistical difference in NGAL levels between the two groups at these time points ($P > 0.05$). There was no statistical difference in Cys-C levels between the two groups at 6 h postoperatively ($P > 0.05$), but the postoperative Cys-C levels at 12 h, 24 h, 48 h and 72 h in the NG were lower than those in the FCG ($P < 0.05$). There was no statistical difference in Kim-1 levels between the two groups at 6 h, 12 h, 24 h, and 72 h postoperatively ($P > 0.05$), but the Kim-1 level in the NG was higher than that in the FCG at 48 h postoperatively ($P < 0.05$) (**Figure 3**).

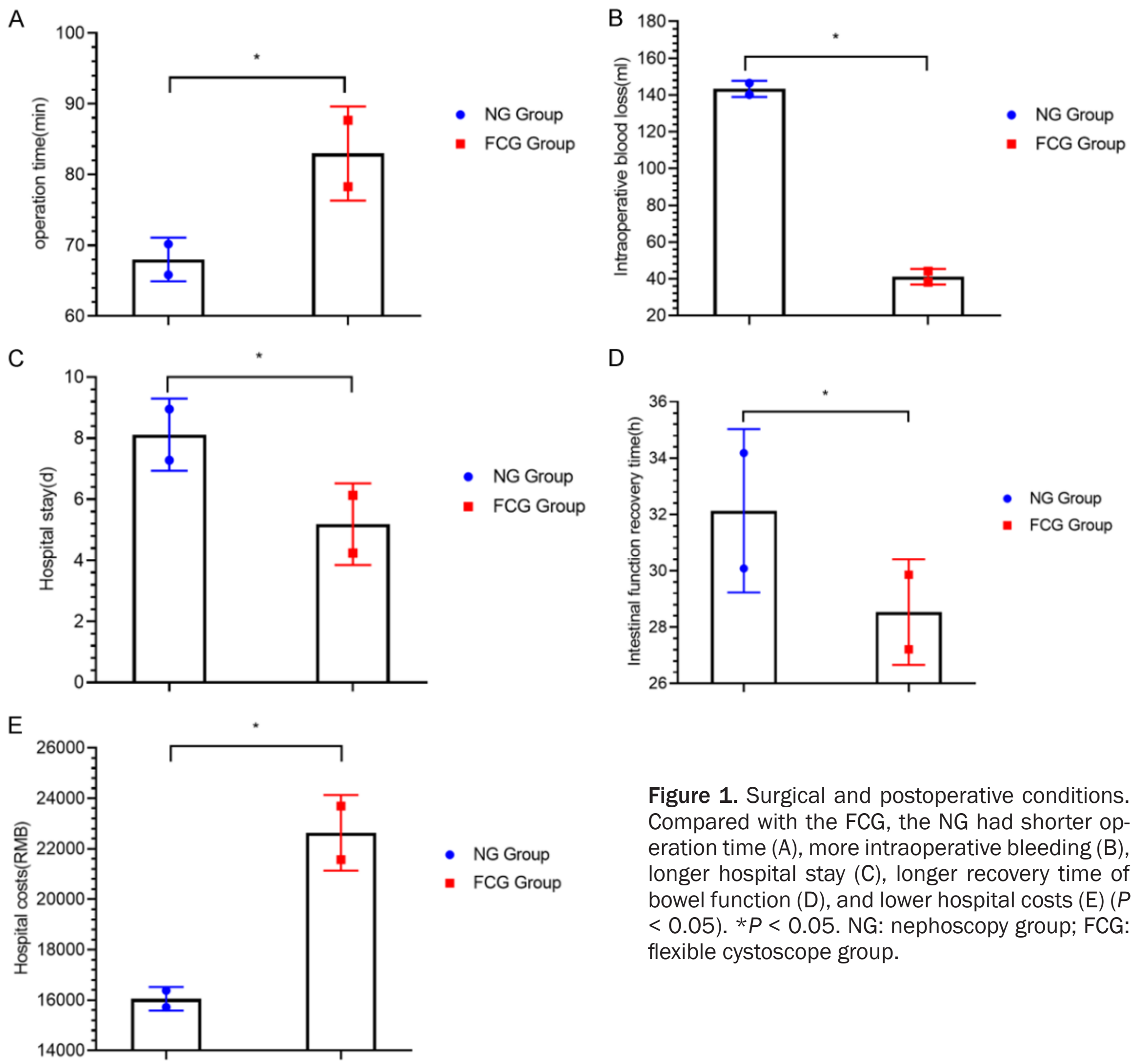


Figure 1. Surgical and postoperative conditions. Compared with the FCG, the NG had shorter operation time (A), more intraoperative bleeding (B), longer hospital stay (C), longer recovery time of bowel function (D), and lower hospital costs (E) ($P < 0.05$). *$P < 0.05$. NG: nephoscopy group; FCG: flexible cystoscope group.

