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**ABSTRACT**

of the dissertation for the degree of Doctor of Philosophy

**ROLE OF FLEXIBLE URETERORENOSCOPIC  
NEPHROLITHOTRIPTY IN THE TREATMENT  
OF KIDNEY STONES**

Speciality: 3234.01 – Urology

Field of science: Medicine

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## GENERAL CHARACTERISTICS OF THE WORK

**Actuality of the problem.** Urinary stone disease is the most common pathology in the world, accounting for 32-40% of all urological diseases. The fact that mainly this disease occurs mainly in 65-70% of cases at the working age (20-60) is an indicator of the social significance of this problem<sup>1,2</sup>. In this regard, the search for and improvement of new minimally invasive methods in the treatment of kidney stone disease is an actual issue. Extracorporeal nephrolithotripsy and percutaneous contact nephrolithotripsy have radically changed the tactics of treatment of kidney stone disease and as a result led to a decrease in the number of open transactions<sup>3,4</sup>.

Although the cause of stone formation has not yet been resolved as a main problem, and stone removal does not save the underlying disease, removal of stones from the urinary tract by various methods remains an important part of the complex treatment of patients. Until the advent of new technologies, the main treatment for patients who has kidney stone was open pyelolithotomy. However, open surgical removal of the stone can lead to many complications, and this prolongs the rehabilitation period. Regardless of the surgical method, there is a possibility of advent of recurrent stone in patients after kidney stone are removed. Repeated open surgery can result in more occurrence of complications in all cases<sup>5,6,7</sup>.

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<sup>1</sup>*Imamverdiyev, S.B.* Urolithiasis: epidemiological and diagnostic analysis/ S.B.Imamverdiyev, R.T.Huseynzada // Health, Baku, – 2010. 9. – s. 185-190.

<sup>2</sup>*Urology Desktop Reference Book.*–Ankara, – 2017. –984 s.

<sup>3</sup>*Ordon, M.* The surgical management of kidney stone disease: a population based time series analysis // J. Urol., – 2014. 192 (5), – p. 1450-1456.

<sup>4</sup>*Donaldson, J.* Systematic review and meta-analysis of the clinical effectiveness of shock wave lithotripsy, retrograde intrarenal surgery, and percutaneous nephrolithotomy for lower-pole renal stones / J.Donaldson, M.Lardas, D.Scrimgeour [et al.] // Eur. Urol., – 2015. 67 (4), – p. 612-616.

<sup>5</sup>*Donaldson, J.* Systematic review and meta-analysis of the clinical effectiveness of shock wave lithotripsy, retrograde intrarenal surgery, and percutaneous nephrolithotomy for lower-pole renal stones / J.Donaldson, M.Lardas, D.Scrimgeour [et al.] // Eur. Urol., – 2015. 67 (4), – p. 612-616.

Extracorporeal and percutaneous contact nephrolithotripsy is a commonly used method in the treatment of kidney stones. However, the presence of complications such as renal trauma, bleeding, perforation of neighboring organs during percutaneous contact nephrolithotripsy, etc. requires the importance of application of minimal invasive retrograde (ureteroscopic) nephrolithotripsy method in kidney stone disease<sup>8,9</sup>.

Currently, ureteroscopic nephrolithotripsy is considered more modern and affordable among the minimal invasive methods currently available. There are three types of ureteroscope: rigid, semi-rigid and flexible. Among those mentioned, the method of treatment of flexible ureteroscopic nephrolithotripsy was proposed by Marshall in 1964. The technical capabilities of a flexible ureteroscope allow you to visually monitor the renal pelvis and calyces, find the stone, cut it into fragments with a Holmium laser and remove them from there with various loops.<sup>10</sup>

Also flexible ureteroscopic nephrolithotripsy treatment method allows high-quality dissection of stones of different localization and composition in the kidney. Flexible ureteroscope has a number of advantages: entering of it to the renal calyces by twisting 270 degrees, compactness, mobility and ease of use<sup>11</sup>. Along with the notes, there are many questions about

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<sup>6</sup>*Brisbane, W.* An overview of kidney stone imaging techniques / W.Brisbane, M.R.Bailey, M.D.Sorensen [et al.] // Nature reviews Urology, – 2016. 13 (11), – p. 654-662.

<sup>7</sup>*Aboumarzouk, O.* Safety and efficacy of ureteroscopic lithotripsy for stone disease in obese patients: a systematic review of the literature / O.Aboumarzouk, B.Somani, M.Monga [et al.] // BJU Int., – 2012. 110 (8), – p. 374-380.

<sup>8</sup>*Wiesenthal, J.D.* A comparison of treatment modalities for renal calculi between 100 and 300 mm2: are shockwave lithotripsy, ureteroscopy, and percutaneous nephrolithotomy equivalent? / J.D.Wiesenthal, D.Ghiculete, R.J.D'A Honey [et al.] // J. Endourol., – 2011. 25 (3), – p. 481-485.

<sup>9</sup>*Sakhaee, K.* Kidney stones 2012: pathogenesis, diagnosis, and management / K.Sakhaee, N.M.Maalouf, B.Sinnott, [et al.] // The Journal of clinical endocrinology and metabolism, – 2012. 97 (6), – p. 1847-1860.

<sup>10</sup>Marshall, V. Fiber optics in urology / J. Urol., – 1964. 91, – p. 110-114.

