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**URETEROSCOPIC TREATMENT FOR PYELOCALICEAL LITHIASIS
BETWEEN 20-40 MM**

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Introduction

Renal lithiasis occurs in a proportion of 5-15% in the global population, not having a well-defined pattern, but especially more frequently among the male population, the percentage being in an increasing trend in the last 25 years. As a potential risk factor for the development of chronic renal failure, the problem of the existence of renal lithiasis has gained momentum in the urological world with the development of the pharmaceutical and technological industries. It is relatively rare in the age group below 20 years and reaching the maximum frequency in the age group 40-60 years.

The first mention of ureteral stones belongs to Ambroise Pare in 1564, but it was not until 200 years later that an intervention to extract ureteral stones was successfully performed.

The term endourology, introduced by Smith in 1982, encompassed the techniques of antegrade and retrograde approach to the urinary tract. Technical advances have made endourology find, in recent years, its applicability in almost all types of diseases that affect the upper urinary system.

Thanks to these advances, modern stone extraction techniques by retrograde or antegrade ureteroscopy could be developed.

Guidance from the Urology Clinic of the Emergency Clinical Hospital "St. Ioan" proved, in this international context, in line with modern, minimally invasive trends. Since 1994, the introduction of the retrograde ureteroscopic approach in the diagnostic and therapeutic armamentarium has radically changed the investigative protocol and the therapeutic attitude in the pathology of the upper urinary tract.

Considering the broad addressability of patients in our Clinic for the treatment of large renal lithiasis, and knowing the renal anatomy and physiology, the opportunity to carry out a work, in which the ureteroscopic treatment of renal lithiasis between 2 and 4 cm in size can be studied, gained a perspective favorable.

GENERAL PART

1. Surgical and endoscopic anatomy of the pelvicalyceal system

The upper urinary tract, composed of the pyelo-calyceal system and ureters, ensures the circulation of urine from the kidneys to the bladder through peristaltic contractions. Recent advances in the field of endourology have led to an increase in interest in understanding the anatomy of the collecting system, considering that the deepening of these notions of anatomy is the basis for performing reliable endourological procedures, as well as for making a reliable uro-radiological analysis. Also, the adaptation of the ureteroscopic technique to the micro- and macroscopic peculiarities of the segments of the upper urinary tract are the key to performing an endoscopic intervention under conditions of maximum effectiveness and safety.

The pyelo-calyceal system consists of the renal calyces and the renal pelvis. Urine from the collecting ducts (which cross the renal pyramids and open at the level of the papillary surface – area cribosa) is collected in small calyces (secondary or minor). The minor calyces are defined as the calyces located in the immediate continuity of the papilla. They drain the renal papillae, being approximately 5-14 in number (on average, 8). It is believed that in about 70% of cases between 7 and 9 small calyces are found at the renal level. Small calyces can be simple (draining a single papilla) or compound (draining two or three papillae).

Understanding the endoscopic anatomy of the upper urinary tract is essential for performing endoscopic interventions under appropriate conditions for both diagnostic and therapeutic purposes.

With the introduction of the ureteroscope into the bladder, the trigone of the bladder becomes visible, being delimited by the posterior lip of the neck and the two ureteral openings. The base of the trigone is represented by a prominence called the interureteral ridge, which extends between the two holes. Normally, the ureteral orifices compress as the bladder fills, which is one of the mechanisms underlying the prevention of ureteral reflux. Bladder emptying, in some cases, may lead to identification of the ureteral orifices and, thus, avoidance of dilatation prior to instrumentation of the upper urinary tract.

From an endoscopic perspective, the ureter is divided into 3 approximately equal segments:

- the distal or pelvic segment;
- the middle segment located between the two extremities of the sacro-iliac joint;

- the proximal segment that is contained between the urinary pelvis and the proximal extremity of the sarco-iliac joint, at the level of the transverse process of the L5 vertebra.

An important anatomical parameter in flexible retrograde ureteroscopy is represented by the infundibulo-pyelic angle. This angle is found between the axis of the upper part of the ureter and the axis of the lower calyx. It is considered to be the equivalent, in practice, of the deflection amplitude of the flexible ureteroscope during the approach to the calyceal groups. The average value of this angle is approximately 40 degrees and is inversely proportional to the difficulty of approaching the lower calyx.

2. Renal lithiasis

Urinary lithiasis is one of the most widespread pathologies at the present time with a prevalence of 5-15%. The incidence is higher in men than in women. At the same time, the incidence of kidney stones has increased in the last 50 years, especially in civilized countries with the increase in the quality of life. The global incidence is increasing due to obesity and diabetes, making these patient populations more likely to suffer from kidney disease. Most of the stones are radiopaque, forming at the level of the kidneys. They form especially in the sloping regions of the kidney, from where they migrate to the renal pelvis and ureter, where they begin to produce symptoms. Some of these stones can be eliminated spontaneously with the help of medical treatment supplemented with hygienic and dietary treatment.

Another category of stones smaller than the previous one requires urological surgery. Due to the formidable evolution of endoscopic instruments, open surgical intervention for renoureteral calculi can now only be performed exceptionally today, the place of this operation being almost completely taken by minimally invasive endoscopic interventions. The most common reason for emergency admission to urology departments is lower back pain due to stone migration (renal colic). Extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), and retrograde ureteroscopy (URS) are the three current methods for the treatment of kidney stones.

3. Diagnostic protocol

3.1. Clinical examination and symptoms

An initial evaluation of any patient begins with a thorough medical history (especially in patients with a known history of urolithiasis) and a clinical examination. Although some patients may be asymptomatic, the dominant symptomatology in renal lithiasis pathology is pain (lumbar, radiating to the abdominal or external genital organs), variably accompanied by hematuria, fever, nausea, vomiting, increased blood pressure, digestive manifestations. Renal colic is mostly unilateral, its duration is variable, and the subjective intensity, depending on the degree of pain tolerance for each individual patient.

3.2. Imaging investigations

KUB (kidney-ureter-bladder) radiography is used as the first method of radiological exploration within the investigation protocol of a suspected urinary tract lithiasis. The role is to provide information regarding the location, shape, number and size of radiopaque or poorly radiopaque calculi. The lack of information regarding radiolucent lithiasis is not at all negligible. It has a specificity of 77%, while the sensitivity is about 44%.

Abdominal ultrasound is usually a method for exploring the urinary tract because it is non-invasive (safe), inexpensive and widely available. This can provide valuable information about the number of stones, their size, location (even if it is not always exact), as well as possible associated phenomena (hydronephrosis, secondary renal abscess, etc.).

Intravenous urography is a useful imaging method in the diagnosis of renal lithiasis because it provides information primarily about the anatomy of the kidneys, their function, and secondarily, regarding the location of a possible lithiasis, its dimensions, if it is single or multiple, as well as the consequences of its existence on the renal parenchyma or possible complications.

Computed tomography without contrast has recently been the gold standard in the diagnosis of urinary tract lithiasis in developed countries. Being an expensive paraclinical investigation, its applicability as a routine investigation is not widely used. Following this investigation, the doctor benefits from useful information such as the location, diameter, density of the stones and the echo on the neighboring structures, and in their absence, highlighting the cause of the symptoms manifested by the patients.

4. Treatment options for renal lithiasis

The role of surgical treatment in the approach to upper urinary tract lithiasis is to remove the stone completely with the lowest possible morbidity rate. Currently, the therapeutic options for pyelo-calyceal lithiasis are represented by ESWL, NLP, the retrograde ureteroscopic approach (usually by flexible ureteroscopy) and, rarely, usually secondary to the appearance of complications, by open surgical treatment, the therapeutic strategy being individualized according to the particularities each patient.

The choice of the therapeutic alternative for the treatment of pyelocalyceal lithiasis is generally influenced by the size of the stone, its configuration (coraliform or non-coraliform), location, chemical composition, individual characteristics of the patient (anatomical variations, comorbidities) and, also, it is taken into account by the patient's preferences.

4.1. Spontaneous passage of the stone

The possibility of spontaneous stone removal should not be neglected, even in the context of the development of increasingly less aggressive interventional treatment methods. This therapeutic attitude is, in many cases, preferred by patients, avoiding the risks and discomfort involved in surgical intervention. However, even this type of therapeutic approach is burdened by potential risks, some of them very serious, reaching up to kidney destruction or sepsis.

