“CAROL DAVILA” UNIVERSITY OF MEDICINE AND PHARMACY BUCHAREST
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THE INCIDENCE, PREVALENCE, AND RISK FACTORS ASSOCIATED WITH PATHOGENIC AGENTS IN LITHIASIS PATIENTS TREATED WITH INTERNAL URINARY DRAINAGE

DOCTORAL THESIS SUMMARY

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Introduction

Urinary lithiasis is a frequent pathology with a variable and often recurrent evolution, whose prevalence in the general population, between 8% and 10%, has tripled in the last 40 years in developed countries.

There are several urological techniques for the treatment of urolithiasis, depending on size, location, chemical composition of the stones, and morphology of the excretory urinary pathways.

In the last 20 years, the strategy for the treatment of urinary lithiasis has changed, with laparoscopic or open surgery being supplanted by extremely efficient minimally invasive methods with few complications, allowing for rapid social reintegration of patients and shortening the convalescence period.

The insertion of JJ ureteral catheters, a common practice in urology services, represents an option for high urinary tract derivation for preventive, curative, or palliative purposes, regardless of their indications.

Today, the indications for ureteral stenting are multiple: obstructive urolithiasis, preventive in extracorporeal lithotripsy, complex pelvic surgical interventions, extrinsic ureteral compressions, trauma, etc. In the case of obstructive urolithiasis, the first indication is the insertion of double J endoprostheses, and in case of failure, performing an ultrasound-guided percutaneous nephrostomy.

The study aimed to evaluate the prevalence of urinary and catheter colonization in patients with obstructive urolithiasis and to highlight the role of stent colonization in the pathogenesis of urinary tract infections (UTI). Possible associations were sought between demographic factors (age, sex), stenting variables (type of insertion, indwelling time), diseases associated with urinary and JJ ureteral catheter colonization. Etiological agents responsible for urinary and stent colonization were identified, and clinical or stent-related complications during their insertion were monitored.

I. General Part

1. Urinary Lithiasis

1.1. History

In antiquity, the Greeks sought to discover the "cause of kidney stone formation".

The surgical approach to urinary lithiasis appears in the Middle Ages.

The emergence of the anesthesia specialty led towards the end of the 19th century to the development of general surgery and its division with the appearance of new specialties. The first Urology service was established in 1907 at Necker Hospital in Paris, led by Dr. Jean Casimir Felix Guyon.

During the 19th century Romania, two personalities are cited in the history of urology: Prof. Dr. Nicolae Turnescu and Prof. Dr. Gh. Assaky [105].

In the 20th century, the treatment strategy for urinary lithiasis developed rapidly with the emergence of extremely efficient minimally invasive methods.

During the 21st century Romanian urology, Prof. Dr. Michael Daudon and Prof. Dr. C. Pricop established the "Center for Morphological and Spectrophotometric Analysis of Renal Calculi" in Iași, and Prof. Dr. Radu Mihai Boja from Tg. Mureș performed the first percutaneous nephrostomy in 1985. The first Urology department in Romania was established in 1909 by Prof. Dr. Petre Herescu at Colțea Hospital in Bucharest, and the Romanian Urology Society was also founded in 1909.

1.2. Epidemiology

In the modern era, both the incidence and prevalence of urolithiasis are increasing especially in developed countries, correlated with the evolution of eating habits. It affects especially the population between 30 and 50 years old, with double the rate for men compared to that of women.

1.3. Etiopathogenesis

The essential elements of lithogenesis are water and urinary constituents.

Urine is stable, so it does not precipitate when its constituents are in equilibrium. Multiple factors are known to trigger lithogenesis or to oppose it [29, 111].

1.3.1. Stages of Calculi Formation

Lithogenesis has three successive stages: nucleation, aggregation, epitaxy

1.3.2. Theories of Calculi Formation

1.3.2.1. Crystalline Retention

Crystalline retention is the process by which solid, insoluble material is retained in the urinary tract. There are several theories that explain crystalline retention [27, 37, 40, 80].

1.3.2.2. Role of Genetic Factors

Correlation between CLDN14 and NPT2 genes in urolithiasis in the Caucasian population is known [47, 105].

1.3.3. Pathogenesis of Urinary Lithiasis

From the point of view of chemical composition, lithiasis can be [126]:

- calcium lithiasis: calcium oxalate; hydroxyapatite; brushed;
- non-calcic lithiasis: uric acid; struvite; cystine; other forms.

1. Calcium lithiasis

The pathogenic mechanism in calcium lithiasis is hyper-calciuria. This results from increased intestinal absorption, increased renal elimination, or bone resorption through demineralization [49].

2. Uric lithiasis

In the pathogenesis of uric acid stones three elements are involved: hyperuricosuria, reduced urinary volume and acidic urinary pH. The essential pathogenic element is considered to be urinary pH.

3. Cystine lithiasis

Cystinuria is an autosomal recessive condition caused by two genes: SLC3A1 located on chromosome 2 and SLC7A9 located on chromosome 19, involved in the synthesis of transmembrane transporters for cystine, ornithine, lysine and arginine.

4. Lithiasis from infection

Urea-producing bacteria (Proteus, Pseudomonas, Klebsiella, Staphylococcus), split urea into ammonia and carbon dioxide, and later into ammonium and bicarbonate. The calculi of infection are crystals of magnesium-ammonia-phosphate (struvite) and invariably calcium carbonate. The bacteria remain enclaved in the core of the stone, giving rise to new nuclei of precipitation and accelerated growth with a tendency towards coraliform stones.