Table 2. Comparison of stone clearance rate at the first treatment and total stone clearance rate [n (%)]

Group	Stone removal at the first treatment		Total stone clearance rate	
	Successful clearance	Not cleared	Successful clearance	Not cleared
NG (n=51)	45 (88.24)	6 (11.76)	50 (98.04)	1 (1.96)
FCG (n=48)	34 (70.83)	14 (29.17)	40 (83.33)	8 (16.67)
X^2	4.645		4.814	
P	0.031		0.028	

Note: NG: nephoscopy group; FCG: flexible cystoscope group.

Serum cytokines

The levels of IL-6, IL-10, Cor, WBC, and CRP showed no significantly difference between the two groups before surgery ($P > 0.05$). The NG showed higher levels of IL-6, Cor, WBC and CRP, and lower level of IL-10 as compared with the FCG at 6 h, 12 h, 24 h, 48 h, and 72 h postoperatively ($P < 0.05$). The levels of IL-10 in both groups at different time-points after surgery were higher than those before surgery, and the levels of IL-6, Cor, WBC and CRP at 6 h, 12 h, 24 h, and 48 h after surgery were higher than those before surgery ($P < 0.05$), whereas

Table 3. Comparison of postoperative complication rates [n (%)]

Group	Hyperthermia	Hemorrhage	Pleural injury	Pneumothorax	Renal failure
NG (n=51)	3 (5.88)	8 (15.69)	4 (7.84)	2 (3.92)	0 (0.00)
FCG (n=48)	2 (4.17)	1 (2.08)	2 (4.17)	0 (0.00)	0 (0.00)
X^2	0.005	4.013	0.119	0.451	/
P	0.945	0.045	0.730	0.502	/

Note: NG: nephoscopy group; FCG: flexible cystoscope group.

Table 4. Comparison of recurrence rates during 1-year follow-up period [n (%)]

Group	Recurrence	No recurrence
NG (n=51)	5 (9.80)	46 (90.20)
FCG (n=48)	3 (6.25)	45 (93.75)
X^2	0.078	
P	0.780	

Note: NG: nephoscopy group; FCG: flexible cystoscope group.

there was no significant difference in IL-6, Cor, WBC and CRP at 72 h after surgery compared with those before surgery ($P > 0.05$) (**Figure 4**).

Discussion

PCNL is a clinical procedure for stone clearance, and is considered by many scholars as the first-line treatment for all types of complex stones [9]. However, PCNL requires expansion of the channel to 30F, which is traumatic and can increase the incidence of intraoperative hemorrhage and cortical tearing [10]. In this study, PCNL was performed with a minimally invasive approach, *e.g.,* the puncture channel was dilated to 16F only, and ureteroscopy was chosen instead of nephroscopy, which reduced bleeding compared with the conventional procedure. It was found that PCNL performed with minimally invasive approach did not increase trauma and could reduce complications compared with conventional PCNL, even with multiple punctures and fistulas [11]. In this study, the thinner diameter selected for the PCNL surgery could swing and rotate to a larger range after placement, and reach the upper ureter, most of the calyceal area, and even renal calyces, showing a high stone clearance rate [12].

With the continuous progress of research, RIRS surgery is gradually applied in the treatment of complex stones. Compared with PCNL, RIRS is more minimally invasive and requires no incision to clear stones (directly *via* internal cavity of the body) [13]. For stones up to 2 cm in diameter, the clearance rates of both RIRS and PCNL were about 90%, without severe postoperative pain or bleeding [14]. RIRS is no longer limited to the treatment of stones less than 2 cm in diameter, and is performed also for different types of complex stones [15, 16]. In this study, we compared RIRS with PCNL and found that the NG had more intraoperative bleeding, longer hospital stay and recovery time of bowel function, shorter operation time and less hospital cost than the FCG ($P < 0.05$), suggesting that RIRS had better short-term surgical outcomes. The reason may be that RIRS has less impact on hemoglobin levels and coagulation function, resulting in less bleeding, shorter hospital stay, and faster gastrointestinal recovery. However, PCNL also has its own advantages, such as shorter operation time and lower medical costs. The hemoglobin level in the NG was lower than that in the FCG at 1 day postoperatively, and the decrease in hemoglobin level of the NG was greater than that of the FCG ($P < 0.05$), which is consistent with the above discussion.

