

Recent Advancements in the Management of Nephrolithiasis: A Comprehensive Review

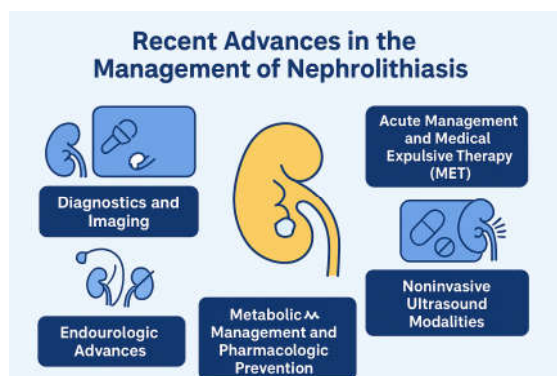
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Graphical Abstract



Abstract

Nephrolithiasis is a prevalent urological condition that is becoming more widespread worldwide and has a recurrence rate of about 50% within ten years. Reducing morbidity and recurrence is still a significant problem even with well-established surgical techniques. In addition to outlining future possibilities, this review highlights current developments in kidney stone disease diagnostics, acute therapy, surgical and noninvasive therapies, and metabolic prevention. Low-dose and dual-energy CT and enhanced ultrasonography are examples of diagnostic imaging advancements that reduce radiation exposure while improving stone characterisation. α -blockers have shown to be a successful medical expulsive treatment in acute care, and better analgesic techniques have maximized patient comfort. Smaller PCNL devices, disposable digital ureteroscopes, and thulium fiber laser technologies have all improved surgical practice by increasing stone-free rates while lowering complications. Clinical research is being done on noninvasive techniques including ultrasonic propulsion and burst wave lithotripsy, which might allow for anesthesia-free, outpatient care. Although the recent NOSTONE experiment has called into question the long-standing reliance on thiazides, preventive care still places a strong emphasis on hydration and nutritional optimization. While new research indicates that SGLT2 inhibitors may lower the incidence of stone formation through beneficial metabolic and urinary effects, potassium citrate is still useful in individuals with hypocitraturia and uric acid or cystine stones. In general, the care of nephrolithiasis is moving toward patient-centered, minimally invasive, and precise methods. Future results might be safer, more efficient, and more long-lasting if metabolomic and genetic profiling for risk assessment, artificial intelligence to aid in intraoperative and diagnostic decision-making, and next-generation ultrasound treatments are combined.

Introduction

One of the most common urological conditions is nephrolithiasis, often known as kidney stone disease, which affects 10–12% of people worldwide at some point in their lives. Recurrence rates can reach 50% within ten years (Scales et al., 2012; Sorokin et al., 2017). Nephrolithiasis causes substantial healthcare expenses, lost productivity, and a decline in quality of life in addition to its clinical burden (Khan et al., 2016). Percutaneous nephrolithotomy (PCNL), ureteroscopy (URS), extracorporeal shockwave lithotripsy (SWL), and conservative observation are examples of traditional management techniques that have proven successful but are constrained by recurrence, invasiveness, complications, and variable success rates based on patient anatomy, stone size, and composition (Assimos et al., 2016).

Significant progress has been made in the diagnosis, treatment, and prevention of nephrolithiasis in recent years. With ultrasound and low-dose or dual-energy computed tomography (DECT) developing as safer, more accurate modalities for stone identification and characterisation, there is an increasing focus on radiation stewardship on the diagnostic front (Zhang et al., 2022; Montatore et al., 2023). Medical expulsive treatment (MET) using α -blockers is still being improved in acute care, and new pain-control techniques increase patient comfort without using opioids (Türk et al., 2023).

However, the most significant advancements have been in noninvasive and surgical stone therapy. Endourologic practice has been transformed by technological advancements such as dusting vs fragmentation methods, downsized PCNL devices, and thulium fiber laser (TFL) for URS, which enable shorter surgical periods and lower morbidity (Ventimiglia et al., 2022). At the same time, noninvasive techniques like ultrasonic propulsion and burst wave lithotripsy (BWL) are rapidly being translated into clinical settings and have the potential to effectively shatter stones without the need for anesthesia or hospitalization (Harper et al., 2025).

