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REVIEW

Management of urinary stones by experts in stone disease (ESD 2025)

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Summary

The formation of kidney stones is a complex biologic process involving interactions among genetic, anatomic, dietary, and environmental factors. Traditional lithogenic models were based on urine supersaturation in relation to the activity of crystallization promoters and inhibitors. However, modern research has added new principles such as the "renal epithelial cell response" and the role of inflammation and oxidative stress leading to the development of a "multi-hit hypothesis".

A strong correlation between urinary stones and kidney damage has been well demonstrated by both cohort and case-control studies. The main contributors to chronic kidney damage associated with urinary stones include crystal deposition within the renal parenchyma, associated comorbidities, repeated obstructive and infectious episodes, as well as the potential adverse effects of stone removal procedures. Most hereditary stones may cause high urinary saturation levels promoting obstruction of the Bellini ducts and consequent glomerulosclerosis and interstitial fibrosis in the cortex. These include hereditary hypercalciurias, primary hyperoxalurias, cystinuria, adenine phosphoribosyltransferase (APRT) deficiency (associated with 2,8-dihydroxyadenine lithiasis) and xanthinuria. Complete distal renal tubular acidosis occurs in childhood and presents deafness, rickets, and a short life expectancy. The incomplete form usually manifests in adulthood, primarily with recurrent urinary lithiasis, and less frequently with nephrocalcinosis.

In all stone formers stone analysis and a basic metabolic evaluation, including blood biochemistry, urine sediment examination, urinary pH and culture are mandatory, in contrast high-risk stone formers require a more specific metabolic evaluation, including a 24-hour urine sample to measure calcium, phosphate, citrate,

oxalate, uric acid, magnesium, sodium and proteinuria. The morpho compositional analysis of kidney stones offers essential insights beyond merely identifying their predominant chemical component. This approach reveals key aspets of the stone formation, such as nucleation sites, crystal growth patterns, and the presence of specific lithogenic processes. The ideal analytical protocol combines stereoscopic microscopy (StM), scanning electron microscopy with energy-dispersive X-ray spectroscopy (SEM-EDS), and, when necessary, Fourier-transform infrared spectroscopy (FTIR).

Recurrence prevention and managing residual fragments require complementary strategies such as lifestyle modifications, dietary interventions, and pharmacological therapies. Among pharmacological options, alkaline citrate salts, particularly potassium citrate, are widely used due to their ability to modify urinary chemistry and inhibit stone formation. Recently, novel molecules have been introduced into the management of renal stone disease. Phytate a naturally occurring polyphosphorylated carbohydrate, exibits a potent inhibitory effect on calcium salt's nucleation, growth, and aggregation. Theobromine, another natural compound, has been shown to effectively inhibit uric acid crystallization. The co-administration of urinary alkalinizing agents, such as potassium citrate, alongside theobromine has been proposed as a therapeutic strategy to optimize uric acid solubility and to reduce the risk of excessive alkalinization and subsequent sodium urate precipitation.

Struvite stones are caused by urinary tract infection with urease-producing microorganisms. Their treatment requires specific measures including complete surgical stone removal, short or long-term antibiotic treatment, to maintain urinary acidification to a pH below 6.2, and a urine volume of at least 2 litres/24 hours. L-methionine has been shown to effectively lower urine pH and the relative supersaturation of struvite. An essential aspect of medical management of urinary stone disease is treatment adherence, which depends on perceived benefit, treatment duration, and side effect profile. The side effects of citrate treatment are mild gastrointestinal disorders whereas thiazide diuretics tend to cause hypokalemia-related symptoms and less frequent metabolic and dermatologic side effects.

Urease inhibitors for struvite stones and drugs used to enhance cystine solubility are more frequently associated with side effects. The use of smartphone applications can support patients by promoting adequate hydration, adherence to dietary recommendations, and compliance with prophylactic medication.

Endoscopic techniques currently play a prevalent role in the removal of renal stones, while extracorporeal shock wave lithotripsy is today marginally used for specific indications.

Different technical modalities can be used for percutaneous nephrolithotomy (PCNL), each with its own advantages and disadvntages (standard vs. mini, prone vs. supine, fluoroscopic vs ultrasound-guided).

Flexible ureteroscopy or retrograde intrarenal renal surgery (RIRS) has extended its indications due to technological advancements in endoscopes and their accessories.

The availability of new laser technologies (thulium fiber laser and pulse-modulated Ho:YAG laser) has enhanced stone fragmentation and dusting capabilities.

However, their use exposes the renal parenchyma to high temperatures and pressures which could potentially contribute to renal damage.

Factors influencing heat release include laser type and settings, exposure time, stone location, fiber-to-stone distance, irrigation volume and fluid circulation. Reduction of heat release can be achieved by limiting the laser settings to reasonable values or by improving fluid circulation with use of ureteral access sheaths, especially those navigable and equipped with suction. High intrarenal pressure is also closely associated with renal damage. Sustained high pressure or even pressure spikes may increase this risk, highlighting the importance of real-time pressure monitoring through sensors integrated on guidewires, scopes, access sheath and use of innovative platforms regulating irrigation/suction systems.

Direct In-Scope Suction (DISS) system was developed to control intrarenal pressure and facilitate the removal of residual fragments. Flexible and Navigable Suction Ureteral Access Sheath (FANS-UAS) is a flexi-bendable UAS equipped with suction capabilities combining mechanical flexibility with continuous irrigation management and stone clearance mechanisms.

Ultra-thin scopes (7.5 F) make it easy to perform RIRS without the need for pre-placed double-J stents or with a 9 F sheath achieving more space for stone fragments expulsion or infusion.

All these technological advancements have enhanced the efficacy of fURS or RIRS which can be an alternative treatment (salvage fURS) when standard stone management techniques, such as percutaneous nephrolithotomy (PCNL), are contraindicated or fail. Salvage fURS has shown favorable outcomes in complex or high-risk cases, including patients with coagulopathies, morbid obesity, renal anatomical abnormalities (e.g., horseshoe or pelvic kidneys), urinary diversion, calyceal diverticula, and altered urinary tracts. In such scenarios it demonstrated favorable outcomes with stone-free rates ranging from 55.6% to 64% for stones > 2 cm.

Although non-invasive, extracorporeal and endoscopic treatments for renal and ureteral stones carry a risk of complications that can be classified according to the Clavien-Dindo system. The complication rate after SWL was estimated at 18.43% for Clavien grade I-II complications (pain, hematuria) and 2.48% for Clavien III-IV complications (hematoma, sepsis). The most frequent complication after RIRS is fever or urinary tract infection observed in 0.2-15% (with 0.1-4.3% of cases of urinary sepsis). Complications after PCNL are more frequent and may include moderate events (hemorrhage requiring transfusion 2-7%, urosepsis 1-2%, bowel injury < 1%) as well as severe events (arteriovenous fistula 0.5-1%, thoracic complications < 1% , loss of access tract 1-3%, death < 0.5%). The risk of bleeding complications is significantly increased in patients on antithrombotic therapy. A personalized, interdisciplinary approach enables optimal decision-making in balancing antithrombotic therapy with surgical safety during urological stone interventions

Finally, it must be considered that endourological procedures can be harmful to the surgeons themselves and their team due to exposure to ionizing radiation. For this reason, procedures must be carried out in strict accordance with safety guidelines and regulations to minimize radiation exposure.

Safety is vital in any surgical intervention, with efficacy being the next most critical consideration. However, cost-effectiveness should be also considered. Endourology involves high costs largely due to the use of sophisticated equipment that requires frequent renewal due to the continuous rapid technological evolution. Using disposable devices brings numerous benefits but also leads to a further increase in costs. Finally, in the cost-benefit assessment, the rate of reintervention associated with some types of procedures must be considered.