The limitations of conservative treatment are determined by the impossibility of establishing with certainty the possibility of spontaneous removal of the stones.

The decision must be based on the corroboration of different factors including: the size, location and chemical composition of the stones, the patient's preference, the costs of the treatment as well as the available therapeutic means.

4.2. Retrograde ureteroscopy

Ureteroscopy is a method of diagnosis and treatment of pathology of the upper urinary tract. Cystoscopy preceded the appearance of ureteroscopy, this being a procedure through which the urinary bladder can be evaluated and, at the same time, the insertion of the ureters at this level. Subsequently, the emergence of rigid, semi-rigid and, finally, flexible ureteroscopy as tools for the diagnosis and effective treatment of ureteral and pyelo-calyceal pathology was described. Ureteroscopy is a minimally invasive, affordable method with low morbidity that provides good results and rapid post-interventional recovery.

4.3. Percutaneous nephrolithotomy

Percutaneous nephrolithotomy (PCNL) is accepted as the procedure of choice for the treatment of large or complex kidney stones. Since its introduction in 1976, operative technique and endoscopic equipment have constantly evolved, increasing success rates and decreasing complications and morbidity.

4.4. Extracorporeal shock-wave lithotripsy

Extracorporeal shock wave lithotripsy (ESWL) is a truly non-invasive procedure, unlike other surgical treatments used, such as retrograde intrarenal surgery (RIRS) and percutaneous nephrolithotomy (NLP). The effectiveness of ESWL lies in its ability to pulverize stones in vivo into smaller segments, which are then spontaneously eliminated. Shock waves are generated and then focused on a point inside the body.

ESWL is the only method that is truly non-invasive and can achieve stone-free rates approaching 75%.

The choice between shock wave lithotripsy (ESWL) and other treatment modalities depends on several factors, including the size of the stone, its composition, etc. Another complex factor in the choice of treatment modality is the patient's preference and expectations.

4.5. Open and laparoscopic pyelolithotomy

The progress made by minimally invasive treatment techniques has given classical surgery a secondary place in the therapeutic armamentarium of renal lithiasis. Open surgical pyelolithotomy is burdened by a prolonged period of hospitalization and convalescence. Classical surgical intervention may be required with the appearance of complications of the other treatment methods (injuries to the ureteral wall, pelvis or neighboring organs) or if nephrectomy is necessary. In the absence of high-performance technical equipment, surgical pyelolithotomy remains a useful method of treatment.

Laparoscopic pyelolithotomy was first introduced over 20 years ago. However, the role of laparoscopy in the management of kidney stones is currently quite limited due to technical difficulties, higher degree of invasiveness, longer operative time, prolonged convalescence.

5. Treatment of pyelocalyceal lithiasis with dimensions between 20 and 40 mm

When discussing stone mass greater than 2 cm, PCNL is considered to be the first-line alternative because it has superior success rates compared to ESWL or flexible ureteroscopy. However, if this is impossible to perform or contraindicated, and also taking into account the patient's preference, stones larger than 2 cm can be treated with the help of the flexible ureteroscopic approach, although it increases the risk of the need for a multistage intervention and, it may also increase the necessity of fitting a ureteral stent post-intervention.

At the same time, for patients with skeletal malformations, morbid obesity, renal malformations or hemorrhagic diathesis in whom the NLP or ESWL approach is difficult to achieve or even contraindicated, flexible retrograde ureteroscopy is an indication of choice. Intradiverticular lithiasis may also be an indication for flexible ureteroscopy.

In recent years, advances in ureteroscope technology and increasingly effective lithotripsy methods have made the retrograde ureteroscopic approach widely used for stones between 20 and 40 mm in size. Therefore, there have been numerous studies comparing the retrograde ureteroscopic approach and percutaneous nephrolithotomy for the treatment of pyelo-calyceal lithiasis between 20 and 40 mm in size.

When discussing the success rate of the retrograde flexible ureteroscopic approach to pyelocalyceal lithiasis, it varies, according to some authors, from 62% to 98%.

The use of the Ho:YAG laser as a method of lithotripsy creates the opportunity for a higher success rate, demonstrating its effectiveness regardless of the chemical structure of the calculus.

Also, the safety profile of the procedure provided by the photothermal effect allows lithotritition of stones into very small fragments that can be easily removed ureterally, without requiring additional extraction measures.

Some studies highlight that for certain patients presenting with multiple intrarenal stones, Holmium laser flexible ureteroscopy may represent a superior therapeutic alternative to ESWL or NLP, with increased efficiency and reduced morbidity.

The reported success rate of the flexible ureteroscopic approach for larger stones has improved as a result of continued development of the technique and instrumentation of this method. However, as previously mentioned, flexible retrograde ureteroscopy can be used in the treatment of large pyelo-calyceal lithiasis.

II. PERSONAL CONTRIBUTIONS

6. Working hypothesis and general objectives

I chose to address this topic because urinary lithiasis is a pathology that, although most of the time does not immediately endanger the lives of patients, it is a debilitating condition including for the young and socially active segment of the population. Thus, its treatment is an important aspect that is the subject of many current studies, given the progress known by minimally invasive interventions. Although, at the moment, there are international guidelines to guide the surgeon in choosing the appropriate therapeutic method, it should not be neglected that this choice involves the analysis of a series of individual factors of the patient as well as the expertise of the doctor.

The choice of therapeutic alternative for the treatment of pyelo-calyceal lithiasis is generally influenced by the size of the stone, its configuration (coraliform or non-coraliform), location, chemical composition, individual characteristics of the patient (anatomical variations, comorbidities) and, last but not least, , patient preferences. Also, the therapeutic decision should be supported by the experience of the surgeon.

The work carried out contains, in the first part, some general aspects of stone disease and the retrograde ureteroscopic technique, followed by the second part of the work presenting a mixed study (retrospective + prospective) carried out on a group of 250 patients with voluminous pyelo-calyceal lithiasis (lithiasis mass between 2 and 4 cm in size) who benefited from treatment either by retrograde ureteroscopic approach or by percutaneous nephrolithotomy, carried out in the Urology Department of the "Sfântul Ioan" Emergency Clinical Hospital, on a period of 3 years (January 2019 – December 2021).

Goals and objectives

The main aim of this study is to evaluate the effectiveness and safety of the retrograde ureteroscopic approach in the treatment of bulky pyelo-calyceal lithiasis.

The objectives of the study are the following:

- Establishing the incidence of surgically sanctioned voluminous pyelo-calyceal lithiasis according to age, gender and the environment of origin

- Evaluation of pyelo-calyceal lithiasis according to the number of existing stones

- Presentation of the operative technique used in the treatment of voluminous pyelo-calyceal lithiasis

- Evaluation of the success rate of ureteroscopic intervention versus the success rate of

percutaneous nephrolithotomy

- Evaluation of the success rate according to the number of ureteroscopic procedures required
- Evaluation of post-interventional complications
- Evaluation of the length of hospitalization of patients treated by retrograde ureteroscopy and those treated by percutaneous nephrolithotomy

7. General research methodology

The present study represents a mixed, retrospective and prospective analysis of patients who presented renal lithiasis between 2 and 4 cm in size, treated in the urology clinic of the Saint John Emergency Clinical Hospital, either by retrograde ureteroscopy or by percutaneous nephrolithotomy, between January 1, 2019, and December 31, 2021.

The mixed, prospective and retrospective observational character of the study allowed during its development the assimilation of some additive variables, reflecting the equivocal nature of the epidemiological context attributed to society in the last 3 years, marked by the Covid-19 pandemic. Implicit changes experienced by the entire population globally, under all aspects of life, are currently materializing in a nucleus of interest for all fields of research. The psychological impact of the set of restrictions related to the pandemic period has the potential to trigger the long-term emergence of medical conditions or to exacerbate pre-existing pathologies. This epidemiological context further favored the late presentation of patients to the doctor.

This research plan was implemented in compliance with the norms of scientific, professional and university ethics, in accordance with the provisions of the code of ethics and professional deontology of the following institutions: "Carol Davila" University of Medicine and Pharmacy and "Sfântul Ioan" Emergency Clinical Hospital from Bucharest.

Through the programs: IBM SPSS Statistics for Windows version 26.0 (IBM Corp. Released 2015. Armonk, NY: IBM Corp), and Microsoft Excel Data Analysis (Microsoft 365 Personal), systematization, grouping, processing and statistical analysis operations were possible of the collected data, which will be presented in detail according to the assigned research plan.

