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URETERAL STENTS: EXPERIMENTAL EVALUATION OF PROPERTIES AND NEW APPROACHES TO PREVENTION OF COMPLICATIONS

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INTRODUCTION

Relevance of the research topic

Ureteral stents are widely used in urological practice. Their main task is to ensure adequate drainage and splinting of the upper urinary tract.

According to economic forecasts, the global ureteral stents turnover will reach US$ 565 million in 2026 with a compound annual growth rate of about 5,8%, and these figures are estimated to grow exponentially [55].

The term ‘stent’ first appeared in medical literature in the 19th century, when British dentist Charles T. Stent made dental impressions of teeth. The material he used allowed for a long-time preservation of the adopted shape. However, this term was not widely used in urological literature until the 1970s. In 1978, R.P. Finney presented to the urological community a prototype of a modern ureteral stent with loops at both ends, which most resembles modern products [52].

Various polymers have been used in the production of ureteral stents, but not all compounds were highly biocompatible, inert and non-toxic to the urinary tract. Currently, most ureteral stents are made of polyurethane and silicone. Advances in science and technology have led to the development of various copolymers of polyurethane and silicone rubber. A lot of research has been directed towards the development of new stent designs, materials and coatings. These efforts have been essential to enhance biocompatibility and, consequently, reduce the risk of complications [1]. Despite this, scientific literature provides little information on the pathogenesis of interactions between specific stent materials or their coatings and the urinary tract.

Adverse effects associated with ureteral stent placement are observed in nearly 80% of cases [65]. The term “stent-associated symptoms” (SAS) encompasses irritative symptoms, suprapubic discomfort, flank pain on the side of the stent

placement, and hematuria [44, 118]. Unfortunately, pharmacological interventions cannot completely eliminate these undesirable phenomena.

The evolution of ureteral stents has involved not only material improvements but also design advancements. For instance, new stent removal techniques have been developed, such as the use of retrieval snares, magnetic retrievers, or spiral-ending devices for women under ultrasound guidance [72, 115, 121]. In routine clinical practice, ureteral stents are typically removed by cystoscopy, a procedure that induces significant dysuria in more than half of patients, especially in males [103]. Developing methods for stent removal without cystoscopy, anesthesia, or radiological control remains a pressing issue in modern minimally invasive urology.

"Forgotten" ureteral stents (FUS) are a rare but severe problem in urology that can lead to life-threatening complications, including sepsis and renal function decline. Other complications of “forgotten” stents include encrustation and fragmentation of stents, and urinary tract infections [54]. Factors contributing to “forgotten” stents may include low social adaptability, poor adherence to medical recommendations, and good stent tolerance without significant stent-associated symptoms [80]. Therefore, the development and implementation of preventive measures are critical to improving the quality of life for patients with ureteral stents. Automated computer programs that remind patients about timely stent removal could reduce the incidence of “forgotten” stents. It is also worth noting that the removal of “forgotten” stents often requires multimodal surgical treatment and incurs significant economic costs. According to the literature, the cost of removing a “forgotten” stent is nearly seven times higher than the cost of removing a routine stent [110].

Prolonged stent retention in the urinary tract leads to crystallization and salt deposition on its surface, a process known as encrustation. Approximately 50% of patients undergoing long-term ureteral stenting experience this complication [102]. Nearly 43% of ureteral stents become encrusted within four months of placement. Moreover, patients with a history of stent encrustation are more likely to develop recurrent encrustation earlier [74]. In patients with long-term indwelling stents, biofilm formation on the stent surface occurs in 100% of cases [21]. Encrustation

is a multistage process beginning with the formation of a conditioning film on the stent surface, followed by precipitation of calcium, phosphorus, and uric acid salts [31]. Severe stent encrustation can result in urinary tract obstruction, impaired renal function, and exacerbation or progression of infection, significantly affecting the patient's quality of life and safety. Understanding the sequence of encrustation processes and developing pharmacological preventive measures is a vital area of clinical research.

In summary, ureteral stents have both advantages and disadvantages. The increasing use of stents will inevitably expose many patients to the undesirable consequences of stenting. Thus, there is a clear need to address complications associated with ureteral stents, such as stent-associated symptoms and encrustation. Additionally, optimizing stent removal methods and addressing the issue of “forgotten” stents remain important objectives.

Aim of the research

Optimisation of the use of ureteral stents taking into account their properties, impact on quality of life, removal methods and prevention of complications.

Research objectives

1. To identify the characteristics of the surface and physico-mechanical properties of polymers used in the production of ureteral stents in an experimental setting.
2. To evaluate the quality of life of patients with urolithiasis who have silicone and polyurethane ureteral stents implanted.
3. To assess the efficacy and safety of removing magnetic ureteral stents under ultrasound guidance in men.
4. To develop a personalized automatic digital registry for patients with ureteral stents and evaluate its clinical effectiveness in preventing “forgotten” and untimely removed stents.

5. To develop and assess the effectiveness of pharmacological modeling of lithogenic urine properties for the prevention of ureteral stent encrustation.

Scientific novelty of the research

For the first time, the surface and physico-mechanical properties of stent polymers (polyurethane and silicone) were experimentally studied, revealing their potential impact on biocompatibility. Differences in the studied material parameters were identified, and key factors influencing the rate of stent material adaptation within the urinary tract were determined.

A comparative assessment of the quality of life of patients with silicone and polyurethane ureteral stents was conducted for the first time, demonstrating the advantages of silicone stents over polyurethane stents.

The impact of magnetic-tip ureteral stents on the severity of stent-associated symptoms was evaluated. For the first time, a study was conducted on the safety and efficacy of their removal from the urinary tract under ultrasound guidance using a specialized extractor.

As part of this work, with the author's participation, an automated digital registry of patients with ureteral stents was created, which is implemented as an application for smartphones based on iOS and Android (certificate of registration of the software for ECM RU 2017610874, date of registration: 18.01.2017). Its effectiveness with regard to the prevention of “forgotten” stents was studied.

The efficacy and safety of an oral mixture of creatine and ascorbic acid for preventing ureteral stent encrustation were assessed for the first time.

Practical significance of the research

Based on the experimental and clinical components of the dissertation research, practical recommendations were formulated regarding the selection of stent material.

The study conducted on a considerable clinical material has shown high efficacy and safety of the use of stents with magnetic tip in men. In turn, their widespread use allows to significantly simplify the method of stent removal and makes it widely available in terms of financial feasibility for medical centres of the Russian Federation.

Preventive measures were developed to address the most common complications of ureteral stenting, such as stent encrustation and delayed removal. These measures are expected to reduce the substantial economic burden associated with the management of these complications.

Main scientific results

1. A significant advantage of silicone stents over polyurethane stents was identified in terms of the frequency and intensity of pain syndrome two weeks after the placement of ureteral stents, as well as just before their removal, with p-values of 0.023 and 0.014, respectively. The average pain levels measured on the Visual Analog Scale (VAS) indicate that patients with silicone stents experienced significantly lower pain compared to those with polyurethane stents ($p=0.0010$) [6]. Pages 127-128. Author's contribution: 85%.

2. The effectiveness and safety of removing magnetic ureteral stents in men using a specialized retriever under ultrasound guidance were studied. It was found that the time required for the removal of the magnetic stent was significantly shorter compared to the removal time of conventional polyurethane stents (40 seconds vs. 142.5 seconds, respectively; $p<0.0001$). Additionally, the removal of magnetic stents caused less discomfort in men compared to the removal of conventional polyurethane DJ stents ($p=0.0008$) [98]. Pages 2894-2895. Author's contribution: 70%.

3. The first Russian mobile application for smartphones based on iOS and Android has been developed for patients with kidney stone disease. This digital registry allows for monitoring and feedback from patients with kidney stone disease,

including those with ureteral stents in place [2]. Page 125. Author's contribution: 50%.

4. A study was conducted on patients with kidney stone disease who have ureteral stents in place. A patent has been obtained for the software program "Kidney Stone Disease: Patient Assistant" (RU 2017610874, registration date: January 18, 2017). This program features an automated digital registry for patients, including a section called "Stent Radar," designed to prevent the occurrence of forgotten stents [5]. Author's contribution: 25%.

5. An analysis of existing ureteral stents, complications associated with their widespread use, and prospective developments in this field has been conducted [1]. Pages 85-93. Author's contribution: 80%.

6. An analysis of the advantages and disadvantages of metallic ureteral stents has been performed [3]. Pages 129-132. Author's contribution: 25%.

7. The main factors influencing the severity of stent-associated symptoms in patients with ureteral stents have been analyzed and identified [4]. Page 30. Author's contribution: 25%.

Theses submitted for defense

1. Modern silicone ureteral stents, due to their physico-mechanical properties, induce less pronounced stent-associated symptoms compared to polyurethane stents. Their use in routine practice can significantly reduce pain syndrome in patients with urolithiasis.

2. When choosing a polyurethane stent for male patients, preference should be given to magnetic-tip ureteral stents. While demonstrating a comparable severity of stent-associated symptoms to conventional polyurethane stents, they offer clear advantages in terms of ease and safety of removal.

3. The implementation of a personalized digital registry for patients with ureteral stents, realized through the mobile application Stone MD, statistically

significantly reduces the likelihood of delayed stent removal, thereby preventing forgotten stents and associated complications.

4. The combined use of ascorbic acid and creatine effectively inhibits the crystallization of calcium phosphate and calcium oxalate salts, which are the primary components of ureteral stent encrustation. This approach is characterized by good tolerability and safety.

Testing and implementation of results in practice

Materials of the thesis were presented at the IV Congress of the Association of Young Urologists of Russia (Kazan, 2017); at the 4th meeting of the Urolithiasis Section of the European Association of Urologists - EULIS 17 (Vienna, 2017); at the VII Annual Congress of Urologists of Siberia (Kemerovo, 2018); at the IV Specialised Medical Exhibition “Health. Crimea 2019” (Republic of Crimea, 2019); at Endourocenter meeting 2019 (St. Petersburg, 2019); at Endourocenter meeting 2021 (St. Petersburg, 2021); at the V Nevsky Urological Forum (St. Petersburg, 2022); at the 6th Scientific and Practical Conference of Urologists of the North-West Federal District (St. Petersburg, 2023); at Endourocenter meeting 2023 (St. Petersburg, 2023); at the IX Scientific and Practical Conference “Urolithiasis – 2023: Russian School” (Moscow, 2023); at the VII Scientific and Practical Conference of Urologists of the North-West Federal District (St. Petersburg, 2024); at the VI Nevsky Urological Forum (St. Petersburg, 2024); at the XXIV Congress of the Russian Society of Urologists (Yekaterinburg, 2024); at the Pomor Urological Readings (Arkhangelsk, 2024).

The results of the work are implemented in the treatment, diagnostic and educational process of the Urology Research Centre of the I.P. Pavlov First St. Petersburg State Medical University, the N.I. Pirogov Clinic of High Medical Technologies of the Saint Petersburg State University and The Federal State Budgetary Institute «The Nikiforov Russian Center of Emergency and Radiation Medicine» of the Emergencies Ministry of Russia.

Publications

The dissertation research resulted in the publication of five articles in journals recommended by the Higher Attestation Commission (HAC). Additionally, one articles were published in international peer-reviewed journals classified as Q1. A certificate of state registration was obtained for a software program for electronic computing machines.

Personal contribution of the author

The author conducted experimental and clinical research, investigated the physico-mechanical properties of stent materials, developed a database, and performed statistical analysis of the collected data.

Structure and size of the dissertation

The dissertation consists of an introduction, literature review, description of materials and methods of researches, two chapters of experimental and clinical studies, summary, conclusions, practical recommendations, and a list of references.

The thesis is set out on 119 pages of typewritten text, illustrated with 23 tables and 49 figures.

The bibliographic index includes 129 works, including 10 domestic and 119 foreign publications.

Chapter 1
URETERAL STENTS IN UROLOGY: CURRENT STATUS OF THE PROBLEM (LITERATURE REVIEW)

1.1 History of development and evolution of ureteral stents

Ureteral stents are a cornerstone of urological practice, with their primary purpose being the provision of adequate drainage and splinting of the upper urinary tract. These devices are employed in various pathological conditions, including the resolution of obstructions, the healing of the ureter following trauma, and facilitating ureter localization during surgeries on pelvic and retroperitoneal organs. However, stents also have drawbacks, including urinary disturbances, pain in most patients, and urinary tract infections. These complications significantly impact patients' quality of life. A considerable number of stent-related complications are associated with the low biocompatibility of stent materials. "Ideal" stent should have the following characteristics: easy insertion and removal, adequate drainage of the upper urinary tract, high resistance to encrustation and bacterial adhesion, chemically stable in prolonged contact with urine and not compromise the patient's quality of life.

The term "stent" first appeared in the medical literature in the 19th century. It was introduced by the British dentist Charles T. Stent, who used gutta-percha combined with talc and stearin to create negative impressions of hard dental tissues for dental molds. These components allowed the material to harden and retain its shape for extended periods [27]. In urological literature, the term "stent" remained uncommon until the 1970s. Earlier publications referred to devices such as "ureteral tubes," "splints," or "catheters." In 1967, Paul D. Zimskind was the first to use silicone tubes for upper urinary tract drainage [129]. The maximum duration of stent placement in the ureter was 19 months. These stents provided effective drainage but lacked mechanisms

to prevent migration of the device. In 1976, R.P. Gibbons refined Zimskind's design, creating a silicone stent with a distal flange and pointed barbs to prevent upward migration [49]. One major drawback of this design was its increased diameter, from 7 to 11 Fr, which made placement more challenging. In 1978, R.P. Finney introduced the modern silicone stent design, featuring curls on both ends, resembling contemporary stents [52]. These stents were available in two sizes, 7 Fr and 8,5 Fr. The curled ends resembled the letter "J" in the English alphabet, leading to the term "double-J stent" (or "DJ stent") in the international medical literature. Nowadays the term "JJ stent" is also widely used. DJ stents gained widespread acceptance in urological practice worldwide and continue to be extensively used today.

1.2 Materials and design of modern ureteral stents

1.2.1 Stent materials

Silicone

The first silicone stent was produced in 1960 [23]. Despite the high biocompatibility of pure silicone stents, characterized by inertness and non-toxicity, these stents were less effective in ensuring urinary drainage from the upper urinary tract compared to stents made of other materials. This limitation was primarily due to the lower resistance of silicone stents at that time to deformation and compression under radial pressure [58]. Silicone is characterized by a high coefficient of friction, as well as significant flexibility, elasticity, and stretchability. These material properties created challenges when inserting pure silicone stents into tortuous ureters or ureters obstructed by impacted stones [47].

Modern technologies, including advancements in synthesis techniques and innovative coatings, have allowed silicone stents to eliminate their historical drawbacks while preserving their core advantages – biocompatibility and resistance

to encrustation over polyurethane stents. Using electron microscopy to measure the degree and thickness of encrustation on various polymers after prolonged exposure to artificial urine, silicone stents demonstrated 69% surface coverage by encrustation after 10 weeks, whereas all other materials exhibited 100% surface coverage over the same period [113].

Lecithin, silver citrate, and liquid silicone combined with various polymers have become the foundation for the next generation of modern silicone stents, including Silitek (Surgitek), UroGuide (Olympus), Black Silicone (Cook), and ImaJin (Coloplast). Applying a hydrophilic coating to the surface of silicone stents not only improves their glide during insertion but also reduces the severity of encrustation [121].

Polyethylene

Polyethylene was first used for ureteral stents in 1979. However, stents made from this material lost their strength after prolonged placement in the urinary tract and were prone to fragmentation and encrustation [75]. Due to low biocompatibility, the use of polyethylene stents in urology was discontinued and is no longer employed.

Polyurethane

Polyurethane stents became widely adopted in the 1980s, replacing stents made from polyethylene and silicone. Polyurethane is associated with a higher frequency of encrustation compared to silicone stents. Mineralogical analysis has shown that encrustations primarily consist of struvite, hydroxyapatite, and calcium oxalate [113]. In terms of upper urinary tract drainage, urine flow generally occurs alongside the stent rather than through its lumen [76]. "Pure" polyurethane stents had several drawbacks, including increased bacterial adhesion and urothelial laceration during prolonged use, resulting in erosions and ulceration [106]. These characteristics negatively impacted the function of the kidneys and urinary tract. The advent of modified polyurethane copolymers has helped reduce the incidence of these adverse effects.

Modified polyurethane materials (copolymer-based)

Tecoflex (PNN medical) – a radiopaque thermoplastic polyurethane (TPUs). After placement in the ureter, it becomes softer. This material is prone

to encrustation, particularly with calcium oxalate and urate stones. An example of a stent made from Tecoflex is the LithoStent (Olympus).

Percuflex (Boston scientific) – a polyurethane copolymer that becomes flexible at room temperature. Despite its improved physical properties, the rates of encrustation and bacterial adhesion remain similar to those of "pure" polyurethane stents [41].

Sof-Flex® (Cook medical) – a polymer with a low coefficient of friction. This material has a high frequency of encrustation, primarily consisting of calcium carbonate and calcium oxalate [41].

C-flex (Cook medical) – exhibits the highest resistance to radial compression among all non-metallic stents [63]. However, its major drawback is its high bacterial adhesion rate.

Metallic stents

Metallic stents were first utilized in cardiac surgery in France in 1986, when Jacques Puel implanted a metallic stent into a coronary artery. In urology, pronounced radial compression is the primary indication for the use of metallic stents, which may occur in cases such as tumor-induced compression or ureteral strictures [116, 121]. Compared to polyurethane stents, metallic stents are more effective at relieving extraureteral compression and can remain in the urinary tract for extended periods [3, 34, 94]. High migration rate is one of the main problems inherent to metallic stents. Encrustation, tumour growth into the stent and development of urothelial hyperplastic reaction occur when a metallic stent remains in the urinary tract for a long time, which reduces its ability to provide adequate ureteral patency over time [111]. Currently, several types of metallic stents are available: self-expanding, balloon-expandable, thermally expandable, and coated metallic stents.

Self-expanding (wallstent (schneider, boston scientific) and balloon-expandable metallic stents (strecker stent, boston scientific) – these are short stents that are not intended for subsequent replacement or removal. Due to the development of hyperplasticity around the stent, its ability to drain the kidney decreases markedly

over time [73]. Due to the frequent development of adverse reactions, these stents are no longer used.

Resonance stent (Cook medical) is corrosion-resistant and made from an alloy of nickel, molybdenum, cobalt, and chromium. This double-J stent lacks a lumen and consists of a tightly coiled spiral. While the Resonance stent effectively relieves ureteral obstruction, long-term studies have shown that it ceases functioning in 28% of cases, which is comparable to traditional stents [117].

Memokath 051 (PNN medical) is a thermally expandable metallic stent made from a nickel-titanium alloy (NiTinol). During insertion, the stent is expanded and shaped using saline heated to 55 °C, while cooled irrigation fluid (<10 °C) softens the material for removal. Both short-term and long-term outcomes indicate high efficacy in relieving obstructions [70]. Complications such as stent migration and encrustation occur in 1-8% of patients [69].

Uventa thermally expandable stent (Taewoong medical) is constructed from a nickel-titanium alloy with internal and external polytetrafluoroethylene (PTFE) coatings. The NiTinol inner layer provides structural support, while the PTFE coating prevents tissue ingrowth during extended placement in the urinary tract.

Allium stent (Allium medical) is a large-caliber (24-30 Fr) nickel-titanium stent. It is coated internally and externally with a biocompatible polymer to prevent tissue ingrowth. Allium was specifically designed for use in the proximal ureter. Currently, there are few publications evaluating the long-term results of this stent, however, the stent retained its function in 95% of cases, with migration occurring in only 14% of cases. No encrustation was observed during a 17-month period following placement [13, 79].

Biodegradable stents

Biodegradable stents are made from high-molecular-weight polymers such as PGA (polyglycolic acid), PLA (polylactic acid), or acrylic acid (AAc), which have high biocompatibility and are completely non-toxic. Controlling the degradation rate is the most challenging aspect of developing biodegradable stents. In an in vitro

study, a stent made of polyglycolic acid showed no encrustation or bacterial adhesion; however, its poor mechanical properties limited its further use [20].

UripreneTM (Poly-Med Inc) – a biodegradable stent composed of L-glycolic acid, polyethylene glycol, and barium sulfate. This stent has two layers: an outer hydrophobic layer with a rapid degradation rate and an inner layer that degrades more slowly, providing structural support. In in vivo studies, 9 out of 10 stents completely dissolved within 4 weeks, with fragmentation occurring in only one case [64]. Additionally, the UripreneTM stent exhibited a lower level of irritation to the ureter wall compared to conventional polymer stents [81].

Tissue engineering

Several ureteral stents have been created for experimental purposes using tissue engineering. Amiel et al. used a polyglycolic acid scaffold coated with bovine chondrocytes. The study was conducted both in vitro and in vivo and showed the ability of the new stent to resist radial compression [109].

1.2.2 Stent design

In most cases, ureteral stents have proximal and distal coils (“pigtail”), which prevent stent migration. This design was first introduced by Finney in 1978 [52]. Ureteral stents can vary in length, diameter, whether or not they have a coil at the end, and in terms of the number of side holes on the coils.

The length of the stent depends on the patient's height. Typically, stents of 24-26 cm in length and 4-6 Fr in diameter are used in adult patients. There are universal ureteral stents (multi-length), which can be used for patients of different heights (Stretch™ VL Flexima (Boston Scientific)). Larger diameter stents (10 Fr/14 Fr) are used after endopyelotomy or for ureteral stricture incisions [8].

A double-lumen stent was created to prevent compression in cases of malignant tumors causing external ureteral obstruction. In a comparative study,

Hafron et al. found that double-lumen stents had better drainage function than single-lumen stents. Additionally, the advantage of a double-lumen stent over two single-lumen stents is that it can be deployed in one procedure [82].

Spirastent (Urosurge) is a DJ stent with helical metallic ridges designed to improve urine flow and the passage of stone fragments by increasing the space between the stent and the ureteral wall. However, published research shows that a regular DJ stent is more effective [101].

Open-Pass стент (Fossa Medical) has 15 to 17 radially expanding basket traps along its length and is designed for ureteral dilation up to 20 Fr and capturing stone fragments after shockwave lithotripsy. The captured fragments can be removed along with the stent. The stent features an anti-reflux mechanism, reducing the risks of vesicoureteral reflux.

3 Fr Microstent (PercSys) is a device consisting of a 3 Fr tube with a distal intravesical coil and a unique fixation mechanism in the proximal part. This mechanism involves a film with holes, which, when activated, secures the stent. Once the stent is placed above the stone level, the stent is secured using an integrated guidewire [39]. Given the small diameter of the stent, this may theoretically facilitate the passage of stones through the ureter. The urine flow rates with the 3 Fr Microstent are better than those of a DJ stent of the same diameter.

Grooved stents (LithoStent, Olympus) show higher overall and extraluminal urine flow compared to regular DJ stents.

URIGLOW® (RocketMedical) – is a luminescent stent used to facilitate ureteral visualization during surgical procedures in the retroperitoneal space or pelvic organs.

1.2.3 Surface coating of stents

The prolonged presence of DJ stents in the urinary tract leads to a number of complications that significantly affect the quality of life of patients.

Numerous studies have focused on the development of new designs, materials, and coatings for stents. These innovations are necessary to enhance biocompatibility and, consequently, reduce the risk of complications. Drug-coated stents consist of three components: a base, a polymer coating with controlled drug release, and an active pharmaceutical component.

Hydrophilic coating

Hydrogels consist of hydrophilic polymers that absorb water, thereby increasing the elasticity of the stent and reducing surface friction. John et al. demonstrated the effectiveness of hydrogel-coated stents with antibacterial coverage in vitro [16]. When comparing hydrophilic and hydrophobic stents with antibacterial coatings (ciprofloxacin, gentamicin, or cefazolin), hydrogel-coated stents significantly retained antibacterial activity for a longer time [16]. The Bard Inlay® stent is a stent with a polyvinylpyrrolidone (PVP) hydrophilic coating. According to Tunney and Gorman, the PVP coating makes the stent smoother compared to polyurethane and silicone stents without coating. PVP-coated stents are less prone to bacterial adhesion [114].

Phosphorylcholine coating

Phosphorylcholine is a component of the phospholipids in the cell membranes of the eye and erythrocytes, and it is characterized by high hydrophilicity. In a study by Stickler et al., a phosphorylcholine-coated ureteral stent was implanted in 44 patients for 12 weeks. The results showed that these stents were less susceptible to encrustation and bacterial adhesion compared to the stents in the control group [102].

Diamond-like carbon coating (DLC)

Another method of improving biocompatibility is the use of a diamond-like carbon (DLC) coating. Polyurethane coated with a 100-200 nm layer of DLC has a lower coefficient of friction and is more resistant to encrustation [48].

Glycosaminoglycan coating

Glycosaminoglycans, along with heparin, are inhibitors of calcium oxalate crystal growth. In vivo studies have shown that stents coated with heparin had a lower rate of encrustation compared to uncoated stents, even with prolonged stent placement [93].

Antibacterial coating

Until recently, the use of stents with antibacterial coatings was in the testing phase, during which it was established that the combination of antibiotic therapy and stents with antibacterial coatings reduces the formation of biofilms [43].

Triclosan coating

Triclosan is commonly used in the perfume industry for the production of soaps and deodorants. It is an organic compound with broad-spectrum antibacterial and antifungal activity. In both in vivo and in vitro studies, ureteral stents coated with triclosan (Triumph®, Boston Scientific) were less prone to bacterial adhesion compared to conventional stents [112]. Additionally, there was a noted reduction in the intensity of stent-associated symptoms when using the Triumph® stent over a short period of time [108].

Coating with drugs with antiproliferative activity

Paclitaxel, an alkaloid derived from the bark of the Pacific yew tree (Taxus brevifolia), has cytotoxic antimitotic activity. Liatsikos et al. used a paclitaxel-coated stent (TAXUS, Boston Scientific) in vivo in the ureter of a pig [17]. A stent coated with paclitaxel was placed in one ureter of the animal, while a metallic stent (R-Stent, Orbus Medical Technologies) was placed in the other. After three weeks, most of the metallic stents were occluded due to urothelial hyperplasia. The development of inflammatory reactions and hyperplastic processes in the ureter where the drug-coated stent was deployed was minimal.

Rapamycin, an immunosuppressant widely used in transplantation, has been shown in experimental studies to suppress the proliferation of fibroblasts. In an in vitro experiment, a rapamycin-coated stent significantly inhibited fibroblast proliferation. In vivo results demonstrated a reduction in the thickness of the connective tissue component in the lamina propria of the rat ureter wall. These results suggest that rapamycin-coated stents may be effective in preventing the development of ureteral strictures following surgical interventions [62].

Unfortunately, current stent coatings are unable to fully eliminate undesirable phenomena such as encrustation, infections, and stent-associated symptoms. It is also

worth noting that drug-coated stents are generally more expensive. Further research is definitely required to enhance the biocompatibility of ureteral stents.

1.3 Complications associated with the use of ureteral stents

1.3.1 Encrustation of ureteral stents

Encrustation is the process of crystallization and deposition of salts onto ureteral stents. A heavily encrusted stent can lead to urinary tract obstruction, reduced kidney function, exacerbation, and progression of infection. Additionally, an encrusted stent loses its tensile strength, which can cause it to fragment when removed from the urinary tract. In cases of urinary stones, the composition of the salts deposited on the stent is most commonly similar to that of the stone: ammonium-magnesium phosphate (struvite), calcium phosphate, calcium oxalate, uric acid salts [77].