In this study, the stone clearance rate at the first treatment and the total stone clearance rate in the NG were 88.24% and 98.04%, respectively, which were higher than 70.83% and 83.33%, respectively in the FCG ($P < 0.05$), suggesting that PCNL is superior to RIRS in stone clearance. However, we believe that in addition to the emphasis on the rapidity and effectiveness of stone removal, attention should also be paid to the rapid release of obstruction to maximize the protection for renal function, reduce renal injury and decrease the incidence of postoperative hemorrhage. In this study, the incidence of postoperative hemorrhage in the NG was 15.69%, which was higher than 2.08% in the FCG ($P < 0.05$), suggesting that the lithotripsy rate of RIRS was lower. Therefore, PCNL should be chosen after comprehensive consideration of safety. It was also

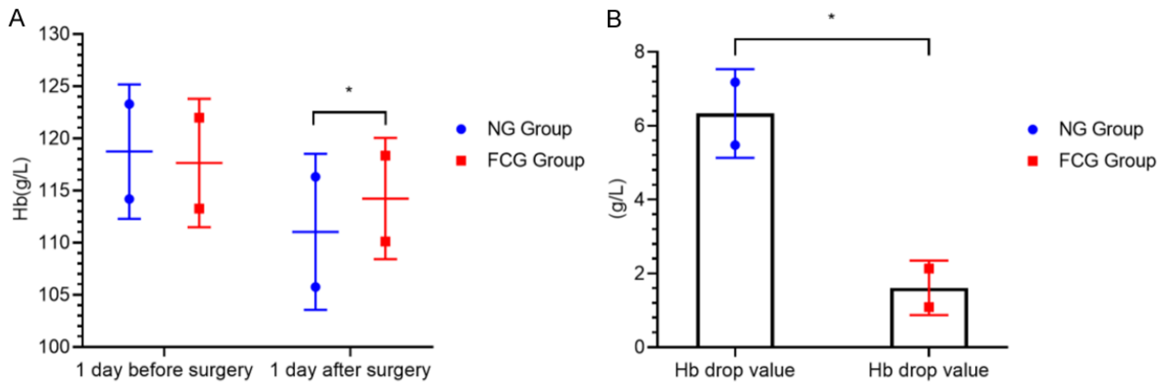
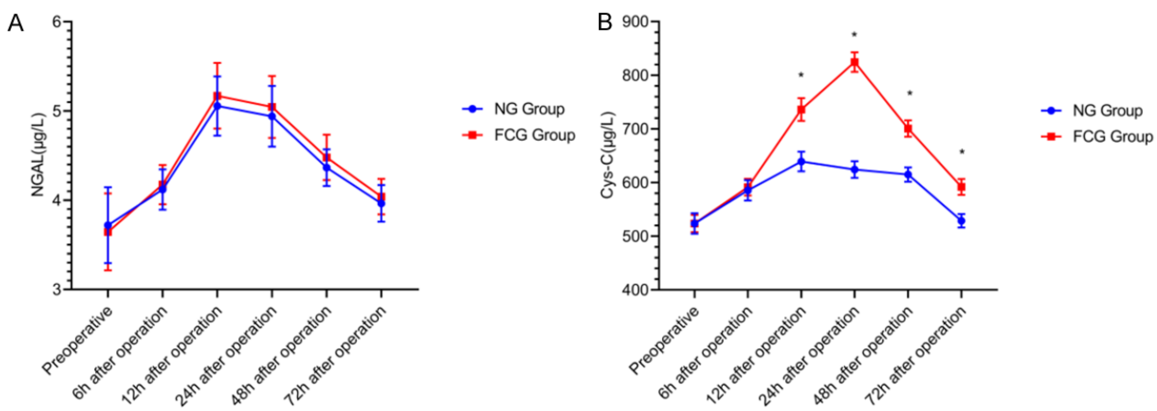


Figure 2. Hemoglobin level. The difference in the hemoglobin levels at 1 day before surgery (A) ($P > 0.05$). The decrease of the hemoglobin levels before and after surgery (B). *$P < 0.05$. NG: nephoscopy group; FCG: flexible cystoscope group.