Study population

The study was conducted on a group of 250 patients with pyelo-calyceal lithiasis between 2 and 4 cm in size, who benefited from either retrograde ureteroscopic treatment or percutaneous nephrolithotomy, admitted to the Urology Clinic of the St. John's Emergency Clinical Hospital,

Bucharest.

Of the 250 patients, 125 were treated by retrograde ureteroscopy (flexible \pm semirigid), and 125 were treated by percutaneous nephrolithotomy. The choice of treatment for patients was stratified according to the presence or absence of associated comorbidities, the presence or absence of congenital malformations, the presence of previous surgical interventions for renal lithiasis (recurrent renal lithiasis), and, last but not least, according to the patient's preference after explaining the risks and the benefits of both surgeries.

Evaluation of the studied group according to gender

Sex FURS					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	female	52	41.6	41.6	41.6
	male	73	58.4	58.4	100.0
	Total	125	100.0	100.0	

Table 1: Distribution of cases treated by flexible ureteroscopy according to gender

Sex NLP					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	female	60	48.0	48.0	48.0
	male	65	52.0	52.0	100.0
	Total	125	100.0	100.0	

Table 2: Distribution of cases treated by percutaneous nephrolithotomy according to gender

In the presented study, carried out between 2019-2021, 250 cases of pyolocaliceal lithiasis with sizes between 2 and 4 cm were recorded. Male patients were more frequent in the group treated by flexible ureteroscopy (58.4%), as in the group treated by percutaneous nephrolithotomy (52%). The data are consistent with other specialist articles showing a higher frequency of kidney stones among males.

Evaluation of the studied group according to age

According to tables no. 1 and 2, in the case of patients treated by retrograde ureteroscopy, an average age of 54.96 years is observed, with a standard deviation of 14.283 years. The minimum

age of the patients is 31 years, and the maximum is 84 years. In the case of patients treated by percutaneous nephrolithotomy, an average age of 57.04 years is observed, with a standard deviation of 8.511 years. The minimum age of patients treated by percutaneous nephrolithotomy was 37 years, and the maximum age was 71 years.

One-Sample Test							
Test Value = 0							
	t	df	Significance		Mean Difference	95% Confidence Interval of the Difference	
			One-Sided p	Two-Sided p		Lower	Upper
Varsta FURS	43.021	124	<.001	<.001	54.960	52.43	57.49
Varsta NLP	74.927	124	<.001	<.001	57.040	55.53	58.55

Table 3: Student T-test on the distribution of cases by age

Therefore, a higher mean age is observed among patients treated by percutaneous nephrolithotomy than among those treated by retrograde ureteroscopy.

At the same time, a percentage of 20.8% of patients treated by flexible ureteroscopy are between 31 and 37 years old, while the youngest age of patients treated by percutaneous nephrolithotomy was 37 years. Considering all this, we can consider that young people prefer ureteroscopy, a minimally invasive intervention, even with the risk of performing several interventions, to the detriment of percutaneous nephrolithotomy, a more laborious surgical intervention.

8. Results

8.1. Evaluation of cases of bulky renal lithiasis according to the size of the pyelocalyceal lithiasis

Technical improvements, including miniaturization of the endoscope, improved deflection mechanism, improved visual quality and instrumentation, and the introduction of flexible disposable ureteroscopes, have led to increased use of ureteroscopy for both renal lithiasis and ureteral calculi. Major technological advances have been made for retrograde ureteroscopy. A recent systematic review of data from the literature on renal stones larger than 2 cm showed a cumulative stone-free rate of 91% with 1.45 procedures/patient.

One-Sample T Test					
				95% Confidence interval	
	Medium stone size(mm)	P(value)	Standard deviation(mm)	Inferior	Superior
FURS	26.38	<0.001	4.453	25.59	27.16
NLP	29.44	<0.001	4.817	28.59	30.29

Table 4: Evaluation of cases according to stone size

In the current study we found a mean stone size of 26.38 mm in patients treated by retrograde ureteroscopy, with a standard deviation of 4.453 mm. In the case of patients treated by percutaneous nephrolithotomy, the mean lithiasis volume was 29.44 mm, with a standard deviation of 4.817 mm. The sizes of the stones were measured by means of tomography.

8.2 Evaluation of patients with bulky renal lithiasis according to operative time

Operative time is an essential factor in influencing postoperative complications. A longer operative time increases the risk of urosepsis secondary to retrograde ureteroscopy and the need for blood transfusion secondary to decreased hemoglobin in the percutaneous nephrolithotomy group.

		Descriptive Statistics				
		Statistic	Bias	Std. Error	Bootstrap ^a	
					95% Confidence Interval	
					Lower	Upper
Time OP FURS	N	125	0	0	125	125
	Minimum	47				
	Maximum	90				
	Mean	69.91	.06	1.02	67.88	71.94
	Std. Deviation	11.762	-.073	.594	10.450	12.784
Time OP NLP	N	125	0	0	125	125
	Minimum	45				
	Maximum	77				
	Mean	63.08	-.02	.66	61.76	64.33
	Std. Deviation	7.074	-.043	.429	6.149	7.832
Valid N (listwise)	N	125	0	0	125	125

a. Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

Table 5: Evaluation of operative time of ureteroscopy and percutaneous nephrolithotomy for stones between 20 and 40 mm in size

According to table no. 5 the mean operative time of retrograde ureteroscopy was 69.91 min, with a standard deviation of 11.762 min, while the mean operative time of percutaneous nephrolithotomy was 63.08 min, with a standard deviation of 7.074 minutes.

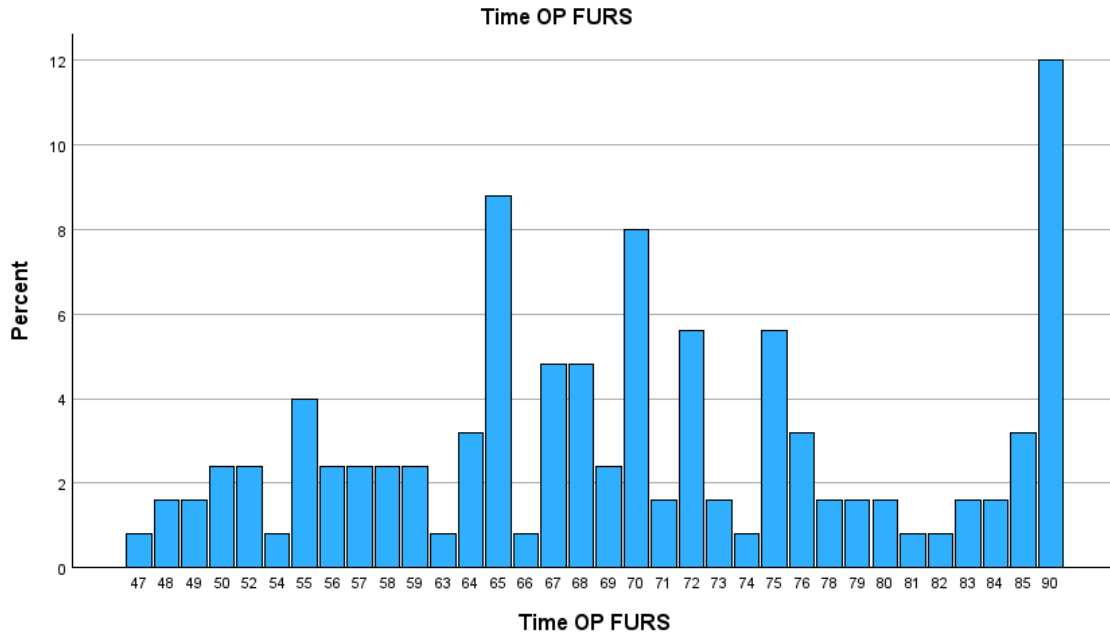


Figure 1: Graphic representation of operative time of retrograde ureteroscopy.

In the case of the group treated by retrograde ureteroscopy, surgery was completed either after therapeutic success was achieved, or if the visibility during ureteroscopy was impaired due to minimal bleeding or environmental blur, or if the maximum operative time was reached. The maximum operative time in the case of ureteroscopy was 90 minutes. According to the specialized literature, an operating time of more than 90 minutes increases the risk of postoperative sepsis, which is why the surgical intervention was stopped at 90 minutes, regardless of whether the patient still had lithiasis or not. It is observed that in 12% of cases the maximum operative time was reached.