Risk factors for encrustation of ureteral stents

Duration of stenting

The primary factor in salt deposition onto the stent is its duration within the urinary tract [15, 120]. About 50% of patients undergoing long-term stenting of the ureter experience this issue [102]. Matthew F. Bultitude et al. found that nearly 43% of ureteral stents become encrusted within 4 months of placement, and patients with a history of stent encrustation were more likely to experience recurrence at earlier intervals [74]. According to a study conducted in 1991 by el-Faqih et al., 9% of polyurethane stents were encrusted within 6 weeks after placement, 48% within 6-12 weeks, and 77% after 12 weeks, respectively [88].

Bacterial composition of urine

The bacterial composition of urine can play a crucial role in the process of stent encrustation. M.M. Tunney et al. found that 90% of ureteral stents retrieved from the

urinary tract were colonized with bacteria, and 55% of these already had bacterial biofilms on their surface [33]. Analysis of bacterial colonization conducted by Shabeena et al. demonstrated a linear relationship between the duration of stenting and the degree of stent colonization with bacteria [30]. This is clearly illustrated in figure 1.

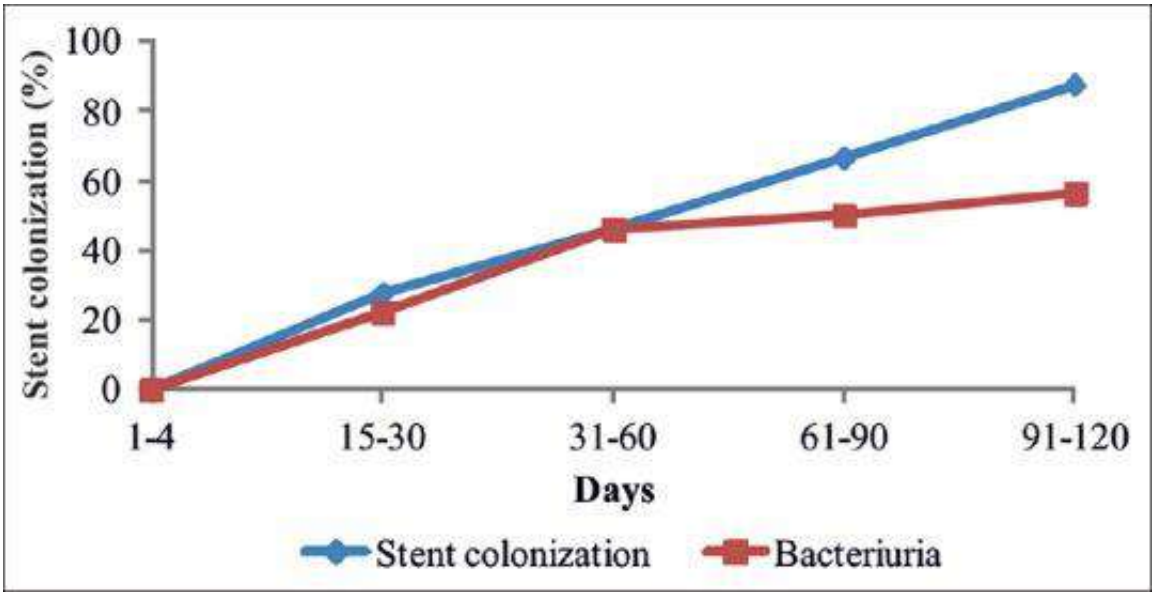


Figure 1 – Relationship between the degree of bacterial colonization of the stent surface and time. adapted from [30]

However, it is not entirely clear how the biofilm formed on the surface of the stent leads to mineral precipitation. Recurring urinary tract infections, diabetes mellitus, chronic kidney disease, and female sex are the main risk factors for stent bacterial colonization [50]. Pregnant women are also at risk. This is likely due to the development of absorptive hypercalciuria and hyperuricosuria during pregnancy, which necessitates more frequent stent changes every 4-6 weeks to avoid stent encrustation [46].

Influence of stent design on encrustation

It is important to consider that the encrustation process may depend on the stent design or, in other words, its physical parameters. Kawahara et al., after studying 330 ureteral stents, reported that the length and inner diameter of the stent

were not associated with the degree of encrustation. However, the external size of the stent plays a crucial role: stents with a diameter of 6 Fr or smaller have a higher rate of encrustation compared to stents with a diameter of 7 Fr or larger [120].

Mechanism of encrustation of ureteral stents

After kidney drainage with a stent, three scenarios may occur: the surface of the stent may remain unchanged, a bacterial biofilm may form on the surface, increasing the risk of urosepsis, or encrustation may develop. The mechanism of stent encrustation is illustrated in figure 2.

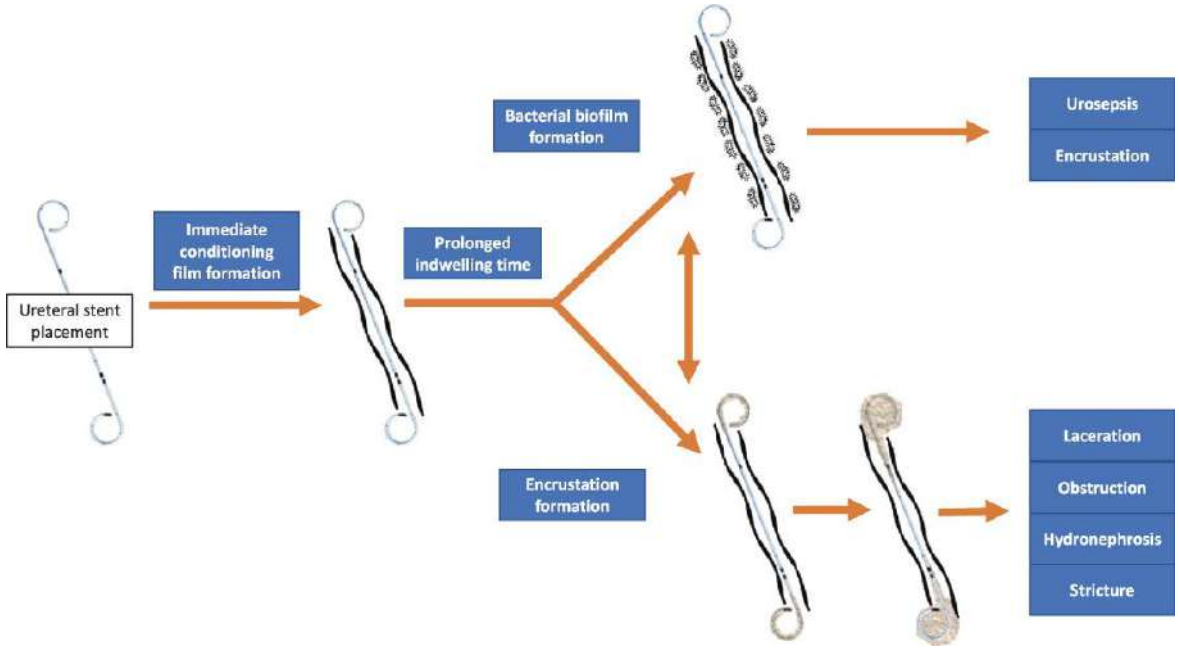


Figure 2 – Mechanism of encrustation of ureteral stents.
Adapted from [119]

Immediately after the stent is placed in the urinary tract, various organic molecules, such as glycoproteins and polysaccharides, are deposited on the polymer surface, leading to the formation of a conditioning film [31].

The second step, after the conditioning film forms, involves the adsorption of organic molecules such as fibrinogen, albumin, and collagen on the surface of the stent, which enables the further development of a bacterial biofilm [41]. A microphotograph of the conditioning film on the surface of the ureteral stent is shown in figure 3.

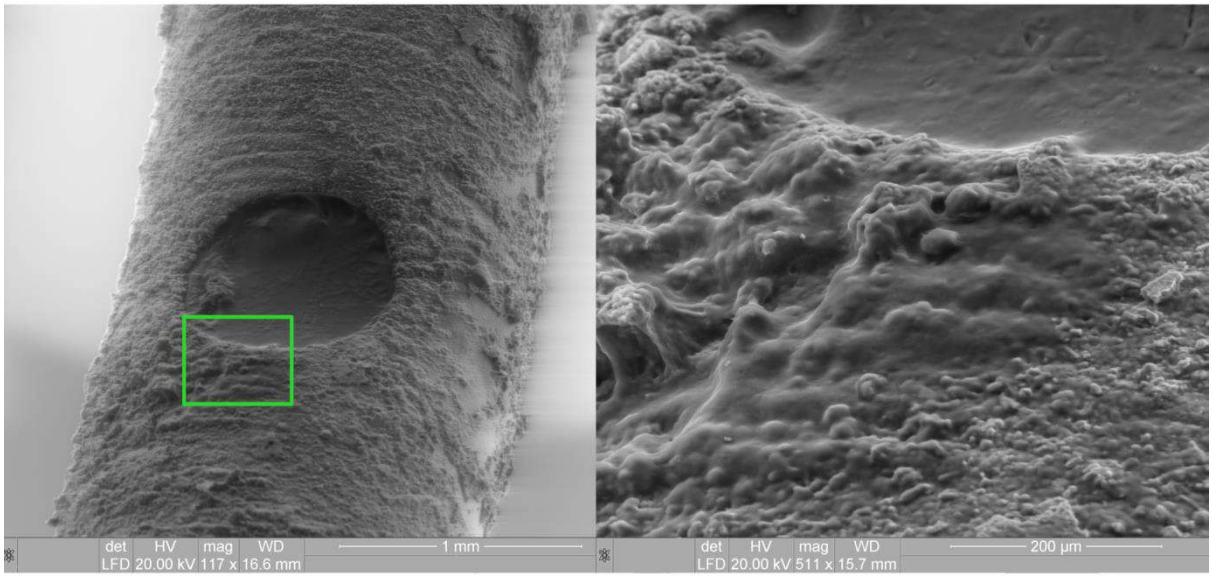


Figure 3 – Electron microscopy of a ureteral stent sample,
on the surface of which a conditioning film has formed.
Magnification 117^{x} and 511^{x}. Electron microscope QUANTA™ 3D
(FEI Company (USA)). "Source: Author's own work"

The mechanism of bacterial attachment to the surface of the conditioning film is not yet fully understood. It is known that urine pH, ionic and electrostatic forces, as well as hydrophobic interactions, play an important role in this process [32]. Research on the proteins involved in the formation of urinary stent encrustations has shown that in most cases, five proteins are always present: alpha-1-antitrypsin, kappa immunoglobulin, heavy chains of immunoglobulin G1, as well as histones H2b and H3a [68]. Several mechanisms of bacterial attachment to the stent surface exist. For example, the surface of *Klebsiella pneumoniae* and *Escherichia coli* cells contains type 3 fimbriae, which are virulence factors for these pathogens and are involved in the adhesion of bacteria to a substrate or other cells [59, 96]. Other bacteria may secrete a specific extracellular polymeric matrix, which participates in biofilm formation, a characteristic of *Pseudomonas aeruginosa* [85]. Figure 4 shows a microphotograph of the bacterial biofilm on the surface of the stent.

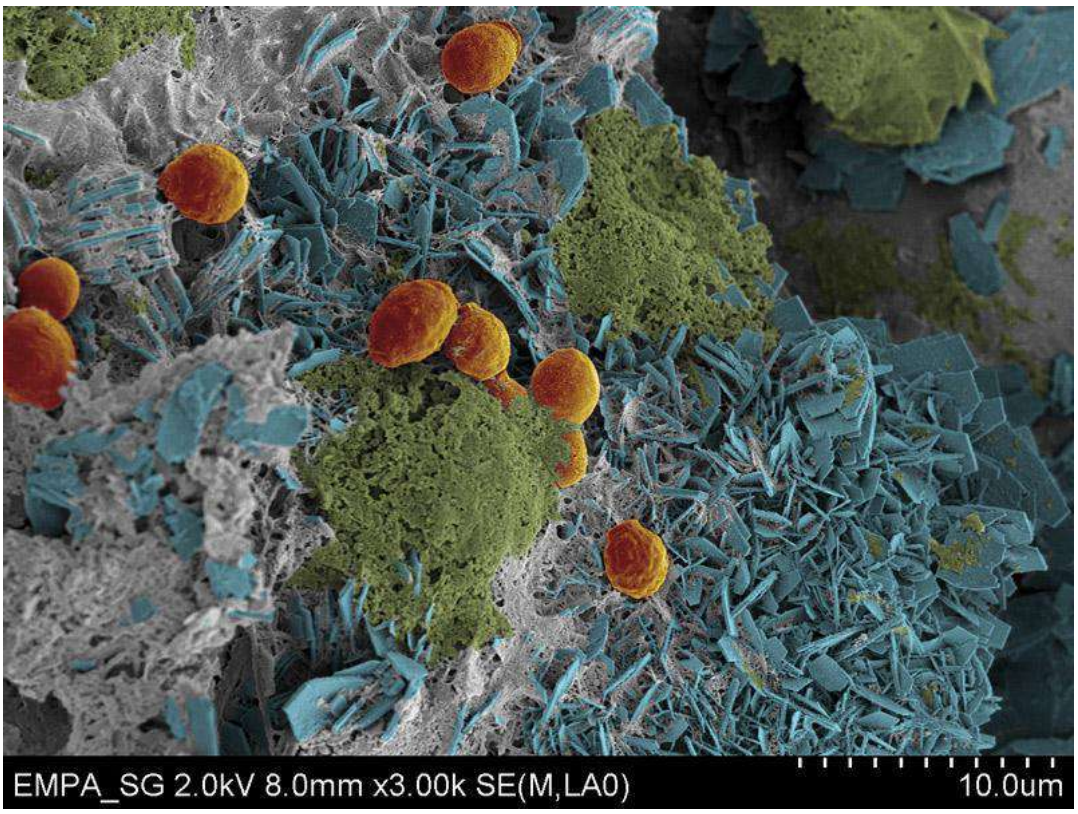


Figure 4 – Electron microphotograph of the biofilm on the surface of a urinary stent. Microorganisms are highlighted in orange, carbonate-apatite crystals in blue, and amorphous crystal-like structures in green. Adapted from [26]

Another method of formation of encrustations should be noted, which is associated with the activity of the enzyme urease produced by certain pathogens. Urease-producing bacteria, through their activity, increase the pH of urine and can cause the formation of encrustations consisting of struvite, carbonate-apatite, or ammonium urate. Figure 5 shows an encrusted stent that had been in the urinary tract of a patient for 8 weeks with the presence of *Proteus mirabilis* in the urine.

The pathogenesis of ureteral stent encrustation caused by the activity of urease-producing bacteria is illustrated in figure 6.

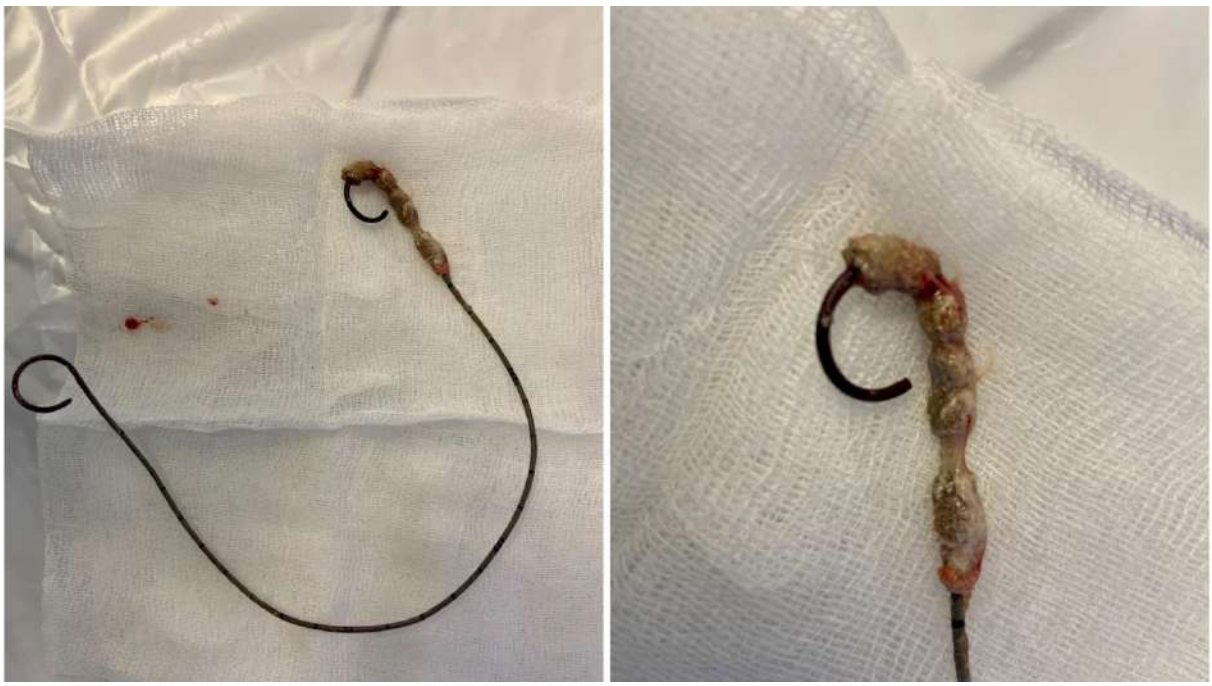


Figure 5 – Severe encrustation of the distal coil of a ureteral stent in a patient, caused by the presence of *proteus mirabilis* in the urine. "Source: Author's own work"

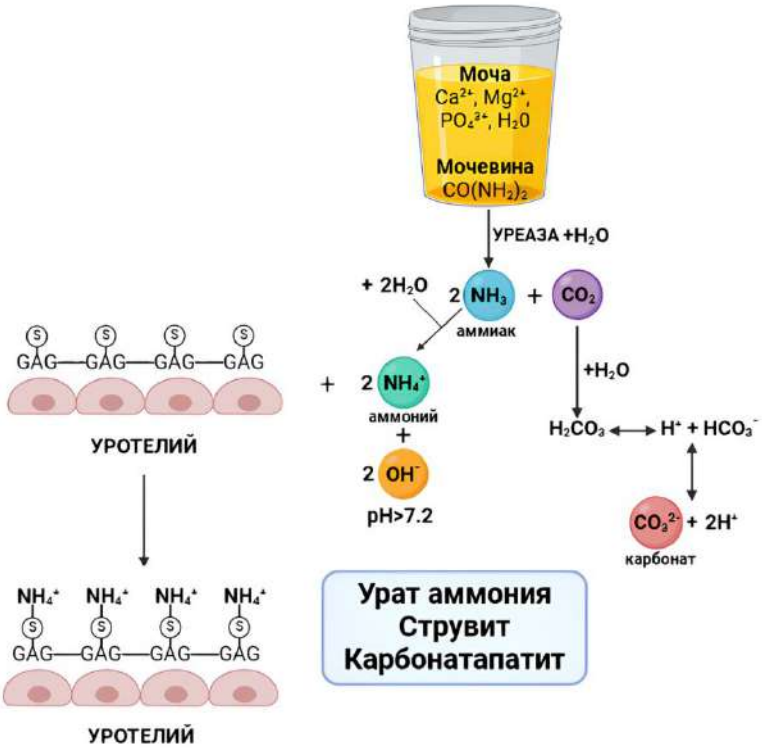


Figure 6 – Diagram of stent encrustation formation associated with the activity of urease-producing bacteria. Adapted from [57]

Recent studies have highlighted that the presence of bacteria in urine is not a prerequisite for stent encrustation, as this process can occur spontaneously. The conditioning film, combined with a urine pH >6, can induce the precipitation of calcium and magnesium phosphates, leading to the formation of brushite, hydroxyapatite, and magnesium ammonium phosphate crystals on the polymer surface [12]. Consequently, urinary supersaturation with calcium, oxalate, phosphate, and uric acid, along with an appropriate urine pH, plays a critical role in the pathogenesis of stent encrustation. The encrustation of a ureteral stent in a patient with hypercalciuria and a urine pH of 7,3, along with its microphotograph, is shown in figure 7.

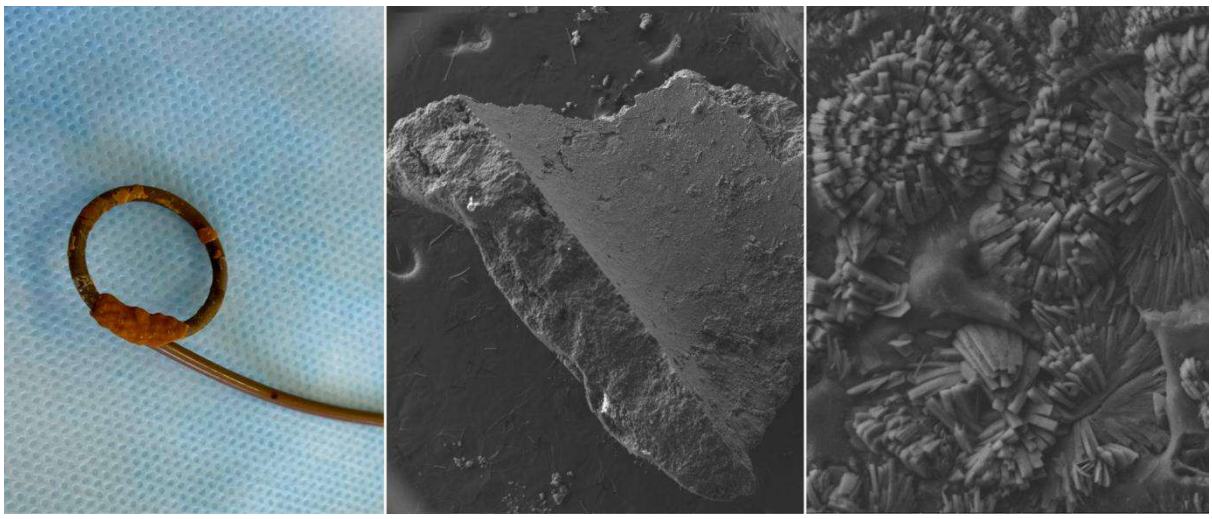


Figure 7 – Encrusted distal end of a stent. electron microscopy of prismatic crystal aggregates, morphologically and chemically corresponding to whewellite ($CaC_2O_4 \times H_2O$) and weddellite ($CaC_2O_4 \times 2H_2O$). Magnification 33^x and 3668^x. Electron microscope QUANTA™ 3D (FEI Company (USA)).
"Source: Author’s own work"

Prevention of ureteral stent encrustation

Pharmacological prevention of stent encrustation

It is well established that urine supersaturation with lithogenic components, combined with an alkaline pH, plays a critical role in the pathogenesis of stent

encrustation. Therefore, modifying the lithogenic properties of urine can help prevent encrustation on ureteral stents. Urine acidification and the use of crystallization inhibitors are effective strategies in addressing this issue.

In 1999, A. Hesse and D. Heimbach detailed the physicochemical process of phosphate stone formation in the urinary tract, emphasizing that urine pH is a key factor in orthophosphoric acid dissociation. A pH above 7, combined with calcium and phosphate supersaturation, leads to the rapid formation of brushite and apatite crystals [57]. Pharmacological management of urine pH is an effective method for the metaphylaxis of infectious urolithiasis recurrence and is included in the clinical guidelines of the Russian Society of Urology and the European Association of Urology [67]. Clinically, various drugs, such as ascorbic acid, L-methionine, ammonium chloride, ammonium sulfate, and methenamine, are used to lower urine pH [128]. However, methenamine, ammonium chloride, and ammonium sulfate are not registered for use in Russia, making their clinical application impossible. Yasser A. Noureldin et al. conducted a study where participants received ascorbic acid at a dose of 1000 mg/day, which resulted in pronounced urine acidification in all patients [66]. Notably, ascorbic acid has not previously been used for the prevention of ureteral stent encrustation.

Urine contains various substances that inhibit calcium crystallization, including magnesium, citrate, glycosaminoglycans, Tamm-Horsfall glycoprotein, nephrocalcin, osteopontin, and pyrophosphate [97]. Pyrophosphate, in particular, can prevent the nucleation of brushite and hydroxyapatite crystals in urine. This process involves the interaction of the hydroxyl group of brushite with the phosphate group of pyrophosphates [56]. Certain foods contain phytate (inositol phosphate), an organic pyrophosphate that can chelate calcium in urine, thus preventing stone formation [124]. In their in vitro experiment, Grases et al. found that the presence of phytate in artificial urine at a concentration of 1,5 mg/L inhibited the formation of calcium oxalate monohydrate crystals on the surface of hydroxyapatite crystals [86]. Creatine, a widely distributed non-protein amino acid (PubChem CID: 586) synthesized primarily in the liver, kidneys, and pancreas, is a potential source of inorganic

phosphate and pyrophosphate. In cells, creatine serves as an important source of ATP, and during its hydrolysis, pyrophosphate anion $[P_2O_7]^{4-}$ is generated [78]. Creatine can diffuse from cells and be excreted in urine (1,7% of its total content in the body), where it spontaneously degrades into creatinine via a monomolecular non-enzymatic reaction dependent on temperature and pH, resulting in inorganic phosphate anion formation [42]. Thus, creatine may potentially be used as an inhibitor of ureteral stent encrustation.

Material and coating of ureteral stents

The material and coating of a stent significantly impact its ability to resist encrustation. Ureteral stents made of silicone are less prone to encrustation than others. Bouzidi et al. reported that silicone stents are 25% less likely to undergo bacterial colonization and 35% less prone to encrustation compared to polyurethane stents, making them more favorable for clinical use [29]. An alternative to silicone is modified polyurethane. Leading companies specializing in ureteral stent development have created various polyurethane copolymers to reduce encrustation rates (Percuflex (Boston Scientific); Sof-Flex® (Cook Medical); PercuShield (Boston Scientific)). Unfortunately, their formulations are proprietary, and information is limited in open sources.

Another approach to reducing deposits on stents involves coating their surface with materials that suppress bacterial adhesion or mineral precipitation. The focus has been on developing biomaterials and stent coatings incorporating antibacterial agents and biocides to inhibit bacterial cell adhesion [102]. Multanen et al. were the first to demonstrate that coating a stent with silver nitrate and ofloxacin reduces encrustation and accelerates the degradation of biodegradable stents made from poly-L-lactic acid [25]. Pentosan polysulfate (PPS), a semi-synthetic glycosaminoglycan, inhibits calcium oxalate crystallization. When comparing silicone discs with and without PPS coating placed in the rabbit bladder for 50 days, PPS significantly reduced material encrustation [84]. Laube et al. deployed DLC stents (diamond-like carbon coating) in 10 patients prone to encrustation. The results showed a significant reduction in encrustation and biofilm formation compared to standard stents previously used in these patients [35].

1.3.2 Stent migration

Stent migration occurs in 4% of cases [28]. The distal and proximal loops of the stent are designed to prevent migration. The primary risk factor for migration is an improperly selected stent length. Correct placement of the stent and monitoring the positioning of its loops are the simplest measures to reduce the likelihood of migration.

1.3.3 Hematuria

Microhematuria develops in most patients with ureteral stents. Macrohematuria occurs in 8% of cases, is associated with urothelial damage, and typically resolves spontaneously after stent removal [60].

1.4 Adverse effects of ureteral stents on patients' quality of life

The term "stent-associated symptoms" (SAS) encompasses irritative symptoms, suprapubic discomfort, flank pain on the side of the deployed stent, and hematuria [4, 44, 118]. Adverse effects related to stent placement occur in nearly 80% of cases [65]. Several questionnaires are used to assess SAS, including the Ureteric Stent Symptom Questionnaire (USSQ). This tool evaluates lower urinary tract symptoms, pain, the impact of stents on sexual function, and overall quality of life. A validated Russian-language version of the USSQ is available and recommended for routine clinical practice in Russia [126].