KEY WORDS: Urinary calculi; Citrate; Phytate; Theobromine; Shock wave lithotripsy; Retrograde intrarenal lithotripsy; Percutaneous nephrolithotomy; Direct scope suction; Flexible and Navigable Suction Ureteral Access Sheath.

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INTRODUCTION

(Almusafer M, Geavlete B, Geavlete P, Jinga V, Mitsogiannis I, Moussa M, Oguz Acar Y, Papatsoris A, Radavoi D)

The *Experts in Stone Disease* (ESD) Conference was founded with a clear purpose: to bring together experts worldwide, foster collaboration, and drive innovation in stone disease treatment. Over the years, ESD has become a recognized global platform for exchanging knowledge, combining traditional and emerging treatment approaches, and advancing technology and pharmacology. Just as importantly, it continues to inspire and educate the next generation of urologists. The 7th Edition of the ESD Conference was held in Bucharest on 11-12 April 2025 under the presidency of *Professors Thanos Papatsoris, Bogdan Geavlete* and *Daniel Radavoi* in conjunction with the *10th Romanian Nephro-Urology Conference*.

ETIOPATHOGENESIS

Lithogenesis processes *(Kyriaki Stamatelou)*

The formation of kidney stones is a complex biologic process involving interactions of genetic, anatomic, dietary, and environmental factors.

The traditional lithogenesis models emphasize 1. urine supersaturation, 2. the role of crystallization promoters and inhibitors, and 3. Randall's plaques, as the primary pathophysiologic stone formation mechanisms (1, 2). Modern research has added the "*renal epithelial cell response*" and the pivotal role of inflammation and oxidative stress to form a "*multi-hit hypothesis*" (3, 4). The scheme describing the physicochemical mechanisms of stone formation has evolved to a multiple-step sequential process involving: supersaturation, oxidative stress, cell apoptosis and/or necrosis, cell injury, crystal nucleation, crystal growth, crystal aggregation, crystal cell interaction, crystal adhesion and stone formation.

An imbalance between stone inhibitors (magnesium, citrate, pyrophosphate, phytate, uromodulin, osteopontin, nephrocalcin, etc) and stone promoters (calcium, sodium, oxalate, uric acid, etc) precedes and triggers supersaturation. In the "*supersaturation zone of urine*" the formation of new crystals occurs spontaneously, the pre-existing crystals may grow, and crystal aggregation is more likely.

The pathogenic components of lithogenesis include:

- The urinary solute supersaturation that provides the necessary milieu for stone formation.
- The nucleus that provides a substrate for crystal growth in supersaturated urine. Injured epithelial cells may serve as nuclei. Nucleation occurs on Randall's plaques.
- The plaques of Randall and plugs which are no longer considered as mere incidental findings but as active pathologic features that act as initiators of calcium-based stones.

Chronic inflammation is increasingly viewed as a trigger and amplifier in the lithogenesis. It influences crystal adhesion, growth, and retention in renal tissue:

- Crystals induce localized inflammation and oxidative stress, leading to renal epithelial injury. Epithelial injury induces the production of 1.pro-inflammatory cytokines (e.g., IL-6, IL-1β, TNF-α), 2. mineralization modulators (e.g. osteopontin, inter-α-trypsin inhibitor, fibronectin, matrix Gla protein) and 3. promotes osteogenic changes in epithelial cells.
- Reactive oxygen species are produced in response to intratubular crystals and induce the expression of molecules known to promote calcification. Oxidative stress and the production of caspases and inflammatory cytokines further promote mitochondrial changes and macrophage infiltration.
- Exposure to crystals favors the expression of the pro-inflammatory M-1 phenotype of macrophages thus perpetuating the inflammatory response.
- Injured cells promote crystal adhesion and aggregation.

Finally, the urinary and gut microbiomes have recently been recognized as pathogenetic elements and modulators of stone risk: oxalate-degrading bacteria (e.g., Oxalobacter formigenes) reduce urinary oxalate, and "*dysbiosis*" is considered to promote lithogenesis. Research is focusing on probiotic or microbiome-modifying therapies as potential treatments. A better understanding of inflammation activation and modulation of the immune response to urine supersaturation and crystal deposition, as well as effective targeting of inflammatory pathways may provide promising new therapeutic options to reduce lithogenesis and kidney stone recurrence.

Renal impairment and ESKD in stone patients

(Alberto Trinchieri)

The correlation between urinary stones and kidney damage has been well described since the beginning of the last century with the description of single cases or small series up to the most recent cohort and case-control studies.

Vupputuri et al. (5) demonstrated that a history of kidney stones was more frequent in a large series of patients with chronic kidney disease compared to controls matched for sex and age. The OR for CKD of patients with a history of kidney stones was 1.9. A meta-analysis of seven studies confirmed that the history of kidney stones was associated with an increased adjusted risk estimate for CKD (RR 1.47, CI1.23-1.76) (6).

The causes of chronic kidney damage associated with urinary stones include crystal deposition in the renal parenchyma, related comorbidities, repeated obstructive and infectious episodes and the effect of treatments for stone removal. In very high urinary saturation levels, obstruction of the Bellini ducts may occur due to crystal plugs with consequent glomerulosclerosis and interstitial fibrosis in the cortex. These conditions are created in the case of most hereditary stones such as hereditary hypercalciurias (e.g. Dent's disease), primary hyperoxalurias, deficiency of adenine-phospho-ribosyl transferase (2,8 hydroxyadenine) and, to a lesser extent, cystinuria. Plugging of the Bellini ducts can also be observed in some forms of acquired stones such as brushite stones which are often associated with high levels of calciuria and are resistant to SWL.

CKD can also be caused by comorbidities frequently associated with renal stone formation, such as type 2 diabetes. The effects of ureteral obstruction are well demonstrated by experimental studies of ureteral ligation in rats. In clinical conditions, obstruction is incomplete and intermittent, still, repeated and prolonged episodes without relief of the obstruction can be associated with a loss of functional nephrons with hyperfiltration and overload of the residual nephrons resulting in the onset of chronic kidney disease over time. For this reason, urinary tract decompression or treatment of ureteral stones should be timely, especially in case of severe obstruction. The maximum waiting time is not well defined by the guidelines, although the AUA recommends definitive stone treatment after conservative treatment of 4-6 weeks (7).

Studies on urinary excretion of renal tubular damage markers have shown that open renal stone surgery causes significant renal tubular damage, especially in treating staghorn renal stones with nephrotomies with temporary clamping of the renal artery (8). However, even noninvasive treatment can cause transient renal damage. Extracorporeal shock wave lithotripsy induces a measurable alteration of urinary renal tubular enzymes related to the number and energy of shock waves which is due to renal vasoconstriction and hemorrhagic microlesions. These renal "*bioeffects*" after SWL are even slightly higher than those observed after *percutaneous nephrolithotomy* (PCNL) and *retrograde intrarenal surgery* (RIRS). In contrast, the bioeffects of PCNL are higher than those of RIRS. Long-term studies after SWL have not shown significant GFR alterations or unexpected blood pressure increases. However, it must be considered that all these forms of treatment can cause obstructive or vascular complications that can cause renal damage in a single case, so their use must be carefully planned to minimize the potential risks of iatrogenic damage. Finally, the recent use of new technologies for intracorporeal lithotripsy potentially exposes the kidney to risks related to high intrarenal pressures or temperatures. These potential causes of morbidity must be carefully evaluated to define better protocols ensuring the safety of the treatment.

