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ORIGINAL PAPER

Enhanced recovery after retrograde intra-renal surgery (RIRS) in comparison with mini-percutaneous nephrolithotomy (Mini-PCNL) for renal stone treatment

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Summary ***Objectives. The study presents a comparative analysis of the mini-percutaneous nephrolithotripsy (mini-PCNL) and retrograde nephrolithotripsy (RIRS) with a logistic analysis of outcomes and complications. Material and methods. The prospective study included 50 patients diagnosed with urolithiasis from 2018 to 2021 in the urological hospitals in Irkutsk. Patients were divided into two groups: RIRS (group I, n = 23) and Mini-PCNL (group II, n = 27). The comparison groups are statistically homogeneous. Results. Both procedures equally lead to high stone free rates (SFR > 1 mm, 91.3% vs 85.1%; p = 0.867; SFR > 2 mm, 95.6% vs 92.5%; p = 0.936). The intergroup analysis of the total operation time (and lithotripsy) demonstrated similar times (p > 0.05). Postoperative complications of classes II-III (Clavien-Dindo) in the early and late postoperative period developed rarely and were comparable (p > 0.05). Class I complications were predominant in the PCNL group (p = 0.007). Some parameters demonstrated the superiority of RIRS over PCNL: less pronounced pain syndrome (p = 0.002), less drainage time (p < 0.001), no postoperative hematuria (p = 0.002), shorter hospitalization and total treatment period (p < 0.001).***
Conclusions. The study highlighted the positive effect of the one-day surgery principle on the risk of developing postoperative hematuria, urinary infection, or severe postoperative pain. RIRS and mini-PCNL have similar effectiveness, but RIRS meets the criteria of the enhanced recovery program more than PCNL.

KEY WORDS: Fast track surgery; RIRS; PCNL; mini-PCNL; Enhanced recovery.

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INTRODUCTION

Enhanced recovery is the conventional name of various protocols or programs for optimizing the perioperative period (*for example, fast track surgery, Enhanced Recovery After Surgery or ERAS*) aimed at restoring health, working capacity, and improving the quality of treatment.
Urolithiasis is a widespread disease affecting up to 12% of the human population, with pronounced social and economic significance. The social aspect is related to the long duration of the illness, the high recurrence rate (up to 50%), and its frequent urgent presentation, leading to sudden disability (1). The economic aspect is related to high personal and government costs for treatment, and loss of working activity. Mortality from urolithiasis has recently increased (2, 3).
The multifactorial process of stone formation leads to a wide variety of clinical presentations. One of the most common forms of urolithiasis is the formation of calcium oxalate stones (4). The increased concentration of salts in the urine, inflammation, the presence of papillary plaques and plugs in the collecting system of the kidney, and other factors contribute to the development of the disease (5).
A complex of metaphylactic measures, such as lifestyle changes, hyperhydration, dietary modifications, correction of concomitant diseases and hormonal disorders, is considered extremely important to prevent relapses after surgical treatment. In addition, the prevention of postoperative recurrence depends on minimizing intraoperative trauma, reducing the risk of infectious complications, and avoiding residual fragments that can act as initial nucleus of stone formation (6).
It is important to note that the recommendations for stone treatment have been changed in the context of the pandemic. The *International Endourological Society* has reached a consensus on several recommendations for urolithiasis treatment. Thus, it was recommended to conduct remote counseling, avoid intubation methods of anesthesia, reduce indications for surgical treatment of asymptomatic concretions, etc. (7).
Currently, there are two most effective alternative methods for minimally invasive removal of kidney stones with a high level of *stone-free rate* (SFR) that are the retrograde nephrolithotripsy or *retrograde intra-renal surgery* (RIRS) and the *percutaneous nephrolithotomy* (PCNL) using flexible optics (8, 9). These methods are superior to the alternative method, shock-wave lithotripsy, in terms of SFR and complications (10, 11). An effective combination of both methods is possible in complex cases (12, 13). Both

methods lead to several postoperative complications, such as hematuria, fever, extravasation, pain. However, complications after RIRS are less pronounced and less likely to require surgical treatment (14, 15). Nevertheless, reducing the diameter of the working tool can reduce the severity of complications after PCNL and even surpass RIRS (10).

There is a small number of publications devoted to RIRS (according to *PubMed*, 601 works on 02.02.2022 from 1988 to 2022), and only 48 comparative studies of RIRS and PCNL (according to *PubMed*, 48 works on 02.02.2022 from 2008 to 2022). Moreover, there are practically no comparative studies on optimization of the perioperative period to improve the treatment effectiveness and enhance recovery.

The study presents a comparative analysis of the use of *mini-percutaneous nephrolithotripsy* (mini-PCNL) and *retrograde nephrolithotripsy* (RIRS) with a logistic analysis of outcomes and complications.

