

## Advances in Urology: A Comprehensive Literature Review on Urolithiasis Management and Innovations

Reza Dwi Ramadhan<sup>1\*</sup>, Mangkubumi Putra Wijaya<sup>2</sup>, Dzaky Ramadhan Hidayat<sup>3</sup>

<sup>1</sup>*Faculty of Medicine, University of Muhammadiyah Malang, East Java, Indonesia, 65145*

<sup>2</sup>*Department of Urology, Ngudi Waluyo General Hospital, Blitar, East Java, Indonesia, 66183*

<sup>3</sup>*Emergency Department, Melati Husada Hospital, Malang, East Java, Indonesia, 65517*

### \*Corresponding Author

Reza Dwi Ramadhan

Faculty of Medicine, University of Muhammadiyah Malang, East Java, Indonesia, 65145

Email:

[rezadwiramadhan@gmail.com](mailto:rezadwiramadhan@gmail.com)

**Introduction.** Urolithiasis is a prevalent condition, affecting approximately 12% of the global population at some point in their lives, with higher incidence rates reported in industrialized nations. This condition poses significant health challenges worldwide due to its recurrence and the associated healthcare burden. Recent innovations in imaging, minimally invasive techniques, and pharmacotherapy have revolutionized the field. This review aims to explore recent updates and innovations in the management of urolithiasis, from diagnosis to therapy.

**Methods.** A systematic search using predefined keywords in multiple databases was done. Peer-reviewed articles, clinical trials, meta-analyses, and systematic reviews focused on urolithiasis management, diagnostic techniques, therapeutic innovations, and preventive strategies were analyzed. Articles from January 2015—December 2023 were included, reviewed for its eligibility, and extracted.

**Results.** Emerging pharmacological agents (eg. empagliflozin, thiosulfate) offer new avenues for prevention and recurrence reduction, particularly for patients with recurrent urolithiasis, although not as primary therapy. Additionally, the integration of artificial intelligence and machine learning is beginning to play a role in predicting stone recurrence and optimizing treatment plans.

**Conclusion.** This review highlights the importance of a personalized, patient-centered approach in managing urolithiasis, emphasizing the need for ongoing research and clinical trials to further refine these innovations.

**Keywords:** artificial intelligence, disease management, urinary stone disease, urolithiasis

## Introduction

Urolithiasis is a global health issue occurring when calculi form in the urinary tract. The management of urolithiasis has changed overtime following the present day technology and surgical procedures and understanding the pathological mechanisms. An estimated 10-15% people worldwide will experience urolithiasis sometime in their lifetime [1-2]. The widespread and increasing urolithiasis prevalence requires a multifaceted solution. . If left untreated, urolithiasis may predisposes individuals to recurrent urinary tract infections [3].

Current research shows that conservative treatment measures such as extracorporeal shock wave lithotripsy (ESWL), minimally invasive surgeries like ureteroscopy (URS), and percutaneous nephrolithotomy (PCNL) are

preferred in the management of kidney stones [4-5]. The European Association of Urology (EAU) guidelines advise to distinguish the treatment strategy by taking into account the characteristics of the stones, the patient's preference, and the capabilities of the healthcare provider, to yield better outcomes, shorter recovery periods, and higher safety levels [6-8].

In terms of surgical management, the application of laser technology has become a significant importance. Laser lithotripsy, especially with the enhanced use of high-power lasers, has brought significant advancement in the management of urolithiasis due to its increased stone fragmentation rate and less risk of procedural complications [9-10]. The International Alliance of Urolithiasis (IAU) Guidelines are optimizing the use of laser technology in diverse settings, which is essential for developing best practices and

enhancing the quality of surgery [11]. Furthermore, the application of artificial intelligence (AI) in urology has demonstrated the potential in improving the care of urolithiasis. The AI-enhanced imaging and predictive analysis helps in the proper categorization of stones, more effective operation planning, increasing the success rate and patients' satisfaction, and lowering the relapse rate [12-13]. This review aims to explore recent updates and innovations in the management of urolithiasis, from diagnosis to therapy.

## Materials and Method

This literature review was conducted by systematically searching multiple electronic databases, including PubMed, Science Direct, and Web of Science, to identify relevant studies on urolithiasis management and innovations. The search terms used were combinations of keywords such as "urolithiasis," "urinary stone disease," "minimally invasive surgery," "laser lithotripsy," "artificial intelligence in urology," and "diagnostic advances." The search was limited to articles published between January 2015 and December 2023 to ensure the inclusion of the most recent advancements. Additionally, manual searches of reference lists from key articles were performed to identify further relevant studies.