Pharmacological management of stent-associated symptoms

Bladder wall irritation can result in unbearable urinary urgency, frequent urination, hematuria, and dull suprapubic pain. M-anticholinergics and a1-

adrenoceptor blockers can be used to manage irritative symptoms, either as monotherapy or in combination [105]. However, according to Sivalingam et al., no statistically significant differences were observed in patients receiving a combination of tamsulosin and tolterodine for SAS [36]. Considering the side effects of these medications, a patient may start with one, such as an a1-blocker, and add an M-anticholinergic if the initial therapy proves ineffective. Other drugs under investigation for alleviating SAS include selective β3-adrenoceptor agonists (mirabegron) and phosphodiesterase type 5 inhibitors (sildenafil citrate) [11, 37]. Intravesical therapy may serve as an alternative for treating SAS. In a study by Beiko, intravesical administration of oxybutynin, ketorolac, and lidocaine was used to reduce irritative symptoms after upper urinary tract stenting. Among these drugs, only ketorolac demonstrated significant relief of pain and dysuria one hour after stent placement [38]. However, it is important to consider the potential side effects of nonsteroidal analgesics.

Risk factors for stent-associated symptoms

A prospective study in 2011 involving 86 patients with DJ ureteral stents assessed SAS using the USSQ [90]. Analysis revealed that male gender, high body mass index, excessive stent length, and contact between the distal loop of the stent and the contralateral bladder wall were associated with increased use of nonsteroidal analgesics and M-anticholinergics. Multivariate analysis showed that improper positioning of the distal loop, particularly crossing the midline of the bladder, affected most USSQ domains at 7- and 28-days post-stenting. However, patient height did not significantly influence SAS severity. Visualization of the distal loop contacting the opposite bladder wall can identify patients at risk for SAS. If this is noted during cystoscopy or fluoroscopy, the stent should be repositioned. In summary, the primary risk factor for SAS is an overly long distal stent end located contralaterally in the bladder. Other risk factors include bacteriuria at the time of stenting and placement of the proximal stent end in the calyces rather than the renal pelvis [99].

The impact of stent design on stent-associated symptoms

To minimize stent-associated symptoms and improve patients' quality of life, ureteral stents with varying stiffness and soft bladder ends have been developed. The Polaris™Ultra stent (Boston Scientific) features a firmer proximal segment and a softer bladder end to reduce irritative symptoms. Theoretically, removing the distal stent loop could decrease irritative symptoms. The Polaris™Loop sten (Boston Scientific) replaces the distal loop with two soft Percuflex material loops. Studies by Lingeman and Taguchi found that patients with the Polaris™ Loop stent reported fewer irritative symptoms compared to those with standard DJ stents [18]. In 2015, Vogt et al. created a customized ureteral stent by replacing the distal loop with surgical thread positioned in the bladder during stent placement. This stent modification reduced SAS severity [127]. A commercially available alternative is the JFil stent (ROCAMED), which lacks not only a bladder loop but also a distal ureteral segment, reducing the likelihood of vesicoureteral reflux. A randomized study by Bosio et al. demonstrated that the JFil stent significantly decreased SAS, particularly lower urinary tract symptoms and pain, compared to conventional DJ stents [87].

Beyond stent design and shape, the material used to manufacture ureteral stents also affects stent-associated symptoms severity [6].

Important directions for improving patients' quality of life include addressing the adverse effects associated with stent placement. This involves refining pharmacological strategies for managing stent-associated symptoms. Additionally, advancing stent design and materials is essential for enhancing their functionality and biocompatibility. Collectively, these measures will contribute to reducing SAS and improving the overall quality of life for patients.

1.5 "Forgotten" ureteral stents and associated complications

“Forgotten” ureteral stents (FUS) represent a rare but potentially serious issue, often leading to significant complications. These include stent encrustation and

fragmentation, urinary tract infections, and even sepsis, along with impaired kidney function [54]. Figure 8 depicts a "forgotten" ureteral stent that remained in the urinary tract of a female patient for seven years. Arrows indicate severe encrustation of both the distal and proximal coils. This encrustation caused obstruction of the upper urinary tract, resulting in hydronephrosis and a decline in the function of the right kidney.

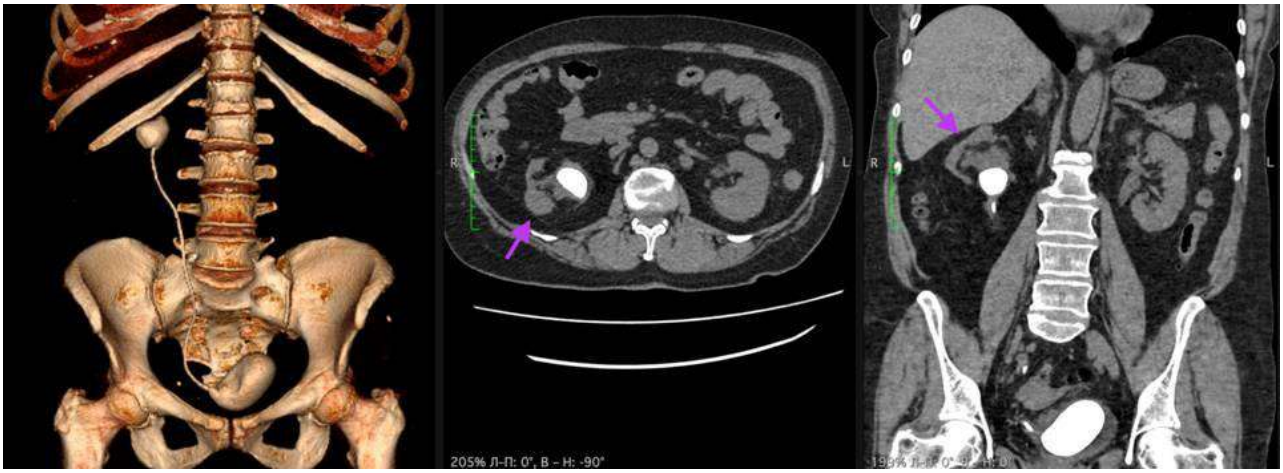


Figure 8 – A "forgotten" ureteral stent in the right kidney.
"Source: Author’s own work"

The literature reports that the incidence of forgotten ureteral stents (FUS) varies widely across studies, ranging from 3% to 51% of all stents deployed [91, 92, 122].

Risk factors for complications associated with "forgotten" stents

The maximum duration a stent can remain in the urinary tract depends on the manufacturer's guidelines, which are based on the stent's material and coating. For instance, the Universa®Soft polyurethane stent (COOK MEDICAL, USA) is approved for up to 3 months, whereas the Black Silicone ureteral stent (COOK MEDICAL, USA) is approved for up to 12 months. Lin et al. defined forgotten stents as those not removed or replaced within 14 days after the recommended maximum period of use [107].

Currently, there is no consensus among urologists regarding the optimal timing for stent removal or the timeline for encrustation. However, the 2024 clinical guidelines of the European Association of Urology recommend stent removal within

three weeks of placement. Prolonged stent retention increases the risk of infection from 6% to 40% [40]. The primary risk factor for complications related to "forgotten" ureteral stents remains the duration the stent has been in situ [88]. Beysens and Tailly noted that ureteroscopy performed on patients with stents retained for over 30 days carries a higher risk of postoperative sepsis [24]. Similarly, Somani et al. found that the risk of acute febrile postoperative urinary tract infections increases from 6% to 14% when stents remain in the urinary tract for more than two months [89].

Causes of "forgotten" stents

Factors contributing to "forgotten" stents include low social adaptation, cognitive impairments, non-adherence to medical recommendations, and good tolerance of the stent without significant stent-associated symptoms [80, 100]. Therefore, developing and implementing preventive measures is a critical component of modern healthcare strategies. Before discharge, patients should be thoroughly informed about the necessity of timely stent removal [10]. Efforts should focus not only on minimizing unnecessary stent placements and reducing retention time but also on devising strategies to prevent "forgotten" stents.

Strategies to address "forgotten" stents

Various monitoring and follow-up systems have been introduced to prevent "forgotten" stents, falling into two main categories. The first category includes manual logbooks, where healthcare staff record patient details and stent removal dates. However, this approach has proven inefficient, as 25,1% of patients failed to have their stents removed on time due to staff errors [122]. The second category involves automated and digital registries, which have shown considerable efficacy in managing stented patients [2, 5]. Modern technologies can track and schedule stent removal or replacement dates while sending automated push notifications and SMS reminders. In 1997, Ather et al. implemented an automated computer program in routine practice. Data analysis before and after the system's introduction revealed that the rate of "forgotten" stents decreased from 12,5% to 1,2% within the first year of use [19].

The development of biodegradable stents could theoretically eliminate the need for cystoscopic removal and address the issue of "forgotten" stents. To date, only one study has investigated the use of biodegradable stents in humans. According to Lingeman et al., 89% of patients were satisfied with biodegradable stents, and 96,6% experienced complete stent dissolution within 90 days [125].

Management of patients with "forgotten" stents

In some cases, pronounced encrustation can form on the surface of a FUS, making its removal a complex surgical challenge that requires a multimodal approach. Depending on the degree of encrustation, procedures such as percutaneous nephrolithotripsy, retrograde ureterolithotripsy, or transurethral cystolithotripsy may be required to remove the stent. According to scientific data, up to 59% of patients with FUS require combined surgical interventions [53]. This, in turn, leads to significant economic losses. A study by Sancaktutar et al. found that the cost of removing a FUS is, on average, 6,9 times (1,8-21) higher than the cost of removing a routine stent [110].

"Forgotten" stents pose a substantial threat to patient safety and have serious implications for healthcare economics.

1.6 Ureteral stent removal

In recent years, advances in science and technology have significantly improved the design, materials, and coatings of ureteral stents, leading to a reduction in stent-associated symptoms and better biocompatibility [51]. Additionally, the evolution of ureteral stents includes innovations in stent removal methods, such as the use of extraction loops, magnetic retrievers, and spiral-ended devices in women [14, 83, 98, 121]. In most cases, ureteral stents are removed via cystoscopy, which typically causes pain, hematuria, and increased urinary frequency in 64% of patients, particularly among men [103].

A notable advantage of stents with extraction loops is the possibility of removal at home by the patient or healthcare worker by pulling the external thread. The thread, which exits through the urethral meatus and is secured with adhesive tape to the pubic area or penis, poses a high risk of stent migration. Women are four times more likely than men to experience stent dislocation due to anatomical differences and specific genital hygiene practices [95]. Nonetheless, many patients report significant discomfort during self-removal. One study involving 68 patients who underwent ureteroscopy compared stents with and without extraction threads. No statistically significant differences in stent-associated symptoms, as measured by the USSQ, were found between patients with standard DJ stents and those with stents equipped with extraction loops [22, 123].

The development of stent removal methods that eliminate the need for cystoscopy, anesthesia, and radiological control remains a pressing issue in modern urology. A breakthrough in endourology was the introduction of stents with magnets on the bladder end. Magnetip, a silicone DJ stent first described by Macaluso et al. in 1987, served as the precursor to contemporary magnetic stents. Using a specialized retriever, the authors successfully removed magnetic stents in 86% of cases [71]. Taylor et al. demonstrated the feasibility of removing magnetic stents without endoscopic equipment. Retrospective analysis showed successful stent removal in 29 out of 30 patients, with the sole failure attributed to significant median prostatic lobe enlargement [104]. Similarly, Rassweiler et al. reported an unsuccessful removal attempt due to prostate adenoma [72], suggesting that prostate adenoma may be a risk factor for unsuccessful stent removal. Pronounced encrustation of the magnet on the distal end of the stent may also impede successful retrieval [45].

An innovative and straightforward method for stent removal in women under ultrasound guidance was proposed by Gadzhiev et al. [115]. Using a spiral device (hook) inserted into the bladder, the stent's loop is captured and subsequently removed under ultrasound control. This method proved to be more comfortable for patients than classical cystoscopic removal and avoided additional costs associated

with endoscopic equipment. As it does not involve ionizing radiation, this technique is suitable for pregnant patients.

Conclusion

Ureteral stents have a rich history of use. Since their introduction, they have undergone numerous stages of evolution and modernization. However, despite the significant technological advancements, there is still a major issue related to their widespread use: despite the tremendous progress, ureteral stenting is associated with several complications. Stent-associated symptoms, encrustation, and bacterial infections remain unresolved issues in the creation of the "ideal" stent. In contemporary urology, key challenges include not only optimizing and finding new methods of stent removal but also ensuring their timely removal. The ongoing development of new materials, coatings, and designs will lead to the further refinement of this indispensable device, the ureteral stent. Therefore, further research and development in this field are necessary to achieve higher standards in urology and improve the quality of life for patients.

Chapter 2
MATERIAL AND METHODS OF RESEARCH

2.1 Organization, size, and general procedure of the dissertation research

The clinical part of the study involved 378 patients with ureteral stents who underwent surgical treatment in the Department of Urology at Academician I.P. Pavlov First St. Petersburg State Medical University. Additionally, 10 healthy volunteers participated in the research. The clinical research was conducted from June 2019 to April 2024. The detailed patient flow is presented in the diagram (figure 9).

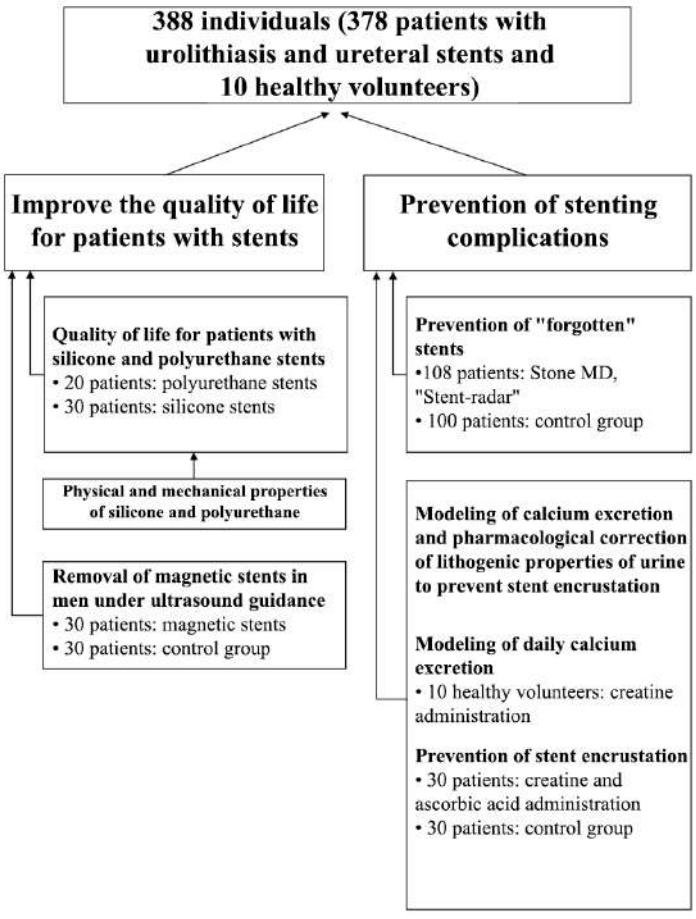


Figure 9 – Diagram of patient group formation

Experimental part of the study, aimed at examining surface and physicochemical properties, was conducted in the scientific laboratory at the Department of "Equipment and Robotics for Plastic Processing" of Saint Petersburg State Institute of Technology (Technical University) under the supervision of Professor, Doctor of Technical Sciences V.P. Britov, as well as at the "Microscopy and Microanalysis" resource center of Saint Petersburg State University under the supervision of Deputy Director, Candidate of Geological and Mineralogical Sciences S.Y. Janson, with the direct participation of the author.

Preoperative examination included the collection of complaints and medical history, as well as the life history. The diagnosis was made after performing a physical examination and multidetector computed tomography of the urinary tract without contrast. Before being admitted to the urology department, all patients underwent necessary standard preoperative testing, which included:

- comprehensive clinical blood test;
- general urine analysis;
- urine culture with antibiotic sensitivity testing;
- coagulation profile: activated partial thromboplastin time, prothrombin index, international normalized ratio, fibrinogen;
- biochemical blood test: total protein, creatinine, total bilirubin, alanine aminotransferase, aspartate aminotransferase, glucose, ionized calcium;
- electrocardiogram;
- blood tests for hepatitis B and C, syphilis, and human immunodeficiency virus;
- chest X-ray;
- consultation with a general practitioner.

If indicated, additional tests were performed (echocardiography, Holter monitoring, duplex scanning of lower limb veins, fibrogastroduodenoscopy, 24-hour urine biochemical testing), as well as consultations with related specialists (cardiologist, nephrologist).

2.2 Evaluation of in vitro surface and physicomechanical properties of stent polymers (experimental study)

The hardness of polymers used for manufacturing ureteral stents ranges from 30 to 50 ShA [61]. For the experiment, samples of polymers with similar hardness values were selected. The study investigated samples of thermoplastic polyurethane (PU) and silicone rubber with varying degrees of hardness. Detailed characteristics of the studied samples are presented in table 1.

Table 1 – Characteristics of the studied polymer samples

№	Main component of the sample	Hardness
1	Silicone	30 ShA
2	Silicone	50 ShA
3	PU	45 ShA
4	PU	50 ShA

To produce a polyurethane plate, a mixture of prepolymer and polyol components from "Era Polymers" – ERACAST RT – was used. The main properties of the components for 45 and 50 ShA polyurethane are presented in table 2.

The PU samples were prepared via cold pressing using a mold and plate, with the mixture pre-vacuumed. Silicone samples were prepared via hot pressing at a temperature of 125 °C under pressure, also using a mold and plate. The obtained polymer samples were then studied in deionized water (density ρ_0=1,0 g/cm^3, refractive index n_0=1,333, dynamic viscosity η_0=1,0 cP) и глицерине (ρ_0=1,26 г/см^3, $n_{0=}$1,47352, $\eta_{0=}$1,41 Pa·s).

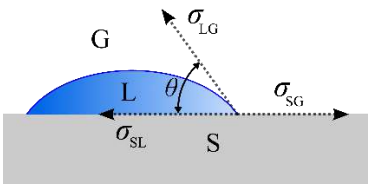
To study the surface and physical-mechanical properties of the obtained polymers, the following parameters were determined: the contact angle, moisture absorption, material hardness, elastic modulus, and the depth of liquid penetration through the material's surface.

Table 2 – Main properties of polyurethane sample components

Material	Properties of the components	Process parameters
PU 45 ShA	The prepolymer is an amber liquid with a viscosity of 4700-5300 cP and a density of 1,02 kg/cm^3 at a temperature of 25 °C. The polyol is a light straw-colored liquid with a viscosity of 240-440 cP and a density of 1,02 kg/cm³ at a temperature of 25 °C.	The prepolymer and polyol were mixed by weight in a ratio of 100:100 g.
PU 50 ShA	The prepolymer is an amber liquid with a viscosity of 4700-5300 cP and a density of 1,02 kg/cm^3 at a temperature of 25 °C. The polyol is a light straw-colored liquid with a viscosity of 120-270 cP and a density of 1,02 kg/cm³ at a temperature of 25 °C.	The prepolymer and polyol were mixed by weight in a ratio of 100:48 g.

Wetting

Wetting is a surface phenomenon involving the interaction of a solid with a liquid in the simultaneous presence of three immiscible phases. The measure of wetting is the equilibrium contact angle θ, defined as the angle between the solid surface and the tangent at the point of contact of the three phases (figure 10) [9].



σ_{SG}, σ_{SL}, σ_{LG} – surface energies of a solid, gas, and liquid.

Figure 10 – Determination of the contact angle

In the experimental part of the study, the contact angle was measured using a laboratory setup with manual dosing to produce droplets of the required volume, DSA-14 (KRUSS, Germany), shown in figure 11. The contact angle can be determined within a range of 1° to 180° with an accuracy of 0,1°. The silicone and polyurethane samples under investigation were immersed in water for 50 hours, which was sufficient to reach a "plateau" level for the contact angle.

Figure 11 – The DSA-14 device for determining the contact angle

Moisture absorption

The spontaneous process of a polymer absorbing liquid or vapor from the surrounding environment, accompanied by an increase in its volume and mass, is referred to as moisture absorption. The primary factor describing this process is the degree of swelling (α), which is determined using the following equation:

$$\alpha = \frac{m - m_0}{m_0} \times 100\ \%\,, \qquad (1)$$

where m – the mass of the polymer after immersion in the liquid;

m_0 – the mass of the polymer before immersion in the liquid.

Two types of moisture absorption are distinguished: limited and unlimited. In the first case, α reaches a constant value and remains unchanged. In the case of unlimited swelling, α reaches its maximum value and then drops sharply, indicating

the dissolution of the polymer [9]. The samples under study were immersed in water, and the degree of swelling of the elastomers was determined using Sartorius CP324S analytical scales (Sartorius, Germany), shown in figure 12. The exposure of polyurethane and silicone samples in water continued until the moisture absorption values reached a "plateau" level.

Figure 12 – Sartorius CP324S analytical scales

Hardness

The property of a polymer material to resist the penetration of another object is called hardness. When an object is pressed into the polymer, local plastic and quasi-plastic deformations occur, which, with further pressure, lead to localized damage [7].

To measure the hardness of a polymer material, a special method called Shore hardness testing is used. This method involves measuring the depth of penetration of a spring-loaded indenter made of hardened steel into the material. The depth of penetration is referred to as Shore hardness, which is measured on a scale from 0 to 100 Shore (ranging from 2,5 mm to 0 mm). Due to the variety of indenter shapes and spring characteristics, there are several different Shore scales. The most commonly used are the Shore A and Shore D scales. For the Shore A scale, the most frequently tested surfaces are elastomers, such as soft rubber, elastomers, and natural rubber. figure 13 shows a durometer for measuring polymers on the Shore A scale.

Figure 13 – Durometer for measuring polymer hardness on the shore a scale

Elasticity and Young's modulus

Elasticity refers to the ability of a material to return to its original shape after being subjected to external forces. According to Hooke's law, the relative deformation of a body is directly proportional to the magnitude of the applied stress. There are two types of stress: normal stress σ_n, which occurs due to stretching or compression, and shear (tangential) stress σ_t, which results from shear deformation (sliding). The response of polymers to such external mechanical stress is characterized by the Young's modulus E. The Young's modulus is a measure that is directly proportional to the applied stress σ and inversely proportional to the relative deformation ε:

$$E = \frac{\sigma}{\varepsilon} = \frac{(\frac{F}{S})}{(\frac{\Delta l}{l_0})}, \quad (2)$$

where F – force of tension, compression, or shear;

S – area on which the force is applied;

l_0 – initial length of the sample;

l – change in the length of the sample when the force is applied.

To determine the Young's modulus experimentally, a testing tensile machine Zwick/Roell Z5.0 was used, as shown in figure 14.

Figure 14 – Zwick/Roell Z5.0 tensile machine

The elastomer samples, in the form of blades with a thickness of 3 mm and a width of 2 mm, were tested on a tensile machine to determine the Young's modulus. The obtained data were compared with the absorption rate and the contact angle measurements of the samples from the experiment described above. This allowed for a correlation to be established between the methods used to study the surfaces of the polymers.

Penetration depth

Penetration depth refers to the distance to which a liquid penetrates into a polymer composition through its surface. This parameter provides a more detailed view of the liquid's spread within the polymer over a length equal to the thickness of the ureteral stents (ranging from 395 to 450 microns). In the research, penetration depth was determined using a LEICA DM4500P polarized light microscope, shown in figure 15.

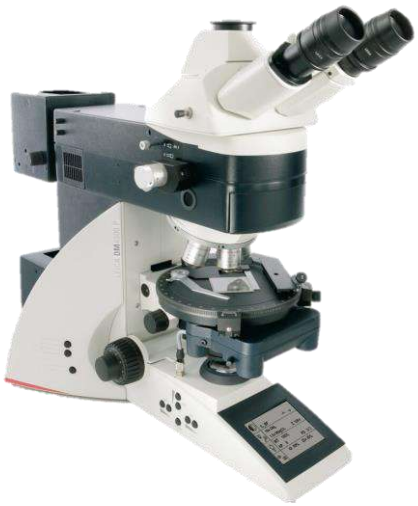


Figure 15 – LEICA DM4500P polarized light microscope

The polymer samples were immersed vertically in a 1% solution of brilliant green for 60 minutes. Every 20 minutes, the samples were removed from the solution to create cross-sections of the material. Then, using the microscope, the depth of the dye penetration into the sample was assessed.

The statistical analysis utilized the standard deviation method.

Thus, in the first stage of the dissertation work, the characteristics of the physical and mechanical properties of the polymers were identified in laboratory conditions, and the advantages of silicone rubber over polyurethane were substantiated.

2.3 Comparative assessment of the quality of life of patients with urolithiasis with placed silicone and polyurethane ureteral stents

In order to evaluate the advantage of the stent material in terms of its impact on the patient's quality of life, especially the incidence of pain syndrome following urinary tract stenting, a clinical study was conducted using polyurethane and silicone ureteral stents.

Ethical requirements

From June to October 2019, 57 patients with renal colic were included in a single-centre prospective study. Patients were divided into 2 groups depending on the material of the stent placed. The study was approved by the local ethical committee of Pavlov First Saint Petersburg State Medical University (FSBEI HE I.P. Pavlov SPbSMU MOH Russia) (№ 217 dated 25.03.2019) and registered on the ClinicalTrials.gov portal (#NCT 04000178).

Study design and evaluation of results

Inclusion criteria were: age from 18 to 65 years, hospitalization for renal colic. The only exclusion criterion was active urinary tract infection. After obtaining informed consent, all patients were divided into two groups. In group № 1, which included 20 patients, polyurethane stents (Rüsch, Teleflex) were deployed. In group No. 2, consisting of 30 patients, silicone stents (Cook Medical) were placed. Due to the presence of acute urinary tract infection 7 patients were excluded from the study.

In all patients the stents had the same length and thickness characteristics (26 cm and 6 Fr), stent placement was performed under anaesthesia using a cystoscope under X-ray control. During the study, the stent remained in the urinary tract for 1 month. Follow-up was performed 1 hour after stent placement, 2 weeks later, and prior to stent removal or contact ureterolithotripsy. At each follow-up visit, patients completed two questionnaires, the visual analogue pain scale (VAS) and the overactive bladder symptom questionnaire (OAB) developed by International Continence Society. The primary indicators assessed were pain intensity and dysuria symptoms severity. Secondary indicators included difficulty in stent placement, presence of blood in urine, deposition of urinary stone crystals on the stent (encrustation) and unscheduled visits of patients. The study diagram is depicted in figure 16.