<sup>11</sup>*Göğüş, Ç.* Üreteroskopik taş manipülasyonu ve mesane taşlarının tedavisi // Türk uroloji derneği, – 2009. – s. 487-497.

the application of the method of treatment of flexible ureterorenoscopic nephrolithotripsy and there is no doubt that more research is needed. Application of the method of treatment of flexible ureterorenoscopic nephrolithotripsy in the form of monotherapy in kidney stones with indicators 2-3 cm in size, extensive research on the conduct of postoperative period has not been conducted<sup>12</sup>.

Thus, regardless of localization, endoscopic operations on kidney stones, damage of soft tissue compared to traditional surgical interventions, pus of wound, formation of urinary fistula and because patients are not likely to stay in the hospital for long periods of time, has undoubted advantages. As a result, flexible ureterorenoscopic nephrolithiasis should be considered as a monotherapy method. The development of endoscopic and minimally invasive surgery in the treatment of kidney stones, its place in clinical practice are promising and relevant areas of modern urology, and taking into account the practical need to improve the results of mini-invasive methods in the treatment of this group of patients, it was decided to conduct the current study by us.

**Object of research:** patients those have urinary stone disease.

**The aim** of the study is to provide optimization of treatment by clinical analysis and evaluation of the main advantages and disadvantages of the method of flexible ureterorenoscopic nephrolithotripsy in the surgical treatment of kidney stone disease.

**Responsibilities of research:**

1. To analyze comparatively different methods of examination and treatment during kidney stones;
2. To determine the effectiveness of flexible ureterorenoscopic nephrolithotripsy on kidney stones larger than 2 cm and on stones located the lower renal calyx;
3. To investigate the technical feasibility of the method of treatment of flexible ureterorenoscopy;
4. Develop an appropriate treatment algorithm for stone size,

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<sup>12</sup>Palmero, J. Comparative study for the efficacy and safety of percutaneous nephrolithotomy (PCNL) and retrograde intrarenal surgery (RIRS) for the treatment of 2-3,5 cm kidney stones / J.Palmero, A.Duran-Rivera, J.Miralles [et al.] // Arch. Esp. Urol., – 2016. 69 (2), – p. 67-72.

location, hardness, body condition, body mass index, anatomical anomalies;

5. Optimize the period of preoperative preparation and postoperative rehabilitation during flexible ureterorenoscopic nephrolithotripsy;

6. To identify technical errors and complications during the operation.

**Research methods:** anamnesis and family history, physical examination; clinical and laboratory examinations; instrumental examination methods; Resorlu-Unsal prognostic assessment system; SFR - stone free rate; American Society of Anesthesiologists physical condition classification system; statistical processing.

**Main thesis of dissertation for defense:**

- Flexible ureterorenoscopic nephrolithotripsy has become the gold standard in the treatment of stones up to 2 cm.
- Highly effective results can be obtained by successfully applying the method of flexible ureterorenoscopic nephrolithotripsy in the treatment of 2-3 cm kidney stones.
- Compared to percutaneous nephrolithotomy, in flexible ureterorenoscopic nephrolithotripsy method does not observed complications such as bleeding requiring hemotransfusion, damage to adjacent organs, or severe urinary tract infection.
- In the treatment of stones located in the renal lower calyx, It is possible to obtain a higher probability of complication compared with extracorporeal shock wave lithotripsy (ESWL) by flexible ureterorenoscopic nephrolithotripsy and it is possible to obtain a less likely complication compared to percutaneous contact nephrolithotripsy (PCNL) to the degree of postoperative stone free.
- This method has a higher efficiency compared to other minimally invasive methods in pregnant women, patients who suffer from various kidney abnormalities and obesity.
- Early complications such as thromboembolism and intestinal paresis are not observed because the activation period after flexible ureterorenoscopic nephrolithotripsy is very short.

### **Scientific novelty of the research:**

- A treatment algorithm was developed depending on the size of kidney stones, location, density and somatic condition of the patient.
- As a result of the study, the effectiveness of flexible ureterorenoscopic nephrolithotripsy in the treatment of kidney stones with a size of 2-2.5 cm was revealed by comparative analysis with other treatments.
- In the treatment of lower calyx stones up to 20 mm in size, a high effect can be achieved with flexible ureterorenoscopic nephrolithotripsy. The low risk of complications and the short rehabilitation period have proven the advantages of retrograde intrarenal surgery.

**Practical significance of the research.** Based on the results obtained, a treatment algorithm providing an optimal approach to the treatment of kidney stones of different sizes and localizations was developed and applied in practice.

By applying the results of the study in practice, as well as optimization of the preoperative preparation period during flexible ureterorenoscopic nephrolithotripsy, shortening the postoperative rehabilitation period, reducing the duration of hospitalization thereby reduction of hospital cost has been achieved.

At the same time, research work will have the opportunity to have a positive impact on the long-term outcome of treatment of patients with nephrolithiasis.

**Approbation.** The results of the research were reported and discussed at various scientific meetings: at the international scientific-practical conference on the topic of "Modern problems of neurosurgery" dedicated to the 50th anniversary of the establishment of Department of Neurosurgery of the Azerbaijan Medical University (Baku, 2019); at the international scientific and practical Internet conference dedicated to the 60th anniversary of the public figure, professor Aliyev Mubariz Yagub oglu (Minsk, 2019); international scientific-practical conference on the topic of "Actual problems of medicine - 2020" dedicated to the 90th anniversary of the establishment of Azerbaijan Medical University (Baku, 2020).

The initial discussion of the dissertation was held at the meeting of the staff of the "Urology" department of AMU (15.03. 2021, protocol 01), the approbation of the work was held at the scientific seminar of the Dissertation Council ED 2.06 operating at Azerbaijan Medical University (26.05.2021, protocol № 05).