5. Rare types of lithiasis

There are rare types: xanthine stones; urate-ammonium acid stones; drug stones [86].

1.4. Imaging Diagnostic Methods

Imaging can be performed to confirm urinary lithiasis, to assess the severity of the disease and to evaluate a spontaneous expulsion of the stone.

Plain Radiography (KUB)

The method allows the visualization of radiopaque calculi (80% of their total), but does not provide data on the complications of urinary lithiasis or the anatomy of the renal collecting duct.

Intravenous Urography (IVU)

IVU reveals radiotransparent calculi, but also possible malformations of the upper urinary system (pyeloureteral junction stenoses, ureteral stenoses, etc.).

It has sensitivity of 52–87% and specificity of approximately 92% [127].

Ultrasound

It is usually performed in combination with KUB [138]. It does not provide data on the complications of urolithiasis or the anatomy of the renal collecting duct.

Tomography (CT-scan)

CT scans can be used both in the acute and chronic phase of prolonged ureteral obstruction, being able to highlight all types of stones, except for medicinal ones. It has a sensitivity of 96% and a specificity of about 98% [128].

Magnetic Resonance Imaging (MRI)

MRI scans can reveal both calculi and hydronephrosis and secondary ureterohydronephrosis. It has a high price and takes a long time. It has a sensitivity of 92%, but can give false positive results.

Scintigraphy and radioisotope studies

Radioisotope methods allow the evaluation of renal function and upper urinary tract obstruction, being used post-operatively, at 3-6 months [92].

Retrograde ureteropyelography and antegrade pyeloureterography

These methods allow the pre- and post-operative evaluation of ureteral or pelvicalyceal abnormalities and the performance of urothelial biopsies [15].

1.5. Treatment Methods

1.5.1. Indications for Urological Treatment

The choice of treatment depends on the patient's morphology and comorbidities; location, size and chemical composition of the stone; urinary tract anatomy [93, 136].

1.5.2. Extracorporeal Lithotripsy (ESWL)

Indications for Extracorporeal Shock Wave Lithotripsy (ESWL) are: kidney stones smaller than 20 mm located in the pelvis or middle calyces, radio-opaque stones and lithiasis in children.

1.5.3. Ureteroscopy

Indications are: stones resistant or with contraindication to extracorporeal lithotripsy, kidney stones larger than 2 cm, stones on the pelvic ureter, infection and coraliform stones.

1.5.4. Percutaneous Nephrolithotomy (PCNL)

It is used for calculi larger than 2 cm and coraliform stones.

1.5.5. Open and Laparoscopic Surgery.

Open surgery in urinary lithiasis consists of polar or total nephrectomy for urinary calculi on a kidney with anatomical anomalies or important parenchymal destruction (pyelo-ureteral junction syndrome) [16, 78, 128].

1.5.6. Bladder Calculi

The indication is for the extraction of stones by open surgery, optical urethrotomy, endoscopic electroresection and anti-infective treatment.

1.5.7. Optimization of Instrumental Urological Treatments

In case of residual fragments after a urological instrumental treatment, there are two possibilities [102]:

- expulsive medical treatment: administration of an alpha-blocker, etc.;
- post-urotherapy performed in ventral decubitus and incline at 30^{o}-45^{o}.

1.5.8. Principles of Medical Treatment

The medical treatment of active lithiasis disease consists in the administration of a thiazide diuretic in persistent hypercalciuria or allopurinol in hyperuricemia. Specific measures consist of urine alkalinization in the case of uric acid stones, urinary infection prevention in the case of struvites, urine alkalinization in the case of cystine stones, etc.

1.6. Risk of recurrence

The risk of recurrence is 26% at 5 years and only half of the lithiasis patients present only a single episode of recurrence [105].

2. Ureteral Catheters

2.1. History

Stents were originally thought as an adjunct to open surgery to ensure upper urinary tract drainage or ureteral continuity. Over the years researchers have searched for the ideal catheter design for high urinary tract diversion [72].

2.2. Indications

The indications for the double J catheter are [45]: ureteral obstruction by calculus; preventively, before an extracorporeal lithotripsy; complicated pelvic surgeries; extrinsic compressions of the ureter; congenital anomalies, trauma or iatrogenic insults.

2.3. Types of Ureteral Catheters

Ureteral catheters must have the following features:

- to be radio-opaque for good visibility on radiography;
- to be provided with gradations visible during endoscopy for good positioning;
- have a low surface tension to limit friction;
- can be inserted antero or retrograde;
- simple to insert, change, extract, biocompatible and resistant;
- have a good caliber for urine drainage and low risk of obstruction;
- have a low price.

Catheters vary in: material, size, design and guide.

2.4. Approach and Insertion Duration

The stent is inserted under general or locoregional anesthesia [97]. Two approaches can be used [103]: naturally through cystoscopy or percutaneously after renal puncture (nephrostomy), under radiological control.

The JJ stent can be kept from a few days to a few months, depending on the indications. Withdrawn early may be ineffective, kept too long complications may occur [99]. Long-life catheters, coated with an inert polymer, can be maintained up to 12 months [87].

2.5. Complications

During the maintenance of the JJ ureteral catheter, various unwanted effects may occur [2, 11, 63, 98, 109]: frequent urination; lumbar pain; bladder discomfort; hematuria; urinary infections. Late complications related to stent retention are: calcification or encrustation of the JJ stent; UTI; fracturing, migration or obstruction of the catheter etc.