Developments in the prevention of stone recurrence are equally significant. The recent NOSTONE study has raised concerns about the function of thiazide diuretics, even though dietary changes and hydration are still the mainstays of metabolic treatment (von Unruh et al., 2023). Novel pharmaceutical approaches, such as sodium–glucose cotransporter-2 (SGLT2) inhibitors, which have been shown to lower urinary supersaturation and stone risk in both diabetic and non-diabetic populations, are supported by emerging data (Anderegg et al., 2025; Liu et al., 2025).

This study offers a thorough summary of current developments in the treatment of nephrolithiasis, including advances in imaging, noninvasive and surgical treatments, and developing prophylactic medication. We highlight existing best practices and lay out potential prospects toward safer, less intrusive, and more successful kidney stone management by fusing mechanistic insights with clinical trial data.

2. Imaging and Diagnostics for Nephrolithiasis

Urinary stones must be accurately diagnosed and described in order to inform therapeutic plans. Due to its excellent sensitivity (94–100%) and specificity (92–100%) in identifying urolithiasis across a variety of stone sizes and locations, non-contrast computed tomography (NCCT) has long been regarded as the gold standard (Brisbane et al., 2016; Scales et al., 2012). Nonetheless, a paradigm change toward radiation-sparing techniques has been spurred by worries about radiation exposure, especially in younger patients and those with recurrent stone disease (Zhang et al., 2022).

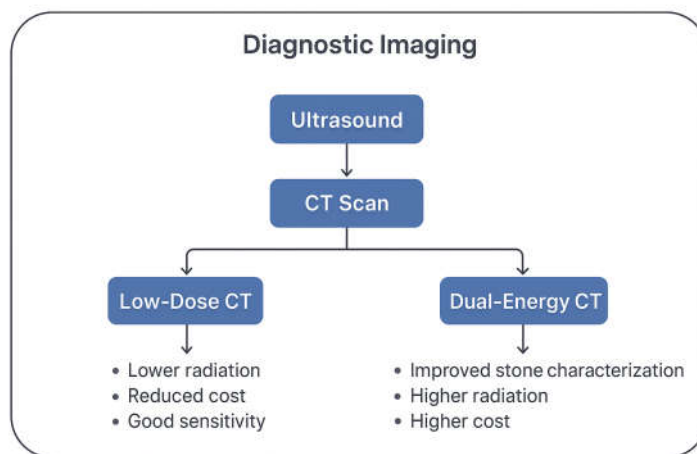


Fig.1 Diagnostic Imaging

2.1 First-Ultrasound Methods

An ultrasound-first diagnostic approach is advised for first examination by a number of professional bodies, such as the European Association of Urology (EAU) (Türk et al., 2023). Ultrasonography avoids ionizing radiation and is safe, accessible, and reasonably priced. Despite having a somewhat reduced sensitivity for stones smaller than 5 mm, recent prospective studies have demonstrated that an ultrasound-first approach produces patient results that are equivalent to those of CT-based pathways (Wang et al., 2022). Clinical decision-making is aided by the real-time information that ultrasound offers on hydronephrosis, ureteral blockage, and bladder emptying.

2.2 Computed Tomography Developments

CT is nevertheless essential when ultrasound results are unclear or surgery is being considered, despite radiation concerns. Significant radiation exposure reductions have been attained without compromising diagnostic accuracy because to recent advancements in low-dose CT procedures, which are frequently improved with deep learning reconstruction algorithms (Zhang et al., 2022). Dual-energy CT (DECT) also helps distinguish between calculi that contain calcium and those that contain uric acid, giving important information regarding the composition of stones. This difference has real-world applications since urinary alkalinization can be used to therapeutically remove uric acid stones, perhaps avoiding surgery (Montatore et al., 2023).