Rare stones *(Maria Ramos)*

These stones are not prevalent, accounting for just 1-3%. Many have a genetic basis and a high recurrence rate (9-11). Cystinuria is considered one of the most complex conditions to treat and is suspected in young patients with a high recurrence rate and weakly radiopaque, bilateral stones. The diagnosis can be made by analysing kidney stones, observing cystine crystals (pathognomonic) in the urinary sediment, or detecting an abnormal excretion of cystine and dibasic amino acids in the urine. Genetic analysis is not mandatory, and the incidence of end-stage kidney disease remains relatively low. Treatment consists of increasing fluid intake, modifying the diet and taking citrate to increase cystine solubility and maintain urine pH at 7-7.5. We use D-penicillamine and tiopronin to bind cystine in the urine in refractory cases. However, they have serious side effects and are often poorly tolerated, which is why some alternative drugs have been investigated, such as tolvaptan, alpha-lipoic acid and iSGLT2, but the results are not conclusive. *Adenine phosphoribosyltransferase* (APRT) deficiency is an inherited disorder that leads to 2,8-dihydroxyadenine lithiasis. It can present as urolithiasis or crystalline nephropathy, and the stones are radiolucent with no metabolic alterations in urine or blood. These stones do not respond to alkali therapy. The treatment consists of high fluid intake and allopurinol. Hereditary xanthinuria is caused by a xanthine oxidase deficiency, resulting in hypouricaemia and hypouricosuria. Since the solubility of xanthine is unaffected by urinary pH, alkalisation is ineffective.

Distal tubular acidosis in idiopathic stone patients
(Jordi Guimerà Garcia)

Distal renal tubular acidosis (DRTA) has two clinical forms: complete and incomplete. The complete form mainly occurs in childhood and presents deafness, rickets, and a short life expectancy. The incomplete form generally occurs in adulthood and presents recurrent urinary lithiasis, and, sometimes, nephrocalcinosis. The etiopathogenesis of incomplete DRTA is the partial inability to excrete acid (H+) into the urine. Incomplete DRTA has the following biochemical characteristics: normal serum pH, alkaline urinary pH (pH > 6), hypercalciuria, and hypocitraturia. Hypercalciuria is due to elevated bone resorption; the patient does not have metabolic acidosis because they compensate with calcium from the bone (buffer effect) (12). Renal stones commonly associated with incomplete DRTA are calcium oxalate dihydrate, hydroxyapatite, and brushite.

The diagnosis of incomplete DRTA can be made using the furosemide test or the acid overload test (gold standard). If the furosemide test is performed on patients with the aforementioned characteristics, it has a specificity and sensitivity equivalent to the gold standard (13). Treatment for incomplete DRTA is not well established. Traditionally, treatment involved alkalizing the patient to offset the buffering effect and reduce bone resorption. A recent study demonstrated the efficacy of phytate (300-400 mg every 12 hours) as an inhibitor of bone resorption and reduction of hypercalciuria in patients with incomplete DRTA (14).

DIAGNOSTICS

Metabolic workup *(Maria Ramos)*

Metabolic studies are necessary to diagnose and evaluate the response to preventive measures (15-17). The lithogenic risk of a patient is determined by metabolic disturbances, as well as urine pH and volume. Urine pH is critical in cystinuria, uric acid stones and infectious stones. Changes in urine composition can be caused by increasead crystallization promoters (such as calcium, phosphate, oxalate, uric acid or cystine) or a deficit of crystallization inhibitors (such as citrate, magnesium and phosphate). Stone analysis and basic metabolic evaluation are mandatory for all stone formers. Crystalluria is valuable in assessing the probability of stone recurrence and indicating treatment efficacy. Adult patients who have had a single episode of calcium lithiasis require a basic evaluation including blood tests for glucose, urea, creatinine, sodium, potassium, magnesium, chloride, uric acid, calcium, phosphate, bicarbonate, *parathyroid hormone* (PTH) and vitamin D, as well as urine tests for sediment, pH and culture. High-risk stone formers (those with recurrent nephrolithiasis, persistent residual lithiasis or nephocalcinosis, as well as children and young adults) require a more specific metabolic evaluation, which also includes a 24-hour urine sample to measure calciuria, phosphaturia, citraturia, oxaluria, uricosuria, magnesiuria, natriuresis and proteinuria. Alternatively, spot urine samples can be used, particularly when a 24-hour urine collection is difficult. The first follow-up 24-hour urine measurement should be taken eight to twelve weeks after starting pharmacological prevention of stone recurrence. Once urinary parameters have normalized, an evaluation every twelve months is sufficient.

Stone analysis *(Bernat Isern)*

The morpho-compositional analysis of kidney stones offers essential insights beyond merely identifying their predominant chemical component (18). This type of analysis reveals crucial information about the conditions of stone formation, including nucleation, growth patterns, and the presence of specific lithogenic processes. It reconstructs the patient's lithiasis history sequentially evaluating the stone from nucleus to surface, guiding tailored diagnostic and therapeutic decisions.

While metabolic analyses are helpful, they often provide only a snapshot of current urinary conditions, which may not reflect the original lithogenic environment. In contrast, the stone itself serves as a record of past events, making morpho-compositional analysis a more reliable approach to understanding stone formation (19).

The ideal analytical protocol combines *stereoscopic microscopy* (StM), *scanning electron microscopy with energy-dispersive X-ray spectroscopy* (SEM-EDS), and, when necessary, *Fourier-transform infrared* spectroscopy (FTIR) (20). StM is used first to assess external and internal morphology. SEM-EDS provides highly detailed information about elemental composition and minor components often missed by other methods. FTIR complements the analysis in complex or drug-induced stones, though it is limited in detecting minor components and lacks structural context. The Renal Lithiasis Research Laboratory at the University of the Balearic Islands has conducted over 15,000 such analyses, delivering dual reports: one for clinicians with specific therapeutic recommendations, and a simplified version for patients.

In conclusion, morphocompositional analysis should be routine practice. It significantly enhances diagnostic accuracy, explains stone etiology, and informs more precise treatment strategies, far surpassing the capabilities of traditional chemical or infrared-only methods.

MEDICAL TREATMENT AND PREVENTION

Dietary measures *(Mohamed Elhowairis)*

Kidney stone formation is a prevalent and recurrent condition influenced significantly by dietary and lifestyle factors. Evidence-based dietary strategies for preventing stones, with a focus on calcium oxalate stones, include increasing fluid intake to achieve optimal urine dilution, maintaining adequate dietary calcium, reducing sodium and animal protein intake, and limiting oxalate-rich foods. Additional emphasis should be placed on enhancing citrate intake through citrus fruits, avoiding excess vitamin C and sugars, and promoting a balanced, plant-rich diet. Special attention is given to patients with malabsorption syndromes or gastrointestinal surgeries, who are at heightened risk for enteric hyperoxaluria. Emerging therapies are microbiome-targeted probiotics, oxalate-degrading bacteria, and precision nutrition. These comprehensive, personalized nutritional interventions aim to reduce stone recurrence and improve patient outcomes through non-pharmacological means.

Citrates *(M. Can Kiremit)*

Active treatment modalities remain the cornerstone In the comprehensive management of urinary system stone disease. However, recurrence prevention and managing of residual fragments also require complementary strategies such as lifestyle modifications, dietary interventions, and pharmacological therapies. Among these, *alkaline citrate* salts (AC), particularly potassium citrate, are widely used due to their ability to alter urinary chemistry and inhibit stone formation (21). The efficacy and safety of AC therapy has been demonstrated in various age groups, including pediatric population (22-24) and therefore it is recommended in the current EAU Guidelines (25) for the management of calcium oxalate stones associated with hypocitraturia, hypercalciuria, hyperoxaluria, or distal renal tubular acidosis, as well as in the management of uric acid and cystine stones.