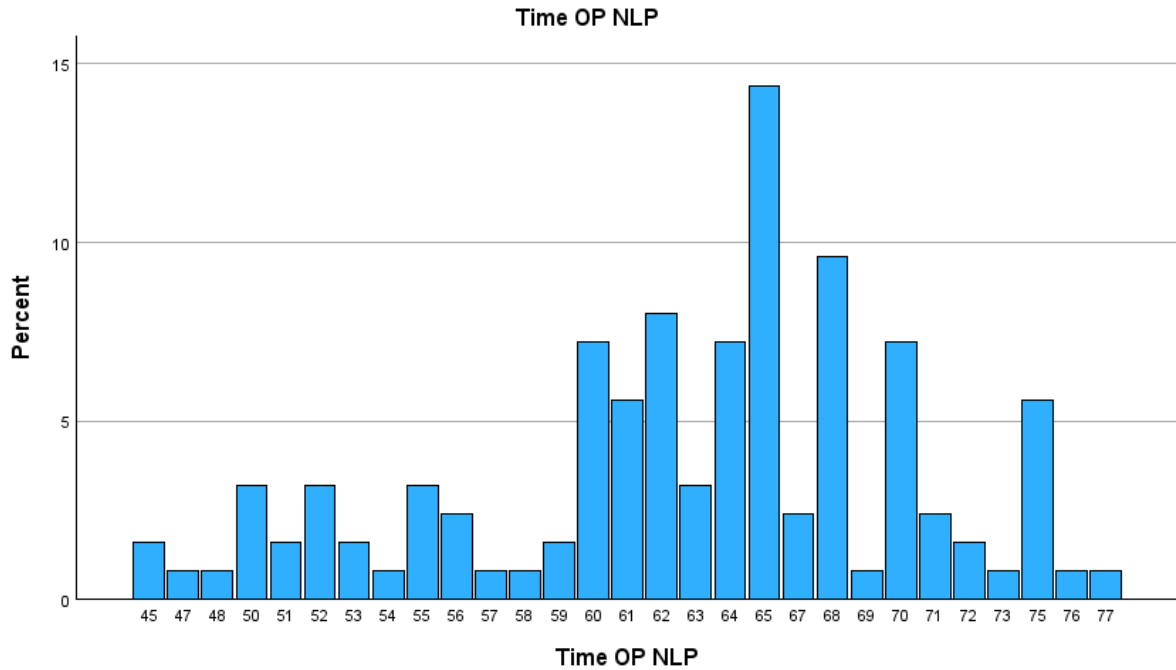


Figure 2: Graphic representation of the operating time of percutaneous nephrolithotomy

One-Sample Test							
Test Value = 0							
	t	df	Significance		Mean Difference	95% Confidence Interval of the Difference	
			One-Sided p	Two-Sided p		Lower	Upper
Time OP FURS	66.456	124	<.001	<.001	69.912	67.83	71.99
Time OP NLP	99.696	124	<.001	<.001	63.080	61.83	64.33

Table 6: Student T-test for operative time of retrograde ureteroscopy and percutaneous nephrolithotomy

According to the T-test for operative time, the confidence interval set at 95% for retrograde ureteroscopy operative time had the lower limit at 67.83 min and the upper limit at 71.99 min. For the operating time of percutaneous nephrolithotomy, the confidence interval set at 95% had the lower limit at 61.83 min, and the upper limit at 64.33 minutes. The test has statistical significance, p value being <0.001.

8.3 Evaluation of cases according to fluoroscopy time

The diagnosis and treatment of nephrolithiasis is associated with high levels of exposure to ionizing radiation. Currently, there are no studies that estimate the lifetime radiation exposure of

stone formers or the subsequent risk of developing malignancies. The radiation exposure of endourologists has been studied extensively. However, there are no studies evaluating the risk of radiation-induced malignancy in urologists or operating room staff.

The International Commission on Radiological Protection (ICRP) recommends a maximum occupational exposure of 50mSv. However, the risk of radiation-induced malignancy follows a probabilistic model, given that no safe exposure threshold is known. Considering this, as well as the length of a urologist's career, the upper limit of 50mSv is still extremely concerning.

According to our study, the fluoroscopy time in patients treated by ureteroscopy had a mean duration of 30.10 seconds, with a standard deviation of 7.914 seconds, while in the group treated by percutaneous nephrolithotomy, the fluoroscopy time had a mean duration of 55.25 seconds, with a standard deviation of 11.987 seconds.

One-Sample Test							
Test Value = 0							
	t	df	Significance		Mean Difference	95% Confidence Interval of the Difference	
			One-Sided p	Two-Sided p		Lower	Upper
Time Fluoroscopy FURS	42.516	124	<.001	<.001	30.096	28.69	31.50
Time Fluoroscopy NLP	51.530	124	<.001	<.001	55.248	53.13	57.37

Table 7: T-test for fluoroscopy time in patients treated by retrograde ureteroscopy and percutaneous nephrolithotomy

In the case of flexible ureteroscopy, fluoroscopy was used for initial ureteral catheterization, pyelography, insertion of the ureteral access sheath guide, and then insertion of the access sheath. At the end of the lithotripsy, a control pyelography was performed for the finding of a possible residual fragment, then a JJ stent was inserted, through fluoroscopic control.

In the case of percutaneous nephrolithotomy, fluoroscopy was used for ureteral catheterization and ureteral probe insertion, then for performing pyelography in order to puncture the pyelocalyceal system. Puncture and dilation of the puncture path, as well as placement of the Amplatz sheath, was performed under fluoroscopic guidance. At the completion of lithotripsy, pyelography was also performed, and a nephrostomy tube was placed under fluoroscopic control.

8.4 Evaluation of cases of large renal lithiasis according to the duration of hospitalization

Regarding the length of hospital stay, Abdullah Erdogan found that the length of hospital stay was longer in the NLP group than in patients who underwent URS, which is similar to the

data obtained by Akman et al. This can be explained by the presence of nephrostomy and the need for a longer postoperative follow-up in the case of NLP.

Our study presented the same results, finding that the duration of hospitalization was longer in the PNL group (162.62 ± 31.802 h) than in the URS group (78.14 ± 23.393 h). In the NLP group, the patient was discharged after the suppression of the nephrostomy tube and when he was clinically stable, without hematuria or the presence of a lumbar fistula, while in the FURS group, the patient was usually discharged the day after the intervention if was clinically stable. The minimum duration of hospitalization for patients treated by retrograde ureteroscopy was 48 hours and the maximum was 168 hours, while the minimum duration of hospitalization for patients treated by NLP was 144 hours and the maximum was 336 hours hours.

One-Sample T Test					
				95% confidence interval	
	Medium hospitalization time(hours)	P(value)	Standard deviation(hours)	Inferior	Superior
FURS	78.14	<0.001	23.393	74.00	82.29
NLP	162.62	<0.001	31.802	156.99	168.25

Table 8: Student T-test for length of hospital stay in patients treated by retrograde ureteroscopy and percutaneous nephrolithotomy

8.5 Evaluation of cases of large renal lithiasis according to the number and location of the stones

The single stone or multiple stone categories refer strictly to lithiasis in the same renal unit.

Of the 125 cases of voluminous pyelo-calyceal lithiasis treated by retrograde ureteroscopy, 77 patients presented single stones, representing 61.6% of all cases of voluminous pyelo-calyceal lithiasis, and 48 patients presented multiple stones, representing 38.4% of the total number of cases of voluminous pyelo-calyceal lithiasis. Of the 125 cases of large pyelocalyceal lithiasis treated by percutaneous nephrolithotomy, 76 patients presented single stones, representing 60.8% of the total number of cases, and 49 patients presented multiple stones, representing 39.2% of the total number of cases.