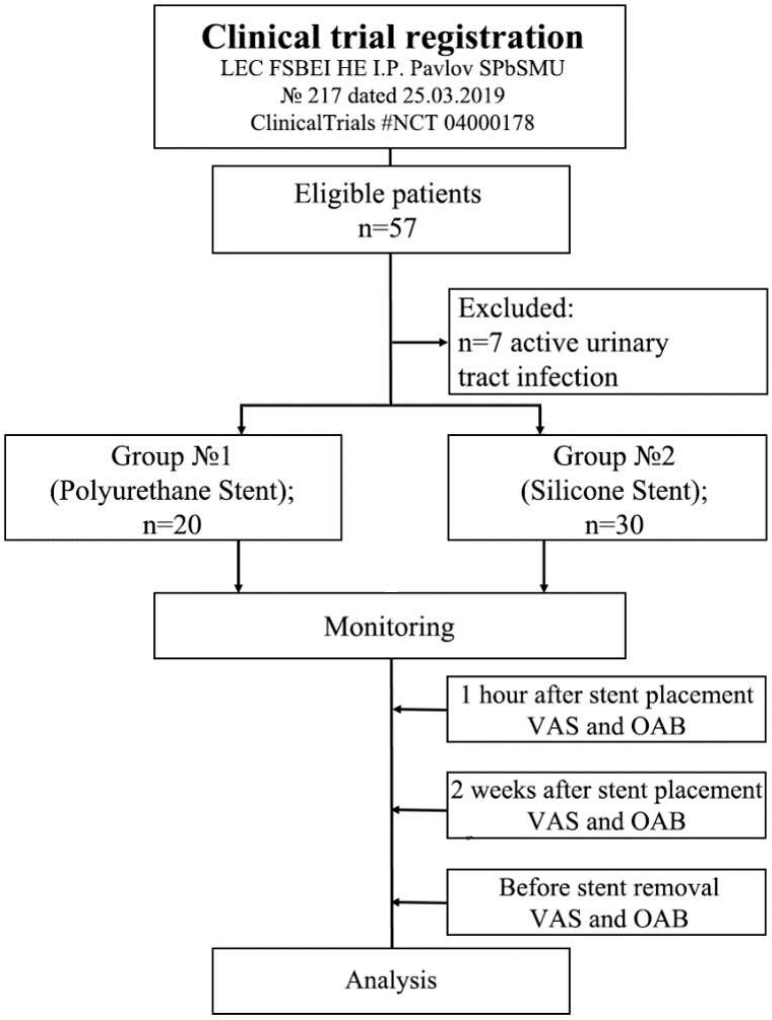


Figure 16 – Diagram of a quality-of-life study of urolithiasis patients with silicone and polyurethane ureteral stents deployed

Statistical methods

For hypothesis testing, a value of 0,05 was used as the critical significance level (α). 95% confidence intervals (CI) were calculated for all parameters. The MOVER methodology implemented in the spreadsheets MOVER-D.xls and MOVER-R.xls was used to calculate CI for differences and/or ratio. For ease of understanding the CI, a compact format was used, with the upper and lower bounds located on the sides of the mean value. PAST software was used to test whether the observed values conformed to a normal distribution as well as for statistical estimation of parameters and their comparisons. Exact nonparametric methods implemented in the StatXact package were used to analyse discrete data. Box plots were generated online using BoxPlotR.

2.4 A study of the safety and efficacy of ultrasound-guided removal of magnetic-tip polyurethane ureteral stents in men

Considering the importance of improving the methods of ureteral stent removal, a clinical study was conducted to study the safety and efficacy of magnetic stents, to assess the severity of stent-associated symptoms, as well as the pain syndrome level during their removal with a special extractor under ultrasound guidance.

Ethical requirements

From October 2020 to March 2022, 60 male patients undergoing transurethral ureterolithotripsy (TUL) or retrograde intrarenal surgery (RIRS) were included in a single-centre prospective randomized study. Randomization was performed in parallel groups, single-blinded – the outcomes of the randomization performed were unknown to patients only. The study was approved by the local ethical committee of the FSBEI HE I.P. Pavlov SPbSMU MOH Russia (№ 228 dated 20.03.2020), all included patients provided informed consent. The study was also registered on the portal ClinicalTrials.gov (#NCT 04582019).

Study design

Inclusion criteria: all male patients aged 18 to 70 years who had an indication for TUL or RIRS. In addition to the above criteria, the ASA (American Society of Anesthesiologists) scale score was used, which should not exceed 3 points. Exclusion criteria: exacerbation of urinary tract infection, as well as patients taking a1-adreno- or m-choline blockers. After obtaining informed consent, all patients were randomized into two groups (figure 17).

Group A (n=30) included patients who underwent postoperative placement of a conventional 6 Fr size polyurethane DJ stent (Coloplast, Denmark). Group B (n=30) included patients who underwent postoperative placement of a polyurethane DJ stent with a magnetic tip [Blackstar, Urotech (Achenmühle, Germany)], size of 7 Fr. All patients were scheduled for stent removal 30 days after stent placement. Block

randomization method was used for equal distribution of patients between the groups. A computer algorithm based on https://randomize.net allowed automatic randomization of all patients. The stents were placed under general anaesthesia with X-ray control. All manipulations were performed by endourologists with extensive experience in working with stents of different types; it should be noted that they were not involved in obtaining and evaluating the results of the study.

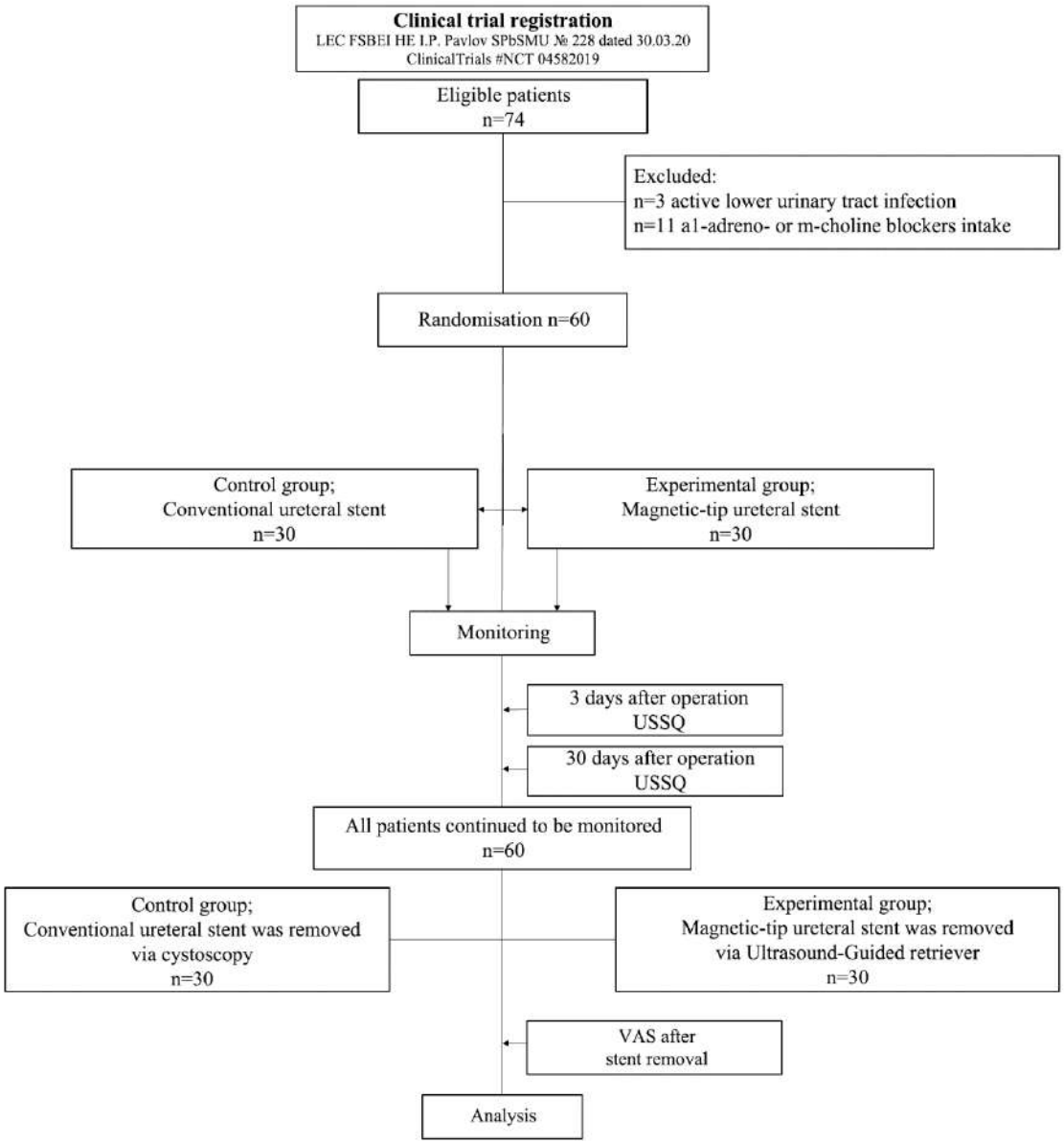


Figure 17 – CONSORT diagram of the study of the safety and efficacy of ultrasound-guided removal of magnetic ureteral stents

Black Star magnetic stent (Urotech (Achenmühle, Germany)) – is a standard 7 Fr polyurethane DJ ureteral stent with a 9 Fr cylindrical magnet at the distal end. The magnet is fixed to the end of the stent with a non-absorbable thread. The stent retrieval device, or retriever, measuring 15 Fr, is also made of soft polyurethane and has the shape of a Tiemman catheter with a magnet at the end. The retriever is colour-coded so that the end with the magnet can be easily oriented in the bladder in the desired direction (figure 18).

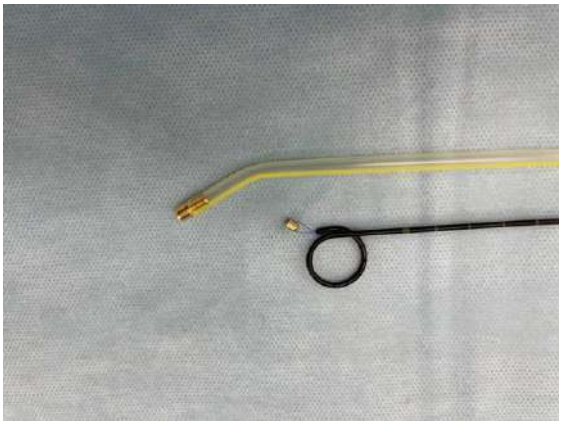


Figure 18 – Special magnetic retriever with tiemman tip
and magnetic ureteral stent

Stent removal in both groups was performed on an outpatient basis without any anaesthesia. Sterile ultrasound gel was used as lubricant during stent retrieval. In group A, all patients had the stent removed with forceps using a flexible 16,5 Fr video cystoscope (Karl Storz, Germany). In group B, stents were removed using a magnetic retriever under ultrasound guidance (figure 19). A special magnetic retriever was inserted transurethrally into the bladder. A convex ultrasound transducer was placed midline in the suprapubic region, and it was used to visualise the magnetic parts of the retriever and stent in the bladder in the axial and sagittal plane. During stent removal, in most cases, the magnetic retriever was in the dominant hand, whereas the ultrasound transducer was controlled by the free hand. When the bladder is full, it is not technically challenging to perform this manoeuvre. When the rotational movement was performed, the end of the retriever was connected to the magnet of the ureteral stent with a characteristic click, and then the retriever and stent were pulled outwards.

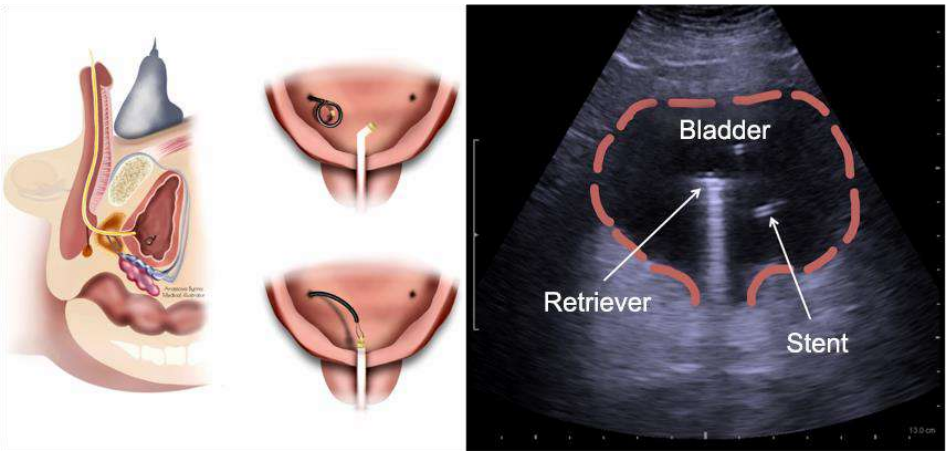


Figure 19 – Ultrasound transducer placed along the midline of the suprapubic region and ultrasound image showing hyperechogenic magnetic parts of the stent and retriever

Evaluation of results

The obtained results were presented according to CONSORT standards. The previously validated and translated into Russian USSQ questionnaire was used to assess the severity of stent-associated symptoms (SAS). In the postoperative period, patients completed the USSQ at 3 and 30 days after surgery, immediately prior to stent removal. The time required for stent retrieval was also measured, which was calculated from the beginning of instrument insertion into the urethra to complete stent removal. Immediately after stent removal, all patients were assessed for pain syndrome caused by stent retrieval using visual analogue pain scale (VAS). Secondary outcomes included the need to use a cystoscope in case of unsuccessful attempt to remove the magnetic stent with a retriever.

Statistical methods

Statistical analysis and visualisation of the obtained data were performed using the R 4.1.2 statistical computing environment (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics are presented as the observed number of observations (relative frequency) for qualitative variables and mean (standard deviation) and median (1st and 3rd quartiles) for quantitative variables. The Mann-Whitney test was used to compare quantitative variables and Fisher's exact test was used to compare

qualitative variables. Mixed regression models were used to compare the components of the USSQ questionnaire over time. The LOCF method was used to fill in missing values of the USSQ questionnaire responses included in the component scores. The Holm method was used to control for inflation of type I errors in multiple comparisons.

2.5 Study of the effectiveness of a digital registry of patients with ureteral stents deployed, implemented on the basis of the stone md mobile application, on the prevention of "forgotten" stents

Untimely removal of ureteral stents is a fairly common problem. To prevent "forgotten" stents in patients with urolithiasis, a clinical trial was conducted to study the effectiveness of the "Stent Radar" section of the Stone MD mobile application.

Ethical requirements

From December 2022 to October 2023, 208 female (39,9%) and male (60,1%) patients undergoing upper urinary tract drainage with a ureteral stent were included in a single-centre prospective study. The study was approved by the local ethical committee of the FSBEI HE I.P. Pavlov SPbSMU MOH Russia (№ 268 dated 26.12.22) and registered on the ClinicalTrials.gov portal (# NCT 06022952).

Study design

Inclusion criteria: all female and male patients from 18 to 80 years of age who had a polyurethane ureteral stent Fr 4,8-6,0. Exclusion criteria: no smartphone with internet access, active urinary tract infection, and insufficient social adaptation. After obtaining informed consent, all patients were divided into two groups. The experimental group (n=108) included patients who used the "Stent Radar" section of the Stone MD mobile application to prevent the occurrence of "forgotten" ureteral stents. The control group (n=100) included patients who did not use the Stone MD app. All patients were scheduled for ureteral stent removal 30 days after surgery.

"Stent Radar" is a section of the mobile application "Stone MD. Urolithiasis». "Stent Radar" was specifically designed for patients to remove a ureteral stent in a timely manner within the time period specified by the treating physician. Immediately after the operation that ended with the drainage of the upper urinary tract with a DJ stent, the patient independently enters data about the placed stent into the app in the "Stent Radar" section. This information includes: the name of the stent, the side of stent placement, and the recommended date of stent removal. After a certain number of days, a push notification from the Stone MD app appears in the patient's smartphone about the need to contact the doctor for timely stent removal. This makes it virtually impossible to forget to remove the ureteral stent. At discharge, we strongly recommend that all patients with a ureteral stent install the Stone MD mobile app on their smartphone. The Stone MD app is available for installation on iOS and Android smartphones. The "Stent Radar" section of the Stone MD mobile app is shown in figure 20.

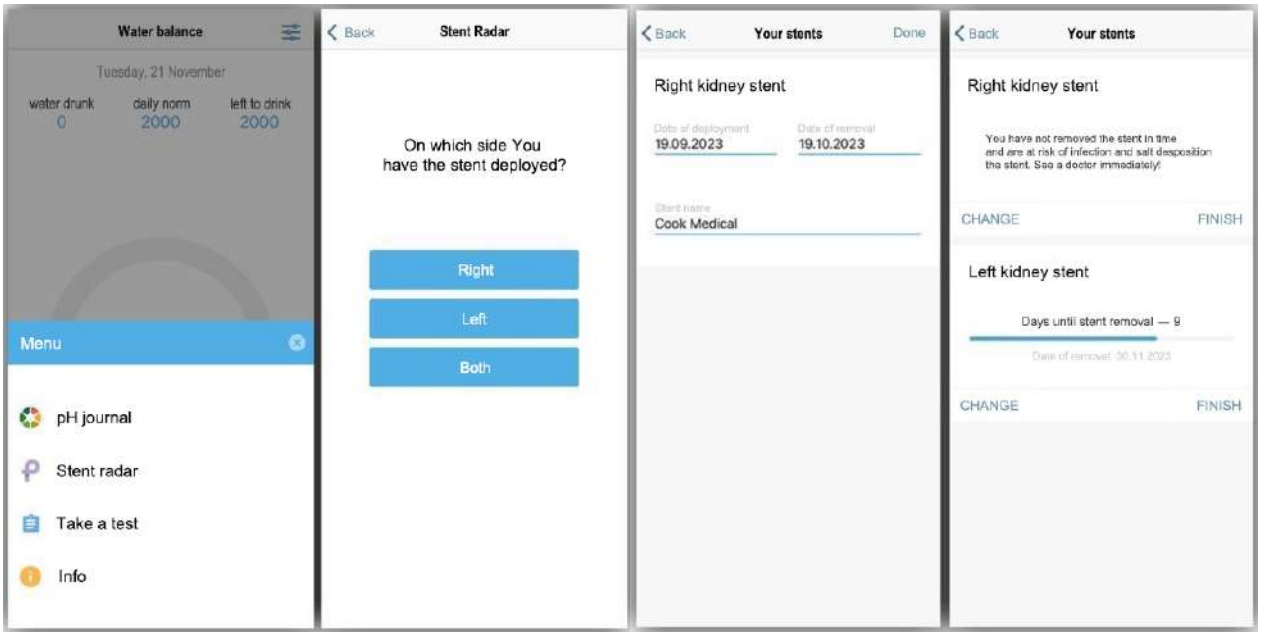


Figure 20 – "Stent Radar" Section of the Stone MD Mobile Application

All patients were closely monitored in the postoperative period. If the patient failed to contact the clinic 2 weeks after the expected date of removal, he/she received a call from the clinic with a reminder of the necessary visit for stent removal.

The severity of stent-associated symptoms, clinical signs of cerebrovascular disease (CVD), and the patient's employment status were also assessed. The study diagram is depicted in figure 21.

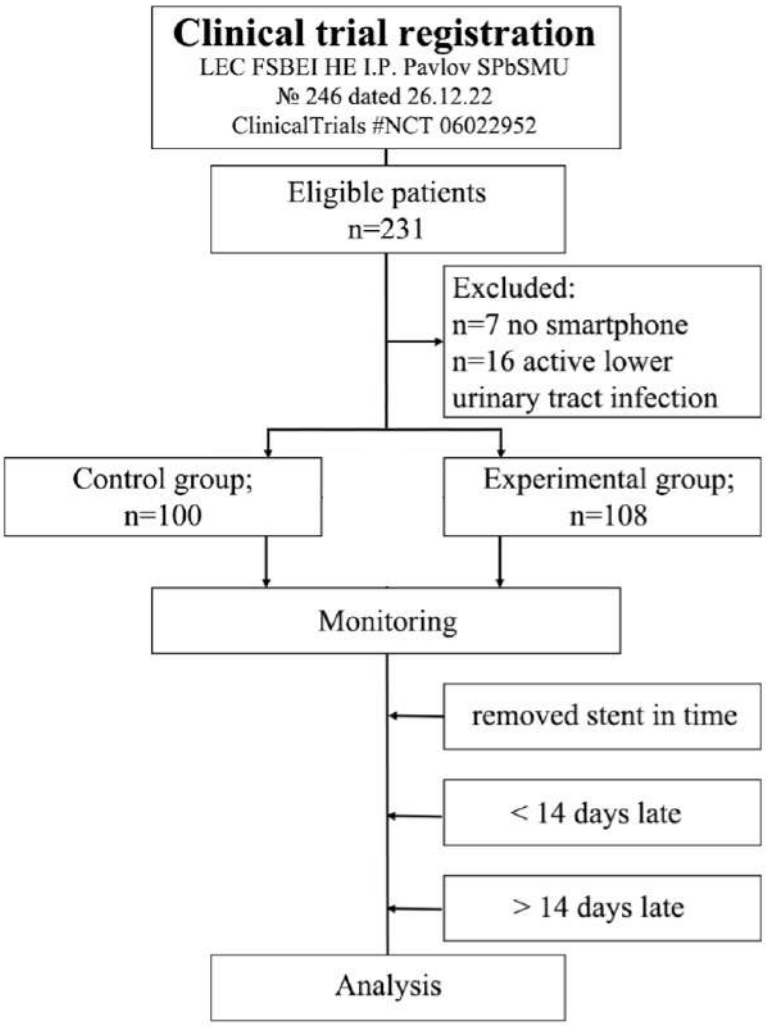


Figure 21 – CONSORT Diagram of a Study of the Impact of the Stone MD Mobile Application on the Prevention of "Forgotten" Ureteral Stents in Patients with Urolithiasis

Statistical methods

Statistical analysis and visualisation of the obtained data were performed using the R 4.2.1 statistical computing environment (R Foundation for Statistical Computing, Vienna, Austria), Excel 2019 ("Microsoft", USA), SPSS Statistica v. 26 ("IBM", USA) and JMP Pro 17 ("SAS", USA).

Descriptive statistics are presented as observed number of observations (relative frequency) for qualitative variables and mean (standard deviation) and median (1st and 3rd quartiles) for quantitative variables.

The Kolmogorov-Smirnov test with Lilliefors correction was used to test the distribution of quantitative variables for normality. Fisher's exact test was used to examine the association of categorical variables. The Mann-Whitney test was used to compare quantitative variables. A proportional odds model was used to compare ordinal outcomes (proportional odds ratio with corresponding 95% CI was used as an estimate of effect size). An association was considered statistically significant at $p<0,05$.

Changes in absolute and relative probabilities of outcome were analysed by calculating the absolute risk reduction ratio (ARR) and relative risk reduction ratio (RRR) with 95% CI. In order to assess the effectiveness of treatment, the number needed to treat (NNT) to prevent one case of adverse outcome was calculated compared to the control group.

2.6 Modelling of calcium excretion and pharmacological correction of urine lithogenic properties for prevention of ureteral stent encrustation

Currently, one of the promising directions of stent encrustation prevention is the search for new inhibitors of calcium crystallization and other lithogenic substances in urine. It is known that pyrophosphate has the ability to chelate calcium in urine. Therefore, creatine, being a source of inorganic phosphate and pyrophosphate, was the subject of our prospective study to evaluate its potential ability to bind calcium in urine.

Ethical requirements

In October 2020, 10 healthy female (30%) and male (70%) volunteers were included in a single-centre prospective study. The study protocol was approved at the meeting of the local ethical committee of the FSBEI HE I.P. Pavlov SPbSMU MOH Russia (№ 240 dated 28.09.2020).

Study design

Inclusion criteria: healthy female and male volunteers from 18 to 65 years of age without hypercalciuria. Exclusion criteria: taking calcium and vitamin D preparations, hyperparathyroidism. All patients were informed of the study objectives, effects and phenomena studied, expected benefits and potential risks. All patients included in the study signed informed written consent.

All included patients were advised to take creatine in a dosage of 3g per day for 28 days, to follow their usual lifestyle and diet. The graphic design is presented in figure 22.

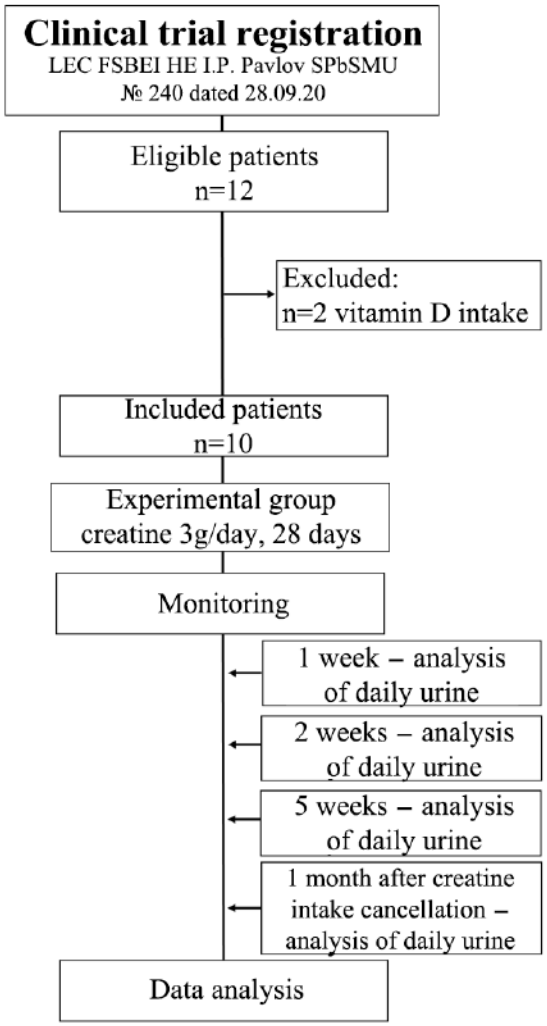


Figure 22 – CONSORT diagram of the study of the effect of creatine on the level of daily calcium excretion in healthy volunteers

Evaluation of results

The results were presented according to CONSORT standards. During the follow-up period, four daily urinalysis studies were performed to determine the daily excretion of calcium, phosphorus and creatinine: at the end of the 1st week and at the end of the 2nd week of creatine administration. Also 5 weeks after the start of the study and 1 month after creatine withdrawal, daily excretion rates of calcium, creatinine and phosphorus were also assessed in all volunteers.

Statistical methods

Statistical analysis and visualization of the obtained data was performed using Excel 2019 statistical computing environment ("Microsoft", USA). The evaluated quantitative indicators were described through median and quartiles, minimum and maximum values were also given. Spearman Rank Order Correlations coefficient was calculated to investigate the relationship between the indicators. The dynamics of the indices was investigated for the whole population of patients using Friedman ANOVA. The association was considered statistically significant at $p<0,05$.

Taking into account that ureteral stents encrustation is one of the main problems associated with their use, it was decided to evaluate the efficacy of the method of pharmacological modelling of urine lithogenic properties to prevent ureteral stents encrustation.

Ethical requirements

From December 2023 to April 2024, 60 patients with urolithiasis undergoing upper urinary tract drainage with a ureteral stent were included in a single-centre prospective randomized study. Randomization was done in parallel groups, blinding was simple – the outcomes of randomization were known only to the investigators. The study was approved by the local ethical committee of FSBEI HE I.P. Pavlov SPbSMU MOH Russia (№ 244 dated 25.01.2021).

Study design

Inclusion criteria: female and male patients from 18 to 80 years of age without recurrence of urolithiasis, who underwent a Fr 4,8-6,0 polyurethane ureteral stent deployment, and were able to measure urine pH independently on a daily basis.

In addition to the above criteria, the ASA (American Society of Anesthesiologists) scale score was used, which should not have exceeded 3 points. Exclusion criteria: exacerbation of urinary tract infection, intolerance to at least one of the components of the mixture, hypercalciuria and hyperuricosuria, patients with one or more recurrences of urolithiasis. After obtaining informed consent, all patients were randomized into two groups, CONSORT diagram of the study is presented in figure 23.