The inclusion criteria comprised peer-reviewed articles, clinical trials, meta-analyses, and systematic reviews focused on urolithiasis management, diagnostic techniques, therapeutic innovations, and preventive strategies. Studies not written in English, case reports with fewer than 10 participants, and articles lacking full-text availability were excluded. The initial search yielded a broad range of articles, which were then screened based on titles and abstracts. Full-text articles were reviewed for eligibility, and data were extracted based on relevance to the research objectives.

## Result

### Pathophysiology on Urolithiasis

The key factor in kidney stone formation is the condition called "urinary supersaturation" where the concentration of stone-forming substances is higher than their solubility in the urine. This supersaturation results in nucleation, the formation of the first stone crystals [14-15]. Calcium oxalate stones are the most common type of kidney stones

found in clinical practice, representing around 80% of overall cases [16-17]. Calcium oxalate crystallization is distinctive by the pH and the ionic strength of urine, which also define the inhibition or promotion of crystallization [17-18]. For example, the low urinary pH favors the formation of uric acid stones, whereas the high urine pH promotes the formation of struvite stones [17,19]. Conditions such as hypercalciuria, hyperoxaluria, and hypocitraturia are commonly observed in patients with stone formation [20-21].

Other important factors that contribute to the development of urolithiasis include the high consumption of sodium, animal protein and oxalate containing foods. On the other hand, drinking more water and adopting a healthy diet, such as by consuming more fruits and vegetables, are useful to dilute and minimize the amount of stone forming chemicals in the urine [22-23]. Comorbid conditions such as obesity, diabetes mellitus, and metabolic syndrome have also been important contributors to urolithiasis. These conditions can change the composition of urine and facilitate stone formation through insulin resistance and renal action on electrolytes [2,24].

Metabolic syndrome, characterized by obesity, insulin resistance, hypertension, and dyslipidemia, has emerged as a significant contributor to the pathogenesis of urolithiasis. Insulin resistance, a hallmark of metabolic syndrome, alters renal tubular handling of electrolytes, leading to an increased urinary excretion of calcium, oxalate, and uric acid, which were key components of kidney stones. Additionally, the chronic low-grade inflammation associated with obesity promotes oxidative stress, which further disrupts urinary solute balance and crystal formation. Studies have shown that obese individuals often exhibit lower urinary pH, favoring the precipitation of uric acid stones. These metabolic disturbances create a supporting environment for stone formation. Thus, explaining the higher prevalence of urolithiasis in patients with metabolic syndrome compared to the general population [25-27].

There are also certain important genetic concerns involved in the development of urolithiasis. Some of the primary metabolic disorders that include cystinuria and primary hyperoxaluria put people at higher risk of recurrent stone formation due to the lack of renal amino acid and oxalate handling [28-29]. Polymorphisms in genes regulating urinary solute transporters (e.g., CLDN14) and inhibitors of crystallization (e.g., OPN) further modulate individual susceptibility to stone disease [30-32]. Thus, family history is a risk factor of urolithiasis.

## Diagnostic Advances in Urolithiasis

Non-contrast computed tomography (NCCT) remains the best imaging technique for diagnosis of urolithiasis due to its sensitivity and specificity of 95% to 100% [33-35]. NCCT exhibits certain advantages over other methods as it does not rely on contrast media, hence reduces the time required to perform the test while providing satisfactory results in the detection of urinary stones of various sizes and compositions [33]. The high sampling rate and the possibility to visualize the entire urinary tract make NCCT irreplaceable in acute conditions, particularly in case of renal colic [34]. The use of low-dose CT protocols has also emerged in recent studies as concerns regarding the total radiation of multiple imaging scans received by a patient started rising [34,36]. Ultrasound (US) is widely used for most diagnostic purposes as it does not interfere with ionizing radiation and is preferred for specific age and groups of patients, such as pregnant women and children. Though ultrasound is useful for defining large stones and evaluating the severity of hydronephrosis, it may have limited sensitivity for small stones, leading to missed diagnoses [37-38]. Thus is used as first-line imaging in suspected renal disease by the European Association of Urology (EAU) guidelines [37,39]. The integration of ultrasound with other imaging techniques such as NCCT can improve the specificity of diagnosis and offer a comprehensive assessment of the urinary tract [37].