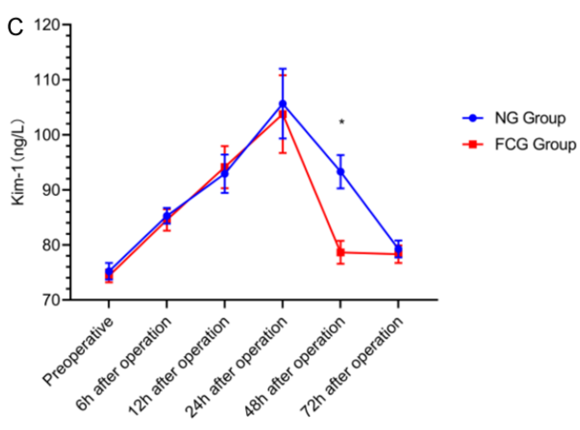


Figure 3. Renal function. NGAL (A), Cys-C (B), and Kim-1 (C), *$P < 0.05$. NG: nephoscopy group; FCG: flexible cystoscope group.

found that RIRS could reduce postoperative bleeding more effectively as compared with PCNL [17]. In this study, The NG showed higher levels of IL-6, Cor, WBC and CRP, and lower level of IL-10 as compared with the FCG at 6 h, 12 h, 24 h, 48 h and 72 h postoperatively ($P < 0.05$); the levels of IL-10 in both groups at different time-points after surgery were higher than those before surgery, and the levels of IL-6, Cor, WBC, and CRP at 6 h, 12 h, 24 h and 48 h after surgery were higher than those before surgery ($P < 0.05$), whereas the levels of IL-6, Cor, WBC, and CRP at 72 h after surgery showed no significant difference within the group compared with those before surgery ($P > 0.05$), suggesting that both types of surgery produce surgical stimuli that lead to abnormal expression of inflammatory cytokines. PCNL