II. Personal Contributions

3. Hypothesis and General Objectives

3.1. Hypothesis

Urinary tract infections and urinary colonization are common in patients with JJ ureteral catheters. In order to anticipate and institute an optimal treatment, it is necessary to know the prevalence and incidence of colonization and urinary infections among JJ ureteral catheter wearers, regardless of the bacteriological status of the stents.

It is also important to know the risk factors that can be associated with an increased rate of infections and urinary colonization in these patients.

Once the risk factors associated with urinary or stent infections are known, control measures can be instituted: optimizing the duration of stent indwelling, careful bacteriological monitoring, prophylactic antibiotic treatment etc.

4.2. General Objectives

In order to verify the working hypotheses, we set the following general objectives:

1. Evaluation of the prevalence of urinary colonization and JJ ureteral catheters in patients with obstructive urolithiasis, indwelling JJ stents.
2. Highlighting the role of colonization of JJ ureteral stents in the pathogenesis of urinary tract infections and their chronicity in these patients.
3. Determination of the role of the indwelling and the type of insertion of JJ ureteral stents on the prevalence of urinary colonization.
4. Association of risk factors for urinary and/or ureteral catheter colonization among diseases associated with obstructive urolithiasis.
5. Identification of common etiological agents of urinary colonization and JJ stents.
6. Follow-up of post-stenting evolution and complications of patients with JJ ureteral catheters for obstructive urolithiasis.
7. The use of new digital and online patient-medical team communication technologies necessary under the restrictions imposed by the Covid-19 pandemic, to monitor the risk of post-stenting complications in patients wearing JJ ureteral catheters for obstructive urolithiasis.

4. General Research Methodology

4.1. Study Type

4.1.1.The clinical study

I performed a retrospective, longitudinal, descriptive, monocentric study, which included 292 stented obstructive urinary lithiasis patients, within the Urology service of the Central Military Emergency University Hospital "Dr. Carol Davila" Bucharest.

4.1.2. Quantitative study

I conducted a quantitative study to assess the perception of urologists regarding the use of new online communication technologies with their stented patients for obstructive urolithiasis in case of imposed restrictions.

4.2. Inclusion and Exclusion Criteria

4.2.1.The clinical study

The study group included all patients with obstructive urolithiasis with JJ ureteral catheters inserted, regardless of age, sex and associated comorbidities, excluding pregnant women. The study spans three years, from 01.01.2020 to 31.12.2022.

It should be noted that this period overlaps with the period of the Covid-19 pandemic.

4.2.2. Quantitative study

The study was conducted between January and February 2023, on a group of 108 urologists from public and private hospitals, using the "snowball" method.

4.3. Data Collection and Analysis

4.3.1.The clinical study

Statistical analysis was performed using ***z-test*** and ***χ2 (chi square)*** to compare the association between stent and urinary colonization with different factors. The level of significance was set at $p < 0.05$.

The studied parameters were: marital status data; comorbidities; stent location and JJ catheter insertion conditions; type of urinary infection and or ureteral stent; etiology of urinary and stent colonization JJ; catheters indwelling time; post-stenting complications.

4.2.2. Quantitative study

The data was used in a multiple linear regression model, their analysis being done with the ANOVA method in the SPSS program.

5. Urinary and Ureteral JJ Catheter Colonization: prevalence, complications, post-stenting surveillance, new communication techniques.

5.1. Introduction

The objectives proposed for this study are:

1. Evaluation of the prevalence and incidence of urinary colonization and JJ stents in known patients stented for obstructive urolithiasis.
2. Highlighting the role of stent colonization in the pathogenesis of urinary tract infections.
3. Follow-up of the post-stenting evolution and complications.
4. Improving communication between the stented patient and the medical team, after discharge, during and after the Covid-19 crisis.

5.2. Results

5.2.1. Indication for JJ Ureteral Stent

The indication for a stent was urinary lithiasis complicated with bilateral uretero-hydronephrosis in 39% of cases (114 patients) and unilateral in 61% (178 patients).

5.2.2. Post-Insertion Evolution of JJ Ureteral Catheter

Clinical signs and symptoms

Were of low intensity, rarely requiring treatment.

Imaging

Different imaging examinations (ultrasound, TDM and uro-TDM if necessary) were performed to visualize the calculus and evaluate the dilatation of the renal cavities.

5.2.5. Complications in JJ Ureteral Catheter Carriers

Complications induced by the time indwelling of JJ ureteral catheters occurred especially in long-term wearers (more than 30 days), (Table 5.3).

Table 5.3. Complications occurring in JJ stent wearers.

Complications	Number of patients	Percentage
Urinary tract infections	67	23%
Stent encrustation	114	39%
Stent fragmentation	18	6%
Stent obstruction	6	2%

5.2.4. Post-Stenting Patient Surveillance

Since the study was conducted during the Covid-19 pandemic, many of the patients did not keep their urological consultation appointments for fear of contracting the disease.

5.3. Improving communication between the stented patient and the urologist

In order to improve the communication between the patient and the medical team (doctor, nurse), a quantitative study was conducted to evaluate the perception of urologists regarding the use of new communication technologies (telemedicine) [139].

The method used was that of the "snowball". A questionnaire was sent online to physicians with questions regarding the respondent's profile, difficulties encountered in communicating with the stented patient after discharge, and their opinion on new communication technologies.

5.4. Discussions

5.4.1. Retrospective clinical study

This study showed a stent colonization rate of 34.9% and a urinary colonization rate of 22.9%. Colonization of ureteral stents may be considered a factor associated with the bacteriurias and UTIs that usually precede them [98, 139, 140, 141]. Most of the time urine cultures have low sensitivity and high specificity because urine cultures are negative when stents are not colonized, but not all stent colonization is followed by urinary colonization. In the conducted study we obtained a sensitivity of 39.2% and a specificity of 92.1%.