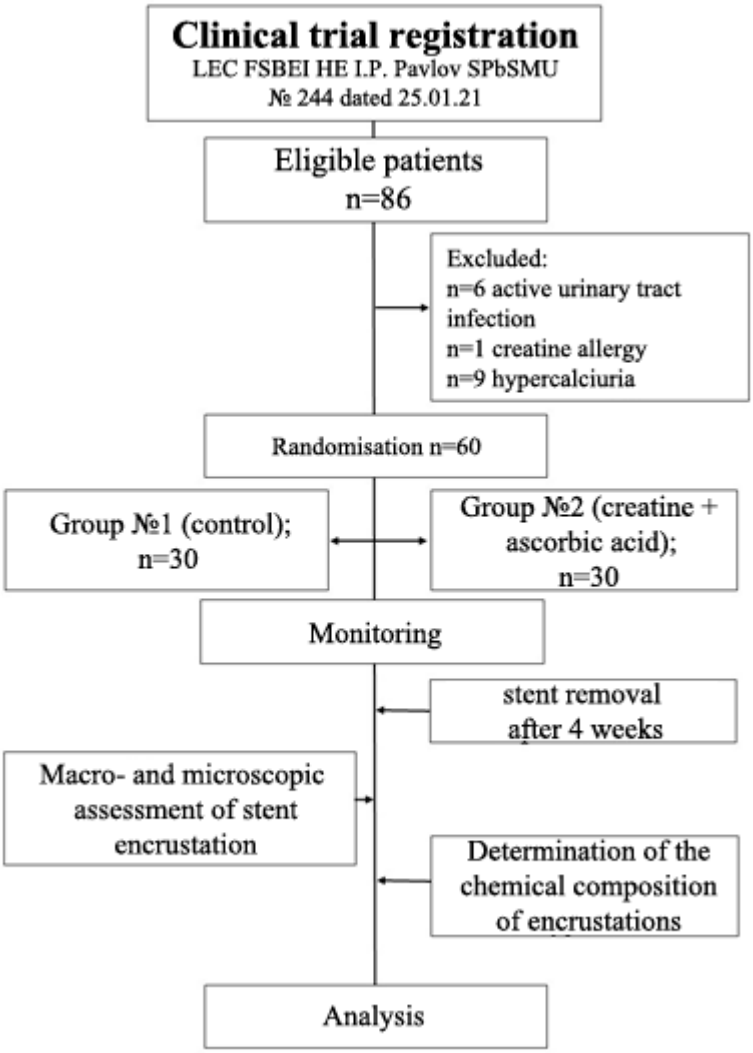


Figure 23 – CONSORT diagram of the study of the effect of combined ascorbic acid and creatine intake for the prevention of ureteral stent encrustation

In the main group of patients in which ureteral stent encrustation prophylaxis was performed, 30 patients were included. In the control group (n=30), modelling of urine lithogenic properties was not performed. All patients were scheduled for stent

removal 4 weeks after stent placement. Block randomization method was used for equal distribution of patients between the groups. A computer algorithm based on https://randomize.net allowed automatic randomization of all patients. Prior to the study, all subjects underwent biochemical analysis of 24-hour urine to determine the daily excretion of calcium, phosphorus, creatinine and uric acid, and blood tests to determine the level of total calcium. This was done to identify and exclude patients with hypercalciuria and hyperuricosuria. Also, only patients without bacteriuria, as confirmed by urine culture test, were included in the study.

In both groups, patients independently measured urine acidity daily in the morning using a portable electronic pH-meter ECOSTAB (ЭКОСТАБ) PH201, which has a pH measurement range from 0 to 14 and an accuracy of ±0,1. All ureteral stents were placed under general anaesthesia and X-ray guidance. Combined intake of ascorbic acid and creatine (IUPAC 2-[Carbamimidoyl(methyl)aminoacetic acid) was used as an inhibitor of ureteral stent encrustation. Patients in the main group took 500 mg of ascorbic acid per os twice daily to acidify the urine and 3 g of creatine per os once daily to increase the excretion of crystallization inhibitors. The combined therapy was continued for 28 days. The capsule preparations were placed in blister packs for convenience of intake. Stent removal was performed either by cystoscopy in men or by hook in women. Separate collection of renal and vesicular coils of the stent was done in closed dry containers, which were labelled and sent for further evaluation.

Evaluation of results

The results obtained from the study were formalized according to CONSORT requirements. Immediately after stent removal, macroscopic evaluation of the stent was performed. This was followed by microanalysis of the thickness and composition of the ureteric stent incrustatum in low vacuum mode without preliminary magnetron plasma spraying using a microscope with focused electron and ion probes QUANTA 200 3D. The QUANTA 200 3D electron microscope is shown in figure 24. The chemical analysis of the incrustate composition was also performed using the electron microscope software.

Figure 24 – QUANTA™ 3D electron microscope (FEI Company (USA))

Statistical methods

Statistical processing of data was performed using Excel 2019 application software ("Microsoft", USA), SPSS Statistica v. 26 ("IBM", USA). The Shapiro-Wilk criterion was used to test the distribution of quantitative indicators for normality. Continuous indices corresponding to normal distribution were described by the mean value and standard deviation ("M±SD"), in case of distribution different from normal distribution – in the form of median and quartiles ("Me [Q25%; Q75%]"). The significance of differences between quantitative data in two independent groups was assessed using the nonparametric Mann-Whitney U test. Qualitative data are presented as absolute and relative value – n (%). Statistical significance of the difference between the studied groups for qualitative indicators was performed using Pearson's $\chi 2$ test or Fisher's exact test for small samples. The relationship between the studied indicators was analysed using multiple regression analysis with calculation of the coefficient of determination (R2) and multiple correlation coefficient. The level of significance in testing statistical hypotheses was fixed at $p<0,05$.

Chapter 3

STENT POLYMER CHARACTERISTICS AND IMPROVING THE QUALITY OF LIFE OF PATIENTS WITH URETERAL STENTS

3.1 In vitro evaluation of surface and physicomechanical properties of stent polymers (experimental study)

This section presents the results of the evaluation of a number of surface and physicomechanical properties of polymers used for the production of urological stents.

The contact medium (water) was found to have various different effects on polyurethane (PU) and silicone.

For a silicone sample with a hardness of 50 ShA, the contact angle θ before soaking in water was 93,4°. As the exposure time of the 50 ShA silicone to the liquid increased, θ decreased, ultimately leading to hydrophilization of the surface. The θ values obtained for the 50 ShA PU sample changed exponentially, the material is hydrophilic as it contains polar groups (figure 25).

A similar dependence was found after measuring the contact angle for the tested samples of polyurethane 45 ShA and silicone 30 ShA (figure 26).

Based on the graphical analysis of the data, it is possible to determine the dependence of the contact angle of the tested samples on their hardness before exposure to aqueous medium. The result is presented in table 3.

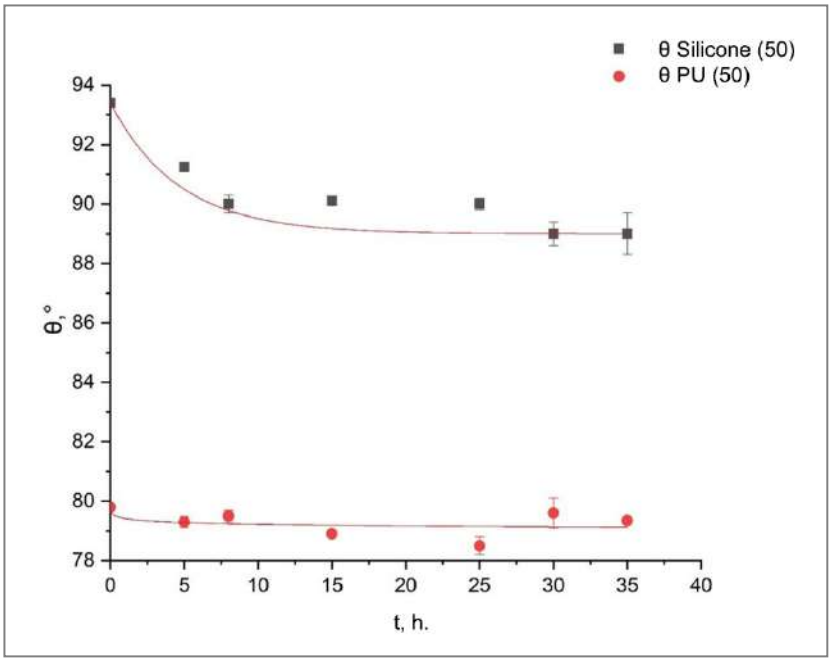


Figure 25 – Dependence of the contact angle on the exposure time to model medium (water) for silicone and polyurethane samples with a hardness of 50 on the shore a scale

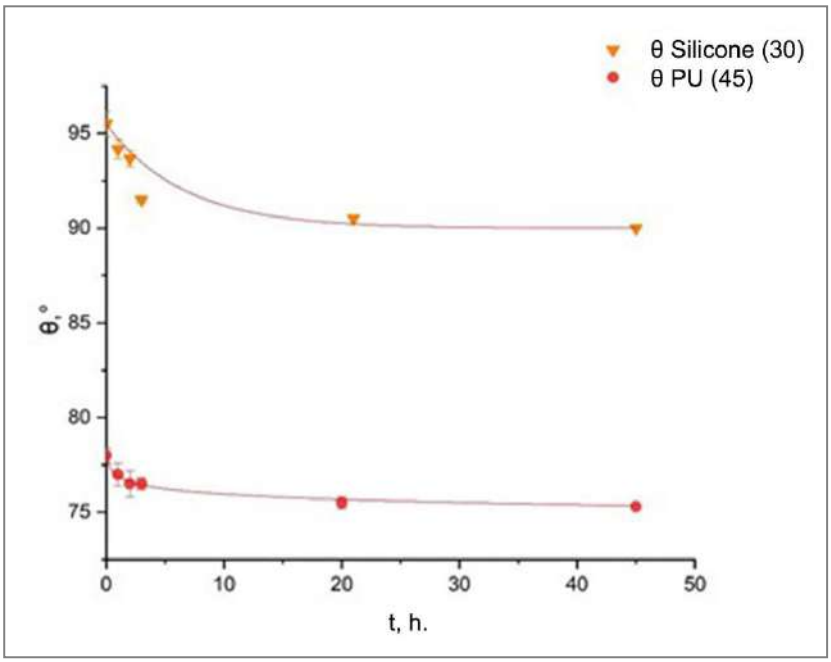


Figure 26 – Dependence of the contact angle on the contact time with the model medium (water) for polyurethane samples with hardness 45 ShA and silicone samples with hardness 30 ShA

Table 3 – Initial contact angle values of investigated polymers before exposure to aqueous media

Sample	Contact angle θ, °
Silicone 30 ShA	95,5
Silicone 50 ShA	93,4
PU 45 ShA	78,6
PU 50 ShA	79,8

Limited swelling was observed when assessing the moisture absorption (hygroscopicity) of the tested samples. After contact with water for 87 hours there was virtually no change in the weight of the tested samples. In addition, figures 27, 28 show that for polyurethane samples the swelling process is noticeably faster compared to silicone samples, which is due to the hygroscopicity of polyurethane.

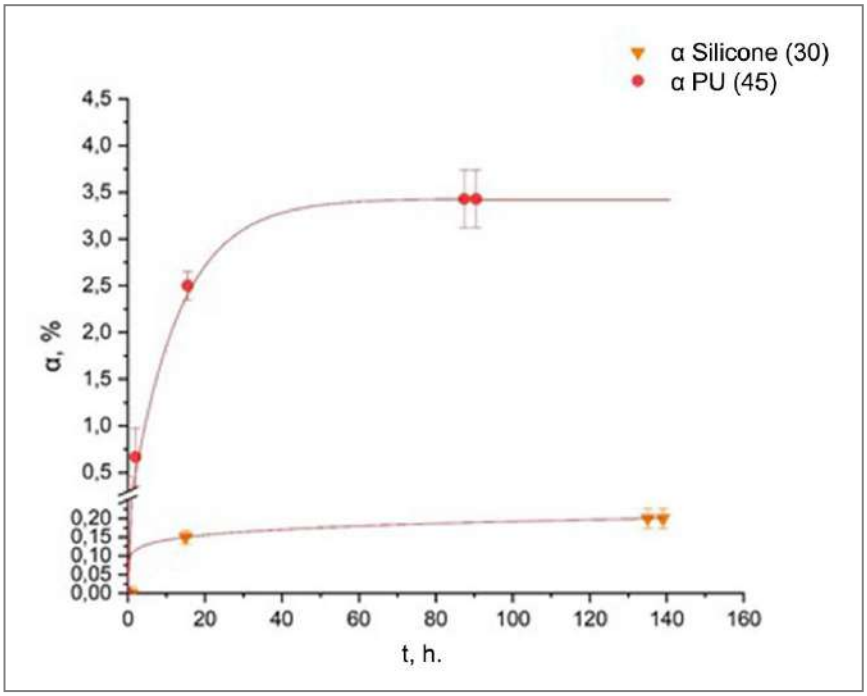


Figure 27 – Changes in the degree of swelling of silicone 30 sha and polyurethane 45 ShA as a function of residence time in water

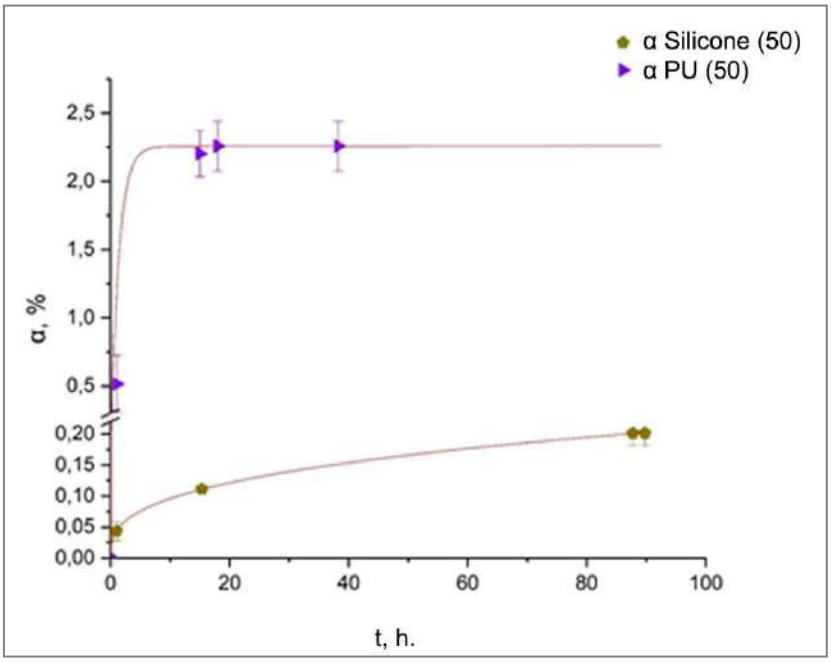
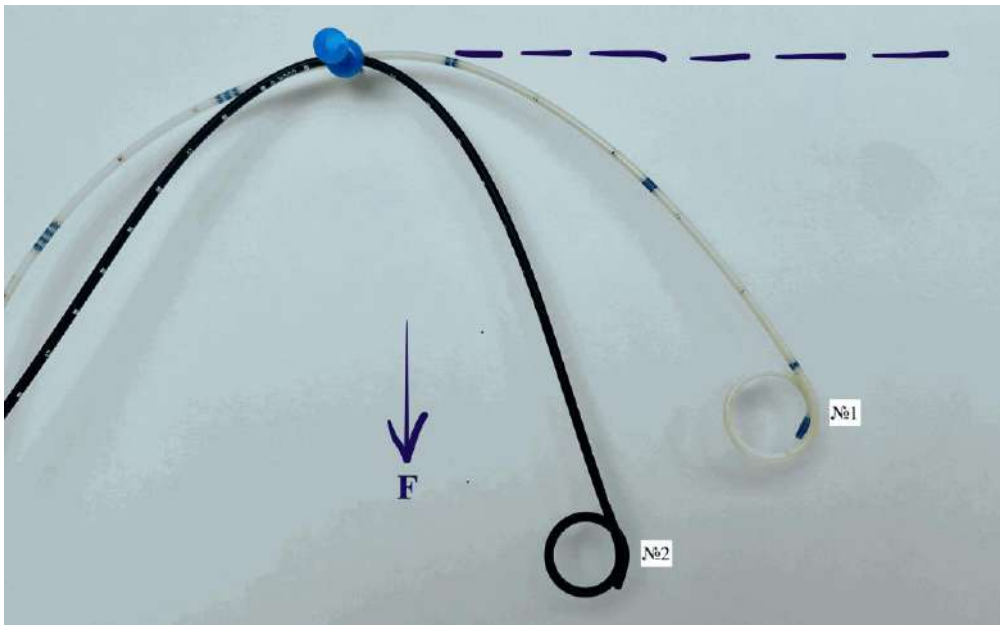


Figure 28 – Time dependence of swelling for silicone and polyurethane sample with hardness of 50 ShA

Figure 29 presents a visual demonstration of the stiffness of ureteral stents.



Stent № 1– Polyurethane Stent (Coloplast, Denmark);
№ 2 – Silicone Stent (Cook, USA).

Figure 29 – Deviation of DJ stents from horizontal under the force of gravity (F) demonstrating the stiffness of ureteral stents

The DJ stents compared have the same diameter – Fr 6. It can be clearly seen with the naked eye that stent № 1 made of polyurethane (Coloplast, Denmark) has greater stiffness, as it deviates less under the force of gravity, compared to stent № 2 made of silicone (Cook, USA) of equal length.

To confirm this supposition, it is necessary to determine the values of the modulus of elasticity of the tested polymers, since the stiffness of the finished product (DJ stent) and the modulus of elasticity of the polymer may differ.

The initial values of Young's modulus of silicone rubber are significantly lower than those of polyurethane of similar hardness (figures 30, 31). In addition, under the influence of the contact medium (water) there is an additional decrease in Young's modulus.

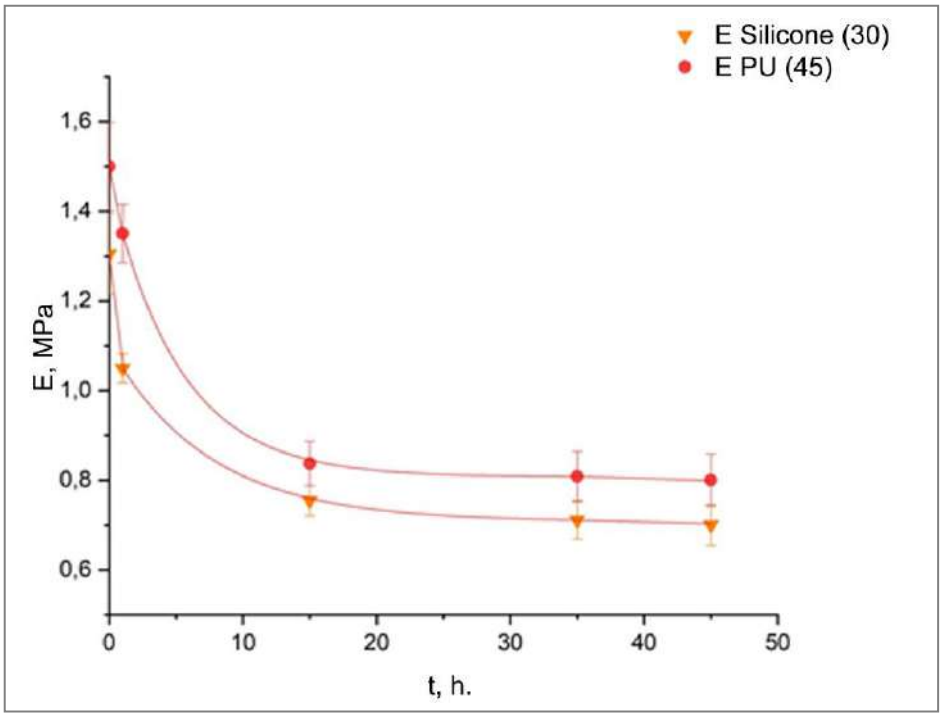


Figure 30 - Modulus of elasticity for polyurethane samples with a hardness of 45 ShA and silicone samples with a hardness of 30 ShA

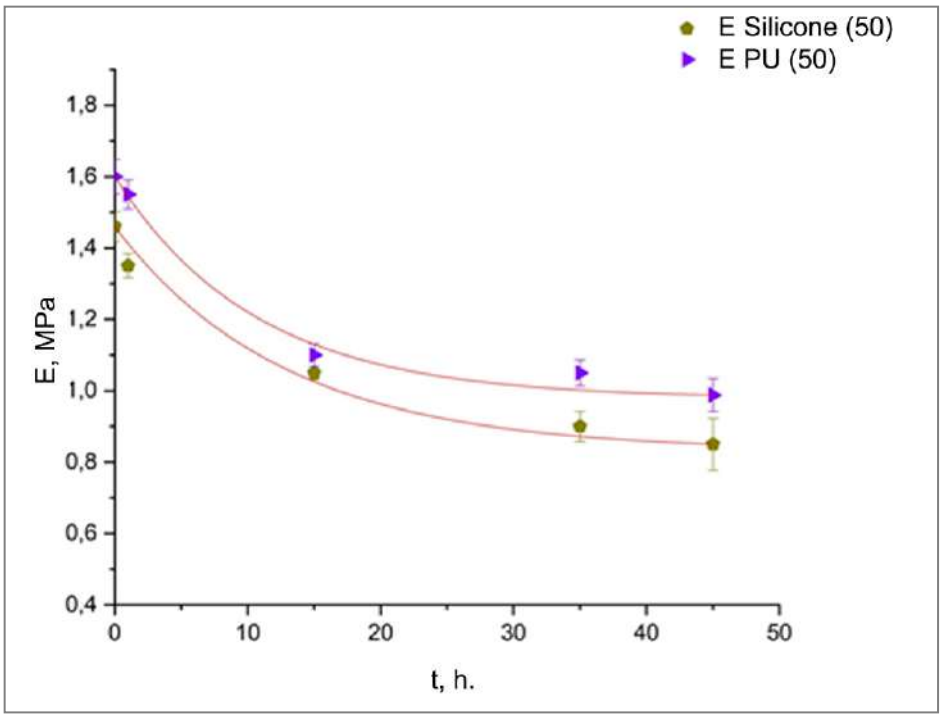


Figure 31 – Young's modulus for a sample of silicone and polyurethane with a hardness of 50 ShA

Since standard test samples have a geometry different from real products (stents), in order to obtain accurate results, it is necessary to scale the obtained results to real stent cross-sections. For this purpose, the time of water penetration into the sample body was determined and the velocity of liquid movement in the polymer volume during its impregnation was estimated. The data were obtained using an optical microscope equipped with a measuring scale. Figures 32, 33 show the dependence of water penetration depth (h) through the surface of the tested polymer samples as a function of time.

The analysis revealed that water penetration through the surface of silicone happens significantly faster. At the same time, the lower the hardness of the material, the faster this process occurs. The microscopic picture of penetration of colouring pigment through the surface of the tested samples is shown in figure 34.

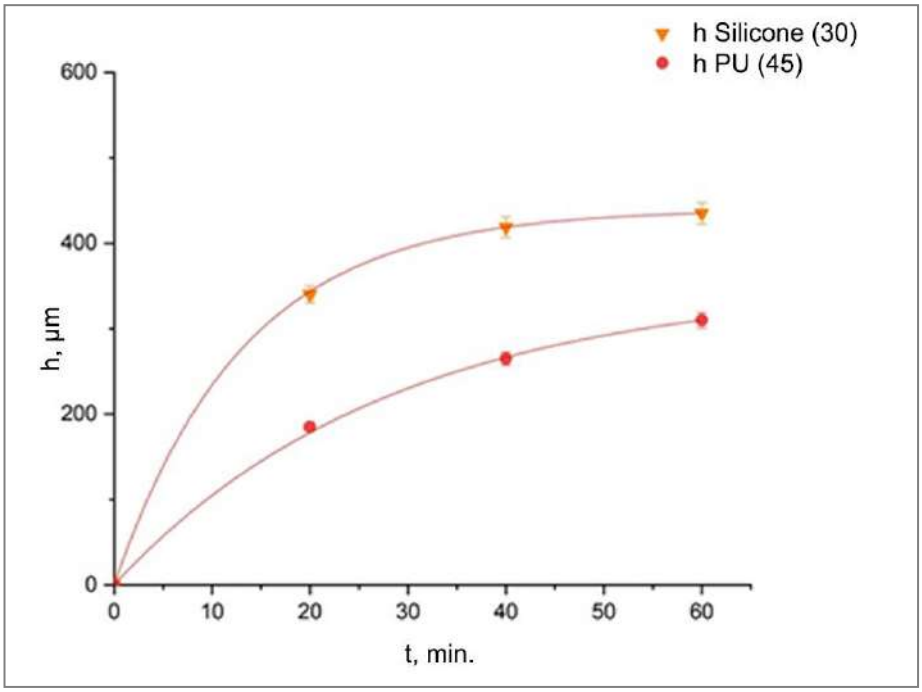


Figure 32 – Depth of dye penetration through the surface for polyurethane samples with a hardness of 45 ShA and silicone samples with a hardness of 30 ShA

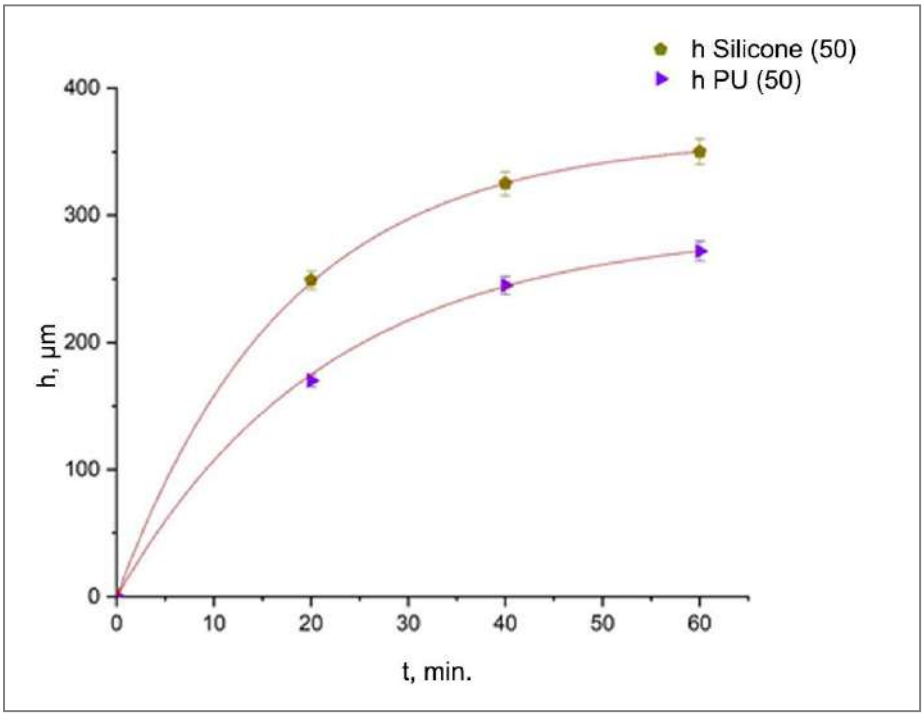


Figure 33 – Depth of dye penetration through the surface of the silicone and polyurethane sample with a hardness of 50 ShA