Methods

Research design

The local ethics committee of the *Irkutsk State Medical University* (ISMU) of the *Ministry of Health of the Russian Federation* approved the clinical trial. It was a prospective, blind, randomized study in Irkutsk urological hospitals.

The study included an analysis of perioperative data and treatment outcomes in patients with urolithiasis who underwent one of the surgical methods established by the protocol from January 2018 to October 2021.

Surgical operations were performed using one of two endourological methods:

mini-PCNL or RIRS.

All the features of the planned treatment methods were explained to the patient.

Inclusion criteria:

– planned surgery for kidney stones;
– indications for the operation meeting the criteria of the approved protocol;
– operation was planned to use one of the methods approved in the study;
– age over 18 years;
– patient signed a voluntary informed consent to participate in the study.

Non-inclusion criteria:

– no indication to treatment;
– presence of concomitant diseases that significantly affect the general conditions of the patient (decompensated diabetes mellitus, heart failure, gross neurological deficits, etc.);
– inability to comply with the protocol of the study.

Exclusion criteria:

– deviation from the study protocol;
– deviation from the criteria of the group.

The inclusion of patients in the study was carried out prospectively and continuously, until reaching the minimum sample size (20 patients in each group) and then within the planned timeframe of the study.

Finally, there were 77 patients recruited to participate in the study, out of them 50 patients completed the study. All the included patients were randomized into two groups based on the approved study protocol. The groups were not artificially aligned. The first group was treated with RIRS, the second group with mini-PCNL.

Deviations from the protocol

Of the 77 patients included in both groups in the study, 27 were excluded (17 - due to deviation from the protocol, and 10 - for personal reasons). The evaluation of the results (per-protocol) included 50 patients who meet all the criteria of the study. RIRS group included 23 patients (group I) and mini-PCNL group included 27 patients (group II).

Outcomes

Primary outcomes of the study were: absence of residual fragments in the postoperative period, not earlier than a month later; need for re-operation, migration of the stone into the ureter during surgery. Secondary outcomes: postoperative examination data; renal colic; urohematomas; urine leakage; recurrence of stone formation.

Comparison of study groups

Table 1 presents the preoperative parameters of patients. The statistical analysis established the homogeneity of the two groups ($p > 0.05$) according to the initial status.

Diagnostic methods

Evaluation included clinical history (history of stone disease, concomitant diseases, etc.), physical examination,

Table 1.
Preoperative status.

Parameter	Group I (n = 23)	Group II (n = 27)	P
Age, years	60 (51; 63)	51 (39; 55)	0.413
Weight, kg	88.2 ± 20.8	81.1 ± 15.7	0.173
Height, cm	1.66 ± 0.1	1.70 ± 0.08	0.147
BMI, units	31 (27; 37)	28 (25; 30)	0.052
Female, n (%)	16 (69.5%)	12 (44.4%)	0.345
Disease duration, days	15 (4; 36)	13 (5; 26)	0.847
Emergency intervention, n (%)	2 (8.6%)	5 (18.5%)	0.384
Re-stenting, n (%)	0 (0%)	2 (7.4%)	0.199
Leukocytosis, n (%)	3 (13.0%)	4 (14.8%)	0.875
Anemia, n (%)	1 (4.3%)	2 (7.4%)	0.668
Ischemic heart disease, n (%)	10 (43.4%)	11 (40.7%)	0.900
Hypertension, n (%)	14 (60.8%)	11 (40.7%)	0.414
Diabetes mellitus, n (%)	3 (13.0%)	3 (11.1%)	0.852
Prostate hyperplasia, n (%)	6 (26.0%)	1 (3.7%)	0.049
Urinary tract cancer, n (%)	1 (4.3%)	0 (0%)	0.284
Kidney cysts, n (%)	4 (17.3%)	1 (3.7%)	0.147
Chronic urinary infection, n (%)	8 (34.7%)	15 (55.5%)	0.367
Area of the largest concretion, mm^2	135 (117;195)	120 (90;228)	0.602
HU density, units	948 (± 298)	909 (± 394)	0.697
Concretion > 20 mm, n (%)	5 (21.7%)	8 (29.6%)	0.626
More than one concretion, n (%)	8 (34.7%)	11 (40.7%)	0.771
Calcium oxalates, n (%)	15 (65.2%)	19 (70.3%)	0.864

biochemistry, imaging (ultrasound, tomography, X-ray) and endoscopy.
The analysis of the composition of the calculi was performed by spectroscopy in a specialized laboratory after surgery.
Multi-slice computer tomography (MSCT) examination helped to assess the urinary system status, including the density and size of concretions.
The severity of postoperative pain syndrome was assessed according to the *Visual Analog Scale* (VAS) of pain.
Before removal of the urethral catheter, nephrostomy, and stent an ultrasound examination was performed to rule out possible uro-hematomas. No earlier than one month after the operation and no later than two months, there was the first control by MSCT to assess SFR.
After the first follow up visit after surgery, patients regularly (once every six months) underwent the examinations established by the protocol of the study: consultation of the operating doctor, blood and urine tests, ultrasound MSCT.
There were several criteria for evaluation of treatment effectiveness: SFR, no re-operation, no complications > Class II according to Clavian-Dindo. SFR was evaluated according to two criteria: fragments > 1 mm and fragments > 2 mm.
The perioperative period was evaluated separately by assessing the length of hospital stay, the total period of disability, the functional status in the postoperative period (pain, temperature, etc.).
The cost-effectiveness of treatment was not evaluated.