However, there are certain limitations to their use. Although generally well tolerated and associated with minimal side effects, gastrointestinal intolerance may reduce patient adherence. Additionally, regular monitoring of serum electrolytes is necessary, to prevent the development of hyperkalemia, particularly in patients with chronic kidney disease or those receiving potassium-sparing medications. Moreover, monitoring urine pH regularly to adjust the dosage properly is another aspect that might reduce patient compliance. If adherence is lacking, the treatment may become ineffective or the risk of uncontrolled urinary pH elevation (≥ 7.5) by over-alkalinization, particularly if sustained over time, may increase the risk of calcium phosphate stone formation.

In conclusion, given its dual role in preventing recurrence and managing residual disease, citrate supplementation is a valuable adjunct to active stone treatment. Its efficacy in stone prevention is well demonstrated, but careful patient selection, individualized dosing, and appropriate monitoring are essential in optimizing therapeutic outcomes and minimizing adverse effects.

Novel molecules *(Adrià Pinero)*

Phytate (myo-inositol hexakisphosphate, $InsP_6$) is a naturally occurring polyphosphorylated carbohydrate in seeds, legumes, nuts, and whole grains. In vitro studies have demonstrated that both $InsP_6$ and its lower phosphorylated derivatives (InsPs) exhibit a potent inhibitory effect on the nucleation, growth, and aggregation of calcium salts, particularly calcium oxalate and calcium phosphate crystals (26). Epidemiological evidence from a large-scale, prospective cohort study involving 96,245 women over eight years revealed that higher dietary phytate intake is significantly associated with a reduced risk of developing symptomatic kidney stones (27).

Furthermore, experimental data indicate a synergistic interaction between phytate and magnesium, enhancing the inhibitory effect on crystal formation (28).

Theobromine, a naturally occurring dimethylxanthine abundant in cocoa beans, has been shown to effectively inhibit uric acid crystallization (29, 30). Due to its structural similarity to uric acid, theobromine can integrate into forming crystals, altering their morphology by producing longer and thinner structures with reduced growth kinetics. Unlike calcium-containing stones, pharmacological options for preventing uric acid crystallization remain limited. Upon ingestion, theobromine is metabolized and excreted in the urine primarily as 7-methylxanthine (36%), unchanged theobromine (21%), 3-methylxanthine (21%), and 3,7-dimethyluric acid (1.3%), all of which retain inhibitory activity against uric acid crystallization. The co-administration of urinary alkalinizing agents, such as potassium citrate, alongside theobromine has been proposed as a therapeutic strategy to optimize uric acid solubility. This combination allows for lower citrate dosages, reducing the risk of excessive alkalinization and subsequent sodium urate precipitation. Additionally, minimizing citrate dosage decreases the risk of hyperkalemia, particularly in patients with impaired renal function or cardiovascular comorbidities.

Management of struvite stones *(Roswitha Siener)*

Struvite (magnesium-ammonium-phosphate-hexahydrate) stones can grow rapidly to large sizes. Struvite stone formers are at high risk for chronic kidney disease and end-stage renal disease. A study of 45,783 stones revealed that 2.1% contained struvite (31). Struvite stones were three times more common in women than men and were most frequent in the youngest and oldest age groups. Factors predisposing to urinary tract infections include vesicoureteral reflux in children and indwelling urinary catheters in the elderly. Struvite stones are always caused by a urinary tract infection with urease-producing microorganisms. The bacterial enzyme urease splits urea to form ammonium and bicarbonate, leading to high urinary ammonium concentrations and pH values above 7.0. Specific measures include complete surgical stone removal, short or long-term antibiotic treatment, urinary acidification to a pH below 6.2, and a urine volume of at least 2 litres/24 hours. Urinary acidification can be achieved with L-methionine. L-methionine is effective in physiologically lowering urine pH and the relative supersaturation of struvite (32). A recent analysis of 1,231 stones containing struvite revealed that only 6% were pure (33). The most common components in mixed struvite stones were carbonate apatite, ammonium urate, calcium oxalate mono- and dihydrate, uric acid and cystine. A previous study found metabolic abnormalities in 57% of patients with pure struvite stones and in 81% of patients with mixed stones (34). Therefore, the search for metabolic abnormalities in 24-hour urine after stone removal and infection control is suggested.

Side effects of stone medications *(Alberto Budia)*

Patient adherence is one of the most critical aspects of medical treatment for urinary stone disease. If the five dimensions of adherence in these treatments are analyzed (social-economic, healthcare system, condition-related, therapy-related and patient-related), the leading causes of low adherence are a lack of perceived benefit from treatment (e.g. lack of symptoms after an acute episode), long duration of therapy and side effects (35, 36).

The most common side effects of citrates are gastrointestinal disorders, such as nausea, diarrhea and abdominal distension. Diuretics can cause weakness, headaches, muscle pain, insomnia and muscle cramps, and long-term thiazide treatment has been associated with non-melanocytic skin cancer. Neurogenic effects (headache and myalgia) have been observed with acetohydroxamic acid and pyridoxine. Specific therapies for cystinuria are associated with a high percentage of side effects (20-30% early and late toxicity). Therefore, to increase adherence to specific treatments for metabolic disorders in stone disease, we must provide accurate information to our patients about the benefits and recommend the use of medical devices such as pH meters or apps that provide immediate feedback on long-term treatment efforts and, of course, ensure continuity of care.

Smart apps for stone patients *(Juan A. Galán-Llopis)*

Challenges faced in managing urolithiasis include problems in maintaining adequate hydration tracking, adherence to specific diets, and prophylactic medication. Mobile apps have also been changing the management scenario of this disease, and long lists of apps for urolithiasis, including those for patient information, dietary recording tools, and herbal and drug remedies and advice, have been reported (37). Coaching patients towards maintaining a high compliance to a low-risk lifestyle is a key factor to prevent stone recurrence, and the new E- and M-health apps may provide the additional coaching needed (38).

These apps may help calculate stone risk, plan specific diets, offer personalized dietary recommendations and hydration advice, a pH diary, and reminders for stent removal.

The *Lito Diagnostic App* allows for precise identification of stone types through the analysis of data on renal stone composition and patient urinary biochemistry, automatically generating a report. The *myLit-Control App* provides monitoring of urine pH, fluid and medication intake, helps patients learning about kidney stones and how to prevent them, and enables a safe and private connection to the patient's portable pH Meter. Nevertheless, the stone apps need scientific validation to ensure high-quality content and should adhere to clinical guidelines. Recently, the latter app was deemed valid and acceptable by urolithiasis patients as a portable tool for urine pH monitoring at home with high usage compliance and satisfaction rates (39). Future research should explore long-term outcomes and strategies to enhance patient adherence, ensuring effective integration of digital health tools in routine clinical practice (40).

PERCUTANEOUS NEPHROLITHOTOMY (PCNL)

Supine PCNL *(Jorge Mora)* (41-43)

The supine position offers advantages in anesthetic management, reduced operative time, and lower complication rates, making it suitable for high-risk or pediatric patients. The choice between positions should be individualized based on patient and stone characteristics, surgeon experience and surgical goals (Table 1).

Table 1.
Advantages or disadvantages of supine PCNL.