**Application of results.** The proposed treatment algorithm is applied in the Uronephrology Department of the Hospital of the Ministry of Internal Affairs of the Republic of Azerbaijan and in the private MedEra Hospital.

**Place of performance of research work.** The dissertation work was carried out at the Department of Urology of Azerbaijan Medical University.

**Publication of the main results of the dissertation work.** The main provisions and results of the research are reflected in 10 scientific papers. 7 of them are scientific articles (2 articles abroad, 5 articles in local journals), 3 theses (1 thesis abroad, 2 theses in the republic).

**Volume and structure of the dissertation work.** The work is presented on 151 printed pages (208962 symbols) and includes an introduction (5 pages), a literature review chapter (24 pages), a chapter of research material and methods (16 pages), 4 research chapters (64 pages), conclusion (14 pages), findings (1 page), practical recommendations (1.5 pages) and bibliography (21 pages). 206 scientific sources were used. 9 of them are in Azerbaijani, 3 in Russian and 194 in English. The dissertation includes 20 tables, 14 figures, 16 charts and 1 scheme.

## **MATERIALS AND METHODS OF THE RESEARCH**

The clinical part of the study was conducted on the comprehensive examination of patients diagnosed with kidney stones at the Hospital of the Ministry of Internal Affairs of the Republic of Azerbaijan and private MedEra Hospital in 2013-2018 and the analysis of the results of surgical treatment. In the research, kidney stones were found in 100 patients aged 22-83 years suffering from urinary stone disease on the basis of complex diagnostic examinations and selective surgical treatment methods have been

developed for them. For objective comparative analysis, patients were divided into 2 groups: Group I (main group) - 50 patients (50%) who underwent flexible ureterorenoscopic nephrolithotripsy; Group II (comparison group) - 50 patients (50%) who underwent percutaneous nephrolithotomy.

The age of the studied patients was 22-83. The mean age of patients was  $53.3 \pm 14.1$  in the first group and  $48.4 \pm 10.9$  in the second group ( $p=0.062$ ). Patients were divided into 3 subgroups according to age. Up to 30 years old, between 30-60 years old and over 60 years old. It was revealed that, the main group of patients who applied with kidney stones consists of persons aged between 30-60 years with high working capacity and social activity.

Of the total number of patients that included in the research group, 58 were male and 42 were female. There were 29 men and 21 women in the main group and 29 men and 21 women in the comparison group.

Depending on the clinical condition and pathogenetically substantiated medical indications, standard clinical-laboratory and instrumental-diagnostic examinations were performed in all patients, the main diagnosis was confirmed once again concomitant diseases have been identified. Properly directed individual treatment tactics were applied to patients and appropriate surgical correction methods were decided. In the postoperative period, each patient was dynamically monitored individually, and the results of the operation were compared on a selective scale. In the course of the work, along with other standard examinations, various clinical laboratory and instrumental examinations were carried out individually.

Anamnestically, the patient's complaints, the duration of the disease, whether he received any conservative or surgical treatment, previously falling kidney stones, and comorbidity diseases were asked. 68 patients (68%) applied for the first time and 38 patients for recurrent kidney stones.

Of the patients suffering from kidney stones, 62 patients (62%) presented with severe pain in the lower back. 26 patients complained of constant dull pain, and 12 patients had no pain complaints.

Periodically, 27 patients (27%) applied with a rise in body

temperature. A sharp rise in temperature was observed in 16 patients (16%), these patients were re-evaluated and operated on after appropriate invasive intervention or conservative treatment.

In addition to pain, dysuria, pollakiuria, microscopic and macroscopic hematuria are also sometimes seen. Dysuria was observed in 17 patients (17%) and hematuria in 11 patients (11%).

In general, in addition to acute pain, 38 patients (38%) had symptoms such as nausea and vomiting.

In total, 38 patients (38%) had symptoms such as nausea and vomiting except severe pain. In 29% of patients, the symptoms of palpitations were positive. No patient had enlarged kidney was not palpated.

Clinical data and physical examination should not be sufficient to assess acute renal failure, and the diagnosis should be confirmed by imaging. Diagnosis and treatment of urolithiasis, published by the European Association of Urologists in 2015, immediate imaging methods should be performed in patients with single kidney and fever.

At the next stage, standard clinical and laboratory examinations were performed in patients belonging to both groups included in the research - general analysis of blood, general analysis of urine, level of creatinine in the blood, erythrocyte sedimentation rate were assessed.

Analysis of pathogenic bacteria that can cause urinary tract infections has shown that the main causative agents of urinary tract infections are Gram-negative bacteria. During the study, we found that in 63% of cases, the causative agent of urinary tract infection is intestinal spores - *Escherichia coli*. Other pathogens detected as a result of cultivation were *Klebsiella*, *Proteus* and *Pseudomonas aeruginosa*, *Candida* fungi and *Staphylococci*.

Urinary tract infection, in 33 confirmed patients (33%) empirical antibacterial treatment was initiated after urine culture examination.

Generation III cephalosporins (Ceftriaxone 1 g x 12 hours), fluoroquinolones (Ciprofloxacin 500 mg x every 12 hours, levofloxacin 500 mg x every 24 hours), aminoglycosides (Gentamicin 80mg x every 8 hours, amikacin 500 mg x every 12

hours) were used as empirical treatment. Patients receiving antibacterial therapy were re-evaluated by general urine analysis on day 8 of treatment. In 18 patients (18%) antibacterial treatment was initiated with a ureteral JJ stent.