Surgical treatment

During the study, a common protocol of enhanced recovery for patients with planned endourological intervention foe renal stones was followed in both groups.
Table 2 presents the protocol scheme.

Table 2.
The enhanced recovery protocol for endourological surgery for kidney stones.

PREOPERATIVE

- Informing the patient about the disease, treatment options, and possible outcomes, indicating the average effectiveness, risks of complications, typical postoperative condition, timing of catheterization, hospitalization, possible methods of pre-rehabilitation, and further rehabilitation methods
- One-day concept: the patient undergoes most of the preoperative examinations in one day, without the need for multiple re-preparation; the order of examinations and tests is optimized and sorted to achieve the desired outcome
- Rigorous evaluation of indications for surgical treatment: symptomatic concretions; chronic urinary infection; concretions > 15 mm; progressive size growth; obstructive disorders; recurrent course
- Assessment of the possibility of patient compliance with the protocol and its feasibility in the medical institution
- Preventive administration of antihistamines and antacids drugs
- Avoiding of preoperative sedation
- Pre-rehabilitation based on indications: age group; obesity; exhaustion; sarcopenia; impaired carbohydrate tolerance or diabetes mellitus
- Preoperative antibiotic therapy according to the indications: latent or obvious infection of the genitourinary system (according to the results of bacteriological research)
- Multidisciplinary examination of patients: Urologist; Anesthetist; General Practitioner/Cardiologist; Radiologist; And other specialists as needed
- CT/MRI of the urinary system, with 3D modeling and contrast, including angiography
- A rich carbohydrate and protein meal (if there are no contraindications) and 200 ml of liquid 2.5 hours before surgery
- The last meal (if the operation is in the morning) at 10 P.M. the day before, if in the afternoon no later than 6 hours before the operation
- Antibiotic prophylaxis 60 minutes before surgery with 3rd generation cephalosporins with a negative result of a urine culture examination
- No shaving of the surgical area
- Preparation of the intestine with laxatives or single micro-clysm
- Prevention of thromboembolic complications by compression of the lower extremities and administration of low-molecular-weight heparins
- No cleansing enemas
- Avoiding of pre-stenting/pre-catheterization

INTRAOPERATIVE

- Preferred method of anesthesia: regional anesthesia/multimodal anesthesia
- Heating of the patient during the operation with the control of normothermia
- Heating of infusion solutions and inhalation gases
- RIRS or mini-(micro)-PCNL using flexible endoscopes
- Using a small diameter access sheath (up to 12-14Fr with RIRS; up to 14Fr with PCNL)
- Laser application in low power mode (up to 10W)
- Avoiding of popcorning. Spraying of fragments > 1 mm with difficult extraction
- Avoiding of the ureteral access sheath for single concretions < 10 mm with RIRS
- Avoiding of multi-access with PCNL
- Administration of tranexamic acid before puncturing during PCNL
- Avoiding of nephrostomy/stenting if possible
- Reduced fluid pressure in the kidney
- Adhesive bandage on the skin
- Intraoperative euvolemia
- Urethral catheters 12-14Ch
- Sealed cosmetic skin suture without loose ends and knots on the skin, adhesive bandages with PCNL

POSTOPERATIVE

- Early fluids intake (2–3 hours after surgery) and food (6 hours after surgery)
- Early activation (2–4 hours after surgery, after evaluation by an anesthesiologist and urologist)
- Physical therapy (breathing exercises, walking, and other exercises)
- Multimodal prevention of nausea and vomiting (Metoclopramide+Ondansetron)
- Early ultrasound control to exclude hematomas and urinomas in the first 3-6 hours after surgery
- Removal of the urethral catheter, nephrostomy, stent after ultrasound control no later than 3 (for PCNL) and 1 (after RIRS) day after surgery, followed by re-evaluation
- Hemostatic drugs (tranexamic acid) in intraoperative or detected postoperative bleeding
- Continuation of prevention of thromboembolic complications by compression of the lower extremities and the use of low-molecular-weight heparins
- Multimodal analgesia for pain control (dexketoprofen + paracetomol)
- Use of alpha blockers
- Chewing gum on the first and second day after surgery
- Monitoring of blood and urine parameters on the first day after surgery
- Strict glycemic control in case of impaired carbohydrate tolerance and diabetes mellitus
- A detailed discussion of the behavior of the patient and the rehabilitation plan before the discharge
- Detailed written instructions in the discharge documents
- Strict plan of control examinations in the postoperative period
- Strict postoperative hygiene of the genitals and postoperative wounds (with an adhesive bandage, the patient is recommended to take a hygienic shower daily from the first day without additional processing)
- Discharge from the hospital within 1-3 days after the operation with the outpatient observation or the recovery