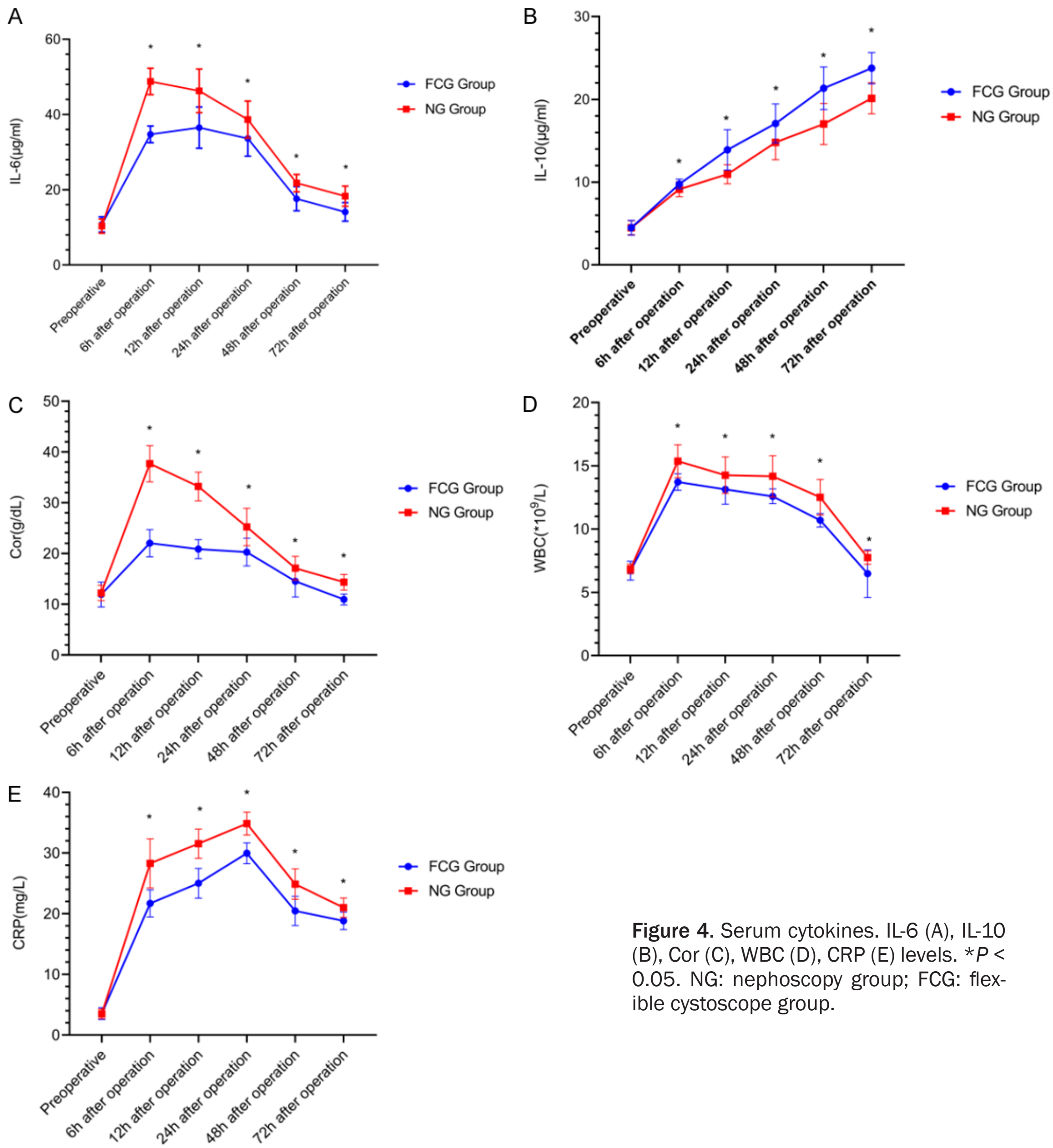


Figure 4. Serum cytokines. IL-6 (A), IL-10 (B), Cor (C), WBC (D), CRP (E) levels. **P* < 0.05. NG: nephoscopy group; FCG: flexible cystoscope group.

exhibited a stronger stress response and a more significant increase in the level of each cytokine, which was also related to the apparent minimally invasive nature of the RIRS.

In this study, the postoperative 1-year recurrence rate in the NG was 9.80%, which was not significantly different from 6.25% in the FCG ($P > 0.05$), suggesting good long-term effects for both procedures, with guaranteed lithotripsy and a lower risk of recurrence. In this study, the level of Kim-1 in the NG was higher than that in the FCG at 48 h postoperatively, and the levels of Cys-C in the NG were lower than those in the FCG at 12 h, 24 h, 48 h, and 72 h postoperatively ($P < 0.05$), whereas there was no statistical difference in NGAL level between the two groups at different time-points after surgery ($P > 0.05$). Cys-C reflects renal function and is highly independent of disease, infection, gender and age [18]. Cys-C is mainly metabolized by the kidney, and is reabsorbed in renal tubular cells and further degraded in the epithelium [19]. Serum Cys-C level is correlated with renal function, especially with glomerular filtration rate, and elevated Cys-C levels suggest glomerular injury, with the greater increase indicating more severe glomerular injury [20]. The Kim-1 level specifically reflects tubular injury [21]. The level of Kim-1 in urine and in renal tubular epithelial cells was increased in patients with early renal impairment, and it was found that the increased level of Kim-1 was positively correlated with the degree of renal impairment [22]. NGAL is closely related to the renal function of the body [23]. In this study, NGAL was used as an observation indicator to determine and compare the influence of the two treatment methods on renal function. The results of this study indicated that both operations affected renal function. RIRS caused more severe damage to the glomerulus, while PCNL had a more pronounced effect on the tubules, but these injuries were reversible. Therefore, it is of importance to conduct precise and meticulous operations with less damage to normal tissue and renal function [24, 25]. Study suggested that PCNL might cause irreversible mechanical damage to renal function due to the establishment of therapeutic access by percutaneous puncture. For patients with isolated kidneys, a slight impairment in renal function will result in more significant damage [26].

In conclusion, for isolated kidney stones, RIRS is more effective, with fewer complications and lower stress response, while PCNL has shorter operation time, lower costs and higher stone clearance rate. Both surgeries have their own advantages and should be selected rationally after comprehensive consideration. The present study also has some deficiencies. We did not clearly elaborate on which surgery has higher overall satisfactory rate. Also, we did not study the differences in the outcomes of patients with single and multiple stones undergoing two surgeries. These areas of interest can be further investigated in the future.

Disclosure of conflict of interest

None.

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