Advantages of supine PCNL	
Anesthetic Management	Easier airway access; reduced cardiopulmonary risks; beneficial for high-risk patients
Operative Time	Generally shorter due to elimination of patient repositioning and easier stone retrieval
Stone-Free Rate (SFR)	Slightly better SFR
Complication Rate	Lower major complication rates; less bleeding and infection risk
Radiation Exposure	Reduced exposure for the surgeon due to lateral puncture site
Access	Access to every calyx. Allows access to upper pole
Patient Positioning	No need for repositioning; facilitates simultaneous retrograde or contraleteral procedures
Hospital Stay	Shorter hospital stay
Ideal Candidates	High-risk patients, combined endoscopic procedures, pediatrics
Disadvantages of supine PCNL	
Surgical team	Requires more than one urologist if the combined approach is used
Access	Longer tract can reduce instrument maneuverability, specially in obese patients
More expensive	Due to more personnel and usage of more instrument and materials *

* *Probably cost/effective due to reduction in time, complications and hospital stay but needs to be proven.*

Prone PCNL *(George Daniel Radavoi)* (44-46) (Table 2)

Table 2.
Advantages and disadvantages of prone PCNL.

Advantages of prone PCNL
Better access to the posterior calyces
Larger working space for instrument manipulation
Lower risk of bowel injury due to retroperitoneal location
Disadvantages of prone PCNL
Requires repositioning under anesthesia (increased time and complexity)
Less favorable for obese patients or those with respiratory compromise
Reduced cardiovascular monitoring access during surgery

Standard PCNL *(Alin Adrian Cumpanas)* (Table 3)

Table 3.
Advantages and disadvantages of standard PCNL.

Advantages of standard PCNL
Good visualization
Low intrarenal pressure
Low risk of bacterial spread/risk of sepsis
Effectiveness/speed of the procedure
Disadvantages of standard PCNL
Hard access in narrow intrarenal spaces (calycean infundibulum, complete staghorn stone) - Lower intrarenal mobility

Mini PCNL *(Kremera Petkova)* (47-51) (Table 4)

Table 4.
Advantages and disadvantages of mini PNL.

Advantages of mini-PNL
Higher stone-free rates and shorter operating times compared to RIRS
Similar stone-free rates compared to standard PCNL
Stone-free rates not affected by stone size and composition
Reduced overall complication rates compared to standard PCNL
Reduced blood loss compared to standard PCNL
Reduced pain compared to standard PCNL
Suitable for: · Small and medium sized stones up to 30 mm · Lower pole stones · Stones resistant to SWL · Failed fURS · Special situations (e.g. stones in calyx diverticula) · Additional nephrostomy tracts during a multi-tract PCNL · Pediatric patients
Disadvantages of mini-PNL
Increased morbidity compared to RIRS
Longer hospital stay compared to RIRS
Longer convalescence period compared to RIRS
Longer OR times compared to standard PCNL
Inability to retrieve larger fragments compared to standard PCNL
Concerns about raised intrarenal pressures compared to standard PCNL
Difficulties in the use of the nephroscopic graspers compared to standard PCNL

Fluoroscopy guided renal puncture *(Petros Sountoulides)* (Table 5)

Table 5.
Advantages of fluoroscopy vs. ultrasound guided renal puncture.

In favour of fluoroscopy-guided access	Comparable results	In favour of ultrasound-guided access
		Radiation exposure
	Needle puncture time	
	Atone clearance rate	
	Single needle puncture success rate	
	Puncture time	
	Operation time	
Access to complicated anatomy		
	Intraoperative bleeding rate	
	Blood transfusion requirement	
	Fever/urosepsis rates	

Ultrasound guided renal puncture

(Mohammed Alameedee) (52-53) (Table 6)

Table 6.
Zero radiation ultrasound-guided PCNL advantages and disadvantages.

Advantages	
1	No radiation
2	Imaging of structures between skin and kidney, depth of access needle, prevent organ injury (colon, pleura, liver, spleen ...etc.).
3	No need for contrast media (in azotemia pt., contrast allergy).
4	Avoids renal vascular injury (color doppler u/s).
5	Used in failed retrograde pyelogram during failure of ureteric catheterization.
6	Safe in pediatric and pregnant patients
	Can performed in supine position.
7	Cost effective (using a portable ultrasound).
8	No need for lithotomy position and ureter stent fixation.
9	Used even in perinephric extravasated fluid.
10	Use hydro dissection to dissect and separate the colon from the lower pole of the kidney, and early diagnoses of colonic injury especially in obese patients.
11	Use optical hydro dissection in ectopic pelvic kidney to prevent bowel injury.
12	Facilitate reentry to the collecting system in case of tangential entry out of the collecting system.
13	Used in prone, supine, semi prone, semi supine and lateral positions.
14	All the abdomen is the field of entrance from posterior axillary line to the umbilicus.
15	Use the Doppler study to detect the residual stones and also the edges of colon.
Disadvantages	
1	Difficult identification of the access needle.
2	Technical difficulty in non-dilated PCS.
3	Difficult visualization and manipulation of guide wire and dilaters, especially the non- metallic dilators.
4	Long learning curve.

RETROGRADE INTRARENAL SURGERY (RIRS)

High power Holmium:YAG laser *(Stefan Rascu)* (54-57)
High Power (HP) Ho:YAG machines represent an improvement over standard Ho:YAG units, allowing a wider variety of settings, with energy settings as low as 0.2 J and frequencies up to 100 Hz. The higher frequencies on high-power holmium devices help achieve faster dusting, smaller fragments and a decrease of 50% in lasing time over the standard machines. Pulse modulation on some HP units (*Moses Technology*®, *Vapour Tunnel* and *Virtual Basket*®) allows for decreased stone movement, improved dusting efficiency and more fragmentation at distance, according to clinical and benchtop studies. While *Thulium Fibre Laser* (TFL) possesses low peak-power, high-power Ho:YAG benefits from high peak-power. According to my experience, high peak-power matters as laser lithotripsy is not only about dusting. A higher-peak power allows you to fragment stones more efficiently, making the HP unit adequate for all scenarios and locations (embedded, impacted, mobile, small, large, ureteral, kidney or bladder stone). I genuinely believe modern urologists should not be keen on using only one laser device but rather consider each device's advantages and disadvantages for the case they are facing. Hence, in the following tables, I tried to summarize a few scenarios for using each laser in my daily practice in Table 7 a/b.

Table 7a.
Scenarios for using each laser: kidney stones.

HP HO:YAG	TFL
Large volume > 2 cm^3	Small Size < 1 cm
UAS – FANS	No UAS
High-Power Settings	Low-power settings
High-Flow Irrigation	Low-Flow Irrigation
JJ stent	No stent

Table 7b.
Scenarios for using each laser: ureteral stones.

HP HO:YAG	TFL
Impacted	Non-Impacted
Low-power settings	Low-power settings
P < 10W, Frequency < 10 Hz	P < 10W, Frequency < 10 Hz

Thulium laser *(Juan Manuel Lopez)* (58-60) (Table 8)

Table 8.
Comparison of lasers for stone treatment.

	Ho:YAG	TFL	p-Tm:YAG	Magneto
Technical specifications				
Wavelength	~2100 nm	~1940 nm	2013 nm	~2100 nm
Max Power	100-150 W	50-60 W	100 W	100-150 W
Frequency	5-80 Hz	10-2400 Hz	5-300 Hz	5-100 Hz
Peak Power	Up to 10 kW	~0.5 kW	~3.7 kW	Up to 10 kW
Tissue Penetration	~0.3 mm	~0.08 mm	~0.15-0.2 mm	~0.3 mm
Design and operational characteristics				
Electrical Needs	16-20 A	Standard 15 A	Standard 15 A	16-20 A
Cooling	Water cooling	Air/water cooling	Closed-loop	Water cooling
Size/Weight	>100 kg	~50-60 kg	~97 kg	>100 kg
Fiber Size	≥200 µm	50-150 µm	≥200 µm	200-1000 µm
Noise	Loud (~70 dB)	Quiet	Mid ≤65 dB	Loud
Lithotripsy performance				
Feature	Ho:YAG	TFL	p-Tm:YAG	Magneto
Retropulsion	Significant	Minimal	Low	Low-Minimal *
Fragmentation	Excellent	Low	Excellent	Excellent
Dusting	Moderate	Excellent	Excellent	Excellent
Predominant effect	Photomechanical	Photothermal	Mixed	Adjustable
Soft tissue surgery				
Feature	Ho:YAG	TFL	p-Tm:YAG	Magneto
Coagulation	Moderate	Excellent	Good	Improved
Dissection	Blunt/pulsed	Smooth	Smooth	Versatile
Char	Low	Hi	Medium	Low
Visibility (bleeding)	Good	Excellent	Very Good	Excellent

* *Based on technical characteristics.*

Impact of intrarenal pressure and temperature *(Razvan Multescu)* (61-63)

Flexible ureteroscopy is generally a procedure with low morbidity and mild complications. However, while performing it we are altering pyelocaliceal system conditions, sometimes with significant clinical consequences.