The final surgical treatment method was chosen before the operation by randomization.
The operating time was estimated from the beginning (including patient positioning) to the complete end of all the actions of the surgical team.
A thulium laser with a power mode up to 10W was used for lithotripsy.
After both procedures, pyeloureterography was done at the end of the operation to assess the need for kidney stenting/nephrostomy.
The main types of operations were mini-perc PCNL with access sheath up to 14 Fr (for multiple and large concretions) and use of flexible optics (to avoid multi-access and to search for possible residual fragments). Puncture of renal cavities was done under *Emergency Operations Center* (EOC) and ultrasound control, after preliminary route planning based on the MSCT angiography results. The patient could be in any position at the discretion of the surgeon, avoiding prone position. Nephrostomy was maintained in most cases for a period of 1 to 3 days. Tubeless procedure was preferred for single, uninfected stones, without ongoing hematuria.
RIRS was performed under EOC control; when ureteral access sheath was not placed, the surgeon inserted the endoscope into the ureter up to the kidney with a guidewire. In absence of signs of perforation or fragments migration, a ureteral catheter was maintained for up to 12 hours from the end of surgery whereas in other situations, a ureteral stent was placed.
After the operation, all patients stayed in the intensive care unit for 2-3 hours.
All patients received multimodal analgesia, prevention of thromboembolic complications (low molecular weight heparin), and protection from stress ulcers (proton pump blockers). On the first day after surgical treatment patients were assessed the pain level.

Statistical analysis

The pre-operative data and the results of surgical treatment were analyzed using STATISTICA software for Windows version 10.0 (*Statsoft, Inc, USA*), SPSS Statistics version 23.0 (*IBM, USA*), and Stata version 16.0 (*StataCorp, USA*).
The significance level for all the methods was set at $p \leq 0.05$ (except multiple logistic regression).
Data of the two groups (RIRS vs mini-PCNL) were compared.

Results

Peri-and postoperative results

In the peri-and postoperative periods, there were no cases of lethality, anesthesiologic complications or critical deterioration of the state of health due to concomitant diseases in both groups.
All registered complications corresponded to classes I-IIIb Clavien-Dindo following the recommendations of the *European Association of Urology* (16, 17). There was one IIIb complication in the PCNL group associated with an increasing paranephric hematoma.
The average surgery duration in groups I and II were 67 ± 34 and 75 ± 21 minutes, respectively (p = 0.350). The time of direct lithotripsy and evacuation of fragments for I and II was 41 ± 31 and 49 ± 20 minutes, respectively (p = 0.276).
Table 3 shows the postoperative status of patients.

Table 3.
Postoperative status of patients.

Parameter	Group I (n = 23)	Group II (n = 27)	P
Clavien-Dindo complications, n (%):			
I class	1 (4.3%)	13 (48.1%)	0.007
II class	1 (4.3%)	6 (22.2%)	0.115
IIIa class	1 (4.3%)	1 (3.7%)	0.911
IIIb class	0	1 (3.7%)	0.360
Migration of concretions fragments, n (%)	0	9 (33.3%)	0.009
Paranephral hematoma > 100 ml, n (%)	0	1 (3.7%)	0.360
Blood transfusion, n (%)	0	2 (7.4%)	0.199
Postoperative hematuria up to 1 day, n (%)	0	13 (48.1%)	0.002
Subfebrility 1st day after surgery, n (%)	0	4 (14.8%)	0.073
Febrility 1st day after surgery, n (%)	0	3 (11.1%)	0.118
Pyelonephritis after surgery, n (%)	0	1 (3.7%)	0.360
Stenting (I)\nephrostomy (II), n (%)	10 (43.4)	17 (62.9)	0.448
Timing of kidney catheterization\nephrostomy, days	1 (1; 1)	2(2; 4)	< 0.001
Perforation, n (%)	1 (4.3%)	1 (3.7%)	0.911
Re-operation, n (%)	0	2 (7.4%)	0.199
VAS more than 5 points on the first day after surgery, n (%)	0	21 (77.7%)	0.002
Postoperative pain, points	4 (4; 4)	6 (6; 7)	< 0.001
Average duration of hospitalization, bed-day	1 (1; 1)	3 (2; 4)	< 0.001
1-day stay, n (%)	13 (56.5%)	0	0.005
Total treatment period, days	1 (1; 2)	10 (3; 14)	< 0.001
SFR > 1 mm, n (%)	21 (91.3%)	23 (85.1%)	0.867
SFR > 2 mm, n (%)	22 (95.6%)	25 (92.5%)	0.936

VAS: visual analog scale; SFR: stone-free rate.