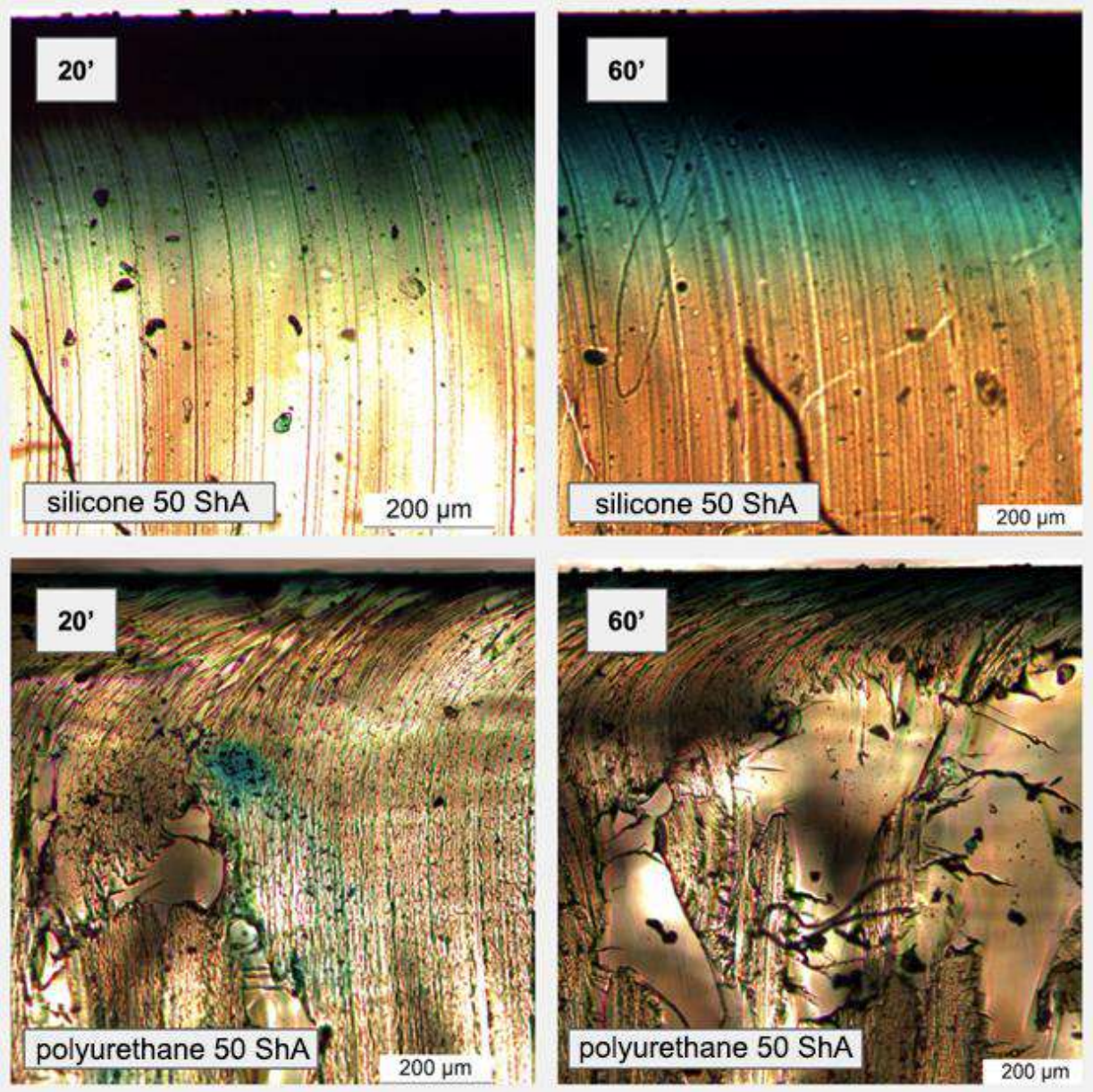


Figure 34 – Dynamics of dye penetration depth through the polymer surface (LEICA DM4500P polarizing microscope)

Summarizing the obtained data, it can be concluded that under the influence of water, the silicone material undergoes hydrophilization significantly faster – within approximately 10 hours – whereas this process takes considerably longer for polyurethane, ranging from 25 to 30 hours. Despite this, the contact angle of silicone remains notably higher than that of polyurethane: 95° and 79°, respectively. Both materials exhibit moisture absorption, but silicone absorbs water at a rate and quantity over an order of magnitude greater. At 50 Shore A hardness, polyurethane shows 0.2% moisture uptake, compared to 2.2% for silicone. The materials also differ

in rigidity: silicone demonstrates lower stiffness, as evidenced by its Young's modulus. Water penetrates silicone's polymer matrix more rapidly. After 20 minutes of water immersion, the penetration depth for polyurethane is 160 μm, whereas silicone reaches 250 μm – a 1.6-fold increase. Furthermore, exposure to water leads to an additional reduction in the Young's modulus of silicone rubber.

3.2 Comparative assessment of the quality of life of patients with urolithiasis with silicone and polyurethane ureteral stents deployed

This section presents the results of comparative assessment of the severity of stent-associated symptoms (SAS) in patients using modern polyurethane and silicone ureteral stents.

Patient data, as well as primary and secondary outcomes are reflected in tables 4-7.

Table 4 – Demographic and clinical data of patients

Characteristic	Group № 1 (polyurethane)	Group № 2 (silicone)	p-value
Number of patients (%)	20 (40%)	30 (60%)	–
Age; mean (range)	50 (19-60)	48 (24-64)	0,96
Men (%)	7 (35%)	18 (60%)	0,19
Women (%)	13 (65%)	12 (40%)	
Body Mass Index (kg/m^2)	$_{26}$ 26 $_{31}$	$_{26}$ 28 $_{30}$	0,71
Stone size (mm)	$_{9}$ 12 $_{13}$	$_{6}$ 8 $_{10}$	0,0013
Stent insertion time (min)	$_{6,1}$ 7,8 $_{9,4}$	$_{6,8}$ 7,8 $_{8,9}$	1,00
Stent indwell time in the urinary tract (weeks)	$_{3,2}$ 3,5 $_{3,7}$	$_{3,6}$ 3,8 $_{4,0}$	0,015

Both comparison groups were statistically homogeneous, except for the size of the concrement, which showed a statistically significant increase in the group of patients with silicone stents (p=0,0013). This value was not relevant for the purpose of the study.

Table 5 – Comparison of VAS and OAB scores one hour, two weeks after stent deployment and immediately prior to stent removal

VAS, score	Group № 1 (polyurethane)	Group № 2 (silicone)	p-value
After 1 hour	$_{1,4}2{,}8_{4,0}$	$_{1,4}2{,}0_{2,5}$	0,23
After 2 hours	$_{1,3}2{,}4_{3,4}$	$_{0,7}1{,}1_{1,5}$	0,023
Prior to removal	$_{1,3}2{,}1_{2,9}$	$_{0,8}1{,}1_{1,4}$	0,014
p-value	0,25	0,0029	
OAB, score			
After 1 hour	$_{4,2}7{,}2_{10}$	$_{4,7}6{,}3_{7,8}$	0,61
After 2 hours	$_{5,1}8{,}2_{11}$	$_{4,8}6{,}2_{7,2}$	0,25
Prior to removal	$_{5,7}8{,}7_{12}$	$_{5,0}6{,}8_{8,5}$	0,27
p-value	0,48	0,76	

Comparison of VAS and OAB 1 hour after stent deployment, 2 weeks after stent deployment and prior to stent removal or operative intervention demonstrates significant differences between mean VAS values 2 weeks after stent deployment and prior to stent removal in favour of the group of patients with silicone stents (p=0,023 and p=0,014, respectively).

To clarify the differences between the patient groups, the summary indices were calculated and compared. Mean VAS scores demonstrate that the level of pain syndrome in the group of patients with silicone stents was significantly lower than in the group of patients with polyurethane stents (p=0,0010).

Table 6 – Comparison of total VAS and OAB scores in patients with polyurethane and silicone stents

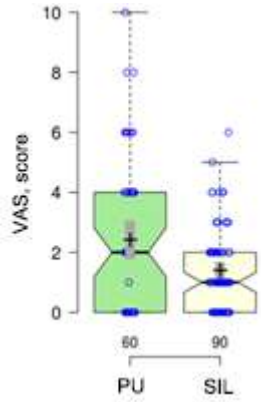
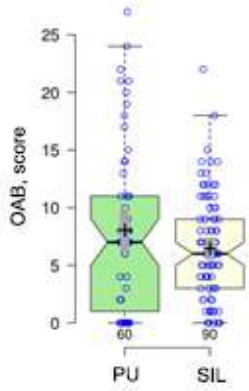
«Box-plots»			
			
M_{PU}	M_{SIL}	M_{PU}	M_{SIL}
$_{1,8}$ 2,4 $_{3,1}$	$_{1,1}$ 1,4 $_{1,7}$	$_{6.2}$ 8.0 $_{39.7}$	$_{5.5}$ 6.4 $_{7.5}$
$M_{PU} - M_{SIL}$		$M_{PU} - M_{SIL}$	
$_{0,3}$ 1,0 $_{1,7}$		$_{-0,5}$ 1,6 $_{3,6}$	
p=0,0010		p=0,098	
Var_{PU}	Var_{SIL}	Var_{PU}	Var_{SIL}
$_{3,7}$ 6,0 $_{8,3}$	$_{1,0}$ 1,6 $_{2,2}$	$_{33}$ 50 $_{67}$	$_{13}$ 20 $_{26}$
Var_{PU}/Var_{SIL}		Var_{PU}/Var_{SIL}	
$_{2,1}$ 3,8 $_{6,6}$		$_{1,5}$ 2,5 $_{4,2}$	
p=0,00016		p=0,0019	
Note – PU – polyurethane; SIL – silicone; M – median; Var – variance.			

Table 7 – Comparison of secondary outcomes

Secondary outcomes		Group		p-value
		Group № 1 (polyurethane)	Group № 2 (silicone)	
Difficulty with stent deployment	no	13 (64%)	26 (85%)	0,09
	yes	7 (36%)	4 (15%)	

Continuation of table 7

Secondary outcomes		Group		*p*-value
		Group № 1 (polyurethane)	Group № 2 (silicone)	
Unscheduled visit	no	17 (83%)	30 (100%)	0,052
	yes	3 (17%)	0 (0%)	
Encrustation	no	17 (83%)	29 (95%)	0,29
	yes	3 (17%)	1 (5%)	
Hematuria	no	9 (45%)	19 (63%)	0,25
	yes	11 (55%)	11 (37%)	

When comparing the secondary outcomes, no statistically significant differences were found between the studied groups.

To summarize the data obtained in the survey, it can be said that the results clearly illustrate the advantage of silicone stents over polyurethane stents in terms of the incidence and intensity of pain syndrome two weeks after stent placement, as well as immediately prior to its removal. When analysing the incidence of complications associated with urinary stenting, no statistically significant differences were found between the studied groups.

3.3 A Study of the safety and efficacy of ultrasound-guided removal of polyurethane magnetic-tip ureteral stents in men

This section presents the results of a study on the safety and efficacy of ultrasound-guided removal of the magnetic ureteral stents. Patient data, as well as primary and secondary outcomes, are displayed in tables 8-10 and figures 35-37.

Table 8 – Demographic and clinical data of patients

Characteristic	Group A, N=30	Group B, N=30	p-value
Age			0,5590
Mean (SD)	50,1 (13,7)	51,6 (14,6)	
Median (IQR)	47,0 (39,5-60,8)	55,0 (40,2-59,8)	
BMI			0,9293
Mean (SD)	27,5 (3,3)	27,5 (3,4)	
Median (IQR)	26,8 (25,2-29,7)	26,6 (25,1-30,0)	
Name of operation, n (%)			0,5889
RIRS	12 (40,0%)	9 (30,0%)	
TUL	18 (60,0%)	21 (70,0%)	

All 60 men who underwent ureteral stent deployment during operative intervention were divided into 2 groups as follows: 30 patients received a conventional DJ stent and the other 30 patients received a Black Star magnetic stent (Urotech (Achenmühle, Germany)). During the follow-up, none of the patients dropped out of the study. There were no statistically significant differences between the patient groups with respect to age, body mass index (BMI) and type of operative intervention.

Table 9 – Components of the USSQ questionnaire

Characteristic	Group A N=30	Group B N=30	p-value
Urinary symptoms (day 3)			0,6553
Mean (SD)	26,2 (8,5)	29,4 (6,5)	
Median (IQR)	22,0 (20,0-35,8)	30,0 (25,2-33,0)	
Urinary symptoms (1 month later)			0,1082
Mean (SD)	25,0 (8,0)	30,1 (7,2)	
Median (IQR)	26,0 (16,8-32,5)	31,0 (24,0-35,0)	
Body pain (3 days)			≈1

Continuation of table 9

Characteristic	Group A N=30	Group B N=30	p-value
Mean (SD)	21,7 (5,2)	20,2 (5,7)	
Median (IQR)	22,0 (17,0-25,5)	18,5 (16,8-25,0)	
Body pain (1 month later)			0,6553
Mean (SD)	18,7 (4,5)	21,1 (6,0)	
Median (IQR)	18,0 (16,0-21,8)	23,0 (17,5-26,0)	
General health score (day 3)			0,6553
Mean (SD)	15,7 (5,1)	13,6 (4,5)	
Median (IQR)	17,0 (13,0-18,8)	14,0 (10,2-16,0)	
General health score (1 month later)			≈1
Mean (SD)	12,9 (4,1)	13,9 (4,9)	
Median (IQR)	13,0 (9,2-14,8)	13,5 (10,2-18,8)	
Additional problems (day 3)			0,0017
Mean (SD)	7,7 (1,9)	5,6 (1,9)	
Median (IQR)	8,0 (6,0-9,0)	5,0 (4,0-7,0)	
Additional problems (1 month later)			≈1
Mean (SD)	6,4 (2,3)	5,9 (2,1)	
Median (IQR)	6,0 (4,0-8,0)	5,0 (4,0-7,0)	
Sexual matters (day 3)			0,2174
Mean (SD)	3,1 (2,7)	1,7 (2,1)	
Median (IQR)	2,0 (2,0-5,0)	0,5 (0,0-3,0)	
Sexual matters (1 month later)			0,6553
Mean (SD)	3,2 (2,5)	2,1 (2,4)	
Median (IQR)	3,0 (0,5-5,0)	1,5 (0,0-3,0)	
Work performance (day 3)			≈1
Mean (SD)	10,6 (3,6)	12,0 (5,9)	
Median (IQR)	10,5 (8,0-12,8)	11,0 (7,0-15,8)	

Continuation of table 9

Characteristic	Group A N=30	Group B N=30	p-value
Work performance (1 month later)			<0,0001
Mean (SD)	5,4 (4,0)	16,6 (12,5)	
Median (IQR)	5,5 (1,2-9,0)	10,5 (9,0-27,0)	

When comparing the components of the USSQ questionnaire, no statistically significant differences were found in the dynamics of Urinary symptoms (p=0,3471), Sexual matters (p=0,6126). However, statistically significant differences were found between groups in the dynamics of components Body pain (p=0,0303), General health score (p=0,0072), Additional problems (p=0,0142), Work performance (p<0,0001). The dynamics of USSQ components is presented in figure 35.

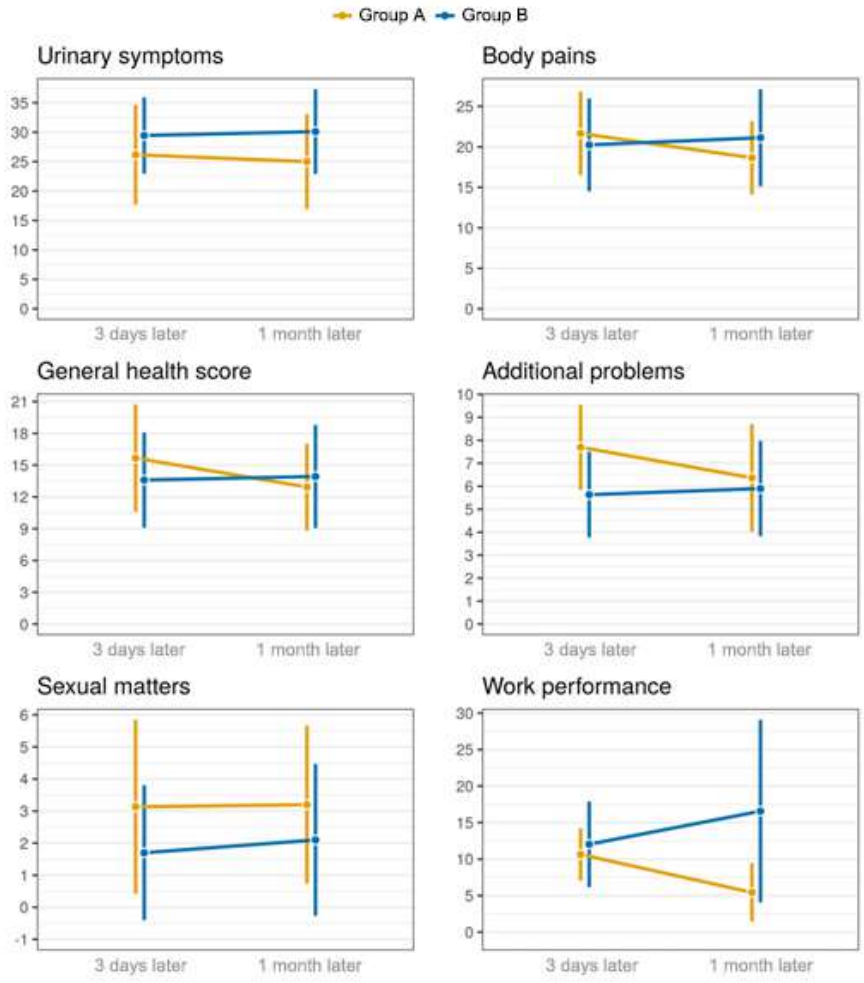


Figure 35 – USSQ components dynamics in both groups

Table 10 – Stent removal time, pain level, stent removal success rate in both groups

Characteristic	Group A N=30	Group B N=30	p-value
Stent removal time, sec			<0,0001
Mean (SD)	151,2 (65,5)	58,1 (41,5)	
Median (IQR)	142,5 (95,0-190,0)	40,0 (25,0-90,0)	
Stent removal success rate, n (%)			–
yes	30 (100,0%)	30 (100,0%)	
Need for cystoscopy, n (%)			<0,0001
yes	30 (100,0%)	0 (0,0%)	
no	0 (0,0%)	30 (100,0%)	
VAS			0,0008
Mean (SD)	4,1 (2,4)	2,0 (2,2)	
Median (IQR)	4,0 (2,0-6,0)	1,0 (0,0-3,8)	

The comparative analysis revealed that the stent removal time was significantly shorter in group B (40 sec (25-90)) compared to group A (142,5 sec (95-190), p<0,0001). In addition, there was a statistically significant lower VAS pain score in group B patients (1 (0-3,8)) compared to group A patients (4 (2-6), p=0,0008). All patients from group B had successful stent removal with magnetic retriever, no cystoscope was required in any case. The dynamics of stent removal time and pain level in group A and group B are shown in figures 36, 37.

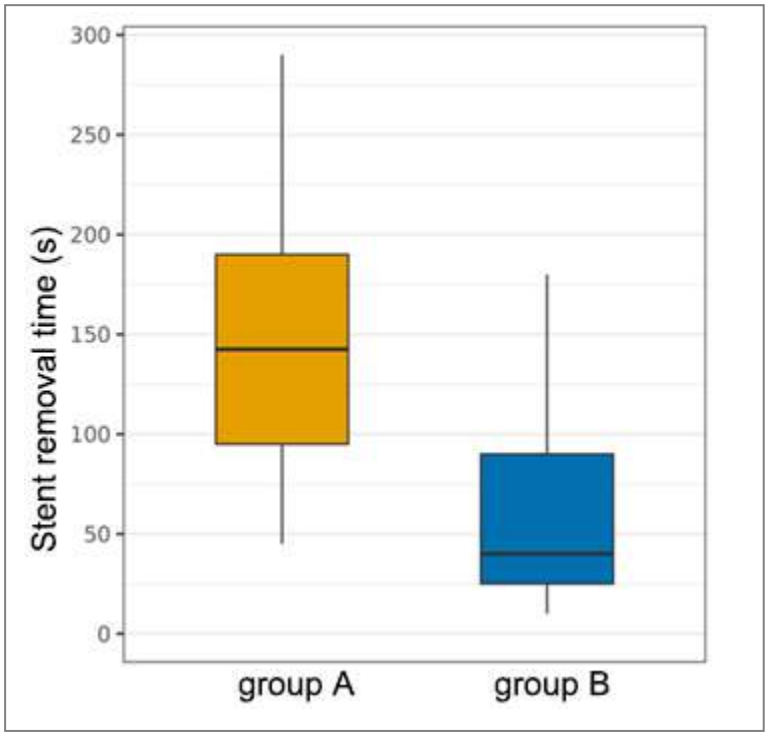


Figure 36 – Ureteral stent removal time

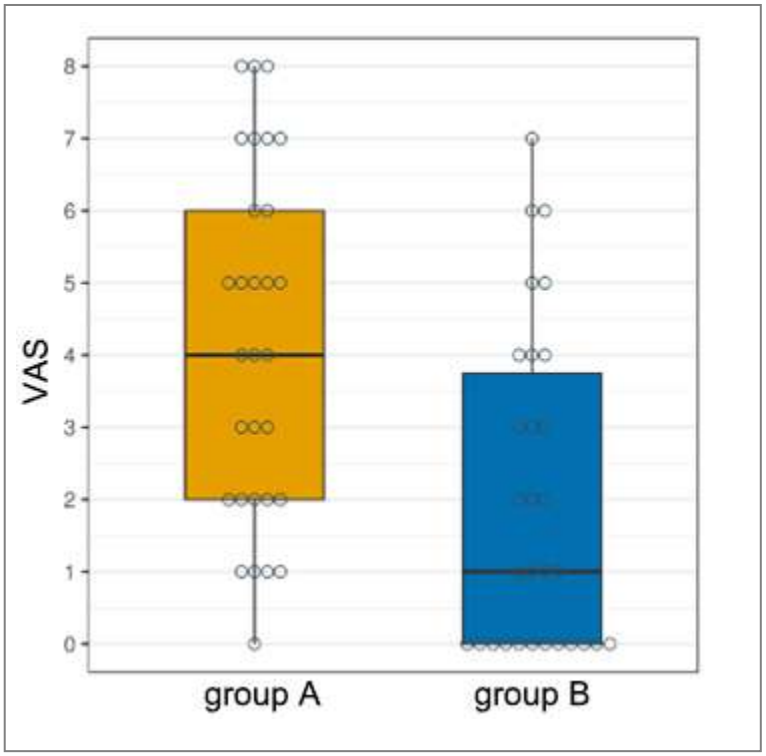


Figure 37 – Pain syndrome level after stent removal

To summarize the data obtained in the study, it can be said that the results clearly illustrate the advantage of using magnetic stents compared to conventional ureteral stents. The procedure of magnetic stent removal by a special retriever under ultrasound guidance is faster and causes less discomfort for the patient, while the severity of stent-associated symptoms is comparable. Also, magnetic stent removal is a completely outpatient procedure, which does not require a visit of the patient to the clinic and eliminates the need for general anaesthesia, which is necessary if stent removal is performed using a rigid cystoscope in men. The magnetic retriever is a disposable instrument that does not require sterilisation, hence eliminating the possibility of cross-contamination of patients with infection. Thus, the use of magnetic stents in urological practice can improve the quality of life of patients without compromising their safety.

Chapter 4
PREVENTION OF COMPLICATIONS ASSOCIATED WITH URETERAL STENTS

4.1 Study of the effectiveness of a digital registry of patients with ureteral stents, implemented on the basis of stone md mobile application, on the prevention of "forgotten" stents

This section presents the results of a study of the effect of the Stone MD mobile application on the prevention of "forgotten" ureteral stents in patients with urolithiasis. Patient data as well as primary and secondary outcomes are presented in tables 11-17 and figures 38-40.

Table 11 – Demographic and clinical data of patients

Characteristic	Control N=100	Stone MD N=108	p-value
Age (years)	53,7 (14,6) 54 (43-65)	51,4 (14) 51 (39-63)	0,2819
Sex			0,8874
female	39 (39%)	44 (40,7%)	
male	61 (61%)	64 (59,3%)	
Social status			0,4405
employed	45 (45%)	57 (52,8%)	
unemployed	29 (29%)	24 (22,2%)	
retired	26 (26%)	27 (25%)	
Diabetes mellitus	8 (8%)	12 (11,1%)	0,4885
Cerebrovascular disease (CVD)	5 (5%)	5 (4,6%)	>0,9999

No statistically significant differences were found between groups with respect to age, gender, social status of patients, and frequency of comorbidities.

Table 12 – Structure of operative interventions in patient groups

Operation name	Control	Stone MD	p
Internal kidney drainage with a stent	49 (49%)	71 (65,7%)	0,1152
Transurethral contact ureterolithotripsy category 1	5 (5%)	6 (5,6%)	
Transurethral contact ureterolithotripsy category 2	38 (38%)	24 (22,2%)	
Transurethral contact ureterolithotripsy category 3	5 (5%)	5 (4,6%)	
Retrograde fibronephrolithotripsy category 1	2 (2%)	2 (1,9%)	
Retrograde fibronephrolithotripsy category 2	1 (1%)	0 (0%)	

The most frequent interventions in both the control group and the Stone MD group were internal kidney drainage with a stent and transurethral contact ureterolithotripsy.

The incidence of stent-associated symptoms was 73% in the control group and 75% in the group of patients using Stone MD (p=0,7542). The use of the Stone MD app was associated with a lower incidence of "forgotten" stents compared to the control group (OR=0,17 [95% CI: 0,04; 0,55], p=0,0073).

Table 13 – Investigated outcomes

Outcome	Control	Stone MD	p
Stent-associated symptoms (SAS)	73 (73%)	81 (75%)	0,7542
Stent removal			0,0073
removed on time	86 (86%)	105 (97,2%)	
delayed less than 14 days	11 (11%)	3 (2,8%)	
delayed more than 14 days	3 (3%)	0 (0%)	

In the group of patients using Stone MD, 105 out of 108 patients (97,2%) removed the stent on time and 3 (2,8%) patients delayed removal for less than 14 days, while in the control group timely stent removal was noted only in 86% of patients, 11% delayed removal for less than 14 days, and 3% of patients removed the stent more than 14 days late. Figure 38 shows the cumulative frequency of timely stent removal in the patient groups.