5.4.2. Quantitative study

The quantitative study performed shows that the insertion of JJ ureteral catheters has become routine for the urologist.

88% of responding physicians experienced difficulties in communicating with their stented patients for obstructive urolithiasis during and post-Covid-19 crisis. The consequences of poor communication are varied, from delay in ablation or JJ lead change, to infection and stent-related complications (obstruction, migration, fragmentation).

92.6% of the urologists participating in the study believe that the new online communication technologies are effective.

5.4. Conclusions

The study shows a colonization rate of JJ ureteral catheters of 35% and an overall prevalence of urinary colonization of 23%. Bacteriological monitoring showed that both

urinary and JJ stent colonization was with Gram-positive and negative germs, with little variation in distribution.

As for complications arising from the catheters indwelling time, they are rare and occur mainly in case of long-term indwelling. Clinically, all signs and symptoms gradually improve and disappear upon ablation of the JJ ureteral catheter. Complications related to the ureteral stent are also much more frequent in long-term indwelling (over 30-45 days) [139, 141].

The clinical study was potentially limited by being a single-centre study, with a relatively small cohort (292 patients) and by the probabilistic antibiotic treatment of patients in J2.

The value of the quantitative study carried out lies in rendering the overall picture of the perception of urologists regarding the use of new online communication technologies with their stented patients for obstructive urolithiasis in crisis situations.

5. 6. Perspectives

It seems necessary to find new methods and mechanisms to control the formation of the biofilm on the surface of the JJ ureteral catheter, the maximum decrease of bacterial adhesion as well as new bactericidal antibiotics with high diffusion power at the level of the biofilm.

A possible solution to improve and minimize the complications related to the stent, seems to be the discovery of resorbable ureteral catheters over time.

6. Bacteriological profile of the stented patient for obstructive urolithiasis: monitoring, etiology, principles of treatment

6.1. Introduction

Urinary tract infections rank second in incidence among community-acquired bacterial infections, after bronchopulmonary infections, and hold first place among nosocomial infections.

Risk factors for urinary infections are: age (children, elderly), pregnancy, immunosuppressed, patients with urinary malformations or urinary catheter, etc.

The occurrence of a UTI usually involves either a deficiency of defense factors or the presence of a virulent, uropathogenic bacterium.

6.1.1. The mechanism of infection

According to the mechanism of infection, there are the following possibilities: infection during probing [58], the endoluminal route [42, 58], the extraluminal route [113], the lymphatic or hematogenous route, particular cases [69, 70].

6.1.2. Epidemiology

Between the ages of 20 and 50, urinary infections are much more common in women (30-50 times), but after the age of 50 their incidence increases in men due to the increase in the frequency of prostatic pathology, finally reaching a sex- ratio of 3/1 (B/F) in the case of the elderly.

6.1.3. **Pathophysiology**

Bacteria that colonize the urinary catheter develop in colonies enclosed in a biofilm that protects them. Bacteria adhere to the surface of the foreign body (catheter, probe), multiply and secrete a "slime" or "glycocalyx" as an extracellular polysaccharide matrix. Salts and urinary proteins (Tamm-Horsfall protein) are incorporated into this matrix forming various incrustations at the level of the probe. The process takes an average of 8 days [33]. This biofilm favors the adhesion of microorganisms, protecting them from defense mechanisms and antimicrobial agents [131, 33, 95].

6.1.4. Principles of treatment

As a rule, in the absence of signs of severity and a special terrain (immunodepression, pregnancy), the introduction of antibiotic therapy will wait for the result of the antibiogram.

As for the duration of the treatment, it is chosen according to the location of the infection.

If possible, it is preferable to withdraw the urinary catheter or change it if drainage is indispensable.

6.2. Results

6.2.1. Monitoring Bacteriological Profile

The clinical study revealed a colonization rate of JJ stents of 34.9% (102 patients), and urinary colonization of 22.9% (67 patients). On the group of patients with non-colonized stents (190), monitoring the bacteriological profile of the urine showed that only 7.9% (15 patients) had subsequent urinary colonization, and 92.1% (175 patients) remained urinary uncolonized. For the group of patients with colonized JJ stents (102) only 49% (50 patients) remained with negative urine cultures throughout the study, while 51% (52 patients) had one or more episodes of urinary infection (Table 6.2 . and Figure 6.2).

Tabel 6.2. Monitorizarea profilului bacteriologic urinar funcție de colonizarea stenturilor JJ

		JJ Catheter		**Total**
		Colonized	**Non-colonized**	
Urine culture	**Pozitive**	52	15	67
	Negative	50	175	225
Total		102	190	292

6.2.2. Etiology of Urinary and JJ Stent Colonization

Different germs were detected both in urine cultures and in JJ ureteral catheters (Table 6.3.)

6.3. Discussions

In the group of patients with non-colonized stents, only 15% presented a subsequent urinary colonization, while in the case of the carriers of colonized stents, 82% subsequently presented one or more infectious episodes, regardless of the associated pathologies. Colonization of ureteral stents may be considered a factor associated with the bacteriurias and UTIs that usually precede them [98].

Both urinary and ureteral catheter colonizations were with Gram-positive or Gram-negative germs with different distribution rates, with Gram-negative ones predominating at the level of stents.

6.4. Conclusion

The study shows a colonization rate of JJ ureteral catheters of 35% and an overall prevalence of urinary colonization of 23% as well as the bacteriological profile with small variations in bacteriological distribution.