	Number of patients		Percentage		P(value)
	FURS	NLP	FURS	NLP	
Solitary stones					

	77	76	61.6%	60.8%	0.854(NS)
Multiple stones	FURS	NLP	FURS	NLP	
	48	49	38.4%	39.2%	0.854(NS)
Total	125		125		

Table 9: Evaluation of the large renal lithiasis according to the number of stones

Location	FURS	PCNL	P(value)	S/NS
Superior calyx	14(11.2%)	0	<0.001	S
Middle calyx	14(11.2%)	0	<0.001	S
Inferior calyx	21(16.8%)	44(35.2%)	0.001	S
Renal pelvis	28(22.4%)	32(25.6%)	0.203	NS
Multiple around the same calyx	3(2.4%)	2(1.6%)	0.312	NS
Multiple	45(36%)	47(37.6%)	0.251	NS

Table 10: Evaluation of the large renal stones according to their location

From the point of view of the location of stones, it was observed that flexible ureteroscopy was practiced for upper calyceal lithiasis in 11.2% of cases, middle calyceal in 11.2% of cases, lower calyceal in 16.8% of cases. Ureteroscopy was performed for pelvic stones in 22.4% of cases, and for multiple stones in 36% of cases.

As for percutaneous nephrolithotomy, it was practiced especially for lower calyceal and pelvis stones, and multiple stones, also located predominantly at the level of the lower calyx and pelvis.

8.6 Evaluation of cases of large renal lithiasis according to therapeutic success

According to many studies on the treatment of stones between 20 and 40 mm in size, the results showed that NLP provided an initial success rate superior to retrograde ureteroscopy for the management of 2-3 cm renal stones. In addition to the inherent flaws of current ureteroscopy techniques and systems, such as narrow working channels and ureteroscopy flexibility, residual fragments are more likely to represent a group of clinically insignificant fragments. This is one explanation for a lower therapeutic success rate after a single stage of FURS.

In the case of the present study, the therapeutic success rate, or stone-free rate, was defined as the absence of stone fragments or stones larger than 3 mm on the control computed tomography 30 days after surgery.

In the current study, the success rate after the first ureteroscopy was higher for the PCNL group (90.4%) than the FURS group (68%). After two sessions of ureteroscopy, the stone-free rate was 88.8% in the first group, and after three procedures, the stone-free rate increased to 95.2%. Our results are consistent with the data found in the literature and confirm that a decent stone-free rate can be achieved after several sessions of flexible ureteroscopy.

	F-URS Group			PCNL-Group
	1 st session	2 nd session	3 rd session	
Stone-Free Rate	68%	88.8%	95.2%	90.4%
<i>p-value</i>	<0.001	0.804	0.180	

Table 11: Therapeutic success rate of the ureteroscopy and PCNL

Hypothesis Test Summary

	Null Hypothesis	Test	Sig. ^{a,b}	Decision
1	The distributions of different values across FURS Stone free after one procedure and PNL Stone free are equally likely.	Related-Samples McNemar Change Test	<.001	Reject the null hypothesis.

a. The significance level is .050.

b. Asymptotic significance is displayed.

Table 12: McNemar test for success rate after first ureteroscopy and percutaneous nephrolithotomy

According to the McNemar test, it is found that there is a statistically significant difference between the success rate after a first ureteroscopy intervention and a percutaneous nephrolithotomy intervention ($p < 0.001$). It follows that performing a single session of flexible ureteroscopy is not enough to have a success rate comparable to percutaneous nephrolithotomy.

Hypothesis Test Summary

	Null Hypothesis	Test	Sig. ^{a,b}	Decision
1	The distributions of different values across FURS Stone free after 2 procedures and PNL Stone free are equally likely.	Related-Samples McNemar Change Test	.804 ^c	Retain the null hypothesis.

- a. The significance level is .050.
- b. Asymptotic significance is displayed.
- c. Exact significance is displayed for this test.

Table 16: McNemar test for success rate after second ureteroscopy and percutaneous nephrolithotomy

Going further, the success rate after two stages of flexible ureteroscopy is comparable to the success rate after a percutaneous nephrolithotomy intervention. According to table no. 11, a success rate of 88.8% is observed for ureteroscopy, while the success rate after PCNL was 90.4%. The results of the two interventions are comparable, according to the McNemar test (p 0.804).

Hypothesis Test Summary

	Null Hypothesis	Test	Sig. ^{a,b}	Decision
1	The distributions of different values across FURS Stone free after 3 procedures and PNL Stone free are equally likely.	Related-Samples McNemar Change Test	.180 ^c	Retain the null hypothesis.

- a. The significance level is .050.
- b. Asymptotic significance is displayed.
- c. Exact significance is displayed for this test.

Table 14: McNemar test for success rate after third ureteroscopy and percutaneous nephrolithotomy

At the same time, after 3 serial interventions of flexible ureteroscopy, the success rate increased to 95.2%, comparable to the success rate of percutaneous nephrolithotomy. According to the McNemar test, there is no statistically significant difference between the stone-free rate after 3 sessions of ureteroscopy and the stone-free rate after percutaneous nephrolithotomy (p 0.180).

8.7 Evaluation of cases of large renal lithiasis according to the incidence of postoperative complications

Postoperative complications varied by group, but those specific to PCNL included sepsis, lumbar fistula, and bleeding requiring transfusion or even embolization. On the other hand, there were fever, urinary tract infections, mild hematuria, specific to FURS. As a result, when we compared Clavien-classified complications, we found that PCNL was associated with a much higher rate of transfusions, which in turn led to a higher frequency of major complications and total complications. Especially in individuals with a solitary kidney, the possible risk of bleeding

resulting from percutaneous nephrolithotomy should be seriously considered. If percutaneous nephrolithotomy is performed, these patients are more likely to develop acute renal failure than those with bilateral kidneys because compensatory hypertrophy makes them more susceptible to bleeding requiring embolization. In addition, functional parenchymal loss after PCNL and urinary obstruction by blood clots both impair the function of a single kidney.

In our study, the overall complication rate was higher in the PCNL group than in the URS group (12% vs. 9.6%), but without statistical significance ($p > 0.05$). In addition, we encountered more grade III and IV complications in the PCNL group (10.4% vs. 4%). No grade V complications were encountered in either group.

	F-URS Complications	Nr. Cases	PCNL Complications	Nr. Cases	<i>p</i>
I	Clavien Fever	5	Fever	4	
	Mild Hematuria	7	Hematuria	11	
	Total	12(9.6%)	Total	15(12%)	0.684
II	Clavien Urinary tract infections	8(6.4%)	Significant bleeding requiring blood transfusion	4(2.3%)	0.388
III	Clavien		Persistent urine leakage requiring double J ureteral stenting	4	
			Arterio- venous fistula requiring angioembolization	5	
			Total	9(7.2%)	0.004
IV	Clavien Sepsis requiring ICU management	5(4%)	Sepsis	4(3.2%)	1.000
Total		25(20%)		32(25.6%)	0.230

Table 17: Presentation of postoperative complications of retrograde ureteroscopy and percutaneous nephrolithotomy

According to table no. 15, in the case of patients treated by retrograde ureteroscopy, 12 cases of Clavien 1 complications were encountered. These consisted of fever and mild hematuria, representing 9.6% of the total number of cases.

According to table no. 15, in the case of patients treated by percutaneous nephrolithotomy, we encountered 15 Clavien 1 postoperative complications, represented by fever and hematuria. Therefore, 12% of the total number of patients had Clavien 1 complications.

Regarding Clavien 3 complications, they were not encountered among patients treated by retrograde ureteroscopy. In the case of patients treated by percutaneous nephrolithotomy, Clavien 3 complications were encountered in 9 cases, representing 7.2% of cases. These were represented by the presence of a lumbar fistula, requiring the installation of a double J stent, in 4 cases, and arterio-venous fistula, with significant bleeding, which required angioembolization, in 5 cases.

Regarding Clavien 4 complications, in 5 cases of patients treated by retrograde ureteroscopy, postoperative sepsis was encountered, requiring transfer to the ATI ward and intensive care measures. In the group treated by NLP, 4 cases of sepsis were encountered, representing 3.2% of the total number of cases.