Dual-energy computed tomography (DECT) has recently been identified as one of the most significant improvements in the imaging of urolithiasis. DECT enables classification of stones based on the chemical composition, and increases the probability to detect uric acid stones which might not be seen on plain NCCT [40-41]. The use of AI to diagnose urolithiasis is certainly a promising innovation to improve the patient treatments approaches. While machine learning (e.g., CNN-based models) achieve >90% accuracy in stone detection on CT scan, current limitations include dependency on high-quality training datasets and poor generalizability across diverse populations. Key challenges such as ethical concerns about data privacy, model interpretability, and integration cost into the existing hospital workflows must be addressed before widespread adoption. AI-driven 3D reconstruction technology is also under development, enabling clinicians to visualize stones in three-dimensional detail and more accurately assess stone size, shape, and anatomical location. In addition, the use of

AI-based software has the potential to improve the assessment of the ultrasound images based on the feedforward and feedback mechanisms, leading to an increased degree of accuracy of diagnostic interpretation. These innovations are paving the way for a future where AI may not only streamline diagnostics but also facilitate surgical planning and predict recurrence risk with unprecedented precision [42-45].

Molecular diagnostics and biochemical assays have also been developed in recent years. The urinary indole-reacted calcium oxalate crystallization index (iCOCI) appears to provide a promising means of distinguishing between calcium oxalate stone formers and non-stone formers, demonstrating high sensitivity and specificity. This diagnostic tool could enhance existing imaging techniques by revealing the metabolic factors associated with stone development [46]. Furthermore, ongoing research is examining the potential of non-invasive outpatient diagnostics through hyperspectral imaging techniques in the context of urinary stone disease. This method may also allow for the detection of spectral signatures in urine, identifying stone-forming agents, which indicates that the conditions can be diagnosed earlier and consequently treated before further progression [47].

## Therapeutic Interventions for Urolithiasis

Minimally invasive procedures have become the cornerstone of urolithiasis management, offering effective treatment options with reduced morbidity. Percutaneous nephrolithotomy (PCNL) remains a preferred method for large or complex kidney stones. Recent studies have demonstrated the feasibility of PCNL in challenging anatomical situations, such as ectopic kidneys, with high stone-free rates and minimal complications [48-49]. This technique has a high success rate but is associated with greater morbidity compared to other minimally invasive options [50]. Ureteroscopy (URS) is a minimally invasive option that allows for direct visualization and removal of stones from the urinary tract. URS is particularly effective for stones located in the distal ureter and can be performed with or without laser lithotripsy for fragmentation [51]. The success rates for URS are high, and it is often preferred for larger stones or those that are not amenable to ESWL [52]. The introduction of the holmium:yttrium-aluminum-garnet (Ho:YAG) laser has revolutionized the treatment of urolithiasis. This laser is recognized as the most efficient for lithotripsy, as the studies have demonstrated its

ability to fragment stones of all types, especially calcium oxalate and struvite [53-54]. Recent studies have demonstrated that the Ho:YAG laser has shown to have high stone free rates (SFRs) with low rates of complications in ureteroscopy and percutaneous nephrolithotomy (PCNL), thus making it a preferred choice [54].

A relatively new laser model is the thulium fiber laser (TFL). TFL offers advantages such as reducing thermal damage to the surrounding tissues and improving stone fragmentation efficiency compared to traditional Ho:YAG laser. A meta-analysis comparing TFL and Ho:YAG laser lithotripsy has found that TFL may result in shorter operative time and lower rate of postoperative complications, suggesting its potential as a superior alternative [55] (Table 1). The advances in laser technology have opened up new possibilities in performing laser lithotripsy, where the fiber bundle laser steering system has been enhanced to deliver lasers at precise and difficult sites in human anatomy[56].

**Table 1.** Comparison of laser technologies in urolithiasis

Parameter	Ho:YAG Laser	Thulium Fiber Laser (TFL)
Stone Types	All (esp. calcium oxalate)	Uric acid, cystine
Penetration Depth	0.5–1.0 mm	0.2–0.4 mm
Operative Time	Moderate	Shorter
Cost	Moderate	High
Best For	Large/hard stones	Small/soft stones

Retrograde Intrarenal Surgery (RIRS) has emerged as a valuable alternative for the treatment of kidney stones, especially in patients who might be unable to handle more invasive procedures. RIRS utilizes a flexible ureteroscope to access the kidney through the ureter, allowing a direct visualization and treatment of intrarenal stones without the need of skin incision. This technique is particularly effective for small to moderate stones and offers high stone-free rates (SFRs) with minimal postoperative discomfort. When combined with advanced laser technologies, RIRS has shown impressive outcomes with fewer complications, making it a preferred choice for patients with stones in anatomically challenging locations or those with underlying comorbidities [57].

Laparoscopic procedures provide another minimally invasive option for treating urolithiasis, particularly where other techniques, such as PCNL and RIRS, are unsuitable for complex and large stones. Laparoscopic pyelolithotomy and ureterolithotomy allow for the removal of stones through small incisions, reducing both recovery time and postoperative pain. While laparoscopic methods generally require more technical expertise, they are associated with lower morbidity and fewer complications than traditional open surgery. Laparoscopy is often reserved for cases with impacted or recurrent stones, or when associated anatomical abnormalities are present, providing both diagnostic and therapeutic advantages in a single procedure [6].