The clinical trial was potentially limited by being a single-centre study, with a relatively small cohort (292 patients) and by the probabilistic antibiotic treatment of patients in J2.

6.5. Perspectives

The discovery of new methods and mechanisms to control the formation of biofilm on the surface of the JJ ureteral catheter and the maximum reduction of bacterial adhesion as well as bactericidal antibiotics with high diffusion power at the biofilm level.

7. Risk Factors Associated with Urinary and JJ Stent Colonization

7.1. Introduction

The study aims to highlight the risk factors associated with both, urinary and JJ stents colonization in patients with ureteral catheters for obstructive urolithiasis.

7.2. Results

7.2.1. Distribution according to demographic factors.

Distribution according to sex.

The batch of 292 patients is made up of 175 men (60%) and 117 women (40%) and corresponds to a sex-ratio of 1.49 (M/W).

Distribution according to age

The average age of the population in the studied group is 50.28±15.33 years, with extremes at 19 and 86 years. The most affected population is between 51 and 65 years old, (Figure 7.2.).

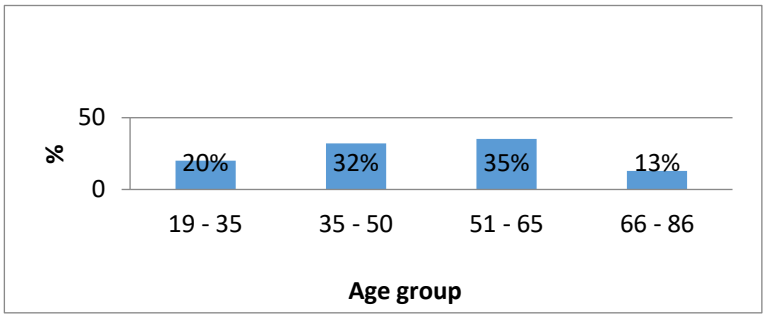

Figure 7.2. Distribution of the study group according to age.

7.2.2. JJ Ureteral Catheter Insertion Type

Following the distribution of colonization of JJ stents according to the type of insertion (emergency or scheduled), we observe an increase in the colonization rate for the patients with the catheter inserted in emergency mode (Table 7.1.).

Table 7.1. Distribution of urinary and JJ stents colonization according to insertion type.

Batch	JJ Catheters				Urine			
	Colonized		Non-colonized		Colonized		Non-colonized	
	Number	%	Number	%	Number	%	Number	%
Emergency	88	86,3	46	24,2	63	94	71	31,6
Scheduled	14	13,7	144	75,8	4	6	154	68,4
Total	102		190		67		225	

7.2.3. Catheter indwelling time

In this study, the mean value of of JJ ureteral stent indwelling time was 33.91±13.18 days with extremes between 10 and 90 days. We notice an increase in the rate of both urinary and catheters colonization along with the increase of the indewlling time (Table 7.3.).

Table 7.3. Distribution of colonized JJ stents according to age and average indwelling time.

JJ catheter indwelling time	Number of patients	Colonized catheters	Mean age Value	Average indwelling time
Less than 30 days	131	29	68,31±12,44	23,58±3,54
30 – 45 days	96	37	59,86±9,77	36,81±7,13
Over 45 zile	65	36	61,15±8,81	55,65±10,00

7.2.4. Associated Pathologies

General Pathologies

54 patients in the studied group were known to have DM, 29 with colonized stents (53.7%) and 25 with non-colonized stents (46.3%), 29 with positive bacteriuria (53.7%) and 25 with non-colonized urine (46 .3%) (Figure 7.5.).

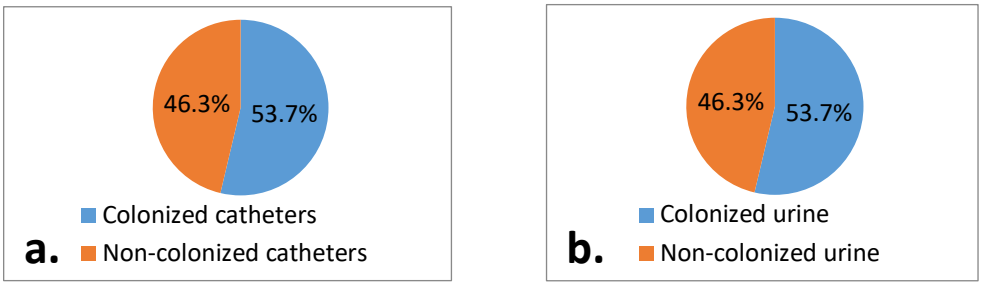

Figure 7.5. Distribution of colonization in DM patients: a. stent; b. urine.

96 patients from the studied group are known to have hypertension, of which 44 with colonized stents (45.8%) and 52 with non-colonized stents (54.2%), 41 patients with positive bacteriuria (42.7%) and 55 with non-colonized urine (57.3%) (Figure 7.6.).