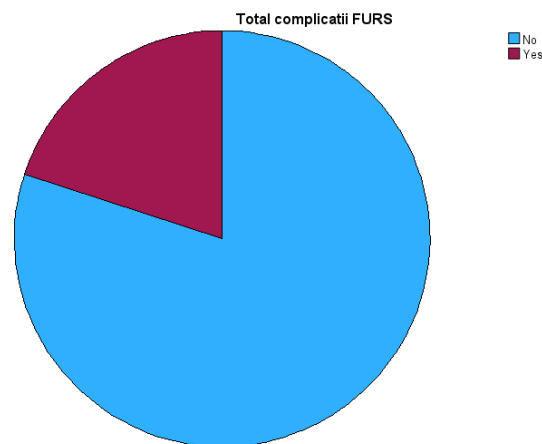


Figure 3: Total number of postoperative complications encountered during flexible ureteroscopy

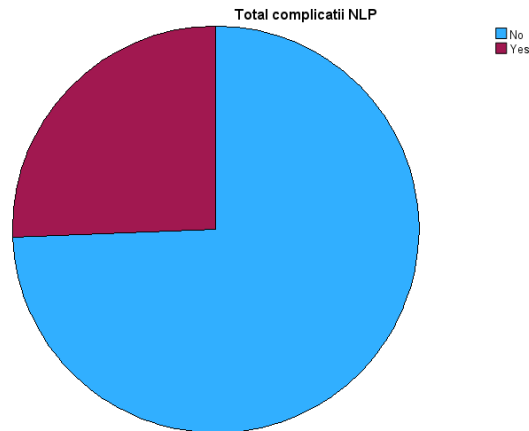


Figure 4: Total number of postoperative complications encountered during PCNL

In conclusion, retrograde ureteroscopy, although it has a higher number of Clavien complications than percutaneous nephrolithotomy, most of them are Clavien 1 and 2, while in case of percutaneous nephrolithotomy most complications were Clavien 3 and 4.

9. Discussion

In the presented study, carried out between 2019-2021, 250 cases of pyolocaliceal lithiasis with sizes between 2 and 4 cm were recorded. Male patients were more frequent in the group treated by flexible ureteroscopy (58.4%), as in the group treated by percutaneous nephrolithotomy (52%). The data are consistent with other specialist articles showing a higher frequency of kidney stones among males.

According to a recent meta-analysis, PCNL provided a superior initial stone-free rate to retrograde flexible ureteroscopy in the management of 2–3 cm renal stones, consistent with the majority of included studies. In addition to the inherent flaws of current FURS techniques and systems, such as constrained working channels and flexibility of ureteroscopes, residual fragments are more likely to represent a clinically insignificant fragment pool. This is one explanation for the lower initial stone-free rate of flexible ureteroscopy. Bryniarski et al. first described the technique by changing the patient's position to move stones from the lower pole, which improved the initial stone-free rate of FURS. Because dust can make the visibility of the operative field difficult and because it can be difficult to distinguish a small, fragmented calculus in the midst of dust, Mułtescu et al. and Cho et al. suggested that the dusting technique followed by fragmentation may be preferable for stones larger than 1 cm. According to Kuo et al., thin fibers (200-270 microns) are preferable to larger ones (365 microns) because they allow fluid irrigation and flexibility without

reducing fragmentation effectiveness. Chen et al. developed a novel technique of aspiration of fragments directly using the ureteral access sheath with vacuum suction and artificial water circulation, made possible by infusing saline into the distal end of the ureteral catheter. This technique also helped to save surgical time because it used fewer steps to extract stones with basket probes. We should be able to greatly increase the success rate of a single flexible ureteroscopy procedure in the near future due to advances in laser fibers with higher energy transmission and the combination of improved flexibility and smaller diameter endoscopes.

Among the included investigations, there was a discrepancy as to whether FURS gave a final stone-free rate equal to that obtained by PCNL. One month after the intervention, Zengin et al. reported that the final stone-free rate of the PCNL group was 95.5%, while Chen et al. stated that the final stone-free rate of the FURS group was identical to that of the PCNL group (89.1 vs. 92.5%). We can accept the discrepancy with caution because several sessions of FURS can lead to a satisfactory success rate, as shown by the most recent study, which found that single-session FURS had a success rate of 67.2% and that the final success rate following multiple procedures was 89.1%. This conclusion was supported by similar investigations. Surgeon judgment and individual patient preferences also played an important role in the choice of subsequent therapy.

In the case of the present study, the therapeutic success rate, or stone-free rate, was defined as the absence of stone fragments or stones larger than 3 mm on the control computed tomography 30 days after surgery.

In the current study, the success rate after the first ureteroscopy was higher for the PCNL group (90.4%) than the FURS group (68%). After two sessions of ureteroscopy, the stone-free rate was 88.8% in the first group, and after three procedures, the stone-free rate increased to 95.2%. Our results are consistent with the data found in the literature and confirm that a decent stone-free rate can be achieved after several sessions of flexible ureteroscopy.

Tests of statistical significance reveal that there is statistical significance between the success rate of the first intervention of flexible ureteroscopy and percutaneous nephrolithotomy. Going forward, the success rate after two stages of flexible ureteroscopy is statistically comparable to the success rate after a percutaneous nephrolithotomy procedure. At the same time, after 3 serial interventions of flexible ureteroscopy, the success rate increased to 95.2%, comparable to the success rate of percutaneous nephrolithotomy. According to the McNemar test, there is no

statistically significant difference between the stone-free rate after 3 sessions of ureteroscopy and the stone-free rate after percutaneous nephrolithotomy (p 0.180).

Postoperative complications varied by group, but those specific to PCNL included hematuria, lumbar urinary fistula, and bleeding requiring transfusion or even embolization. On the other hand, there were ureteral lesions and strictures specific to FURS. As a result, when we compared Clavien-classified postoperative complications, we found that PCNL was associated with a much higher transfusion rate, which in turn led to a higher frequency of major complications. Especially in people with a single kidney, the possible risk of bleeding due to NLP should be seriously considered. When NLP is performed, these patients are more likely to develop acute renal failure than those with bilateral kidneys because compensatory hypertrophy makes them more susceptible to bleeding requiring embolization.

In our study, the overall complication rate was higher in the PCNL group than in the URS group (12% vs. 9.6%), but without statistical significance ($p > 0.05$). In addition, we encountered more grade III and IV complications in the PCNL group (10.4% vs. 4%). No grade V complications were encountered in either group. In the case of patients treated by retrograde ureteroscopy, 12 cases of Clavien 1 complications were encountered. These consisted of fever and mild hematuria, representing 9.6% of the total number of cases. In the case of patients treated by percutaneous nephrolithotomy, we encountered 15 Clavien 1 postoperative complications, represented by fever and hematuria. Therefore, 12% of the total number of patients had Clavien 1 complications. As for Clavien 3 complications, they were not encountered among patients treated by retrograde ureteroscopy. In the case of patients treated by percutaneous nephrolithotomy, Clavien 3 complications were encountered in 9 cases, representing 7.2% of cases. These were represented by the presence of a lumbar fistula, requiring the installation of a double J stent, in 4 cases, and arterio-venous fistula, with significant bleeding, which required angioembolization, in 5 cases. Observing Clavien 4 complications, postoperative sepsis was encountered in 5 cases of patients treated by retrograde ureteroscopy, requiring transfer to the ATI ward and intensive care measures. In the group treated by PCNL, 4 cases of sepsis were encountered, representing 3.2% of the total number of cases. In conclusion, retrograde ureteroscopy, although it presents a number of postoperative complications statistically compared to percutaneous nephrolithotomy, most of them are Clavien 1 and 2, while in the case of percutaneous nephrolithotomy most complications were Clavien 3 and 4.

10. Conclusions and personal contributions

10.1. Conclusions

The research aimed at identifying the urological peculiarities associated with renal lithiasis with sizes between 2 and 4 centimeters defined some essential strategies for the proper implementation of the study plan, described in detail in the section regarding the general methodology of the research. The rigorous application of all the predetermined stages led to the possibility of compiling a complex database that would provide the necessary data for the related statistical analysis, with the aim of achieving the specific objectives of each individual study plan.

Analyzing retrospectively all the activities carried out mainly empirically, but respecting a methodological character, as well as the data processing processes that required a persistent attitude in the acquisition of new statistical and analytical skills, the entire design of the study led step by step to the achievement progressive of all objectives according to the original plan.

The perfect involvement in reaching the final goal associated a pragmatic attitude of transposing intuitive ideas into practice, with maintaining a realistic, conscious vision regarding the dynamics of epidemiological transitions characterizing the surrounding reality.