Patients admitted to the clinic with renal pain were examined by ultrasound and computed tomography (CT). Under the leadership of the American Association of Urologists and the American Society of Radiologists, CT is the first method of choice, and under the leadership of the European Association of Urologists, ultrasound is the first method of choice.

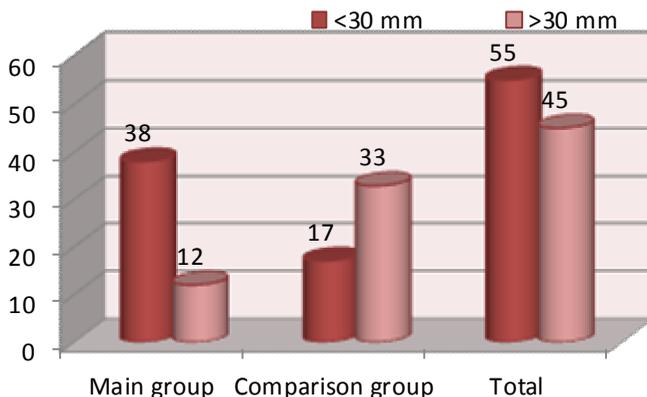
In 47 (47%) of the patients involved in the study, an initial ultrasound examination was performed or they appealed to us with the results of the ultrasound examination. The sensitivity of ultrasound in the detection of kidney stones is 45%, and the specificity is 88%. Because stones smaller than 3 mm do not cast shadows, the sensitivity of the examination method is lower.

CT examination was performed on all patients to assess precise localization of kidney stones, size, anatomical and functional condition of the kidneys and urinary tract. CT scan have a higher sensitivity and specificity compared to ultrasound scans in the detection of kidney stones, accordingly is 95% and 98%.

As an indicator of the size of the stone, the size of length of the longest side was taken into account in millimeters. The average total stone size of the patients who involved in the study was  $34.7 \pm 17.3$  mm. To analyze the results of the study in more detail, patients were divided into 2 subgroups according to the size of kidney stones. In subgroup I, patients with a total stone size less than 30 mm, and in subgroup II Patients with a total stone size of 30 mm or more were identified (chart 1).

In 82 (82%) of the patients that included in the study, stone was localized in the renal pelvis, In 12 patients (12%) in the upper group of calyces, in 15 patients (15%) in the middle group of calyces, in 48 patients (48%) it was localized in the lower calyx group. In general, urinary stone was existed in 17 patients at the same time. Push back flexible ureterorenoscopic nephrolithotripsy was executed in 2 patients due to isolated urinary stones. A single stone was found in

37 patients (37%) and 2 or more stones in 63 patients (63%). The number of patients suffering from coral kidney stones was 12.



**Chart 1. Number of patients in the main and comparison groups according to the total stone size**

In our study, 16 (16%) patients did not have hydronephrotic transformation, and I degree hydronephrotic transformation was noted in 18 patients (18%), II degree in 33 patients (36%), III grade in 15 patients (15%). In 18 patients (18%), a JJ urinary stent was placed before surgery.

The mean density of stones found in the patients included in the study was  $764.6 \pm 273.7$  Hounsfield Unit. Patients were divided into 2 groups – those with a stone density of up to 800 HU and larger than 800 HU.

In some patients, additional examinations (descriptive radiography of the chest and abdomen, Ultrasound examination of the abdominal organs, contrast / non-contrast of the abdominal cavity or thoracic cavity CT and / or magnetic resonance imaging examination) were performed with the aim of the diagnosis somatic comorbidities and surgical diseases.

All patients were divided into 2 groups due to comorbidities that found. In group I include renal pathologies along with kidney stones, and in group II includes diseases that are borderline or systemic

comorbidity to another organ.

Simultaneous operations were performed in 1 (1%) patients in the main group with absolute indications.

Taking into account the general condition of the patients, body type, concomitant diseases, parameters of kidney stones and patient desire, we performed flexible ureterorenoscopic nephrolithotripsy on 50 patients and classic percutaneous nephrolithotomy on 50 patients, without going beyond the guidelines provided by the leading urologist associations in Europe and the world.

The Clavien-Dindo classification was used for systematization of postoperative complications and comparison between study groups.

The figures obtained in the course of the study were statistically analyzed in accordance with modern recommendations. The indicators in the groups are arranged in a series of variations, and the average score (M), standard error (m), minimum (min), and maximum (max) of this indicator were calculated for each variation series.

A non-parametric method - the Wilcoxon (Manna-Whitney) criterion - was used to determine the difference between the quantitative indicators in the groups. Collection of research data, processing, making calculations was conducted in Microsoft Excel 2009, the results are placed in tables and graphs.

## **RESEARCH RESULTS AND THEIR DISCUSSION**

Each of the patients included in the study with a diagnosis of kidney stones was treated individually in the choice of surgical treatment and two types of surgeries performed on the basis of instructions applied in modern times, including those improved hints by us.

Fifty patients in the main group underwent mild ureterorenoscopic nephrolithotripsy, taking into account the size and location of the stone, the patient's constitutional condition, comorbidities, as well as social activity and desire. The total stone size of the examined patients was  $27.6 \pm 10.7$  mm. Isolated renal pelvis stones were found in 13 patients (26%) and isolated lower calyx stone in 8 patients (16%). In 29 patients (58%) stones were placed in a disorderly. Two

patients underwent “push back” (throwing a stone back from the urethra, into the kidney) retrograde intrarenal surgery for stones in the upper 1/3 of the urethra, and these patients were also considered as kidney stones in the study.