2.3 Clinical Algorithms and Decision Support Tools

Decision assistance technologies like the STONE score and ultrasound-first algorithms have been created and shown to reduce the number of needless CT scans in emergency situations. These techniques classify patients according to their risk of developing stone disease by combining clinical presentation, test results, and early imaging. Research shows that these procedures can safely lower CT use without sacrificing the quality of the diagnosis (Valencia et al., 2014; Wang et al., 2022).

2.4 Imaging's Future Directions

Image analysis powered by artificial intelligence (AI) is showing promise as a supplement to stone identification and categorization. According to early research, machine learning algorithms can automate the assessment of stone load and perform better than radiologists in identifying tiny calculi (Kuo et al., 2023). Furthermore, preoperative planning for difficult patients may be enhanced by integrating virtual endoscopy and 3D reconstructions from CT scans.

With DECT as a composition-defining technique, low-dose CT as a confirmatory modality, and ultrasound as the first-line tool, diagnostic imaging in nephrolithiasis is shifting toward individualized, radiation-sparing approaches. It is anticipated that the use of AI and decision-support systems would improve diagnostic precision and effectiveness even more.

Medical Expulsive Therapy (MET) and Acute Care

Relieving discomfort, promoting spontaneous passage where feasible, and identifying individuals in need of surgery are the goals of acute therapy of nephrolithiasis. The main symptom is pain, and if left untreated, ureteral blockage can result in infection, hydronephrosis, or renal impairment.

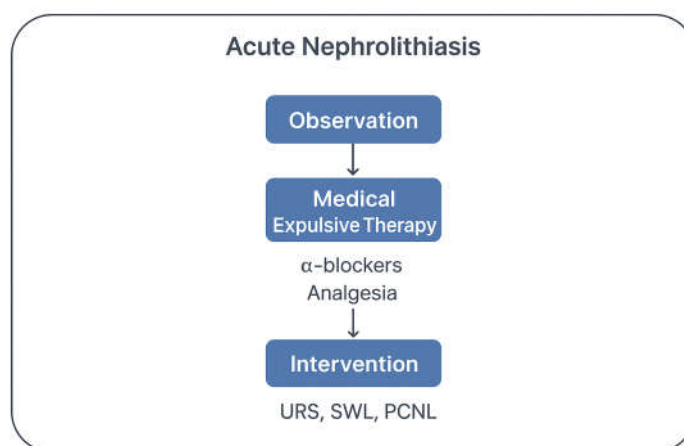


Fig.2 Acute Nephrolithiasis

3.1 Management of Acute Pain

Because of their effectiveness in lowering prostaglandin-mediated renal pelvic pressure and ureteral smooth muscle spasm, nonsteroidal anti-inflammatory medications (NSAIDs) are regarded as the first-line treatment for renal colic (Holdgate & Pollock, 2004). NSAIDs are just as effective as opioids, according to randomized studies, but they have less side effects such as drowsiness and nausea (Pathan et al., 2018). Although recommendations recommend reducing the use of opioids due to the danger of dependence, they are nevertheless an option for refractory patients or when NSAIDs are contraindicated (Türk et al., 2023). In some situations, adjuncts such as intravenous acetaminophen have also shown promise (Serinken et al., 2012).

3.2 MET, or Medical Expulsive Therapy

Over the previous 20 years, MET's function has changed. It has been demonstrated that α -adrenergic antagonists, namely tamsulosin, accelerate the passing of stones, particularly for distal ureteral calculi that are 5–10 mm in size (Furyk et al., 2016). They work by reducing intraluminal pressure, peristaltic frequency, and ureteral smooth muscle relaxation. Although

outcomes have differed among populations, meta-analyses and guidelines advocate MET for some individuals (Ye et al., 2018).

Although they were researched in the past, calcium channel blockers such nifedipine showed less effectiveness than α -blockers, and their usage is now mostly no longer needed (Seitz et al., 2009). Although corticosteroids and α -blockers have been studied together, regular usage is not advised because of the side-effect profiles (Miller & Kane, 2011).