Epidemiological transitions in the context of the Covid-19 pandemic have hampered all sectors of activity worldwide, creating unique turbulence in history, including in the health systems. As far as the Romanian medical system is concerned, it has suffered to the same extent as those in highly developed states, with the daily activity undergoing dramatic transformations, with the complete restoration of priorities. These elements constituted a real impediment regarding the initial plan for carrying out the current research, so the assimilation of additional measures to ensure compliance with ethics and deontology norms constituted a necessary and essential element of adaptability. Most of these measures revolved around respecting social distancing rules and preventing the spread of the viral infection, with the aim of carrying out the research activity safely, without associating compromises of a medical or organizational nature. The transformation of the health unit into a COVID-support hospital constituted another obstacle regarding the conduct of the study, as it was necessary to transform it from a prospective study into a mixed, retrospective and prospective study, in order to create a database as complex as possible.

10.2. Personal contributions

Examination of the results obtained in the current research plan led to the possibility of tracing the following personal contributions:

1. A higher incidence of large kidney stones was observed among male patients. This may be due to the fact that men show some reluctance to go to the doctor for specialist consultations.

2. Patients treated by retrograde ureteroscopy had a mean age of 54.96 years, with a standard deviation of 14.283 years. The minimum age of the patients is 31 years, and the maximum is 84 years. In the case of patients treated by percutaneous nephrolithotomy, an average age of 57.04 years is observed, with a standard deviation of 8.511 years. The minimum age of patients treated by percutaneous nephrolithotomy was 37 years, and the maximum age was 71 years. Therefore, a higher mean age is observed among patients treated by percutaneous nephrolithotomy than among those treated by retrograde ureteroscopy.

3. At the same time, a percentage of 20.8% of patients treated by flexible ureteroscopy were aged between 31 and 37 years, while the youngest age of patients treated by percutaneous nephrolithotomy was 37 years. Considering all this, we can conclude that young people prefer ureteroscopy, a minimally invasive intervention, even at the risk of performing several interventions, to the detriment of percutaneous nephrolithotomy, a more laborious surgical intervention.

4. 18.4% of patients treated by retrograde ureteroscopy are between 70 and 84 years old. This fact is due either to the appearance of contraindications to percutaneous nephrolithotomy (patient with an influenced cardio-pulmonary status, under oral anticoagulant treatment), or to patients' preferences for a minimally invasive treatment, considering a more laborious intervention risky.

5. The mean lithiasis volume was 26.38 mm in patients treated by retrograde ureteroscopy, with a standard deviation of 4.453 mm. In the case of patients treated by percutaneous nephrolithotomy, the mean lithiasis volume was 29.44 mm, with a standard deviation of 4.817 mm. The sizes of the stones were measured by computed tomography.

6. The mean operating time of retrograde ureteroscopy was 69.91 min, with a standard deviation of 11,762 min, while the mean operating time of percutaneous nephrolithotomy was 63.08 min, with a standard deviation of 7,074 minutes. In the case of the group treated by retrograde ureteroscopy, surgery was completed either after therapeutic success was achieved, or if the visibility during ureteroscopy was impaired due to minimal bleeding or environmental blur, or if the maximum operative time was reached. The maximum operative time in the case of ureteroscopy was 90 minutes. According to the specialized literature, an operating time of more

than 90 minutes increases the risk of postoperative sepsis, which is why the surgical intervention was stopped at 90 minutes, regardless of whether the patient still had lithiasis or not. It is observed that in 12% of cases the maximum operative time was reached.

7. Fluoroscopy time in patients treated by ureteroscopy had a mean duration of 30.10 seconds, with a standard deviation of 7.914 seconds, while in the group treated by percutaneous nephrolithotomy, fluoroscopy time had a mean duration of 55.25 seconds, with a standard deviation of 11.987 seconds. This is important for both the patient and the urologist, as he is regularly exposed to significant amounts of ionizing radiation, and limiting his exposure is recommended.

8. The duration of hospitalization was longer in the PNL group (162.62 ± 31.802 h) than in the URS group (78.14 ± 23.393 h). In the PCNL group, the patient was discharged after the suppression of the nephrostomy tube and when he was clinically stable, without hematuria or the presence of any lumbar fistulae, while in the FURS group, the patient was usually discharged the day after the intervention if was clinically stable. The minimum duration of hospitalization for patients treated by retrograde ureteroscopy was 48 hours and the maximum was 168 hours, while the minimum duration of hospitalization for patients treated by NLP was 144 hours and the maximum was 336 hours.

9. A much higher frequency of pre-stenting is observed in patients treated by retrograde ureteroscopy (80.8%) compared to percutaneous nephrolithotomy (3.2%). 101 of the patients treated by retrograde ureteroscopy underwent stenting preoperatively. Among them, some of them presented as an emergency with obstructive pyelonephritis that required ureteral stenting, and another part presented ureteral stenosis that did not make it possible to overcome it with the semi-rigid ureteroscope or the insertion of the ureteral access sheath. In the case of patients treated by percutaneous nephrolithotomy, only 4 of them required preoperative stenting, either because of an obstructive pyelonephritis or because of the appearance of pyuria at the time of puncturing the pyelocalyceal system. pre-stenting may improve the rate of stone extraction in ureteroscopic treatment of renal stones. Although it may facilitate ureteroscopic management of stones and increase success in access sheath placement, intraoperative complications did not show statistically significant differences.

10. Surgical interventions for renal lithiasis, especially classical interventions or NLP can affect the conformation and anatomy of the kidney, making a percutaneous intervention more

difficult. Moreover, it can be all the more difficult for stone producers to perform percutaneous nephrolithotomy or even classic intervention every time they present to the doctor with a bulky kidney stone. In these cases, it can be decided, together with the patient, to perform minimally invasive interventions, even if they can be serial, represented by retrograde ureteroscopy. Also, in the case of patients with a single functional, surgical or congenital kidney, retrograde ureteroscopy can be opted for, as nephrolithotomy could present complications that could affect the single renal unit, leading to renal failure or even anephric.

11. The success rate after the first ureteroscopy was higher for the NLP group (90.4%) than the FURS group (68%). After two sessions of ureteroscopy, the stone-free rate was 88.8% in the first group, and after three procedures, the stone-free rate increased to 95.2%. Our results are consistent with the data found in the literature and confirm that a decent stone-free rate can be achieved after several sessions of flexible ureteroscopy. Tests of statistical significance reveal that there is statistical significance between the success rate of the first intervention of flexible ureteroscopy and percutaneous nephrolithotomy. Going forward, the success rate after two stages of flexible ureteroscopy is statistically comparable to the success rate after a percutaneous nephrolithotomy procedure. At the same time, after 3 serial interventions of flexible ureteroscopy, the success rate increased to 95.2%, comparable to the success rate of percutaneous nephrolithotomy. According to the McNemar test, there is no statistically significant difference between the stone-free rate after 3 sessions of ureteroscopy and the stone-free rate after percutaneous nephrolithotomy ($p = 0.180$).

12. In our study, the overall complication rate was higher in the NLP group than in the URS group (12% vs. 9.6%), but without statistical significance ($p > 0.05$). In addition, we encountered more grade III and IV complications in the PNL group (10.4% vs. 4%). No grade V complications were encountered in either group.

So, by going through all these aspects described, I believe that the current thesis brings a significant contribution aimed at the treatment of bulky renal lithiasis. Retrograde ureteroscopy can be performed for stones between 20 and 40 mm in size. However, patients should be advised that more than one procedure may be required to remove the entire lithiasis volume. Therefore, it is advisable to weigh the risks and benefits in light of the unique characteristics of each patient and make a decision with the patient after emphasizing the advantages and disadvantages of each surgical intervention.