Significant postoperative complications (Clavien-Dindo ≥ 3) rarely developed in both groups. There is a significant statistical difference in the level of mild and minor complications: in group II, class I complications occurred with a higher frequency (p = 0.007). Migration of concretions fragments was more frequent in group II (p = 0.009), which was probably due to worse visualization caused by the development of intraoperative hematuria. In general, hemorrhagic complications in group II are significantly more common.
An objective examination in the late postoperative period established the groups' comparability (p > 0.05) and a significant difference in the risks of complications, postoperative status, and duration of treatment (p < 0.05).
It should be noted that the development of complications of classes IIIa-b was isolated. Univariate logistic regression analysis of these complications revealed no relationship with perioperative parameters (p > 0.05).
Table 4 partially presents the data of the performed regression analysis of predictors of postoperative complications.
A significant predictor of residual concretions was the duration of lithotripsy for more than one hour (HR 2.40; 95% CI -0.21; 5.02; p = 0.072). The remaining factors were not significant (p > 0.1).

Table 4.
Analysis of predictors of complications in the early and late postoperative period.

Complication	Predictor	Univariate analysis			Multivariate analysis	
		χ^2	OR (95% CI)	P	OR (95% CI)	P
Residual concretion.	Lithotripsy time > 60 minutes	14.61	3.61 (1.32; 5.89)	0.002	2.40 (-0.21; 5.02)	0.072
Multivariate Logit Regression:	Intraoperative hematuria	3.62	1.61 (-0.05; 3.28)	0.057	-	-
χ^2 = 16.89; p = 0.0007	Any concrement migration	6.67	2.31 (0.55; 4.07)	0.010	1.21 (-1.07; 3.50)	0.299
	Area > 500 m^2	9.17	2.8 (0.97; 4.77)	0.003	1.69 (-0.61; 4.00)	0.150
Reoperation. Multivariate	Initial anemia	3.30	3.13 (0.02; 6.24)	0.048	-	-
Logit Regression: χ^2 = -; p =-	Perforation	4.30	3.85 (0.44; 7.25)	0.027	-	-
	Coagulopathy	2.20	2.39 (-.055; 5.35)	0.112	-	-
Postoperative pain syndrome,	Increasing experience of the surgeon	9.59	-0.72 (-1.21; -0.23)	0.004	-0.51 (-1.7; 0.69)	
> 5 points on the VAS scale	Lithotripsy time is more than 30 minutes	8.24	1.79 (0.47; 3.11)	0.008	2.28 (0.26; 4.31)	
	Prescription of acute illness, day	9.44	0.68 (0.20; 1.16)	0.005	0.03 (-0.07; 0.15)	
Multivariate Logit Regression:	1-day surgery	6.96	-1.66 (-2.95; -0.37)	0.011	3.51 (-1.27; 8.31)	
χ^2 = 34.38; p < 0.0001	Preoperative waiting > 3 days	7.14	1.87 (0.39; 3.34)	0.013	1.73 (-1.74; 5.21)	
	Intraoperative hematuria	13.69	2.69 (1.02; 4.37)	0.002	1.78 (-0.88; 4.45)	
	Stenting	15.60	-2.74 (-4.38; -1.10)	0.001	-3.4 (-5.93; 0.87)	
	Any concrement migration	5.85	1.90 (0.21; 3.60)	0.028	1.48 (-1.71; 4.68)	

VAS: Visual analog scale.

Figure 1 shows a model with a very good predictive value (area under curve, AUC = 0.88) presented as a ROC curve. Consequently, the long duration of the operation (lithotripsy) increases the probability of residual fragments by 2.4 times.
Baseline anemia (HR 3.13; 95% CI 0.02; 6.24; p = 0.048; AUC = 0.72) and urinary tract perforation (HR 3.85; 95% CI 0.44; 7.25; p = 0.027; AUC = 0.73) were reliable predictors of the need for re-operation with one-factor regression.
It was not possible to build a reliable multivariate regression model.
Significant predictors of postoperative hematuria were male gender (HR 2.14; 95% CI -0.27; 4.56; p = 0.082), duration of lithotripsy more than an hour (HR 3.53; 95% CI -0.31; 7.38; p = 0.072), chronic pyelonephritis (HR 3.09; 95% CI -0.48; 6.67; p = 0.090) and severe postoperative pain VAS > 5 points (HR 3.35; 95% CI 0.34; 6.35; p = 0.029).
Figure 2 shows a model with excellent predictive value (area under curve, AUC = 0.93) presented as a ROC curve.
The remaining factors were not significant (p > 0.1).
Significant predictors of postoperative exacerbation of urinary infection were chronic hepatitis (HR 3.93; 95% CI 0.15; 7.72; p = 0.041), baseline bacteriuria (HR 2.64; 95% CI -0.40; 5.69; p = 0.089) and any migration of concretion intraoperatively (HR 2.86; 95% CI -0.48; 6.22; p = 0.094). Figure 3 shows a model with excellent predictive value (area under curve, AUC = 0.94) presented as a ROC curve.