In 24 patients (48%) the operation was performed on the left side, and in 25 patients (50%) on the right side. Bilateral retrograde intrarenal surgery was performed in 1 patient (2%). During the operation, general anesthesia was used in 32 patients (64%) and regional anesthesia in 18 patients (36%). Complete analgesia and relaxation were achieved with spinal anesthesia during operations. The use of regional anesthesia during RIRS allows to avoid general anesthetic complications such as pulmonary complications, thromboembolic complications.

All operations were performed within the standards. In our clinical practice, we prefer the use of urinary tract cases during retrograde intrarenal surgery. The use of urinary sheaths shortens the duration of the operation, reduces the risk of infectious complications by maintaining low intrarenal pressure during the operation, by making the flexible ureterorenoscope more durable, it both simplifies the surgeon's work and prevents the possibility of damage to the instrument. So during the research, urinary sheath was used in 26 patients (56%). The duration of the operation was 61.53 minutes in patients whose urinary case was used, and 72.6 minutes in other patients. Fever complications were observed in only 1 patient (3.22%) after operations using US (urinary sheath). Compared to that fever was observed in 2 patients in the group where US (urinary sheath) was not used and urinary tract infection in 1 patient (12.5%). However, the surgeon's lack of experience in this area or his or her rough handling when inserting the urethral sheath can even lead to serious complications such as damage to the urethral wall, bleeding, and even rupture of the urinary tract. Therefore, we recommend that you select the appropriate size of urethral sheath and do not behave rudely during the operation and do not perform the procedure under X-ray control.

Ureteral JJ stents were placed in 34 patients (68%) at the end of the operation. Operation of removal of the ureteral stent was performed after 5-90 days (average  $30.68 \pm 20.78$  days) under local

anesthesia or intravenous sedation.

The operations in the main group of our research lasted 34-127 minutes ( $68.4 \pm 19.6$  minutes), which did not differ statistically from the comparison group. The operating time was  $62.2 \pm 13.6$  minutes in stones with a total stone size of less than 30 mm, and  $68.9 \pm 20.3$  minutes in the comparison group although there was a difference between these indicators in favor of the RIRS group, it was not statistically significant. In general, we explain the lack of a statistical difference between the operating times of both methods in small and medium-sized stones by the fact that during percutaneous surgery, a urinary catheter is inserted first and then the loss of time to change the patient's condition although percutaneous nephrolithotomy method is a method which performed in a shorter period of time than flexible ureterorenoscopic nephrolithotripsy method (table 1).

One of the main problems of stone surgery is the exposure of both the operating room staff and the patient to X-rays despite the use of modern anti-radiation protection devices (aprons, collars). The use of X-rays during the operation in the RIRS group was  $26.59 \pm 11.42$  seconds and this is a significantly shorter period of time compared to patients undergoing percutaneous nephrolithotomy. Thus, in the surgical treatment of kidney stones up to 3 cm in size, we concluded that flexible ureterorenoscopic nephrolithotripsy is superior to percutaneous nephrolithotripsy due to its intraoperative properties.

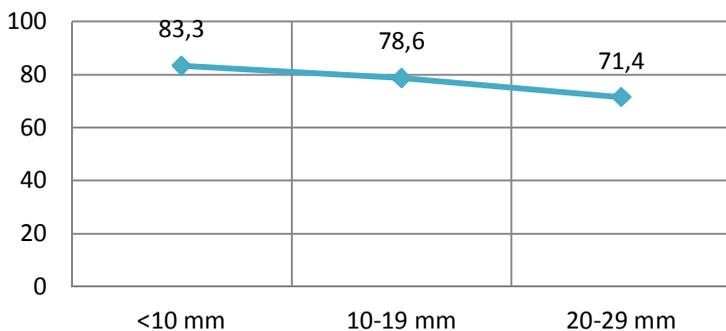
We recommend taking antibiotics for 3 days to prevent infectious complications in the postoperative period. For this purpose, we prefer fluoroquinolones which taken orally. In addition to antibiotic treatment, patients are recommended to have a daily fluid intake of more than 2.5 liters for 1 month and an activity volume of more than 2 hours.

Activation of patients after surgery was possible for an average of  $7.4 \pm 3.6$  hours. Duration of entering into a hospital recorded as an average  $1.1 \pm 0.7$  days. Both indicators were lower in the main group, creating a statistical difference from the comparison group. Early postoperative activation prevents gastrointestinal and cardiopulmonary complications, promotes patients faster recovery of psycho-emotional and somatic conditions and ability to work.

**Table 1**  
**Results of operations which performed in different subgroups**

	Efficiency of operations					$\chi^2$	p
	Main group		Comparison group				
	Abs.	Relative	Abs.	Relative			
<b>Total</b>	41/50	82%	45/50	92%	1,329	0,249	
<b>Total size of stone</b>							
<30 mm	34/38	89.5%	17/17	100%	1,930	0,165	
>30 mm	7/12	58.3%	28/33	84.8%	3,580	0,058	
<b>Gender</b>							
male	22/29	75.9%	25/29	86.2%	1,010	0,315	
female	19/21	90.5%	20/21	95.2%	0,359	0,549	
<b>Number of stones</b>							
Single stone	13/14	92.9%	21/23	91.3%	0,028	0,867	
≥2 stones	28/36	77,8%	24/27	88.9%	1,322	0,250	
<b>Mass index of body</b>							
Normal weight	18/20	90%	20/22	90.9%	0,010	0,920	
Excess weight	14/20	70.0%	16/19	84.2%	1,108	0,292	
Obesity	9/10	90.0%	9/9	100%	0,950	0,330	
<b>Density of stone</b>							
< 800 HU	25/27	92.6%	22/24	91.7%	0,015	0,902	
≥ 800 HU	16/23	69.6%	23/26	88.5%	2,683	0,101	
<b>Hydronephrosis</b>							
No	4/4	100%	8/12	66.7%	1,778	0,182	
Stent	10/15	66.7%	2/3	66.7%	-	-	
I grade	8/8	100%	10/10	100%	-	-	
II grade	13/14	92.9%	19/19	100%	1,400	0,237	
III grade	6/9	66.7%	6/6	100%	2,500	0,114	
<b>Resorlu-Unsal system</b>							
0	5/5	100%	-	-			
1	15/16	93.8%	-	-			
2	14/17	82.3%	-	-			
3	7/12	58.3%	-	-			
<b>Stenting</b>							
Yes	29/34	85.3%	-	-			
No	12/16	75%	-	-			