3.3 MET Patient Selection

Patients without infection, uncontrolled pain, or high-grade blockage who have distal ureteral stones between 5 and 10 mm benefit most from MET. On the other hand, MET is less successful for stones that are bigger than 10 mm and proximal, in which case surgery is typically necessary (Preminger et al., 2007; Türk et al., 2023). Although there is still a lack of long-term safety data, new research indicates that tamsulosin is safe and has a small effect on pediatric patients (Mokhless et al., 2012).

3.4 Acute Management's Future Directions

To improve the management of acute stones, new strategies are being investigated. Potential substitutes for α -blockers include studies on new smooth muscle relaxants and selective phosphodiesterase inhibitors (Matsushima et al., 2018). Additionally, to enhance results and decrease needless procedures, patient-centered decision algorithms that incorporate pain intensity, stone size, and anatomical position are being improved.

4. Endourologic Developments in the Treatment of Nephrolithiasis

Over the past ten years, endourology has seen substantial changes, with improvements in surgical methods, energy sources, and equipment greatly enhancing the prognosis of nephrolithiasis patients. In order to minimize morbidity and hospital stays, there has been a tendency toward miniaturization, less invasiveness, and improved stone clearing.

4.1 URS (ureteroscopy)

The most popular procedure for treating ureteral and intrarenal stones is now ureteroscopy. Compared to their fiberoptic predecessors, digital flexible ureteroscopes provide better image quality, ergonomics, and durability (Knoll et al., 2020). Although their long-term cost-effectiveness is still up for question, innovations like single-use ureteroscopes lower the danger of cross-contamination and minimize replacement expenses (Doizi & Traxer, 2020).

In URS practice, the argument between "dusting" and "fragmentation and basketing" is still crucial. High-frequency, low-energy laser settings used in dusting procedures minimize the requirement for extraction by allowing small particles to pass spontaneously. While basketing still provides greater instantaneous stone-free rates in some situations, comparative studies indicate that dusting may shorten operating time (Patel et al., 2018).

4.2 PCNL, or percutaneous nephrolithotomy

PCNL is still the gold standard for kidney stones that are greater than 20 mm. Access tract miniaturization, which produced mini-, ultra-, and micro-PCNL, is a significant development. These methods preserve high stone-free rates while lowering the risk of bleeding, transfusions, and postoperative discomfort (Sabnis et al., 2013; Zeng et al., 2015). However, the possible necessity for auxiliary procedures and lengthier operating durations must be weighed against their use (Knoll et al., 2020).

Another innovation that has gained favor is supine PCNL, which, in contrast to the conventional prone method, offers simpler simultaneous retrograde access and better anesthetic safety (Falahatkar et al., 2016).

4.3 Innovations in Lasers

There has been a technical revolution in laser lithotripsy. The thulium fiber laser (TFL) is quickly becoming a better substitute for the holmium:YAG (Ho:YAG) laser, which has long been the industry standard. Due to less retropulsion, TFL provides increased safety, smaller fragment sizes, and greater stone ablation efficiency (Ventimiglia et al., 2022). According to early clinical trials, TFL may have fewer complications and shorter operating times than Ho:YAG (Arezzo et al., 2022).

By decreasing retropulsion and increasing fragmentation efficiency, pulse modulation technologies as Moses™ technology have significantly enhanced Ho:YAG performance (Elhilali et al., 2017).

4.4 Trends and Adjunctive Technologies

Additional endourologic innovations include disposable baskets made to minimize mucosal damage and ureteral access sheaths with pressure sensors to lower intrarenal pressure (Patel et al., 2018). While lowering radiation exposure, intraoperative fluoroscopic and ultrasound-guided navigation devices are increasing procedural safety.