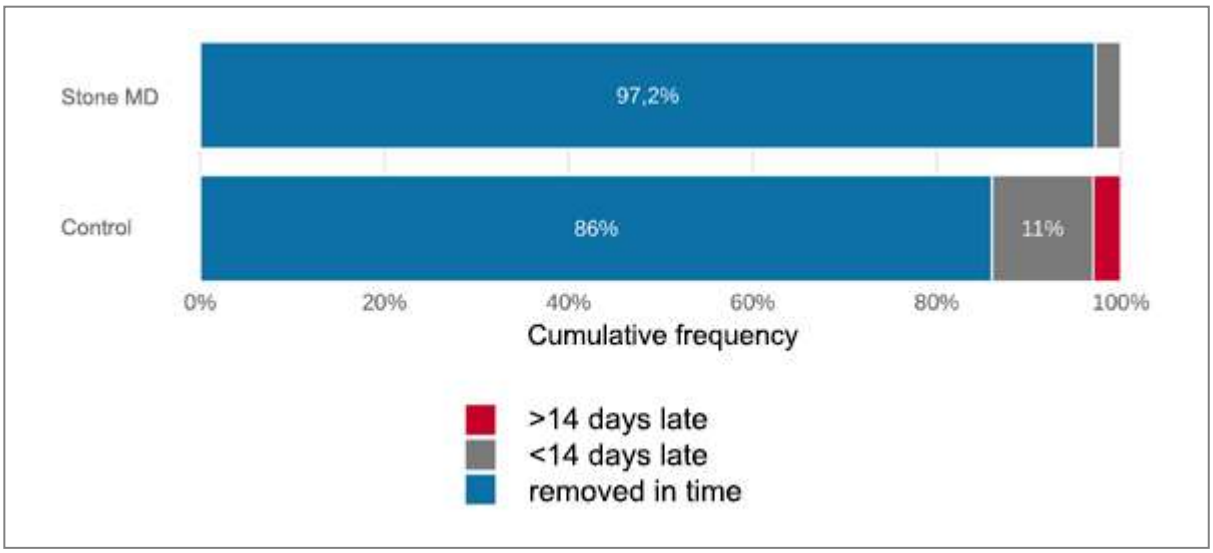


Figure 38 – Timeliness of stent removal in patient groups

Analysis of factors associated with the risk of untimely ureteral stent removal

The results of the single-factor analysis of indicators associated with the risk of untimely ureteral stent removal are presented in table 14.

Table 14 – Results of a single-factor analysis of indicators associated with the risk of untimely ureteral stent removal

Indicator	Risk variation (95% CI)	Relative risk (95% CI)	p
Stent-radar use	-11,2 (-18,7; -3,7)%	0,2 (0,06; 0,67)	**0,0032**
Presence of SAS	-21,5 (-33,2; -9,8)%	0,11 (0,04; 0,32)	**<0,0001**
CVD	22,9 (-5,7; 51,6)%	4,24 (1,45; 12,41)	**0,0098**

Continuation of table 14

Indicator	Risk variation (95% CI)	Relative risk (95% CI)	p
Social status (retired, unemployed)	8,3 (1,0; 15,6)%	3,13 (1,05; 9,28)	**0,0281**
Social status (employed)	-8,3 (-15,6; -1,0)%	0,32 (0,11; 0,95)	**0,0281**
Age ≥55 years	4,0 (-3,6; 11,6)%	1,63 (0,65; 4,13)	0,2931
Male sex	3,6 (-3,7; 10,8)%	1,59 (0,58; 4,36)	0,3566

Figure 39 shows a chart with relative risk scores and 95% confidence interval (CI) for the predictors studied.

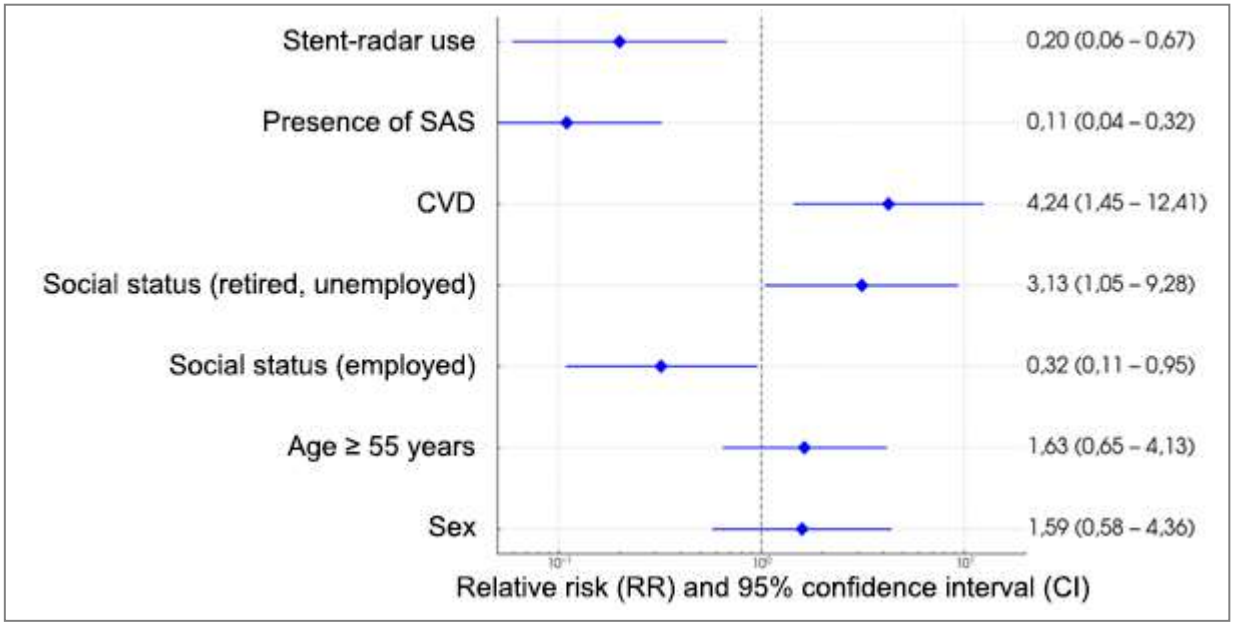


Figure 39 – Factors associated with the risk of untimely ureteral stent removal

Use of the Stone MD app was associated with a significant reduction in the risk of untimely ureteral stent removal, the change in absolute risk (AR) was -11,2% (95% CI: -18,7% to -3,7%) and the relative risk (RR) of untimely ureteral stent removal was 0,2 (95% CI: 0,06 to 0,67; p=0,0032).

The presence of SAS was also significantly associated with a decreased risk of late ureteral stent removal (AR -21,5 (95% CI: -33,2% to -9,8%), RR of late ureteral stent removal was 0,11 (95% CI: 0,04 to 0,32; p<0,0001).

The presence of CVD in patients was associated with a significantly increased risk of untimely ureteral stent removal, with an AR of 22,9% (95% CI: -5,7% to 51,6%). RR was 4,24 (95% CI: 1,45 to 12,41; p=0,0098).

Retirement status or lack of employment was associated with an increased risk of late ureteral stent removal, with an AR of 8,3% (95% CI: 1,0% to 15,6%). RR was 3,13 (95% CI: 1,05 to 9,28; p=0,0281). The presence of employment among patients was associated with a reduced risk of late ureteral stent removal (AR: -8,3% (95% CI: -15,6% to -1,0%)). RR was 0,32 (95% CI: 0,11 to 0,95; p=0,0281).

Age and gender had no statistically significant effect on the risk of untimely ureteral stent removal (p>0,05).

Clinical significance of the use of the Stone MD mobile app, the "stent-radar" section and the pharmacoeconomics of "forgotten" stents

In order to assess the clinical relevance of the "Stent Radar" section of the Stone MD application, the indicators associated with untimely ureteral stent removal were analyzed.

A total of 208 patients participated in the study. 108 (51,9%) were selected to use the Stone MD app, of which 3 patients did not remove the stent in a timely manner despite being reminded in advance by the app. The probability of untimely stent removal using the "Stent Radar" app was 2,8%. Of the 100 (48,1%) patients who did not use "Stent Radar", 14 patients forgot to remove their ureteral stent in a timely manner. Thus, the probability of untimely stent removal without using the app was 14%.

The use of the "Stent Radar" app was found to reduce the absolute probability by 11,2% and the relative probability of untimely stent removal by 80,2% compared to patients not using the "Stent Radar" app (figure 40). The number needed to treat (NNT) of 8,91, indicates that the use of the "Stent Radar" app prevents 1 case

of untimely stent removal for every 9 patients with a ureteral stent. The results of the risk scores for untimely stent removal associated with the use of the Stone MD mobile app are presented in table 15.

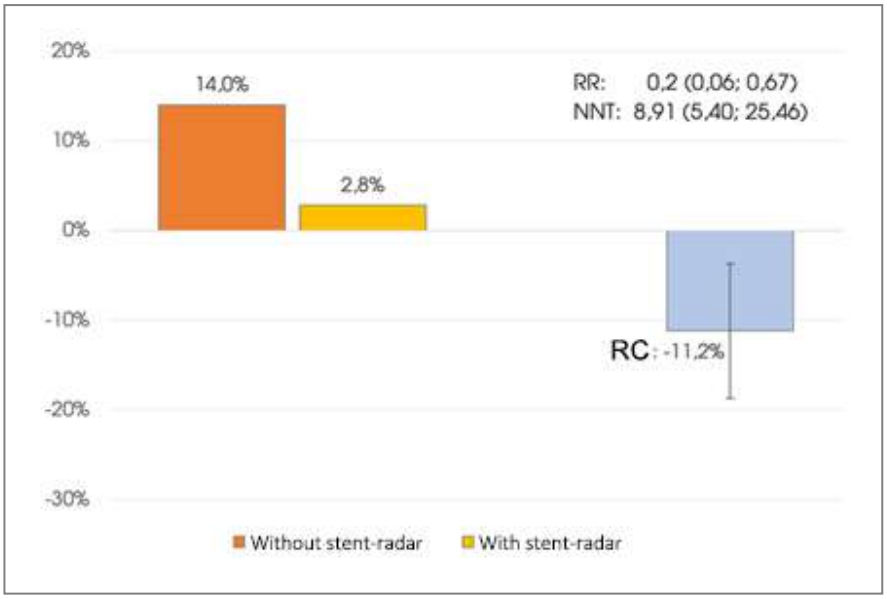


Figure 40 – Change in risks when using the "stent-radar" application

Table 15 – Risk indicators for untimely stent removal associated with the use of the "stent-radar" application

Indicator	Value	95% CI
Absolute Risk Reduction (ARR)	-11,2%	(-18,7; -3,7)
Relative Risk Reduction (RRR)	80,2%	(5,9; 67,0)
Number needed to treat (NNT)	8,91	(5,40; 25,46)

The indicators of potential efficiency of using the "Stent Radar" application in patients with a placed ureteral stent are presented in table 16.

The average costs of treatment of one complete clinical case in the hospital with a "forgotten" ureteral stent are presented in table 17.

Table 16 – Estimated efficacy of the "stent-radar" application in patients with an implanted ureteral stent (per 1000 people)

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Frequency of application use	Base number of "forgotten" stents	Number of "forgotten" stents when using the application	Number of cases of untimely removal prevented
100%	140	28	112
50%	140	14	66
25%	140	7	33

Table 17 – Cost of a completed case of hospitalisation of a patient with a "forgotten" stent according to the rates for the provision of specialised medical care under the basic programme of compulsory medical insurance in 2024

Procedure performed (DRG)	Cost, rub.
catheter removal from the upper urinary tract (st30.010)	~ 29708
transurethral contact cystolithotripsy (st30.012)	~ 44561
transurethral endoscopic ureterolithotripsy (st30.014)	~ 95656
percutaneous nephrolithotripsy with lithoextraction (st30.015)	~ 142005

As a result of the study, it was found that the use of the "Stent Radar" application is associated with a lower probability of FUS. The factors determining timely ureteral stent removal were identified. The use of the "Stent Radar" section of Stone MD mobile application, presence of stent-associated symptoms and employment are associated with decreased risk of untimely ureteral stent removal, while CVD, social status of a pensioner and lack of employment are associated with its increase. Age and gender had no significant effect on the likelihood of untimely ureteral stent removal. Routine use of the Stone MD application in patients, especially those with low compliance who underwent upper urinary tract stenting,

will allow to prevent the occurrence of "forgotten" stents, and thus significantly reduce the economic costs of treatment.

4.2 Modelling of calcium excretion and pharmacological correction of urine lithogenic properties for prevention of ureteral stent encrustation

This section presents the results of a study of the effect of creatine on the daily excretion of key parameters in daily urine in healthy volunteers. Patient data as well as primary outcomes are presented in table 18 and figures 41, 42.

During follow-up, none of the 10 volunteers dropped out of the study. The mean age of the subjects was 34 years (20-65 years). Males accounted for 70% (n=7) of the study cohort. The demographics of the included volunteers are presented in table 18.

Table 18 – Demographics of volunteers

Characteristic	Healthy volunteers (N=10)
Age (years)	34 (20–65)
Sex	
female	3 (30%)
male	7 (70%)
BMI	26,8 (24,1-29,9)
Hypertensive disease	2 (20%)
Tobacco smoking	1 (10%)
Physical activity index	1,8 (1,4-2,2)

When comparing the indicators of daily excretion in urine, no statistically significant differences were found in the dynamics of phosphorus (p=0,34) and creatinine (p=0,75) values. However, statistically significant differences were found

in the dynamics of daily urinary calcium excretion values (p=0,02). The dynamics of changes in the investigated 24-hour urine indicators, as well as the dynamics of their median values are presented in figures 41, 42.

When assessing the indicators of daily excretion in urine in the control points, no significant dynamics was found in the level of phosphorus and creatinine (p=0,34 and p=0,75, respectively). Statistically significant dynamics was noted for the level of calcium excretion in urine (p=0,02). Changes in the investigated indicators of 24-hour urine, as well as their relative values of dynamics are presented in figures 41, 42.

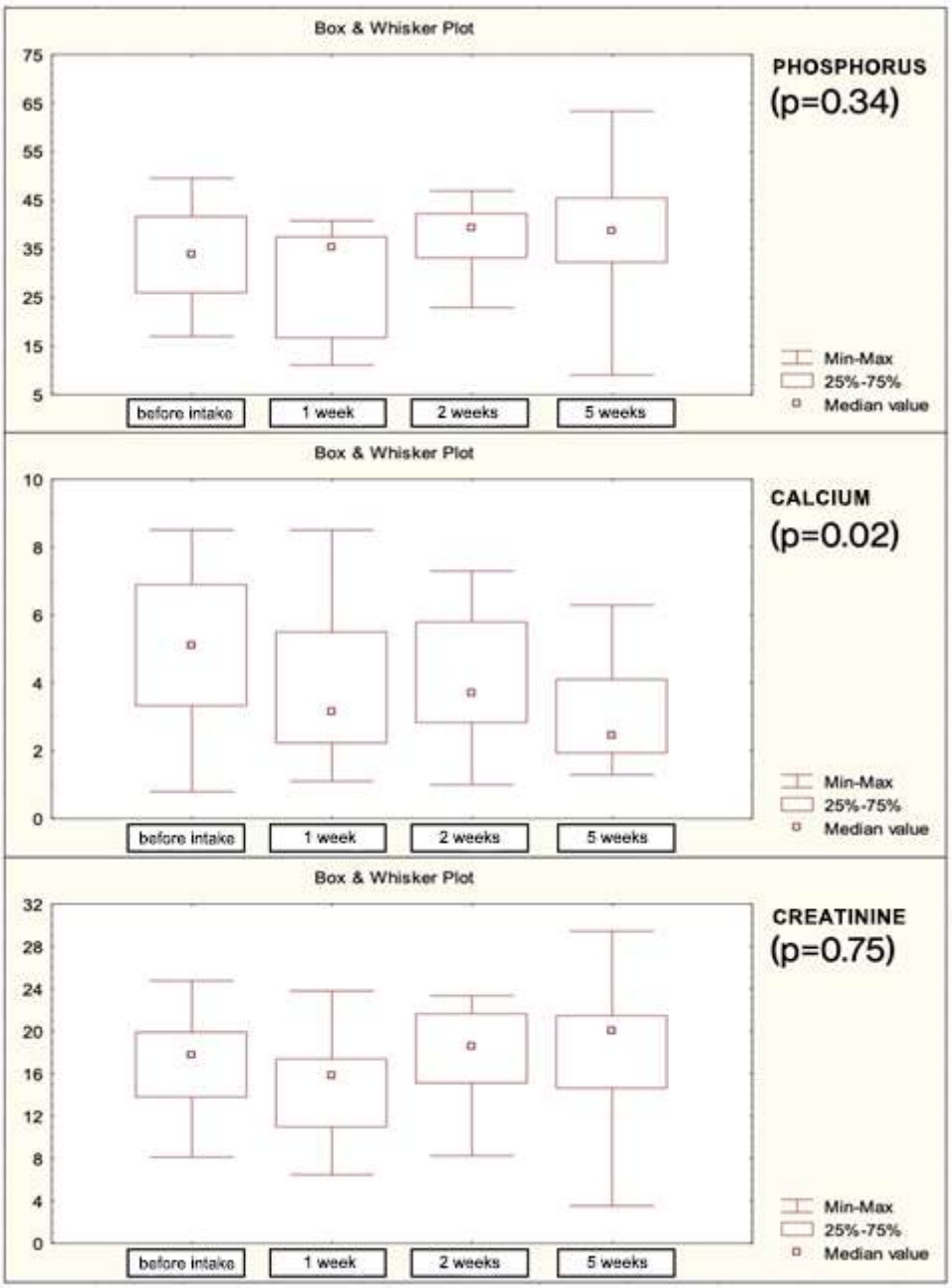
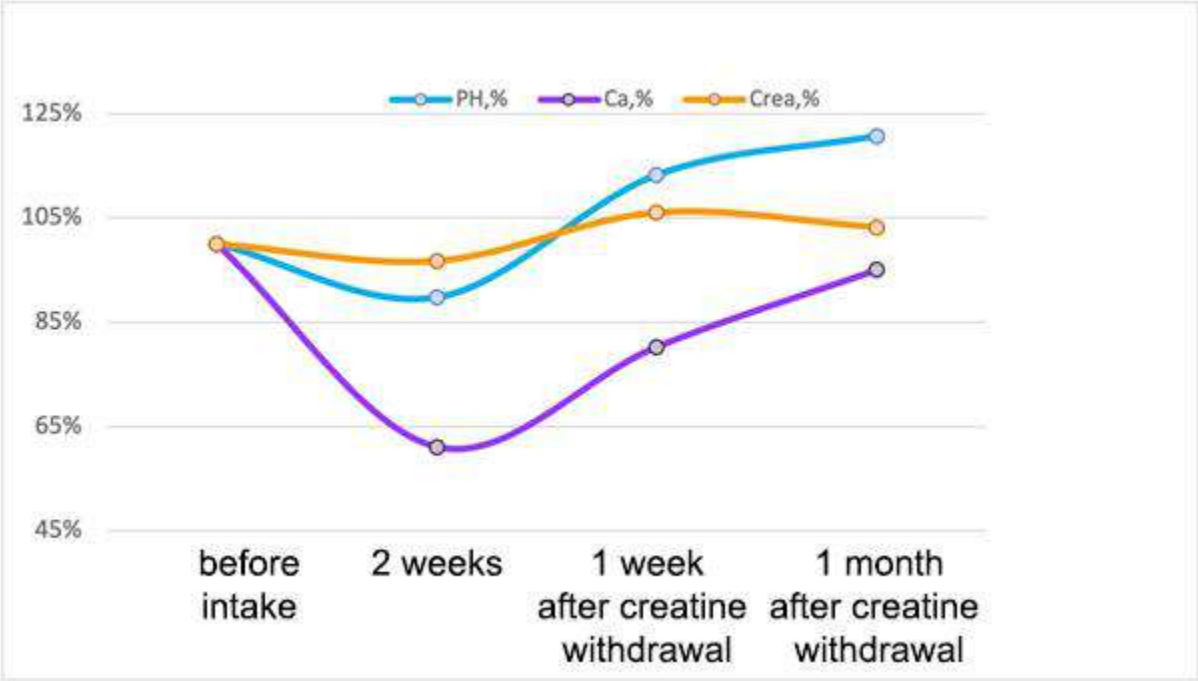


Figure 41 – Diagram of changes in daily excretion of the investigated indicators



PH – phosphorus; Ca – calcium; Crea – creatinine.

Figure 42 – Assessment of the relative dynamics of excretion of investigated indicators in 24-hour urine

The study found that healthy volunteers who received creatine for 1 month had a significant decrease in urinary calcium excretion, which, in turn, may indicate a potential benefit of creatine use in patients with urolithiasis.

This section presents the results of a study on the effect of combined administration of ascorbic acid and creatine as an inhibitor of ureteral stent encrustation. Patient data as well as results are presented in tables 19-22 and figures 43, 44.

60 patients with urolithiasis participated in the present study. The mean age of the patients was 47,1±12,7 years, the minimum age of the included participant was 20 years and the maximum age was 74 years. Male patients constituted 46,7% (n=28) of the study cohort. Transurethral ureterolithotripsy (TUL) was performed in 36,7% (n=22) of patients, internal drainage of the kidney with a stent in 31,7% (n=19), and retrograde intrarenal surgery (RIRS) in 31,7% (n=19).

30 patients each were included in the main group and control group. Comparison of patients according to baseline characteristics is presented in table 19.

The groups were comparable in age, sex and BMI (p>0,05). Patients in the main group underwent RIRS marginally more frequently – 40,0% (n=12), whereas in the control group the more frequent intervention was TUL – 43,3% (n=13), however, the statistical significance of the differences was not achieved (p=0,3507).

Table 19 – Clinical characteristics of patients in the study groups

Indicator	Main (N=30)	Control (N=30)	p
Age, years	46,5±12,4	47,7±13,2	0,7786
BMI, kg/m²	27,8±3,5	29,0±4,1	0,3631
Females	16 (53,3%)	16 (53,3%)	1,0000
Males	14 (46,7%)	14 (46,7%)	
TUL	9 (30,0%)	13 (43,3%)	0,3507
Internal kidney drainage with a stent	9 (30,0%)	10 (33,3%)	
RIRS	12 (40,0%)	7 (23,3%)	

Table 20 presents the results of analysis of daily urine composition of patients before the study. The studied groups did not differ significantly in most indicators (p>0,05), but the patients of the main group had statistically significantly higher calcium level (figure 43) compared to the control group patients (5,6±1,2 mmol/24h vs. 4,6±1,6 mmol/24h, p=0,0127).

Table 20 – Indicators of a baseline study of 24-hour urine composition

Indicator	Main (N=30)	Control (N=30)	p
Phosphorus, mmol/24h	23,9±9,0	26,5±10,6	0,7117
Calcium, mmol/24h	5,6±1,2	4,6±1,6	**0,0127**
Creatinine, mmol/24h	7,4 [5,8; 12,5]	10,7 [6,8; 13,6]	0,1578
Uric acid, mmol/24h	2,9±1,2	3,0±1,2	0,8766

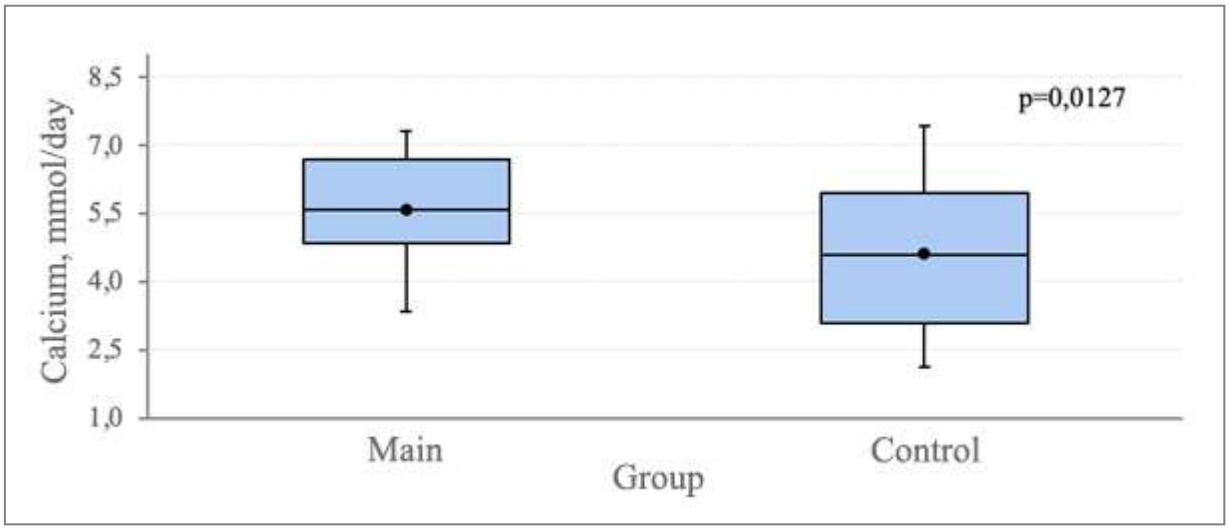


Figure 43 – Calcium levels in 24-hour urine,
in patients in the studied groups (p=0,0127)

In terms of total plasma calcium levels, both groups were comparable: the concentrations in the main and control groups were 2,5±0,2 mmol/L and 2,4±0,1 mmol/L, respectively, at p=0,4869 (figure 44).

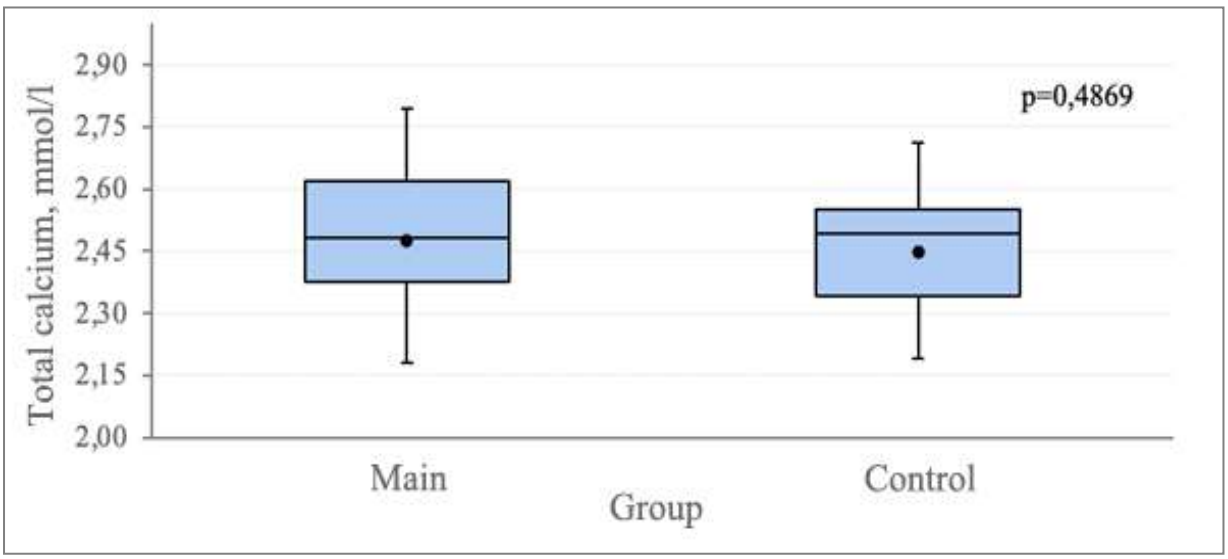


Figure 44 – Results of baseline study of total plasma calcium in the study groups (p=0,4869)

Table 21 and figure 45 present the results of analysing the dynamics of urine pH in the patients of the main group and the control group. During the follow-up

period of 28 days, the decrease in pH among patients in the group receiving ascorbic acid was 14,05% (p<0,0001), while in the control group no statistically significant pH dynamics were observed (p=0,9892) (figure 46).