Open surgery, once the mainstay of urolithiasis management, has shown a significant decline due to the advent of minimally invasive techniques that offer comparable or superior outcomes with fewer complications. Although rarely indicated today, open surgery may still be considered in cases with extremely large or complex stone burdens, anatomical abnormalities that preclude other techniques, or recurrent stones after multiple failed minimally invasive attempts. However, open surgery is associated with higher morbidity, prolonged recovery, and greater risk of postoperative complications, which has led to its relegation to a last-resort option in urolithiasis management [58].

Pharmacologic intervention remains an important part of, not only the therapy, but also the prophylaxis of urolithiasis. Medical expulsive therapy (MET) using alpha-blockers, such as tamsulosin and silodosin, has shown to facilitate the passage of ureteral stones by relaxing smooth muscle in the ureter [59]. Recent studies also review the use of sodium-glucose cotransporter 2 (SGLT2) inhibitors, such as empagliflozin, regarding its altering supersaturation states and further stone formation rate [60]. Studies have indicated that certain plant extracts, such as those from *Cymbopogon proximus* and *Enhydra fluctuans*, exhibit antiurolithic properties by inhibiting calcium oxalate [61-62]. Probiotics and other natural remedies are also being investigated for their potential role in preventing stone formation and recurrence [63-64]. Moreover, researchers are exploring the utilization of nanoparticles for photothermal therapy to eliminate bacteria associated with kidney stones, which may reduce the risk of infection and subsequent stone formation [64].

## Economic Burden and Patient-Reported Outcomes of Urolithiasis Management

The management of urolithiasis imposes a significant economic burden on healthcare systems worldwide, driven by high treatment costs, recurrent hospitalizations, and loss of productivity. Surgical interventions are associated with substantial expenses, particularly for complex or recurrent cases. In industrialized nations, where the prevalence of urolithiasis is rising, the annual healthcare expenditure for stone-related treatments has increased markedly. For example, studies estimate that the United States spends billions annually on urolithiasis care, with the costs further amplified by postoperative complications and the need for repeating procedures. The economic impact is even more pronounced in low-resource settings, where limited access to advanced technologies and trained specialists exacerbate disparities in care [65–67].

Indirect costs, such as missed workdays and reduced productivity experienced by the patients and their helper, further burden the patients and society. Recurrent stone formation often requires multiple interventions, leading to prolonged recovery period and long-term disability. Preventive measures, including dietary modification and pharmacotherapy, offer cost-saving potential but are underutilized due to gaps in patient education and adherence. Addressing these economic challenges necessitates a shift toward value-based care, emphasizing early diagnosis, minimally invasive treatments, and personalized prevention strategies to reduce both direct and indirect costs associated with urolithiasis [65,68].

Patient-reported outcomes (PROs) and quality of life (QoL) measures are critical for evaluating the holistic impact of urolithiasis and its treatments. Acute episodes of renal colic and recurrent stone events are associated with severe pain, anxiety, and diminished physical functioning, significantly impairing patients' daily lives. Studies have shown that the patient often reported lower scores in mental health, vitality, and social functioning compared to the general population, thus interventions should address not only stone clearance but also psychosocial well-being. Emerging evidence highlights the role of minimally invasive techniques in improving PROs. For instance, ureteroscopy with laser lithotripsy has been linked to shorter recovery times and fewer complications, leading to faster resumption of normal activities. However, disparities persist in QoL outcomes based on treatment modality, stone burden, and socioeconomic factors. Integrating

QoL metrics into clinical decision-making can enhance treatment adherence and satisfaction. This integration ultimately serves to connect technological advancements with the actual experiences of patients undergoing management for urolithiasis [69-71].

## Conclusion

Over the years, urolithiasis management has developed almost hand in hand with technology improvement, surgical techniques, and pathological discoveries. Integration of AI in diagnosis and treatment protocol determination has also enhanced treatment results. An understanding of the chemistry involved in stone formation, dietary requirements, and genetic factors are important in preventing the formation of the kidney stones.

Future research should prioritize: (1) longitudinal studies on AI-assisted diagnostics to validate real-world efficacy, (2) randomized trials comparing TFL vs. Ho:YAG lasers in complex stone anatomies, and (3) development of targeted pharmacotherapies for genetic subtypes (e.g., cystinuria). Collaborative efforts between urologists, data scientists, and geneticists are essential to translate innovations into practice.

## Conflict of interest

The authors declare no conflict of interest.

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