5. Modalities of Noninvasive Ultrasound in Nephrolithiasis

One of the most promising areas of stone treatment is noninvasive ultrasound-based therapy. Although endourological operations now account for the majority of surgical treatments, advancements in acoustic energy technology have the potential to bring noninvasive therapies back to the forefront in the treatment of nephrolithiasis.

5.1 Shockwave Lithotripsy Extracorporeal (SWL)

SWL has been a fundamental component of stone management since its inception in the 1980s. With little morbidity and the possibility of outpatient therapy, it provides a noninvasive method. SWL works well on individuals with favorable body habitus and for stones less than 20 mm, especially in the upper ureter or renal pelvis (Assimos et al., 2016).

However, because of inconsistent stone-free rates, the requirement for numerous sessions, and the emergence of more dependable options like ureteroscopy and PCNL, SWL utilization has decreased over the past 20 years (Türk et al., 2023). Improved coupling devices, acoustic lens designs, and low-frequency shockwave protocols are some of the strategies being used to optimize SWL. These techniques may increase fragmentation efficiency while reducing renal damage (Sapozhnikov et al., 2019).

5.2 Lithotripsy by Burst Wave (BWL)

In contrast to high-pressure shockwaves, BWL is a new, experimental technique that produces brief harmonic ultrasonic bursts. According to preclinical and early human research, BWL outperforms SWL in terms of controlled fragmentation and cavitation-related damage (Maxwell et al., 2020). The prospect of office-based therapy has increased due to clinical trials showing that ureteral and renal stones may be effectively fragmented without the requirement for anesthesia or fluoroscopy (Harper et al., 2025).

BWL may lessen the requirement for supplementary treatments since it produces finer pieces that are more receptive to spontaneous passage than SWL (Hall et al., 2022).

5.3 Propulsion by Ultrasonic

Another experimental method is ultrasonic propulsion, which uses focused acoustic radiation force to move stones or pieces around in the urinary system. According to early clinical trials, ultrasonic propulsion can help remove stones by moving calculi into better places, which frequently speeds up passage after spontaneous fragmentation or SWL (Sahota et al., 2018). For patients with tiny, symptomatic, non-obstructing stones, when care could otherwise be postponed, this technique holds great promise.

5.4 Prospects for the Future

Outpatient stone treatment that is entirely noninvasive may be made possible by the incorporation of BWL and ultrasonic propulsion into clinical procedures. To determine their long-term efficacy, safety, and cost-effectiveness in comparison to existing endourologic standards, more research is required. These technologies have the potential to significantly decrease the need for invasive operations, hospital stays, and anesthesia if they are verified.

6. Pharmacologic Prevention and Metabolic Management

The aim of managing nephrolithiasis is still long-term avoidance of recurrence, even while surgical and noninvasive therapies address acute stone occurrences. According to Rule et al. (2014), over half of patients have a recurring stone within ten years, highlighting the need of customized metabolic screening and focused therapy.

6.1 Dietary and Hydration Techniques

Guidelines indicate a urine production of at least 2 to 2.5 liters per day, making adequate hydration the most often recommended preventative intervention (Türk et al., 2023). A high fluid intake reduces the supersaturation of salts that cause stones and dilutes urine solutes. Dietary changes are also essential, such as consuming less salt, limiting animal protein, and keeping dietary calcium levels normal. Since it may improve oxalate absorption and paradoxically increase the risk of stones, excessive calcium restriction is suggested (Taylor & Curhan, 2007).

6.2 Diuretics with Thiazide

Thiazide diuretics have been used for decades to lower calcium excretion in the urine of those who frequently have calcium stones. This paradigm was questioned, nonetheless, by the recent NOSTONE randomized controlled study, which found that gout and hypokalemia were more common side effects and that hydrochlorothiazide did not significantly lower recurrence as compared to a placebo (von Unruh et al., 2023). As a result, thiazide usage has been reevaluated, and many specialists now support a more customized, selective strategy.