References

1. Petrisor A. Geavlete, ELSEVIER, 2016. RETROGRADE URETEROSCOPY, HANDBOOK OF ENDOUROLOGY
2. Arthur D. Smith MD, Glenn M. Preminger MD, Louis R. Kavoussi MD, Gopal H. Badlani MD, 2019. Smith's Textbook of Endourology, Fourth Edition
3. Geavlete, P., Multescu, R., Geavlete, B., 2007. Influence of pyelocaliceal anatomy on the succes of flexible ureteroscopic approach. J. Endourol. 21
4. Victor Papilian – Anatomia omului vol.II. Splanhnologia, Editura Bicall, București, 2001
5. Mihail Ștefăneț – Anatomia omului vol.III, Ministerul Sănătății al Republicii Moldova; USMF "Nicolae Testemițanu". - Chișinău : Medicina, 2010
6. G Lupu- Anatomia omului. Aparatul Genital , Editura Universitară ” Carol Davila”, București, 2007
7. Viorel Ranga- Anatomia Omului, Editura Cerma, București, 2002;
8. Zelenko N, Coll D, Rosenfeld AT, and Smith RC. Normal ureter size on unenhanced helical CT. AJR Am J Roentgenol 2004;182(4):1039–1041
9. Cetti RJ, Biers S, and Keoghane SR. The difficult ureter: what is the incidence of prestenosing? Ann R Coll Surg Engl 2011;93(1):31–33.
10. Bourdounis A, Tanabalan C, Goyal A et al. The difficult ureter: stent and come back or balloon dilate and proceed with ureteroscopy? What does the evidence say? Urology 2014;83(1):1–3.
11. Ambani SN, Faerber GJ, Roberts WW et al. Ureteral stents for impassable ureteroscopy. J Endourol 2013;27(5):549–553.
12. Kaplan AG, Lipkin ME, Scales CD, Jr., and Preminger GM. Use of ureteral access sheaths in ureteroscopy. Nat Rev Urol 2016;13(3):135–140.
13. Nicolae Angelescu – Tratat de Patologie Chirurgicală. Edituta Medicală, București, 2003.
14. Constantinou, C.E., Djurhuus, J.C., 1981. Pyeloureteral dynamics in the intact and chronically obstructed multicalyceal kidney. Am. J. Physiol.
15. Gilpin, S.A., Gosling, J.A., 1983. Smooth muscle in the wall of developing human urinary bladder and urethra. J. Anat. 137, 503–512.

16. Walsh C. Patrick, Alan B. Retik, E.Darracott Vaughan Jr., Alan J. Wein - Campbell's Urology. Seventh Edition
17. Morales, P.A., Crowder, C.H., Fishman, A.P., Maxwell, M.H., 1952. The response of the ureter and pelvis to changing urine flows. *J. Urol.* 67, 484.
18. Muhbes, Fakhria,. 2012., Risk factors for renal stone formation: A field study. *Health Science Journal.* 6. 714-725
19. Acalovschi, I., Aldea, A., Ancă r, V., & Angelescu, N. M. (2003). Litiaza urinară. In *Tratat de patologie chirurgicala* (pp. 2825-2839). Bucureș ti: Editura Medicală .)
20. Bigoniya, Papiya & Sohgaurya, Atul. (2017). A Review on Epidemiology and Etiology of Renal Stone. *American Journal of Drug Discovery and Development*
21. Alatab S, Pourmand G, El Howairis Mel F, Buchholz N, Najafi I, Pourmand MR, Mashhadi R, Pourmand N. National Profiles of Urinary Calculi: a Comparison Between Developing and Developed Worlds. *Iran J Kidney Dis.* 2016 Mar;10(2):51-61.
22. Stoller, M. L., & Meng, M. V. (2016). Epidemiology and Incidence of Stone Disease. In *Urinary Stone Disease The Practical Guide to Medical and Surgical Management* (pp. 27-34). Totowa: Humana Press.
23. Geavlete, P., Arabagiu, I., & Jecu, M. (2013). Litiaza aparatului urinar. In *Urologie: Curs pentru studenți* (pp. 82-110). Bucureș ti: Editura Universitară "Carol Davila
24. Acalovschi, I., Aldea, A., Ancă r, V., & Angelescu, N. M. (2003). Litiaza urinară. In *Tratat de patologie chirurgicala* (pp. 2825-2839). Bucureș ti: Editura Medicală
25. Tekgöl, S., Dogan, H., Hoebeke, P., Kočvara, R., Nijman, J., Radmayr, C., & Stein, R. (2016). EAU Guidelines on Urolithiasis. *European Association of Urology*, 69(3), 475-482
26. David Chon and Elspeth M Mc.Dougall Md. Cap 1.1 Endoscopic imaging and instrumentation –Advanced Endourology: The complete clinical guide –Stephen Y. Nakada Md, Margret S. Pearle, Md., Phd, Editura Humana Press Totowa, New Jersey, 2006, pag 3-19
27. Geavlete, P. A., & Geavlete, P. A. (2016). Instruments. In *Retrograde ureteroscopy: Handbook of endourology* (pp. 21-52). Amsterdam Netherlands: Academic Press.
28. Smith, A. D. (2019). Rigid Ureteroscopes. In *Smith's textbook of endourology* (4th ed., Vol. 1, pp. 465-474). Hoboken, NJ: Wiley-Blackwell.
- 29.6 Krambeck AE, Murat FJ, Gettman MT et al. The evolution of ureteroscopy: a modern single-institution series. *Mayo Clin Proc* 2006;81:468–473.

30. Yayıcioglu O, Guvel S, Kilinc F et al. Results with 7.5Fr versus 10Fr rigid ureteroscopes in treatment of ureteral calculi. *Urology* 2004;64:643–646.
31. Proietti S, Dragos L, Molina W et al. Comparison of new single-use digital flexible ureteroscope versus nondisposable fiber optic and digital ureteroscope in a cadaveric model. *J Endourol* 2016;30(6):655–659
32. Marshall VF. Fibe 33. Smith, A. D. (2019). Flexible Ureteroscopes. In Smith's textbook of endourology (4th ed., Vol. 1, pp. 475-485). Hoboken, NJ: Wiley-Blackwell.
34. Smith, A. D. (2019). Digital Ureteroscopes. In Smith's textbook of endourology (4th ed., Vol. 1, pp. 497-505). Hoboken, NJ: Wiley-Blackwell.
35. Andonian S, Okeke Z, and Smith AD. Digital ureteroscopy: the next step. *J. Endourol* 2008;22: 603–606
36. Binbay M, Yuruk E, Akman T et al. Is there a difference in outcomes between digital and fiberoptic flexible ureterorenoscopy procedures? *J Endourol* 2010;24:1929–1934.
37. Smith, A. D. (2019). Ureteroscopy Energy Sources. In Smith's textbook of endourology (4th ed., Vol. 1, pp. 532-541). Hoboken, NJ: Wiley-Blackwell.
38. Tawfik, E.R., Grasso, M., Bagley, D.H., 1997. The initial use of the Browne Pneumatic Impactor. *J. Endourol.* 11, 121–124.
39. Bach T, Geavlete B, Herrmann TR, and Gross AJ. Working tools in flexible ureterorenoscopy—influence on flow and deflection: what does matter? *J Endourol* 2008;22(8):1639–1643.
40. Watterson JD, Girvan AR, Cook AJ et al. Safety and efficacy of holmium: YAG laser lithotripsy in patients with bleeding diatheses. *J Urol* 2002;168(2):442–445.
41. Traxer O, Keller EX. Thulium fiber laser: the new player for kidney stone treatment? A comparison with Holmium:YAG laser. *World J Urol.* 2020 Aug;38(8):1883-1894. doi: 10.1007/s00345-019-02654-5. Epub 2019 Feb 6
42. Jansen ED, van Leeuwen TG, Motamedi M, Borst C, Welch AJ. Temperature dependence of the absorption coefficient of water for midinfrared laser radiation. *Lasers Surg Med.* 1994;14(3):258-68. doi: 10.1002/lsm.1900140308
43. Blackmon RL, Irby PB, Fried NM. Holmium:YAG ($\lambda = 2,120$ nm) versus thulium fiber ($\lambda = 1,908$ nm) laser lithotripsy. *Lasers Surg Med.* 2010 Mar;42(3):232-6. doi: 10.1002/lsm.20893

44. Kronenberg P, Traxer O. Update on lasers in urology 2014: current assessment on holmium:yttrium-aluminum-garnet (Ho:YAG) laser lithotripter settings and laser fibers. *World J Urol*. 2015 Apr;33(4):463-9. doi: 10.1007/s00345-014-1395-1. Epub 2014 Sep

45. Kronenberg P, Traxer O. The laser of the future: reality and expectations about the new thulium fiber laser-a systematic review. *Transl Androl Urol*. 2019 Sep;8(Suppl 4):S398-S417. doi: 10.21037/tau.2019.08.01

46. Fritzsche P, Moorhead JP, Axford PD et al. Urologic applications of angiographic guide wire and catheter techniques. *J Urol* 1981;125(6):774–780. Optics in urology. *J Urol* 1964;91.