Elevated temperature may impair cell viability and renal function. Many papers are using the critical threshold of 43°C. However, *Dewey* and *Sapareto* arbitrarily chose this value and reported it as dangerous if the renal cells were exposed for 120 minutes (61). Factors influencing heat release include laser type and settings, exposure time, stone location, fiber-to-stone distance, irrigation volume, fluid circulation. Efficient irrigation and use of ureteral access sheaths, especially those navigable and with suction (FANS), help temperature control by improving fluid circulation. Limiting the laser settings to reasonable values may also prevent such significant lesions. However, experimental in vivo porcine models demonstrated that although laser induced thermal lesions were still severe at one week, they may improve by healing in a short period (62).

High *intrarenal pressure* (IRP) is closely associated with septic complications, pain or bleeding. While normal IRP ranges from 0-20 cm H_2O, pyelovenous backflow occur beyond 41 cm H_2O and fornix ruptures above 81 cm H_2O (63). Sustained high pressures or even pressure spikes may increase risk, suggesting importance of real-time monitoring. Innovations include pressure sensors on wires, scopes, UAS and innovative platforms with AI-regulated irrigation/suction systems. FANS and direct in-scope suction help maintaining a low IRP.

Understanding and controlling time-dependent changes in temperature and pressure can enhance procedural safety and efficacy.

Direct in-scope suction (DISS) *(Bogdan Geavlete)*

Flexible ureteroscopy (fURS) utilization is increasing, *surpassing shock wave lithotripsy* (SWL), with experience of over 1,500 procedures a year, worldwide. EAU guidelines suggest percutaneous nephrolithotomy for stones > 20 mm and retrograde renal surgery is not recommended as a first-line treatment for stones > 20 mm (25). However, it may be a first-line option in patients where PCNL is not an option or contraindicated or in selected patients.

Technical improvements and disposable tools have increased URS use. Miniaturization of flexible ureteroscopes improves access. Single-use scopes enhance safety, though cost and sustainability remain concerns. The goal is to minimize residual fragments, aiming for < 63 µm. Suction techniques like Irrigation/Suctioning systems and *Direct in Scope Suction* (DISS) are being developed to control pressure and remove the residual fragments (64-66).

Advantages of suction during fURS include lower intrarenal temperature and pressure, reduced infection risk, and improved visibility. Pusen offers single-use fURS with suction (DISS) that can provide low intrarenal pressure and better vision. DISS can be combined with flexible-tip suction UAS. Finally, recent studies support DISS, showing it could be more efficient and helps improve stone-free rates. Large, randomized, multicenter studies are now needed to standardize the results and draw definite conclusions regarding the benefit of these procedures. The true practical impact over the medium- and long-term success rates of the procedure still needs to be further studied.

Flexible and Navigable Suction Ureteral Access Sheaths UAS (FANS-UAS) *(Petros Sountoulides)*

Retrograde intrarenal surgery (RIRS) has evolved into a cornerstone of modern endourological management for renal calculi, especially for patients with anatomical constraints or those at higher surgical risk. A pivotal component facilitating RIRS is the *Ureteral Access Sheath* (UAS), which enables repeated scope access, improves irrigation outflow, and contributes to procedural safety and efficacy. The latest advancements have introduced flexi-bendable UAS equipped with suction capabilities – *Flexible and Navigable Suction UAS* (FANS-UAS) – which combine mechanical flexibility with continuous irrigation management and stone clearance mechanisms (67).

The advantages of Flexi-Bendable UAS are:

– *Enhanced Navigation and Access*: traditional UAS are limited by rigidity, potentially restricting access to the lower pole or extreme calyces. Flexi-bendable sheaths feature a soft, passively bendable distal tip that can follow the ureteroscope's movement into difficult-to-reach areas, significantly improving navigation and clinical access in complex renal anatomies (68).

– *Suction Capability and Improved Visualization*: FANS-UAS incorporate a vacuum-assisted side port, allowing active removal of stone dust, blood clots, and irrigation fluid during lithotripsy. This functionality creates a clear operative field (avoiding the 'snow globe' effect), enhancing stone visualization and procedural control. Improved vision correlates with better fragmentation accuracy and shorter operative times (68).

– *Reduced Intrarenal Pressure (IRP)*: Elevated IRP during RIRS is associated with pyelovenous backflow, increased risk of urosepsis, and renal injury (69). FANS-UAS have demonstrated the ability to maintain IRP under 20-30 cm H_2O, particularly with larger sheaths (> 12/14 Fr) and effective suction mechanisms. Real-time digital ureteroscopes monitoring confirms safer pressure profiles than non-suction approaches (68, 70).

Higher Stone-Free Rates (SFR): Clinical trials and multicenter studies show that bendable suction UAS significantly outperform traditional sheaths in achieving stone-free status. One study reported an 81.3% immediate and 87.5% three-month SFR for FANS-UAS compared to 49.4% and 70% for standard sheaths (70). Real-world data echo these findings, with a 30-day SFR of 86.8% across 25 centers.

Decreased Postoperative Complications: Continuous suction and pressure control reduce the risk of infectious complications, including postoperative fever and sepsis. The use of FANS-UAS also minimizes the need for stenting and auxiliary procedures, thus decreasing the overall healthcare burden.

Clinical Utility and Expanded Indications

Flexi-bendable suction UAS are particularly useful in scenarios involving:

– Large stone burdens (> 2 cm)
– Pus or turbid urine with infection risk
– Solitary kidneys or cases with impaired renal function
– Same-session bilateral ureteroscopy (RIRS)
– Challenging lower pole stone access.

For large stones, FANS-UAS have shown comparable effectiveness to mini-percutaneous nephrolithotomy (mini-PCNL), with lower complication rates and potential for single-session clearance (71).

Despite their many advantages, flexi-bendable UAS are not without limitations. Maneuvering the flexible tip requires frequent adjustments, particularly in narrow calyceal infundibula. Fragment removal may still require basketing for stones in the lower calyx due to limited deflection angles (68). Additionally, operator training, cost, and the need for more robust data on long-term outcomes and equipment durability remain essential considerations for widespread clinical adoption.

In conclusion, FANS-UAS represent a transformative step in endourology, combining flexibility, suction, and safety. They improve access, visibility, pressure control, and stone-free rates, while minimizing complications and intervention times. While further research is needed to optimize design and validate cost-effectiveness, these systems have the potential to redefine standard RIRS protocols.

Slim disposable fURS *(Athanasios Papatsoris)*

Flexible ureteroscopy (fURS) has been increasingly used as the first-line treatment for urolithiasis (72,73). Disposable (single-use) fURS has enormously progressed because novel slimmer scopes provide both safety and cost/efficacy in *retrograde intrarenal surgery* (RIRS) (74). The slimmest diameter of most commercially available models is 7.5 Fr (*e.g. the EndoView HU-30S by HugeMed*). HugeMed was the first to launch the 6.3 Fr fURS in the global market which has already received clinical praise from many colleagues (75).