6.3 Supplementing with Citrate

Potassium citrate is still a mainstay treatment, especially for those with uric acid stones or hypocitraturia. Numerous randomized trials have shown that citrate lowers the risk of stone recurrence by alkalinizing the urine and binding calcium (Barcelo et al., 1993). Due to their great sensitivity to urinary alkalinization, it is particularly advantageous for cystine and uric acid stones (Pak, 1991).

6.4 Inhibitors of Sodium-Glucose Cotransporter-2 (SGLT2)

SGLT2 inhibitors, which are often used to treat diabetes and heart failure, may also lower the incidence of kidney stones, according to recent observational and mechanistic research. Changes in urine citrate and volume, decreased uric acid supersaturation, and enhanced excretion of glucose and ketones are some of the hypothesized processes (Liu et al., 2025). Compared to other glucose-lowering medications, SGLT2 inhibitor-treated patients had decreased incidence and recurring nephrolithiasis rates, according to a large population-based

investigation (Anderegg et al., 2025). Although randomized trials are still pending, these findings have sparked interest in repurposing SGLT2 inhibitors as a potential preventative treatment.

6.5 New and Supplementary Treatments

Research on new pharmaceutical targets includes crystal growth inhibitors such citrate analogs, gut microbiota modification (e.g., supplementing with *Oxalobacter formigenes*), and inhibitors of oxalate synthesis (Lieske et al., 2014). Despite their promise, these treatments are still in the research stage and have not yet been included in recommendations.

7. Prospects for the Future

Nephrolithiasis treatment is at a turning point thanks to developments in noninvasive techniques, imaging, surgery, and medication prophylaxis. Three key areas are anticipated to be the focus of future research and clinical practice: integrated care models, precision medicine, and technology innovation.

7.1 Personalized and Accurate Medicine

Less than 10% of patients receive a thorough examination following a first stone occurrence, indicating that metabolic stone evaluation is still underused (Stamatelou et al., 2015). Clinicians may be able to stratify patients based on recurrence risk and adjust treatments in accordance with these findings thanks to developments in genomes, metabolomics, and urine proteomics (Lieske et al., 2014). For instance, instead of using the existing "one-size-fits-all" strategy, pharmaceutical treatments and precision-based nutritional recommendations might be tailored to the unique metabolic phenotypes of each patient.

7.2 Innovation in Technology

With more advancements in single-use digital ureteroscopes, mini-PCNL systems, and thulium fiber laser platforms, the trend toward downsizing and disposability in surgery will continue (Ventimiglia et al., 2022). As they advance through clinical trials, noninvasive technologies like burst wave lithotripsy (BWL) and ultrasonic propulsion have the potential to drastically change practice by offering anesthesia-free, outpatient treatment alternatives (Harper et al., 2025). According to Kuo et al. (2023), the use of artificial intelligence into imaging and

intraoperative navigation systems has promise for improving accuracy, minimizing complications, and optimizing stone removal.

7.3 Patient-Centered, Integrated Care

Multidisciplinary approaches of therapy are crucial since kidney stone disease increasingly coexists with systemic diseases such as diabetes, obesity, and chronic kidney disease (Khan et al., 2016). Primary care and chronic disease treatment must include preventive measures that prioritize long-term kidney protection, cardiovascular risk reduction, and lifestyle adjustment. Particularly in environments with limited resources, telemedicine platforms and digital health applications may provide access to recurrence monitoring, dietary counseling, and follow-up (Tasian et al., 2017).

8. Conclusion

From radiation-sparing diagnostic imaging and cutting-edge endourologic tools to next-generation ultrasound treatments and new pharmacologic preventives like SGLT2 inhibitors, the treatment of nephrolithiasis has advanced significantly in recent years. However, there are still big gaps in cost-effectiveness, recurrence prevention, and fair access to cutting-edge technology.

In the future, care pathways will be redesigned through the use of AI-enhanced decision assistance, minimally invasive or noninvasive therapies, and individualized preventative initiatives. The future of managing nephrolithiasis promises safer, more effective, and more sustainable results for patients everywhere by fusing technology innovation with comprehensive, patient-centered methods.

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