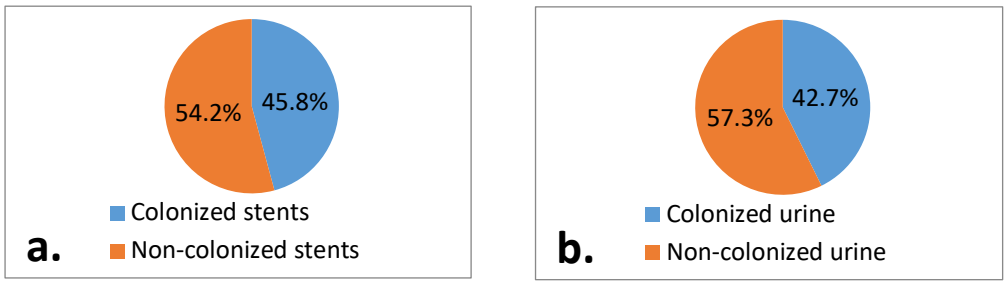

Figure 7.6. Distribution of colonization in patients with hypertension: a. stent; b. urine

In the study group, 23 patients contracted Covid-19, 9 having colonized stents (39.1%) and 14 non-colonized stents (60.9%), 13 patients with positive bacteriuria (56.5%) and 10 with non-colonized urine (43.5%) (Figure 7.7.).

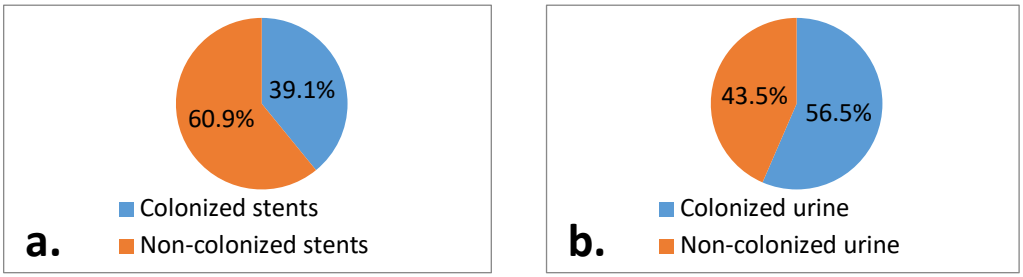

Figure 7.7. Distribution of colonization in patients with Covid-19: a. stent; b. urine.

Reno-Vesical Pathologies

CKD is present in 64 patients in the group, 31 of them with colonized stents (48.4%) and 33 with non-colonized stents (51.6%), 37 patients with positive bacteriuria (57.8%) and 27 non-colonized urine (42.2%) (Figure 7.9.).

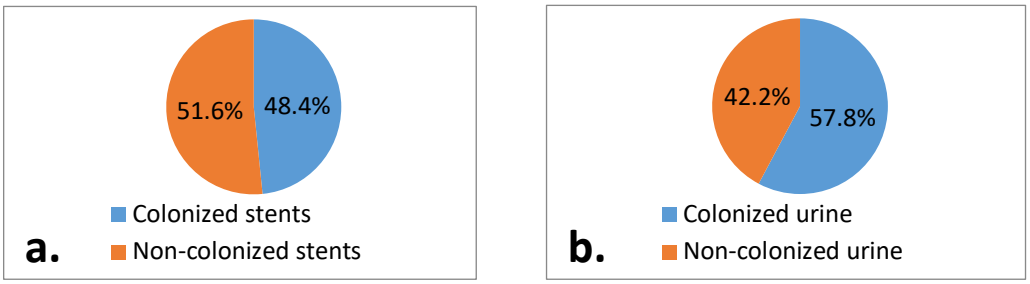

Figure 7.9. Distribution of colonization in patients with CKD: a. stent; b. urine.

In the studied group, 55 patients had prostate tumors (adenoma, cancer), 26 with colonized stents (47.3%) and 29 with non-colonized stents (52.7%), 34 with positive bacteriuria (61.8%) and 21 with non-colonized urine (38.2%) (Figure 7.10.).

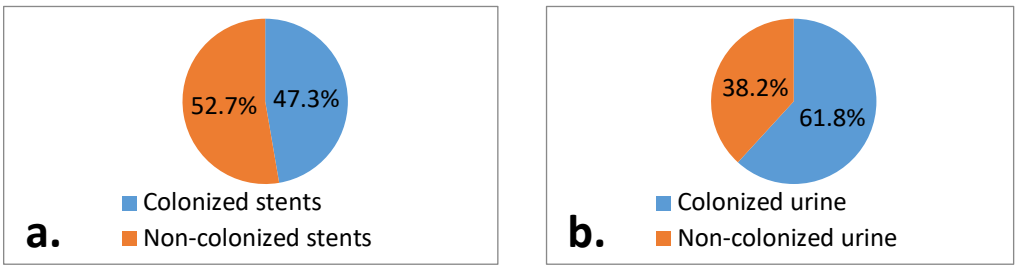

Figure 7.10. Distribution of colonization in patients with prostate tumors: a. stent; b. urine.

7.2.5. Statistical Analysis

The results of the study were centralized in Microsoft Office Excel.

I used the z test to compare the association between continuous variables and stent/urinary colonization. The association between categorical variables and urinary or stent bacterial colonization in these patients was analyzed using the ***χ2 (chi square)*** test.

I set the level of significance at $p < 0.05$, with p values less than 0.05 being considered statistically significant.

7.3. Discussions

The most affected ***age group*** in the present study is 51-65 years. In our study the mean age value is 50.28±15.33 years, for men 50.31±15.31 years and for women 50.24±15.37. With mean values of 62.64±11.16 years and 66.52±8.57 years for colonized catheters and colonized urines respectively, and a statistically significant difference $p<0.0001$, the conclusion is that age influences bacteriuria and stent colonization.

According to the study, it could be concluded that ***gender*** does not influence the incidence of stent colonization nor urinary colonization, the small difference in the probabilistic value p, between the one imposed by 0.05 and the one obtained by 0.06, makes us have reservations about the dissociation of female gender with the incidence urinary colonization in stented patients. One explanation could be the exclusion of pregnant women from our study group.