The ultra-thin HU-30S makes it easy to perform RIRS without pre-placed double-J stents (avoidance of another procedure) and insertion of ureteral access sheaths (avoidance of ureteral injury), resulting in lower costs. If a ureteral access sheath is used the HU-30S is easily manipulated through a slim 9 Fr sheath and more stone expelling space is achieved. Moreover, the ultra-thin HU-30S, provides greater infusion space between the scope and the ureter. This will prevent temperature rise during laser (i.e. *Thulium*) lithotripsy, relieve renal pressure and improve the stone-clearance rate and reduce the likelihood of post op steinstrasse.

Weighing less than 300g, the HU-30M effectively prevents the operator's fatigue during longstanding surgeries. Its standard parameters, including an adjustable angle knob, the 285° bending range in both directions, the 1080P optimization algorithm, and the passive bending function, support surgeons in efficiently tackling even the most demanding surgical cases. A unique characteristic of the HU-30M is

that the scope is produced with a 3 or 9 o'clock working channel for right and left FURS, respectively. Additionally, there is no time limit in working with the HU-30M; therefore, the term disposable is preferred over single use.
Having been one of the first endourologists to use the HU-3OM in recent years, it's my first choice for fURS even for large stones. Once the wire is inserted in the kidney the scope can be easily advanced over it just as we advance a 6 Fr JJ stent. With the HU-30M, I've stopped pre-stenting patients, and I've minimized the use of ureteral access sheaths. I found it ideal for impacted ureteral and lower pole stones, special populations (i.e. children, anatomical anomalies) while slimmer size does not obscure vision or irrigation.

Salvage Flexible URS, Pushing the Boundaries
(Syed Jaffry)

Salvage *Flexible Ureterorenoscopy* (fURS) is a minimally invasive endourological approach used when standard stone management techniques, such as *percutaneous nephrolithotomy* (PCNL), are contraindicated or fail. It has become a key alternative in complex or high-risk cases, including patients with coagulopathy, morbid obesity, renal anatomical abnormalities (e.g., horseshoe or pelvic kidneys), urinary diversion, calyceal diverticula, and altered urinary tracts. In salvage scenarios, fURS demonstrates favorable outcomes with *stone-free rates* (SFRs) ranging from 55.6% to 64% for stones > 2 cm, reaching up to 90% for fragments < 2 mm when multiple sessions are utilized (average 1.6 sessions). Studies show safety and effectiveness across challenging patient groups, with no major intraoperative complications or mortality reported (25). Technological advancements have enhanced the efficacy of salvage fURS. High-powered holmium:YAG lasers, particularly systems featuring *Vapor Tunnel™* and *MasterPULSE™*, allow customization of lithotripsy based on stone composition and size. Short pulses deliver aggressive fragmentation for hard stones, while long pulses enable controlled ablation with minimal retropulsion. Suction access sheaths further optimize outcomes by facilitating fragment evacuation and maintaining clear visualization. These tools are particularly advantageous in salvage procedures involving large or multiple stones. Salvage fURS provides a safe, repeatable, and effective option in modern stone management. Are we truly seeing the end of an era, or are we simply witnessing a redefinition of indications? With salvage fURS and suction-enabled RIRS pushing boundaries, perhaps the question is no longer '*Can we do PCNL?*', but rather '*Do we need to?*

COMPLICATIONS OF STONE TREATMENT

Classification & Reporting *(Elenko Popov)*

Surgical procedures carry intraoperative or postoperative complications risks, which can have significant outcomes. Therefore, accurate documentation of adverse events and thorough preoperative assessments are crucial. These practices help identify systematic errors and improve patient care. Unfortunately, inaccuracies in reporting complications are common among surgeons. A consistent and precise classification system for complications is essential and can only be achieved through a reliable and validated reporting and grading system recognized in clinical practice. The *Clavien-Dindo Classification System* (CDC) classifies complications based on the interventions required for treatment. Its strengths include applicability across various surgical contexts (76). However, a key limitation is that it only considers the highest-grade complication, potentially underestimating overall patient morbidity. Modifications such as the *Memorial Sloan-Kettering Cancer Centre Secondary Events System* (77) and the *Accordion Severity Grading System* (78) have been introduced. Yet they do not fully address the conceptual challenges of the CDC. Each classification and reporting approach has advantages and disadvantages. CDC is the central system for documenting complications due to its ease of use; however, it offers a broad overview of surgical adverse events, creating new reporting frameworks. A urology-specific complication reporting system is needed to monitor complications in urological procedures, facilitating better data collection and analysis and enhancing patient safety. The system should be comprehensive and replicable, ensuring accuracy and reliability. Improving the complication reporting system is essential for Urologists to enhance surgical outcomes.

SWL *(Athanasios Dellis)*

The advent of *shockwave lithotripsy* (SWL) in the 1980s revolutionized the management of kidney stones, replacing open surgery and its associated risks of morbidity and mortality. However, it became evident that SWL was not universally effective for all stone types and carried its own risks and potential complications. As *retrograde intrarenal surgery* (RIRS) and *percutaneous nephrolithotomy* (PCNL) advanced, the scope of SWL applications narrowed. According to the European Association of Urology (EAU) guidelines, SWL remains a first-line treatment for proximal or distal ureteral stones smaller than 1 cm, renal stones up to 2 cm, and lower pole stones in patients with suitable anatomical conditions (25). SWL has fewer overall complications compared to PCNL and *ureteroscopy* (URS) (Table 9) (25).

Table 9.
Complications of SWL.

Complications of SWL	
Regrowth of residual fragments	21-59%
Dysrhythmia	11-59%
Bacteriuria in non-infection stones	7.7-23%
Macroscopic haematuria	17.2%
Pain	12.1%
Auxiliary procedure	6.9%
Steinstrasse	4%
Renal colic	2-4%
Haematoma, asymptomatic (renal)	1.2%
Haematoma, symptomatic (renal)	0.21%
Sepsis	0.15%
Morbid cardiac events	Case reports
Liver, spleen haematoma	Case reports
Bowel perforation	Case reports

A meta-analysis of 115 RCTs reported 18.43% Clavien I-II and 2.48% Clavien III-IV complications (79). The connection between SWL and conditions like hypertension or diabetes remains uncertain. While published data are inconsistent, no conclusive evidence suggests SWL leads to long-term adverse effects. Management of SWL complications involves monitoring and addressing adverse events such as pain, hematuria, or infection. Pain is managed with analgesics, while infections require antibiotics.

Persistent obstruction or fragments may need auxiliary procedures like ureteroscopy or nephrostomy placement. Severe complications, including hematoma, require close observation or intervention based on the patient's clinical stability.

RIRS *(Elenko Popov)*

The ongoing advancements in endoluminal endourology in the upper urinary tract have considerably broadened the applicability of *retrograde intrarenal surgery* (RIRS) within clinical practice. RIRS has transitioned from serving as an alternative modality to a primary intervention for treating renal stones measuring up to 20 mm in maximum diameter, as stated in both the *European and American Association of Urology guidelines*. Nonetheless, this technique can be associated with various potential complications akin to any surgical procedure. The most frequently cited complications include discomfort associated with a ureteral stent, injury to the ureteral wall, and the migration of residual stone fragments (1).

Among the early and most serious postoperative complications, fever is identified as the most prevalent, closely followed by urinary tract infections, which exhibit an incidence range of 0.2% to 15% (80). A particularly alarming complication is sepsis, with an incidence rate fluctuating between 0.1% and 4.3% (81). In rare instances, sepsis may become life-threatening and is recognized as a primary contributor to postoperative mortality, alongside other significant complications such as cardiac events, respiratory distress, multiorgan failure, and haemorrhagic incidents (80).