Reducing stationary hospitalization days minimizes nosocomial complications, making the surgical method is more cost-effective - cost-effective helps patients return to their social lives as soon as possible. Residual stone was found in 9 patients (18%) at the first follow-up approximately 1 month after surgery. The stone free rate 82% were obtained. The highest results were obtained in stones with a total stone size of up to 20 mm. Thus, any residual stones were not detected in any patient, and the total stone free rate 100% was identified. Patients with a total stone size of 20-30 mm we divided into two and a half groups the patients that included this group: patients with kidney stones measuring 20-24 mm and 25-29 mm. Any statistical difference was not found in the results of flexible ureterorenoscopic nephrolithotripsy and percutaneous nephrolithotomy in the first half group (91.7% and 100%, respectively). In the second subgroup, 83.3% of patients who performed RIRS, in patients who underwent PNL, a 100% effect was obtained (chart 2) Based on these results, we can say that high efficiency and short postoperative rehabilitation and hospitalization period make flexible ureterorenoscopic nephrolithotripsy a complete alternative method to percutaneous nephrolithotomy for the treatment of kidney stones measuring 20-24 mm. For stones larger than 30 mm, significantly lower results were obtained in the main group. Although 84.8% stone free rate was registered in the comparison group, this figure was 58.3% in the main group.



**Chart 2. The degree of postoperative stone free in the patients with stones located the lower renal calyx**

When examining the results for the location of the stone inside the kidney, the highest result was obtained in the isolated pelvic stones, and the lowest result was obtained in the stones located in the isolated lower calyx. Residual stone was found in one of the 6 patients where the stones were located only in the lower calyces. The stone free rate in this group was calculated as 83.3%. The initial size of the stone was 29 mm in a patient with a residual stone. From treatment of stones with a total stone size of less than 20 mm and located only in the lower calyx group with flexible ureterorenoscopic nephrolithotripsy was obtained a 100% effect (table 2), based on the literature, we can say that this is higher than the results of treatment with ESWL (41-73%) of stones of the same size and localization.

**Table 2**

**Statistical indicators of surgical treatment of subgroup calyceal stones with RIRS and PNL**

	The duration of the operation (min)	The use of X-ray (seconds)	Activation period after surgery (hours)	Stationary hospitalization days (days)
RIRS	68,3±19,2*	28,1±12,3***	7,3±1,1**	1,1±0,6*
PNL	77,3±21,4	211,4±47,5	18±7,7	6,2±4,8

Note: \*p>0,05, \*\* p<0,05, \*\*\* p<0,001.

We have determined as a result of research, the density of the stone has an effect on the outcome of flexible ureterorenoscopic nephrolithotripsy. Thus, although 92.6% effect was achieved in stones with density less than 800 HU, the degree of stone free was 69.6% for stones with density more than 800 HU. When examining the effect of surgical outcomes on ureteral stent placement after RIRS, it was found that patients with ureteral stent had a higher rate of stone free (accordingly is 85.3% and 75%) than the other group. In addition, the presence and degree of body mass index and preoperative hydronephrosis are factors that do not affect the outcome of the operation. However, we consider flexible ureterorenoscopic nephrolithotripsy to be the preferred method in obese patients with a high body mass index. Thus, the thickening of

the subcutaneous fat layer prolongs the distance from the skin to the stone, resulting in greater absorption of extracorporeal shock waves by the tissues, and reduces the effectiveness of the method. On the other hand, percutaneous nephrolithotomy is increasingly difficult to perform in such patients. In some cases, lack of the length of the tool is observed. In addition, percutaneous access becoming increasingly difficult, because the kidneys are more mobile in patients with highly developed pararenal adipose tissue.

In the early postoperative period complications generally were observed in 6 patients (12%), small was in 3 patients and large one was in 3 patients. Postoperative fever was recorded in 3 patients, pain in 1 patient, urinary tract infection in 1 patient, and stone pathway in 1 patient. Postoperative fever was treated with taking oral antipyretics. A patient diagnosed with a urinary tract infection was hospitalized and antibacterial treatment was started. On the 5th day after the operation, the patient who presented with pain was prematurely removed, thinking that the pain was related to the urinary stent. Stone pathway which one of the specific complications of flexible ureterorenoscopic nephrolithotripsy was observed in 1 patient and it was also treated conservatively, without surgical intervention, with a combination of  $\alpha$ -blockers and analgesics. Any life-threatening complications were not observed in the main group, such as serious blood loss with the need for blood transfusion, which was observed in 4 patients in the comparison group. We concluded that the soft ureterorenoscopic nephrolithotripsy method, which is executed including from a natural hole, is superior to percutaneous nephrolithotomy in terms of both quantity and the degree of severity of postoperative complications (table 3).