Regarding the ***insertion type***, 66% of stents inserted in emergency mode are colonized and only 9% of those scheduled inserted. 47% of positive bacteriurias are associated with emergency stent insertion and only 3% of scheduled ones. The study therefore shows with significant statistical differences, $p<0.0001$, that the emergency insertion type is associated with both stent and urinary colonization.

The mean ***indwelling time*** of JJcatheters in the study was 33.91±13.18 days with extremes between 10 and 90 days. Analyzing from a statistical point of view, with a significance level of probability in the case of stent colonization of $p<0.0001$, and in the case of urinary colonization of $p=0.0003$, we can conclude that the indwelling time of JJ ureteral catheters is associated with both stent and urine colonization, so it can be considered predictive of their colonization.

53.7% of the patients who associated ***DM*** have both colonized stents and urinary colonization (without always being colonized simultaneously). Performing the statistical analysis of the data collected for them, we obtain the level of statistical significance $p=0.001$ for stent colonization and $p<0.0001$ for urinary colonization, so, with significant statistical

differences, we note that DM is associated with both stent and urine colonization, and DM can be considered predictive of colonization.

For patients who associated ***hypertension***, we obtained the rates for stent and urinary colonization of 45.8% and 42.7%. With probability values of $p=0.006$ in the case of stent colonization and $p<0.0001$ in the case of urinary colonization, we can report significant statistical differences for the association between hypertension and stent and urinary colonization.

In the case of the association of the ***Covid-19*** disease, we note that 39.1% of these patients had colonized stents and 56.5% colonized urine. From a statistical point of view, we obtain $p=0.659$ for stent colonization and $p<0.0001$ for urinary colonization and with significant statistical differences we notice that Covid-19 disease is associated with urinary colonization, but not with stent colonization.

Referring to ***CKD***, we notice that 48.4% of these patients had colonized stents and 57.8% colonized urine. Calculation of probability values reveals values of $p=0.01$ for stent colonization and $p<0.0001$ for urinary colonization. Obtaining significant statistical differences, we report that CKD is associated with stent and urinary colonization.

In the group of patients who associated obstructive urolithiasis with ***prostate tumors***, 47.3% of them had colonized stents and 61.8% had bacteriuria. Statistically, with probability values of $p=0.033$ and $p<0.0001$ for stent colonization and urinary respectively, we can state that in the conditions of significant statistical differences, prostate tumors are associated with both stent and urinary colonization.

7.4. Conclusions

The research highlights the association between stent and urinary colonization rates with age. Insertion variables, ureteral catheter indwelling time and emergency mode insertion, were associated with increased rates of both stent and urinary colonization [139, 141]. At the same time, diseases such as DM, hypertension, CKD, Covid-19, prostate tumors can be considered risk factors, predictive of urinary colonization [139,140,141]. Only Covid-19 could not be associated with colonization of JJ stents.

8. Conclusions

General Conclusions

1. Urinary lithiasis is a common pathology nowadays, with increasing incidence.
2. There are several types of reno-ureteral stones, but calcium oxalate predominates.
3. Urolithiasis is revealed by a renal colic, hematuria, urinary infection, acute renal failure or simply discovered by chance and its evolution can be simple (spontaneous expulsion of the stone) or complicated by infection, ureterohydronephrosis, acute renal failure.
4. Untreated urolithiasis has a high recurrence rate and often requires long-term prophylaxis.
5. There are several urological techniques for the treatment of urinary lithiasis, depending on the size of the stone, location, chemical composition or anatomy of the urinary system; general and specific measures for each type of lithiasis are added to these.
6. In the last 20 years, microinvasive techniques have taken the place of classical or laparoscopic urological surgery.
7. Urinary tract infection can be considered both a risk factor and a severity factor for urolithiasis.
8. The insertion of the JJ ureteral catheter is a mini-invasive option for the derivation of the upper urinary system in obstructive urolithiasis, and in case of failure an ultrasound-guided percutaneous nephrostomy will be performed.
9. Clinical or stent-related complications may occur during ureteral stents insertions.
10. Colonization can involve both the ureteral catheter and the urine, and it seems obvious that the role of the stent is essential in the pathogenesis of the urinary colonization.
11. Different factors can be considered predictive for stent and urinary colonization.

Personal Conclusions

1. The study reveals a colonization rate of JJ ureteral catheters of 35% and an overall prevalence of urinary colonization of 23%.
2. Risk of urinary colonization is higher in patients with colonized JJ ureteral stents, regardless of age, sex, comorbidities.
3. Stents and urinary colonization are associated with the demographic factor of age, having reservations about the dissociation of the female sex from urinary colonization due to the study limits.
4. The prevalence of urinary colonization increases depending on the insertion variables.
5. Ureteral catheters should be changed periodically, or withdrawn before 30 days.

6. Diseases such as DM, hypertension, CKD, Covid-19, prostate tumors are associated with an increased risk of urinary colonization and can be considered predictive factors.
7. Colonization of urine as well as of JJ stents was shown to be with Gram-positive or negative germs, with small variations in distribution.
8. Conducting the study during the Covid-19 pandemic allowed research into the association of urinary colonization with a disease whose pathogenesis is not as of yet fully known.
9. Complications due to the ureteral catheter indwelling are rare and occur especially in the case of long-term indwelling.
10. Insertion of ureteral catheters in obstructive urolithiasis is a minimally invasive option, safe, effective and well tolerated by patients for less than 30 days of indwelling time.
11. The specialist aims to shorten hospitalization, ensure quality of life by reducing complications and social and professional reintegration of the patient as quickly as possible.
12. The high technical standard of the team of specialists and compliance with sterility practices is reflected in the study's low rate of urinary colonization.
13. Despite potential limitations, the study makes a complex analysis of both stents and urine colonization for the common urological patient, allowing the doctor to make correct decisions regarding the indication, the optimization of the indwelling time and the dynamic monitoring of both urinary and stent bacteriological profile.
14. Telemedicine can be used under conditions of restrictions imposed by various causes, in order to improve communication between the patient and the medical team.