Figure 1.
ROC curve for multivariate logit regression of predictors of postoperative residual concretions.

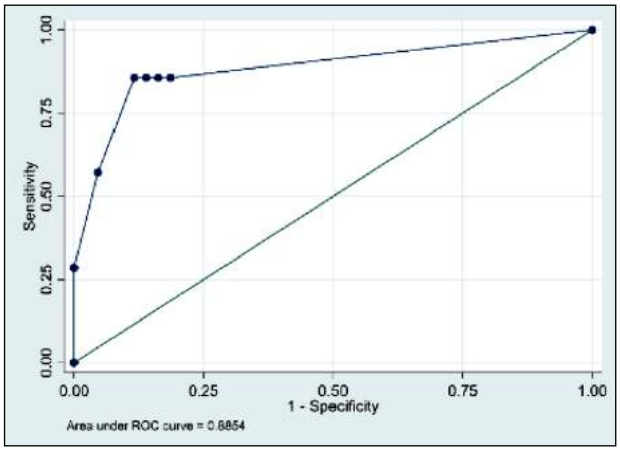


Figure 2.
ROC curve for multivariate logit regression of postoperative hematuria predictors.

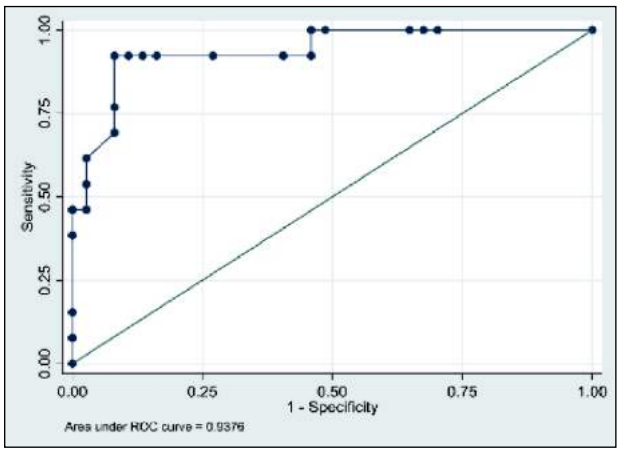


Figure 3.
ROC curve for multivariate logit regression of predictors of exacerbation of urinary infection.

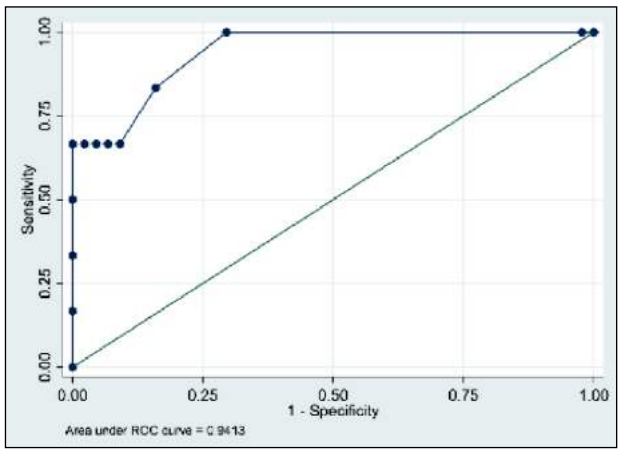


Figure 4.
ROC curve for multivariate logit regression of predictors of moderate postoperative pain.