Surgical treatment of kidney stones in children and adults has evolved over the past thirty years from open surgery to minimally invasive endoscopic surgery. Nowadays, open surgical interventions account for 1%. Currently, extracorporeal shock wave lithotripsy is the most widely used method of treating kidney stones (40-50%). Percutaneous nephrolithotomy and mild ureterorenoscopic nephrolithotripsy are the main methods of choice for stones 2 cm or more in size.

**Table 3**

**Frequency of postoperative complications encountered according to the modified Clavien-Dindo classification**

Complications encountered	Main group (n=50)		Comparison group (n=50)	
	Abs.	Relative	Abs.	Relative
<b>I grade</b>	3	6%	6	12%
• Rise of temperature	3	6%	6	12%
<b>II grade</b>	2	2%	4	8%
• Urinary tract infection	1	2%	-	-
• The way of tone	1	2%	-	-
• Hemotransfusion	-	-	4	8%
• Extravasation	-	-	-	-
<b>III grade</b>	1	2%	-	-
• 3a. Severe pain	1	2%	-	-
<b>Total</b>	6	12%	10	20%
• <b>Minor</b>	3	8%	6	12%
• <b>Major</b>	3	6%	4	8%

Percutaneous nephrolithotomy, considered the primary treatment for staghorn and large kidney stones, is an invasive surgical procedure performed through a small opening in the lumbar region into the renal calyx-pelvis system. In terms of short-term removal of large kidney stones and high efficiency, it can be considered a fairly convenient method for both the urologist and the patient.

In addition to the above, it would be wrong not to mention a number of the existing technical disadvantages of percutaneous surgery. These include pulmonary complications and transient paresis of the upper limbs due to the position of the patient on the operating table, prolonged X-rays during surgery, damage to adjacent organs during surgery, especially the pleura and intestines, postoperative renal and peritoneal urine leaks into the peritoneum.

The most frightening complication of percutaneous nephrolithotomy for urologists is intraoperative and postoperative bleeding. Intraoperative bleeding usually results from damage to segmental arteries or renal parenchyma.

Postoperative bleeding manifests itself mainly in the form of severe hematuria, the main cause of which is the appearance of

postoperative arteriovenous malformations. Retroperitoneal bleeding is also possible. Although treatment for bleeding is sometimes limited to observation and blood transfusion, angiography and selective embolism and even emergency nephrectomy may sometimes be required.

The disadvantages of percutaneous nephrolithotomy include a long hospital stay. This results in patients returning late to work and social life, as well as increased hospital treatment costs.

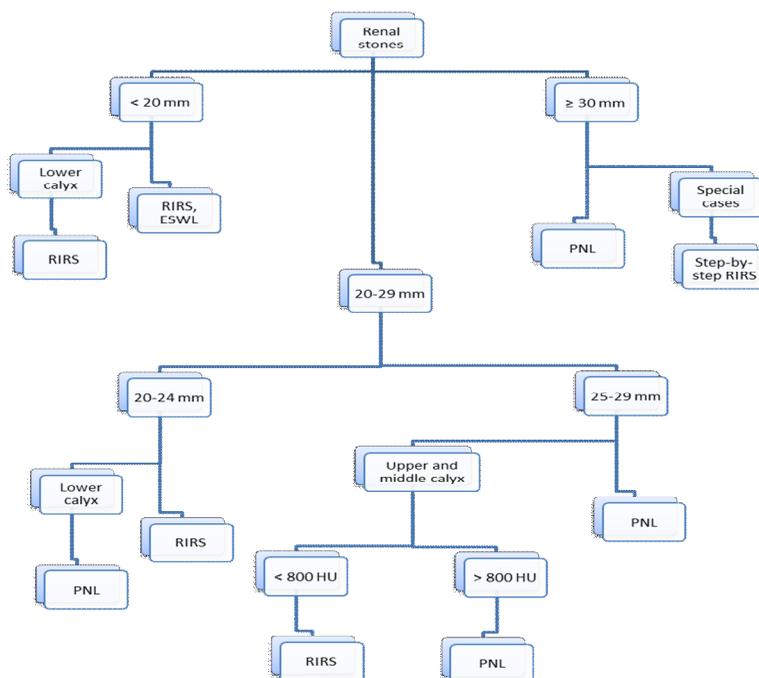
Currently, retrograde intrarenal surgery is widely used in the treatment of small and large kidney stones, as well as stones of the lower calyx group and the upper 1/3 of the urinary tract, in the diagnosis and treatment of malignant tumors of the urinary tract and renal pelvis, in the diagnosis and visualization of urinary tract stenosis.

The advantages of this method in the treatment of kidney stones are that the integrity of the skin is not compromised, the operation can be performed under spinal anesthesia, and there are few intraoperative and postoperative complications. It should be noted that it is very effective in treating small to medium sized stones. One of the advantages of the method is the possibility of several sessions of treatment of large stones, which are contraindicated in percutaneous nephrolithotomy, as well as in patients and pregnant women with spinal deformities and bleeding problems.

In the course of the study, we also found such advantages as faster rehabilitation after mild uretero-renoscopic nephrolithotripsy and shorter hospitalization times. This means lower medical and financial costs in the postoperative period. Thus, retrograde intrarenal surgery is one of the key elements of surgery in the 21st century, when incisions are made through a natural opening, are less painful and bloodless, patients return to social life faster and have less expenses in the postoperative period.

The disadvantages of this method are its low efficiency in the treatment of stones of the lower calyx group and large stones in comparison with percutaneous surgery, as well as the fact that not all clinics have all the instruments and equipment necessary to perform the operation, and the surgeon requires a lot of experience.