Perspectives

1. Pharmacological research in the field of bactericidal antibiotics with high diffusion power at the level of the bacterial film;
2. New technologies and materials for reducing adhesion at the biomaterial level and controlling biofilm formation;
3. Use of resorbable ureteral catheters;
4. To eliminate the limitations of the study, a multicenter study could be performed on a large group of stented obstructive urolithiasis patients, including pregnant women, in the absence of any prophylactic antibiotic therapy;
5. An interesting further study could be the association between the catheter indwelling time and the quality of life, regardless of age, sex, comorbidities;
6. Given that Covid-19 tends to become seasonal, a study focused on highlighting the association of this disease with urinary colonization and UTI may be appropriate.

Bibliography

16. Blaja, C. Litiaza urinară (Boala litogenă urinară) în Patologia Chirurgicală, vol VI, sub redacţia Th. Burghele, Ed. Medicală, 1972, pg. 494-566.

40. Finlayson, B.; Reid, F. The expectation of free and fixed particles in urinary stone disease. Invest Urol 1978; 15(6): 442–8.

46. Goodwin, W.E. Splint, stent, stint. Urol Dig 11: 13–14,1972

60. Jones, R.; Young, P.; Marasseky, J. Treatment of infection in the presence of an indwelling urethral catheter. Br J Urol 1982; 54: 316-9.

86. Matlaga, B.R.; Shah, O.D.; Assimos, D.G. Drug-induced urinary calculi. Rev Urol 2003;5:227–31.

87. Mischianu, D.; Cumpănaș, A.; Pricop, C.; Bratu, O. Urgențele în urologie. Editura Academiei Române, 2018, www.ear.ro

97. Nourparvar, P.; Leung, A.; Adam, B. Safety and efficacy of ureteral stent placement at the bedside using local anesthesia. J Urol 2016; 195: 1–5.

98. Ozgur, B.C.; Ekici, M.; Yuceturk, C.N.; Bayrak, O. Bacterial colonization of double J stents and bacteriuria frequency. Kaohsiung J Med Sci. 2013;29(12):658-61

105. Pricop, C.; Mischianu, D.; Bucuraș, V.; Cumpănaș, A. Profilaxia și metafilaxia în litiaza renală. Editura PIM. 2021

138. Arhiva imagistică a Serviciului de Urologie din Spitalul Universitar de Urgență Militar Central "Dr. Carol Davila", București

139. Vintilă, M.; Mischianu, D.; Honțaru, O-S.; Dobra, M.; Sterian, A.G. Use of Digital Healthcare Communication to Improve Urologists' Surveillance of Lithiasis Patients Treated with Internal Urinary Drainage Pre- and Post-COVID-19 Period. Healthcare 2023, 11, 1776., https://www.mdpi.com/journal/healthcare, https://doi.org/10.3390/healthcare11121776

140. Vintilă, M.; Spînu, D.; Marcu, D.; Mischianu, D.; Nica, S. Risk Factors for Urinary Colonization in Patients with Double J Catheters Implanted for Treating Obstructive Urolithiasis. Vol. CXXVI, No. 4/2023, November, Romanian Journal of Military Medicine, https://doi.org/10.55453/rjmm.2023.126.4.4

141. Vintilă, M.; Spînu, D.; Marcu, D.; Mischianu, D. The Current State of Knowledge Regarding the Use of Double J Catheters in Treating Obstructive Urolithiasis. Vol. CXXVI, No. 3/2023, August, Romanian Journal of Military Medicine, https://doi.org/10.55453/rjmm.2023.126.3.15

List of scientific papers published

1. **Vintilă, M.**; Spînu, D.; Marcu, D.; Mischianu, D. The Current State of Knowledge Regarding the Use of Double J Catheters in Treating Obstructive Urolithiasis. Vol. CXXVI, No. 3/2023, August, Romanian Journal of Military Medicine, https://doi.org/10.55453/rjmm.2023.126.3.15 (chapter 5.5, pag. 49; chapter 7.4, pag. 80)

2. **Vintilă, M.**; Mischianu, D.; Honțaru, O-S.; Dobra, M.; Sterian, A.G. Use of Digital Healthcare Communication to Improve Urologists' Surveillance of Lithiasis Patients Treated with Internal Urinary Drainage Pre- and Post-COVID-19 Period. Healthcare 2023, 11, 1776., https://www.mdpi.com/journal/healthcare, https://doi.org/10.3390/healthcare11121776 (chapter 5.3, pag. 40, 41, 43, 44; chapter 5.4, pag. 49, chapter 5.5, pag. 49; chapter 7.3, pag. 79, 80)

3. **Vintilă, M.**; Spînu, D.; Marcu, D.; Mischianu, D.; Nica, S. Risk Factors for Urinary Colonization in Patients with Double J Catheters Implanted for Treating Obstructive Urolithiasis. Vol. CXXVI, No. 4/2023, November, Romanian Journal of Military Medicine, https://doi.org/10.55453/rjmm.2023.126.4.4 (chapter 7.3, pag. 80, chapter 7.4 pag. 80)