Table 21 – Dynamics of urine ph level in patients in the studied groups

Day	Main group M±S (N=30)	Dynamics, %	Control group M±S (N=30)	Dynamics, %	P* level
0	6,43±0,79	–	6,40±0,73	–	0,8531
1	6,21±0,57	-3,37	6,49±0,59	1,41	0,0879
2	6,17±0,56	-3,99	6,52±0,58	1,93	0,0550
3	5,83±0,53	-9,38	6,52±0,43	1,98	**<0,0001**
4	5,82±0,45	-9,43	6,54±0,50	2,24	**<0,0001**
5	5,79±0,44	-9,95	6,55±0,54	2,40	**<0,0001**
6	5,76±0,40	-10,37	6,41±0,52	0,21	**<0,0001**
7	5,73±0,46	-10,83	6,48±0,55	1,25	**<0,0001**
8	6,01±0,34	-6,58	6,46±0,61	0,99	**0,0017**
9	5,76±0,40	-10,37	6,44±0,69	0,63	**<0,0001**
10	5,91±0,37	-8,09	6,52±0,52	1,93	**<0,0001**
11	5,79±0,38	-9,95	6,57±0,58	2,76	**<0,0001**
12	5,93±0,40	-7,83	6,43±0,41	0,57	**<0,0001**
13	5,84±0,38	-9,12	6,42±0,57	0,36	**<0,0001**
14	5,81±0,39	-9,64	6,47±0,45	1,09	**<0,0001**
15	5,81±0,39	-9,69	6,46±0,53	0,94	**<0,0001**
16	5,80±0,42	-9,80	6,46±0,59	0,99	**<0,0001**
17	5,84±0,41	-9,12	6,42±0,49	0,36	**<0,0001**
18	5,84±0,40	-9,23	6,36±0,45	-0,63	**<0,0001**
19	5,74±0,43	-10,68	6,49±0,51	1,46	**<0,0001**
20	5,74±0,38	-10,68	6,35±0,48	-0,78	**<0,0001**
21	5,65±0,43	-12,13	6,46±0,61	1,04	**<0,0001**
22	5,69±0,44	-11,56	6,46±0,55	0,99	**<0,0001**

Continuation of table 21

Day	Main group M±S (N=30)	Dynamics, %	Control group M±S (N=30)	Dynamics, %	P* level
23	5,66±0,42	-11,98	6,53±0,47	2,14	**<0,0001**
24	5,59±0,48	-13,01	6,47±0,50	1,09	**<0,0001**
25	5,58±0,48	-13,17	6,36±0,51	-0,63	**<0,0001**
26	5,61±0,41	-12,70	6,35±0,50	-0,78	**<0,0001**
27	5,55±0,43	-13,63	6,49±0,52	1,51	**<0,0001**
28	5,53±0,42	-14,05	6,41±0,49	0,16	**<0,0001**
P** level	***<0,0001***		*0,9892*		
Note – * – Mann-Whitney U-test; ** – Friedman test.					

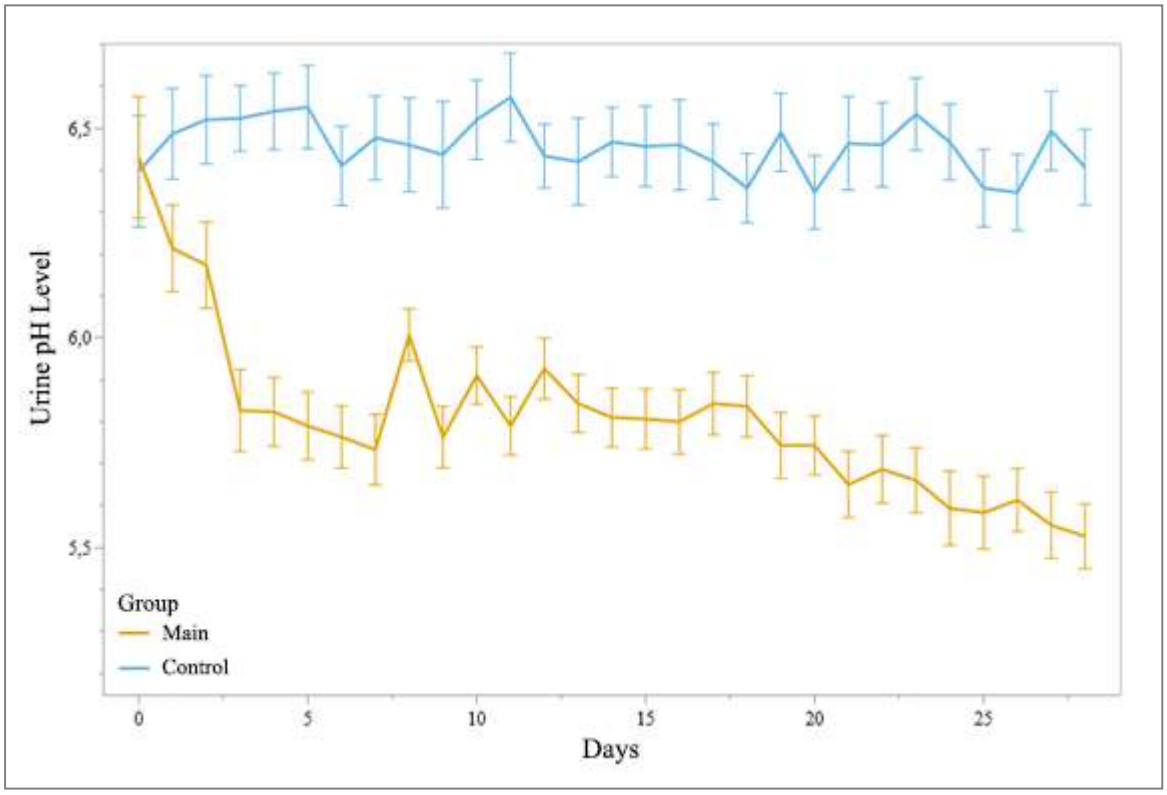


Figure 45 – Absolute dynamics of urine pH level in the studied groups

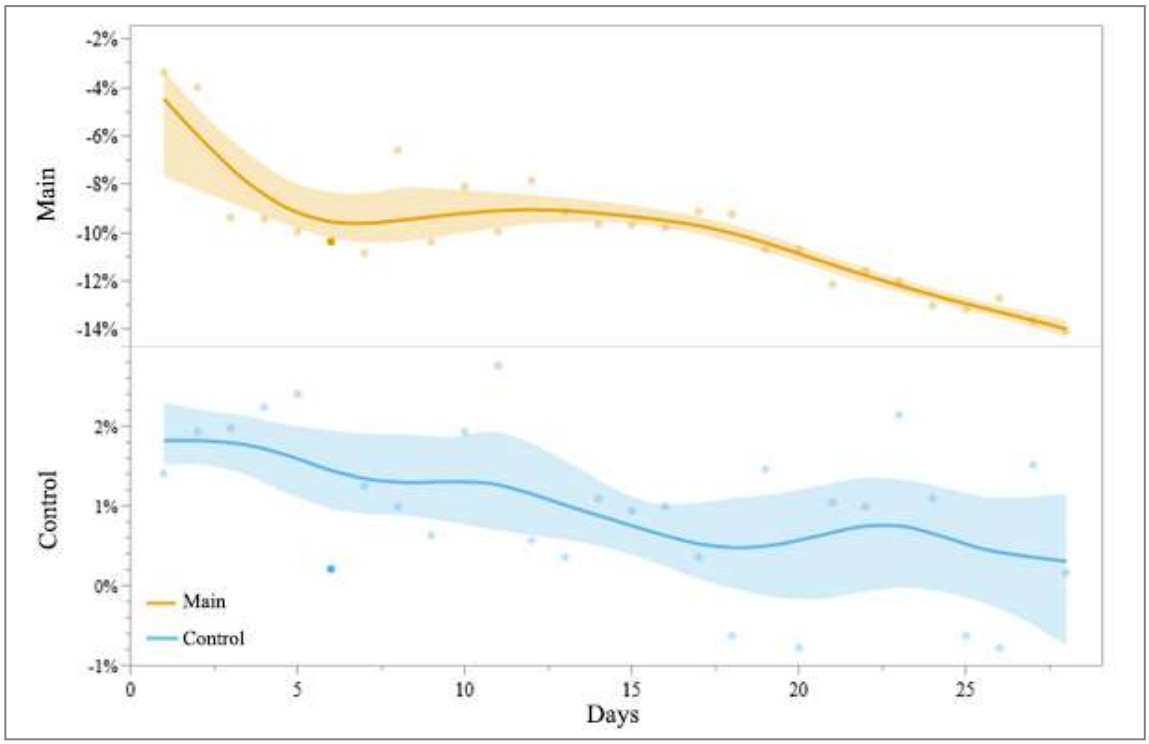


Figure 46 – Relative dynamics of urine pH level in the studied groups

Multiple regression analysis using the least squares method demonstrated that taking ascorbic acid, adjusted for follow-up time, had a statistically significant effect on urine pH. Patients taking ascorbic acid were characterised by lower urine pH levels (coeff. -0,6492). The value of the coefficient of determination R^2=0,3109 indicates that the model explains about 31,09% of the variation in urine pH, indicating that there are other factors that may also influence this indicator. The multiple correlation coefficient of 0,5576 indicates a moderate relationship between predicted and actual pH values.

The results of the analysis of variance also showed high significance of the model as a whole (F-ratio=391,85, p<0,0001), confirming the relevance of the variables included. Normality of the residuals, however, was not confirmed (Shapiro-Wilk test: W=0,9938, p<0,0001), which may indicate the presence of additional sources of variability or non-linear effects that may not have been accounted for in this model.

In summary, the analysis revealed a significant association of ascorbic acid intake with urine pH during the 28-day follow-up, but the findings indicate the possible influence of some confounding factors on the outcome, which may require

further investigation and construction of complex models in order to better explain the variability in the data.

At macroscopic evaluation, no incrustation was detected in any case in the patients of the main group, whereas in the control group macroscopic incrustation was observed in 10,0% (n=3) of patients (p=0,2373). Microscopically, encrustation was detected in 10,0% (n=3) of patients in the main group, and in 40% (n=12) of patients in the control group (p=0,0087). The thickness of encrustation (table 22) in the distal part in the main group was 4 [3,5; 4,5] μm, and in the control group 20 [15,8; 110,3] μm, the revealed differences were statistically significant (p=0,0367). Electron microscopy of the stents is presented in figure 47.

Table 22 – Microscopic evaluation of the thickness of encrustations (μm)

Encrustation level	**Main (N=3)**	**Control (N=12)**	**p**
Proximal part	12 [12; 12]	15 [11,8; 100,5]	0,4386
Distal part	4 [3,5; 4,5]	20 [15,8; 110,3]	**0,0367**

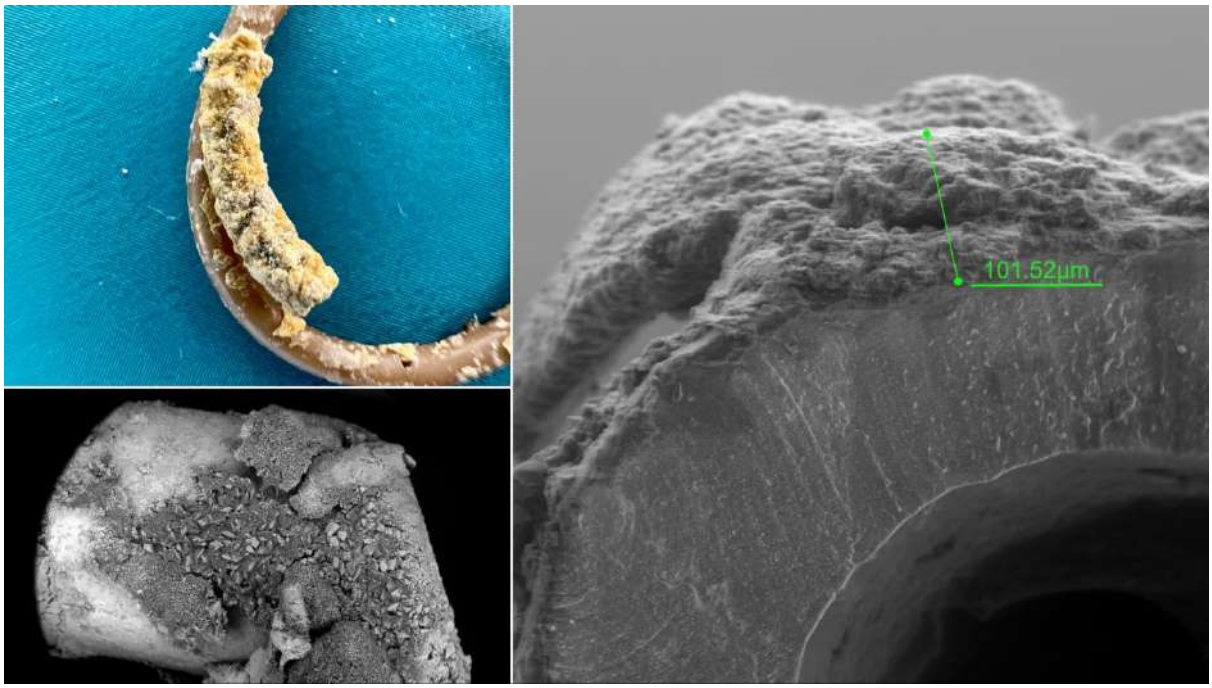


Figure 47 – Macroscopic and microscopic evaluation
of ureteral stent encrustation thickness. Magnification 101× and 313×.
QUANTA™ 3D electron microscope (FEI Company (USA))

Table 23 presents the results of analysing the composition of the excreted incrustation. Urate was excreted in 100,0% (n=3) of cases in patients of the main group, in the control group calcium-oxalate was registered in 83,3% (n=10), in 1 case urate and in 1 case calcium phosphate (p=0,0058) (figures 48, 49).

Table 23 – Distribution of encrustations by composition in the studied groups

Composition of encrustations	**Main (N=3)**	**Control (N=12)**	**p**
calcium-oxalate	(0,00%)	10 (83,3%)	**0,0058**
urate	3 (100,00%)	1 (8,3%)	
calcium phosphate	(0,00%)	1 (8,3%)	

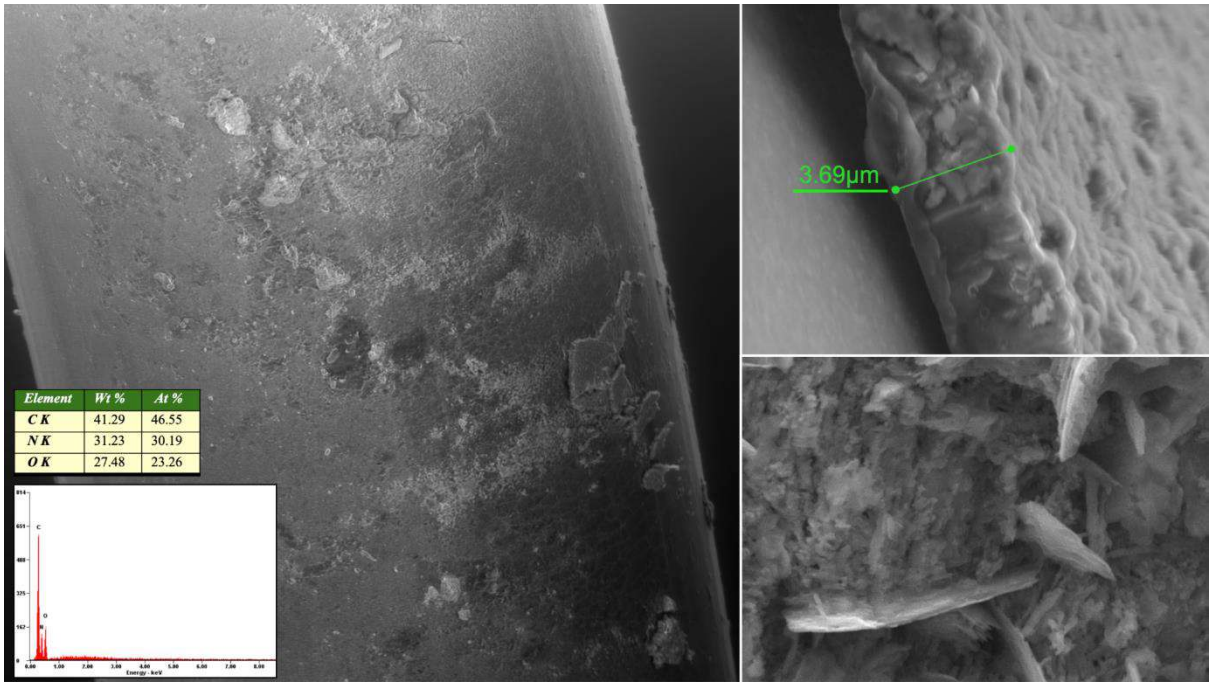


Figure 48 – Microscopic evaluation of the thickness and chemical composition of the ureteral stent encrustation from the main group. The transverse split is morphologically and chemically heterogeneous. Lamellar aggregates and uricite crystals (C5H4N4O3) and urea (CO(NH2)2) crystals. Magnification of 128×, 1356× and 2167×. QUANTA™ 3D electron microscope (FEI Company (USA))

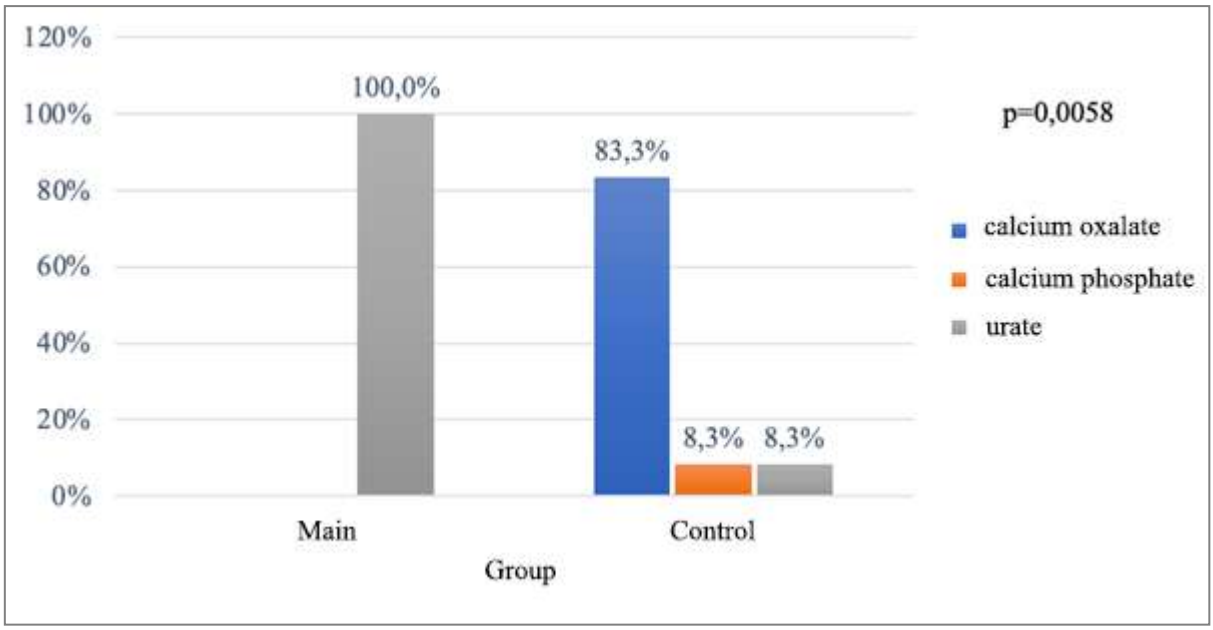


Figure 49 – Distribution of incrustations by composition in the studied groups (p=0,0058)

To summarize the data obtained in the study, it can be said that creatine and ascorbic acid are able to correct lithogenic properties of urine, preventing nucleation of calcium phosphate and oxalate crystals, as well as lowering its pH.

In the main group of patients microscopic encrustation of stents was revealed in 10% of cases, urate was found in the composition of encrustations, the formation of which, apparently, is associated with urine acidification. Absence of calcium-containing salts on the stent surface in the main group is associated with chelating activity of creatine and acidifying ability of ascorbic acid, which have synergism and potentiate the protective effect directed against polymer surface encrustation.

The observed results indicate statistically significant efficacy of the investigated preparations in relation to the degree of ureteral stent encrustation, with good tolerability and safety.

CONCLUSION

Ureteral stents are nowadays an integral and important part of routine urological practice, with a number of significant advantages over other methods of upper urinary tract drainage. The frequency of stent use in various urological interventions is quite high, but at the same time the incidence of adverse effects, such as stent-associated symptoms, "forgotten" ureteral stents, and encrustation, reaches 80%. The presence of a large number of patients who have encountered complications of ureteral stenting creates an urgent problem for modern healthcare. It is necessary to strike a balance between the advantages and disadvantages of ureteral stents. Prospective directions for the control of stent-associated symptoms are reduction of the frequency of ureteral stents use, decreasing the duration of their indwelling in the urinary tract and timely removal, which will definitely lead to improvement of patients' quality of life.

In-depth study of adverse side effects associated with ureteral stent use, understanding the pathophysiology of the interaction between the stent polymer and the urinary tract wall is a key factor necessary to understand the ways to modernize ureteral stents, which is necessary to improve the quality of life of patients. This knowledge also allows researchers to determine the relationship between stenting complications and stent design, material or coating. These are the three main factors responsible for the majority of complications associated with the use of ureteral stents.

Ureteral stents have a rich history and have undergone numerous stages of evolution. However, stent-associated symptoms, encrustation remain and these are obstacles that have yet to be overcome on the way to creating the "perfect" stent.

The aim of this study is to enhance the utilization of ureteral stents through a comprehensive evaluation of their material characteristics, effects on patient quality of life, extraction techniques, and strategies for mitigating complications.

The dissertation consists of experimental and clinical parts.

The goal of the experimental part was to study the peculiarities of surface and physicomechanical properties of polymers used for the production of ureteral stents. The experimental part of the study was carried out in the scientific laboratory on the basis of the Department of "Plastics Processing Equipment and Robotics" of Saint Petersburg State Institute of Technology (SPSIT), as well as on the basis of the resource centre of "Microscopy and Microanalysis" of Saint Petersburg State University (SPbU). For this purpose, samples of thermoplastic polyurethane and silicone rubber with hardness similar to that of polymers used to make ureteral stents were selected. During the analysis of the obtained data, it became obvious that the contact angle as well as the percentage of water absorbed is higher in polyurethanes, but the stiffness of the investigated materials differs significantly. Silicone rubber hydrophilizes faster and has less elasticity. Moreover, in the process of water penetration into the polymer body, the stiffness of silicone decreases. Therefore, it can be said that ureteral stents made of silicone adapt faster in the lumen of the urinary tract compared to stents made of polyurethane.

To assess the quality of life of patients with silicone and polyurethane stents, a clinical study was conducted in the urology clinic of Pavlov First Saint Petersburg State Medical University (FSBEI HE I.P. Pavlov SPbSMU MOH Russia). All patients were divided into two homogeneous groups depending on the material of the deployed stent. Comparison of the visual analogue pain scale indices as well as the severity of overactive bladder symptoms 1 hour and 2 weeks after stent deployment and immediately prior to its removal demonstrates a significant superiority of silicone stents over polyurethane stents. At the same time, the assessment of the incidence of complications associated with urinary stenting did not reveal statistically significant differences between the studied groups.

A study of the safety and efficacy of ultrasound-guided removal of magnetic ureteral stents, all other things being equal, demonstrates the undeniable advantage of magnetic ureteral stents over conventional polyurethane stents. With a comparable degree of stent-associated symptoms, the procedure of magnetic stent removal requires less time and causes less discomfort for the patient. Furthermore, magnetic

stent removal is a completely outpatient procedure that does not require the patient to visit the clinic. This can be very important for implementing de-escalation of surgical activity and freeing up additional patient beds, such as was needed during the COVID-19 pandemic. In addition, the possibility of cross-infection is eliminated because the magnetic retriever is a disposable instrument that does not require re-sterilisation.

The creation of an automatic digital registry of patients with ureteral stents and its mobile realization allowed to implement a personalised approach to timely removal of ureteral stents. It was found that the use of the "Stent Radar" section of the Stone MD mobile application in patients with ureteral stents, especially with low adherence to treatment, is associated with a lower probability of untimely stent removal. In turn, this may lead to a reduction in the number of "forgotten" stents and lower economic costs of treatment.

On the basis of the urology clinic of the FSBEI HE I.P. Pavlov SPbSMU MOH Russia, the effectiveness of oral combined intake of creatine and ascorbic acid on the degree of ureteral stent encrustation was studied. It was found that daily creatine intake for one month reduces daily urinary calcium excretion in healthy subjects. In the course of this study in patients with urolithiasis it was possible to correct lithogenic properties of urine, in particular, to prevent nucleation of calcium phosphate and oxalate crystals on the stent surface, also reducing its pH. The observed results of microscopic evaluation of the thickness and chemical composition of the ureteral stent encrustation indicate the effectiveness of the combined application of creatine and ascorbic acid.

KEY FINDINGS

1. Silicone in the product adapts faster than polyurethane and becomes more elastic due to decreased elastic modulus, high rate of moisture absorption combined with increased hydrophilicity. The adverse effects of polyurethane stents do not depend on surface forces, but are related to the stiffness of the product, which should be taken into account when choosing a ureteral stent.

2. The quality of life of patients with silicone stents is higher than that of patients with polyurethane stents, as they have a significantly lower incidence and intensity of pain syndrome.

3. The use of magnetic-tip polyurethane stents is safe for patients as they have a comparable level of stent-associated symptoms to conventional polyurethane stents. Removal of magnetic-tip stents does not require the use of a cystoscope, is quicker and involves less discomfort.

4. Application of a personalised digital registry of patients with ureteral stents, implemented on the basis of the Stone MD mobile application, is an effective method of prevention of "forgotten" and untimely removed stents.

5. Peroral mixture of ascorbic acid and creatine corrects the lithogenic properties of urine and prevents encrustation of the stent polymer surface by acidifying the urine and preventing nucleation of calcium salts.

PRACTICAL RECOMMENDATIONS

1. Silicone stents are recommended for those patients who have previously had a negative experience with polyurethane stents due to the presence of marked stent-associated symptoms.

2. In men, it is expedient to use magnetic stents, as their removal is performed on an outpatient basis, general anaesthesia, operating room, cystoscope are not required.

3. All patients with stents deployed are recommended to use the free mobile application Stone MD with the section "Stent Radar" to reduce the likelihood of untimely stent removal.

4. All patients with urolithiasis and ureteral stents deployed are recommended to take orally ascorbic acid in a dosage of 500 mg twice a day and creatine 3 g once a day during the whole period of stenting, which will reduce the probability of polymer surface encrustation.

LIST OF ABBREVIATIONS AND SYMBOLS

AR – Absolute Risk
ARR – Absolute Risk Reduction
ASA – American Society of Anesthesiologists
ATP – adenosine triphosphate
BMI – body mass index
CI – confidence interval
CONSORT – Consolidated Standards of Reporting Trials
COVID 19 – coronavirus disease 2019
CVD – cerebrovascular disease
DJ stent – double-J stent
DLC – diamond like carbon coating
DRG – diagnosis-related group
F – force of gravity
FUS – "forgotten" ureteral stents
IQR – interquartile range
NNT – Number Needed to Treat
OAB – overactive bladder
pH – potential of hydrogen
PPS – pentosanpolysulfate
PU – polyurethane
PVP – polyvinylpyrolidone
RIRS – retrograde intrarenal surgery
RR – Relative Risk
RRR – Relative Risk Reduction
SAS – stent-associated symptoms
SD – standard deviation
SIL – silicone

TUL – transurethral ureterolithotripsy

US – ultrasound

USSQ – Ureteric Stent Symptom Questionnaire

VAS – visual-analogue scale

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