The development of the most modern and comprehensive treatment algorithm for kidney stones is of great importance for all urologists-surgeons dealing with nephrolithiasis in terms of high postoperative efficiency and patient satisfaction. The main goal of our research was to create an algorithm adapted to modern protocols, taking into account the size, density and localization of kidney stones as the main predictive factor. The results that we obtained and the complications encountered during the research and the accumulation of experimental knowledge allowed us to determine the following treatment algorithm for kidney stones of different sizes, localizations and densities (scheme 1).



**Scheme 1. Algorithm of surgical treatment of kidney stones proposed by us**

Thus, based on the analysis of the data of the conducted research, we found that for the selection of the surgical method, as well as for predicting the degree of postoperative stone free, indicators that play a key predicative role are the size of kidney stones, location of stones, number and density of stones which measured in units of HU. Retrograde intrarenal surgery may be an alternative to percutaneous nephrolithotomy in the removal of stones up to 30 mm. In the surgical treatment of kidney stones larger than 30 mm, RIRS can only be used as a first choice in specific patient groups. These can be severe deformations of the skeletal apparatus, uncontrolled coagulopathy, severe renal pathology. Increasing the density of stone leads to prolongation the duration of flexible ureterorenoscopic nephrolithotripsy and a decrease in operational results. Prolongation of duration of surgery increases the risk of both local and the risk of increased overall complications. Also, operations lasting more than 1 hour increase the risk of injury to the energy source and the soft ureterorenoscope, this reduces the economic efficiency (cost-effectiveness) of the operation. This factor should be taken into account in the treatment of large and numerous stones with surgical RIRS.

## **FINDINGS**

1. 82% complete stone free can be achieved after retrograde intrarenal surgery. This quantity is directly related to the size of the stone, is 100% for stones up to 20 mm, is 91.7% is for stones with a size of 20-24 mm, 83.3% for stones of 25-29 mm, is 58.3% for stones larger than 30 mm [2, 4, 6].
2. The period of activation (7.4 hours) and inpatient hospitalization (1.1 days) after flexible ureterorenoscopic nephrolithotripsy of kidney stones is very short compared to percutaneous nephrolithotomy. This means a reduction in hospital costs, minimization of nosocomial infectious complications, shortening the rehabilitation period and laying the groundwork for patients to return to their social lives as soon as possible [9].
3. Factors that may affect the outcome of flexible ureterorenoscopic

nephrolithotripsy are the size, location, number, and density of kidney stones. The results of the operation are not correlated with the patient's body mass index, age, constitutional and somatic condition, the degree of preoperative hydronephrosis [7].

4. After flexible ureterorenoscopic nephrolithotripsy, deterioration is not observed in general and biochemical parameters of the blood, especially the amount of hemoglobin and creatinine in the blood [5, 6].
5. Becoming "sterile" of the urine before surgery and preoperative single-dose antibiotic prophylaxis significantly reduce the risk of postoperative infectious complications [6].
6. Almost, renal damage does not occur during flexible ureterorenoscopic nephrolithotripsy, performed by entering through the natural hole. The probability of possible postoperative complications is 12%. According to the Clavien-Dindo classification, first- and second-degree complications are observed [3].

## **PRACTICAL RECOMMENDATIONS**

1. In people who applied to the clinic with kidney pain, native CT should be preferred because of its high sensitivity and informativeness as an initial examination option. Determining the degree of postoperative stone free and for dynamic observation, ultrasound is recommended in order to reduce radiation.
2. Properly conducted period (Obtaining "sterile" urine, single-dose antibiotic prophylaxis, thromboembolism prevention) of preoperative preparation lays the groundwork for safer execution of retrograde intrarenal surgery. Regional anesthesia also prevents pulmonary and intestinal complications.
3. Surgical treatment of patients with kidney stones, which is contraindicated in percutaneous nephrolithotomy based on endotracheal anesthesia, is possible with flexible ureterorenoscopic nephrolithotripsy under regional

anesthesia.

4. The use of urinary sheath during flexible ureterorenoscopic nephrolithotripsy maintains intrarenal pressure during surgery, shortens the duration of surgery, and prolongs the life of the suitability of ureterorenoscope. The surgeon should also be aware of the possibility of abusing urinary sheath and causing urinary tract injuries.
5. It is recommended that conducting oral antibiotic treatment (fluoroquinolones) be given for 3 days to minimize the risk of infectious complications in the early postoperative period.
6. Flexible ureterorenoscopic nephrolithotripsy can be considered the gold standard in the treatment of kidney stones with a total size of up to 2.5 cm due to minimal risk of complications and high efficacy. Percutaneous nephrolithotomy should be chosen as the primary treatment because of the prolongation duration and low efficacy of retrograde intrarenal surgery in stones larger than 2.5.
7. For stones located in the lower calyx group, the initial operation selection should be as follows: Extracorporeal shock wave lithotripsy advisable to perform for stones up to 10 mm, flexible ureterorenoscopic nephrolithotripsy for stones 10-20 mm, percutaneous nephrolithotomy for stones larger than 20 mm.
8. Optimal results can be obtained with flexible ureterorenoscopic nephrolithotripsy in situations (single kidney stone, severe spinal deformities, patients suffering from III degree obesity) where percutaneous nephrolithotomy is life-threatening or where it is technically impossible.

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## **LIST OF ABBREVIATIONS**

CT	Computer tomography
ESWL	Extracorporeal Shock Wave Lithotripsy
HU	Hounsfield Unit
PNL	Percutaneous Nephrolithotomy
RIRS	Retrograde Intrarenal Surgery





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