Table 10.
Complications of retrograde intrarenal surgery (RIRS).

Complication	**Incidence**	**Potential Risk Factors**	**Preventive Strategies**
Ureteral Injury	0.5% - 5%	Previous surgeries, anatomical anomalies	Preoperative imaging, proper surgical technique
Hemorrhage	0.5% - 3%	Coagulopathy, significant stone burden, prolonged operative time	Monitor operative time and intrarenal pressure
Infection	1% - 10%	Preexisting urinary tract infections, diabetes, significant stone burden, prolonged operative time	Prophylactic antibiotics, proper sterile technique, control of intrarenal pressure and operative time
Urinary Leakage	1% - 4%	Preexisting urinary conditions, increased intrarenal pressure, forceful technique	Control of intrarenal pressure
Postoperative Pain	30% - 70%	Individual pain threshold, complications, JJ stent	Adequate analgesia, multimodal pain management
Residual Stone Fragments	5% - 10%	Large stone size, inadequate clearance	Thorough exploration of renal collecting system, use of adjunctive techniques (ESWL, ECIRS, second stage RIRS)

PCNL (George Daniel Radavoi) (25, 82, 83)

Table 11
Complications of Percutaneous Nephrolithotomy (PCNL).

Complication	**Estimated rate (%)**	**Notes**
MILD		
Fever	10-30%	Usually self-limited; related to systemic inflammatory response
Bleeding (self-limited)	5-10%	Minor hematuria, no transfusion required
Pain requiring analgesia	10-20%	Often resolves within 24-48 hours
Urinary leakage (self-limited)	2-5%	Usually resolves with conservative management
MODERATE		
Hemorrhage requiring blood transfusion	2-7%	Due to vascular injury or significant bleeding
Urosepsis	1-2%	May require ICU admission if not promptly managed
Prolonged urinary leakage	1-2%	May require stenting or nephrostomy reinsertion
Injury to collecting system requiring repair	< 1%	Includes pelvic perforation
Bowel injury	< 1%	Requires early detection; may need surgical intervention
SEVERE		
Arteriovenous fistula/pseudoaneurysm	0.5-1%	May require angioembolization
Thoracic complications (e.g., pneumothorax)	< 1%	Especially in supracostal access
Loss of access tract	< 1-3%	May necessitate re-puncture or conversion
Death	< 0.5%	Rare; usually related to sepsis or massive hemorrhage

Perioperative management of antithrombotic therapy in urological stone surgery *(Jaffry Syed)* (84-86)

The management of anticoagulant and antiplatelet therapy in patients undergoing urological stone procedures presents a complex balance between minimizing bleeding risk and preventing thromboembolic events. As the prevalence of cardiovascular disease and anticoagulant use increases with an aging population, stone complexity and associated interventions also grow. Commonly used agents include antiplatelets (e.g., aspirin, clopidogrel) for arterial thrombosis and anticoagulants (e.g., warfarin, direct-acting oral anticoagulants or DOACs) for venous thromboembolism and atrial fibrillation. Procedural bleeding risk varies, with low risk for cystoscopy, moderate for ureteroscopy, and high for PCNL. Thrombotic risk is stratified based on clinical history, such as mechanical valves or recent *venous thromboembolism* (VTE). Bridging therapy - typically using *low molecular weight heparin* (LMWH) - is now limited to high thrombotic risk patients due to increased perioperative bleeding and limited efficacy in thrombosis prevention, as shown in recent studies and the BRIDGE trial. DOACs are generally stopped 48-72 hours preoperatively without bridging; warfarin is stopped 5 days prior, with or without bridging depending on risk. Aspirin is usually continued, while clopidogrel requires cessation 5-7 days before surgery, especially if part of *dual antiplatelet therapy* (DAPT).

Multidisciplinary collaboration with cardiology and hematology is advised for complex cases. Evidence-based guidelines, such as those from the EAU and *American College of Clinical Pharmacy* (ACCP), emphasize individualized risk assessment, procedure-specific planning, and structured resumption of therapy postoperatively. For safe outcomes, institutional protocols, pre-assessment planning, and patient education are critical. A personalized, interdisciplinary approach enables optimal decision-making in balancing antithrombotic therapy with surgical safety during urological stone interventions.

PROTECTION AND ECONOMIC ISSUES

Radiation protection *(Juan Antonio Mainez)*

We know that exposure to ionizing radiation is widespread in endourology. It's also known that exposure to high levels of ionizing radiation is associated with an increased risk of cancer and other adverse health effects (87).

It's for this reason that the urologist involved in the care of lithiasis patients should be educated on the safe use of radiation, because the urolithiasis patients will need a multitude of diagnostic and follow-up tests, and surgical interventions (ESWL, URS and fluoroscopy-guided PCNL) in their lives (88).

Different international organisms regulate radiation doses and limits. Different countries have been adapting their laws to meet the requirements of the European directive which was published in February 2018. The legislation sets the limits to which healthcare personnel can be exposed annually, regulates how to carry out the records and finally indicates how professionals should be trained. Healthcare personnel should be aware of the different individual protection systems available to reduce the radiation they receive, such as using aprons and glasses, keeping a distance from the source of the radiation, and reducing the time of use (89).

All these recommendations are based on the ALARA principle: As Low As Reasonably Achievable.

Many studies are being published in which endourological interventions are performed without the use of ionizing radiation to reduce exposure (patient and urologist). I believe that these X-ray-free procedures can be carried out with the idea of never subjecting the patient to extra risk by not using fluoroscopic support (90).

Laser protection in Endourology *(Alin Adrian Cumpanas)*

The urologists must have a core knowledge about the laser system – both for patients and staff members protection – before starting to use it in a clinical setting.

Personnel working in an endourology environment using Ho:YAG, Tm:YAG, or TFLs face minimal ocular risks (if distance from the laser tip to the cornea < 5 cm): safety goggles are optional.

Safety goggles are mandatory for Nd:YAG, KTP (Green Light), diode lasers (visible/near infrared < 1400 nm wavelength).

Patient complications: the injury is more laser user dependent than laser type dependent.

Setting up a cost-effective Endourology Service
(Hammad Ather)

At the turn of the century, the endourological revolution swept the most formidable invention in urology, *extracorporeal shock wave lithotripsy* (ESWL). Surgical interventions are assessed on efficacy, safety, and cost-effectiveness. Endourology is superior to ESWL in terms of efficacy; however, ESWL is a truly minimally invasive modality with a better safety profile. In terms of cost-effectiveness, the jury is still out.

Konnopka et al. (91) recently reported that in a German set-up, in 7 years of follow-up, reintervention was needed in 15, 23, and 26% of patients undergoing URS, PCNL, and ESWL, respectively. The cost for the primary procedure and reintervention was highest for PCNL (5783€), followed by ESWL (3240€) and URS (2979€).

In a recent systematic review by *Ghorai* and *Kumar* (92), the authors noted that reusing single-use devices in endourology has financial, environmental, and practical advantages.

Safety is vital in any surgical intervention, and efficacy is the second most important consideration. However, the value of cost-effectiveness cannot be underscored. The measures described can significantly reduce the cost of most endourology interventions.

CONCLUSIONS

(Geavlete B, Papatsoris A, Radavoi D)

The 2025 ESD Conference held special significance as a tribute to the late *Noor Buchholz* (13.02.2024), whose vision and dedication laid the foundation for ESD. Alongside pioneering colleagues, he established an enduring legacy that we honor through our shared commitment to excellence and progress.

DECLARATIONS

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