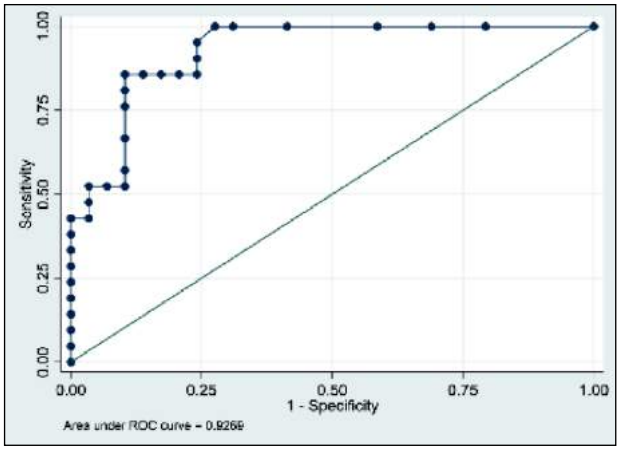
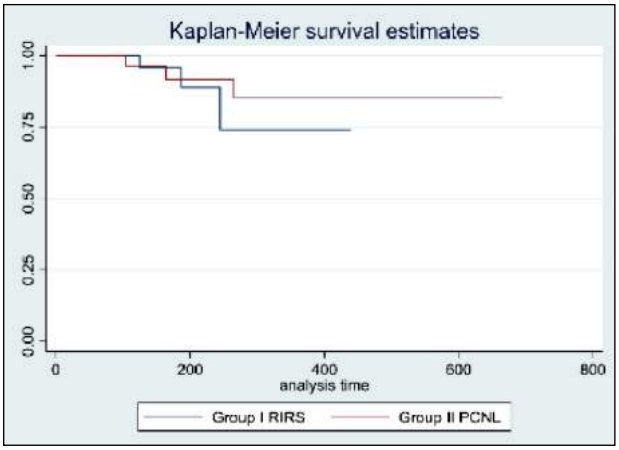


Figure 5.
Freedom from a true relapse of stone formation according to the Kaplan-Meyer method.



Significant predictors of postoperative pain syndrome were lithotripsy time of more than half an hour (HR 2.28; 95% CI 0.26; 4.41; p = 0.027). Postoperative kidney stenting was a protective factor (HR -3.4; 95% CI -5.93; -0.87; p = 0.008). Figure 4 shows a model with excellent predictive value (area under curve, AUC = 0.92) presented as a ROC curve.

Long-term results

General results were reported according to the last observation.

True relapse was considered only when newly identified concretions were observed in patients who were previously considered stone free with a 1 mm cut off (SFR > 1 mm).

Successful primary SFR > 1 mm was observed in 21 (91.3%) *vs* 23 (85.1%) (p = 0.867); false relapse in 2 (8.6%) *vs* 4 (14.8%) (p = 0.555); and true relapse in 2 (9.5%) *vs* 3 (13.0%) (p = 0.742) in group I and II, respectively.

The average clinical observation period was 251 days (95% CI 98-146 days) and maximum duration of follow up was 664 days. For group I, the average follow-up period was 218 days (95% CI 61-112 days) and maximum period of follow up was 440 days. For group II, the average follow-up period was 279 days (95% CI of 108-189 days) and maximum period of follow up was 664 days.

Due to the absence of cases of lethality, survival analysis was not performed, the survival rate for both groups being 100%. There were no significant complications in the long-term postoperative period.

In group I, Kaplan-Meyer's estimate of freedom from true stone recurrence was 95.6 ± 4.25% after the first six months (95% CI 72.9; 99.3%), 88.8 ± 7.6% (95% CI 60.9; 92.2%) after 9 months and 74.0 ± 14.9% (95% CI 32.5; 92.2%) after a year and a half.

In group II, freedom from true stone recurrence was 96.3 ± 3.6% (95% CI 76.4; 99.4%) after the first six months, 91.7 ± 5.6% (95% CI 70.4; 97.8%) after 9 months, and 84.9 ± 8.3% (95% CI 58.6; 95.1%) after a year and a half. The statistical uniformity of the likelihood ratio (Likelihood-ratio test statistical of homogeneity) is comparable (p = 0.620; χ^2 = 0.24).

The log-rank criterion did not reveal statistical differences (p = 0.582; χ^2 = 0.30) in the frequency of relapse over the entire follow-up period, which is graphically expressed by the Kaplan-Meyer method in Figure 5.

Table 5 presents the regression model of proportional Cox risks describing the influence of various factors on the development of relapse.

Multivariate regression analysis of proportional Cox risk (sample from p < 0.05) demonstrated the significance of postoperative fever (HR 23.45; 95% CI 2.14; 256.5; p = 0.010) and initial stone density > 600 HU (HR 0.04; 95% CI 0.004; 0.49; p = 0.010) in predicting possible recurrence of urolithiasis.

The treatment results showed statistical equality for *stone free rate* (SFR), freedom from stone recurrence during the entire follow-up period, and rate of complications of classes II-III Clavien-Dindo (p > 0.05).

Meanwhile, a significant superiority of group I (RIRS) was demonstrated for shorter duration of hospitalization and overall disability, and better objective condition in the early postoperative period.

Economic efficiency was not evaluated.

Consequently, RIRS meets the criteria of the enhanced recovery program more than PCNL with a similar perioperative protocol.

Table 5.
Regression model of urolithiasis recurrence.

Variable	Univariate Cox analysis			Multivariate Cox analysis, χ^2 = 12.66; p = 0.0018	
	Valda χ^2	HR (95% CI)	P	HR (95% CI)	P
Febrility after surgery	3.59	6.77 (1.21; 37.9)	0.029	23.45 (2.14; 256.5)	0.010
Concretion density > 600, HU	6.12	0.12 (0.022; 0.683)	0.016	0.04 (0.004; 0.49)	0.010
Body Mass Index > 25	7.19	2.24 (0.88; 5.70)	0.090	-	-
Duration of postoperative follow-up	4.99	0.88(0.785; 1.00)	0.056	-	-

Limitations

Limitations of the study were the relatively small sample size, the average postoperative follow-up period less than two years, mixing of various surgical techniques within the framework of the protocol (PCNL, RIRS).

Discussion

In the presented study, the outcomes for SFR, I-III class complications development, and surgery duration (lithotripsy) were similar to the data of other authors and meta-analyses of these data. The problem of a longer hospitalization and general treatment period and a more pronounced pain syndrome also corresponds to what reported in previous papers (18-21). A possible solution to align the results of the two procedures and improve compliance with the enhanced recovery program is the transition from mini-PCNL to micro-PCNL (22, 23).

In general, analyzing the results of PCNL and RIRS comparison presented by different authors, attention is drawn to the pronounced spread of SFR indicators, the lack of a clear definition of SFR by the size of the fragments, the lack of a clear definition of the operation duration and its pronounced spread. Probably, such differences are due to different technical conditions, the experience of the surgical team, and other similar reasons. In general, our own experience demonstrates greater ease of implementation and convenience for RIRS patients in comparison with mini-PNCL.

Both treatment protocols are safe, effective, and accompanied by minimal risks of complications. They equally lead to high stone free rates (SFR > 1 mm, 91.3% *vs* 85.1%; p = 0.867; SFR > 2 mm, 95.6% *vs* 92.5%; p = 0.936).

Intergroup analysis of the total operation duration (and lithotripsy) demonstrated a similar duration in the two group (p > 0.05). Postoperative complications (Clavien-Dindo) in the early and late periods developed rarely and were comparable (p > 0.05) although class I complications were predominant in the PCNL group (p = 0.007). Some parameters demonstrated the superiority of RIRS over PCNL: less pronounced pain syndrome (p = 0.002), less drainage time (p < 0.001), no postoperative hematuria (p = 0.002), lower average duration of hospitalization, and total time spent on treatment (p < 0.001).

The analysis of predictors of the complication development based on the results of multivariate analysis showed that exceeding the lithotripsy time by more than one hour increases by 2.4 times (HR 2.40; 95% CI -0.21;5.02; p = 0.072) the risk of presence of residual fragments (SFR > 1 mm). This indicates the expedience of discussing a possible second stage of treatment in certain groups of patients. Postoperative hematuria can be triggered by the following factors: male gender (HR 2.14; 95% CI -0.27; 4.56; p = 0.082), duration of lithotripsy more than an hour (HR 3.53; 95% CI -0.31; 7.38; p = 0.072), chronic pyelonephritis (HR 3.09; 95% CI -0.48; 6.67; p = 0.090) and severe postoperative pain (VAS > 5 points) (HR 3.35; 95% CI 0.34; 6.35; p = 0.029). Significant predictors of postoperative exacerbation of urinary infection are chronic hepatitis (HR 3.93; 95% CI 0.15; 7.72; p = 0.041), baseline bacteriuria (HR 2.64; 95% CI -0.40; 5.69; p = 0.089) and migration of concretions intraoperatively (HR 2.86; 95% CI -0.48; 6.22; p = 0.094). Lithotripsy time of more than half an hour is a significant predictor of severe postoperative pain syndrome (HR 2.28; 95% CI 0.26; 4.41; p = 0.027) whereas a protective factor is postoperative kidney stenting (HR -3.4; 95% CI -5.93; -0.87; p = 0.008).

Special attention should be paid to the prognostic protective effect of the one-day surgery principle and the effect of improvement of the operating surgeon skills on the risk of complications such as postoperative hematuria, exacerbation of chronic urinary infection, severe postoperative pain syndrome (p < 0.05).

Both treatment protocols have a high safety profile without the risk of mortality or relapse. The log-rank criterion did not reveal statistically significant differences in the frequency of survival (p = 1), or relapse (p = 0.582).

The advantages of the performed study are its prospective design, randomization, homogeneity of groups, mandatory strict protocol of the study, in-depth statistical analysis of outcomes, description of the algorithm of patient management with a detailed presentation of the materials and results of the study.

Conclusions

The results of the study have high practical and scientific significance. The design of the study according to a strict protocol, compliance with the *good clinical practice* (GCP) criteria, a clear presentation of diagnostic, surgical, and statistical techniques, specific and objective parameters allowed us to obtain reliable results.

The results led to important conclusions for the selection of treatments. RIRS and mini-PCNL have similar effectiveness, but the path to recovery using retrograde surgery is somewhat simpler and shorter. RIRS meets the criteria of the enhanced recovery program more than PCNL with a similar perioperative protocol.

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