Journal of Advanced Scientific Research

Available online through https://sciensage.info

ISSN

0976-9595

Review Article

Recent Advancements in the Management of Calcium Oxalate Stones: A Comprehensive Review

Dinesh Kamdi[1], Anshu R. Dudhe[2], Rupesh Dudhe[1*]

[1]*Adarsh Institute of Pharmacy, Nandanvan, Nagpur, Maharashtra, India.*

[2]*Nagpur college of Pharmacy, Hingna Rd,Wanadongri, Nagpur, Maharashtra, India.*

*Corresponding author: rdudhe121@gmail.com

Received: 28-03-2025; Accepted: 15-05-2025; Published: 31-05-2025

 https://doi.org/10.55218/JASR.2025160501

ABSTRACT

Urolithiasis, particularly calcium oxalate (CaOx) stone formation, is a prevalent and debilitating condition globally. The management of CaOx stones has seen significant advancements in recent years, driven by technological innovations and a deeper understanding of stone pathogenesis. This review paper provides a comprehensive overview of these recent advancements, focusing on novel diagnostic techniques, minimally invasive surgical interventions, medical expulsive therapy, and preventative strategies. We delve into the latest imaging modalities improving diagnostic accuracy, the evolution of surgical approaches like miniaturized percutaneous nephrolithotomy and flexible ureteroscopy, advancements in medical expulsive therapy with alpha-blockers and other agents, and explore personalized preventative strategies considering dietary modifications, pharmacological interventions, and emerging research on gut microbiome and nanotechnological approaches. This review aims to synthesize current knowledge, highlight the progress made, and identify future directions in the effective management of CaOx stones, ultimately improving patient outcomes and reducing recurrence rates.

Keywords: Calcium oxalate stones, Urolithiasis, Kidney stone management.

INTRODUCTION

Urolithiasis, the formation of stones within the urinary tract, affects a significant portion of the global population, with calcium oxalate (CaOx) stones being the most common composition, accounting for approximately 75 to 80% of all urinary stones.[1] The formation of CaOx stones is a complex multifactorial process involving supersaturation of urine with calcium and oxalate, nucleation, crystal growth, and aggregation, influenced by dietary habits, genetic predispositions, and metabolic disorders (Figure 1).[2] Patients with CaOx stones often experience significant morbidity, including excruciating pain, urinary tract infections, renal colic, and potential kidney damage.[3] The management of CaOx stones has evolved significantly, transitioning from primarily open surgical procedures to minimally invasive techniques and sophisticated preventative strategies. This review aims to provide a detailed overview of the recent advancements in the diagnosis, treatment, and prevention of CaOx stones, focusing on developments that have significantly impacted clinical practice and patient care.

Innovations in Diagnostic Methods

Right and prompt diagnosis holds an essential place in management regarding any CaOx stone. Newer techniques of imaging and stone composition have tremendously aided the accuracy of diagnosis (Figure 2).

Imaging modalities

- *Low-dose computed tomography*

Non-contrast helical CT scanning has become the gold standard for diagnosing urolithiasis by achieving very good sensitivity and specificity.[4,5] Development has been narrowed recently to reducing the level of radiation exposure using low-dose computed tomography (LDCT) protocols and, iterative reconstruction algorithms and automated exposure control without compromising the accuracy of diagnosis. This is even more critical due to the recurrent nature of stone disease requiring repeated imaging.

- *Dual-energy computed tomography*

Dual-energy computed tomography (DECT) has provided rather additional information with respect to traditional CT, by Discriminating materials on the basis of attenuation at two different energy levels. DECT in urolithiasis helps to differentiate uric acid from other non-uric acid stones, i.e., CaOx stones. Also, it quantifies the stone composition and significantly helps in the treatment planning and metabolic evaluation. Improvement is still ongoing on

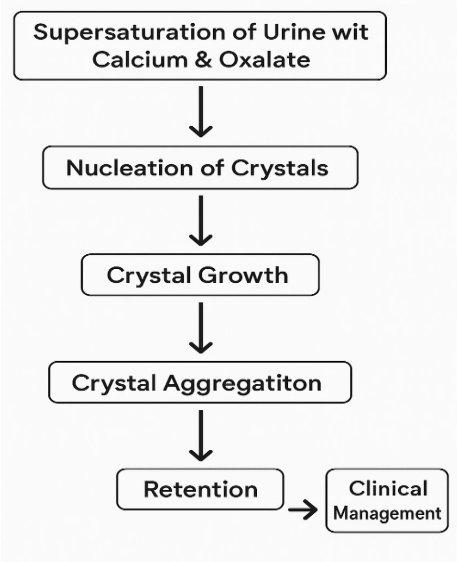

Figure 1: Pathogenesis of CaOx crystals formation[2]

DECT which is intended for accurate characterization of CaOx stones in prediction of stone fragility during lithotripsy.[6]

- *Advances in ultrasound*

Though CT remains the Schrodinger's cat for diagnosis, ultrasound (US) is radiation-free and cheap; it is particularly useful in pregnant women and children for follow-up studies. Advances in US technology include high-resolution transducers, color Doppler, and contrast-enhanced ultrasound. These make the US increasingly valuable for detecting smaller stones and subtle hydronephrosis. One newer US technique under study is elastography, which could potentially be used to assess stone hardness and, thus, predict the success of ESWL.[7]

- *Advanced urine microscopy and crystallography*

Not strictly new, advances in automated urine microscopy and sophisticated crystallization studies make deep in-roads to understanding crystal morphology and crystal composition. An early example is the combination of scanning electron microscopy (SEM) with energy-dispersive X-ray spectroscopy (EDS), which provides detailed analysis of urinary crystals to help understand personal predisposition for the formation of CaOx stones and thus pave the way for individual risk-oriented preventive strategies.[8]

Stone composition analysis (Table 1)

- *Fourier transform infrared (FTIR) spectroscopy*

FTIR is one of the most used and reliable techniques in stone analysis. Recently, these devices are being miniaturized for faster, less expensive analysis for use even in flexible ureteroscopy.[9]

- *Raman spectroscopy*

It is the ability for rapid, non-invasive analysis of stones that allows the possibility of the technique being performed in-vivo with specialized probes during ureteroscopy. This technique represents the potential for real-time stone characterization and application to intraoperative decision-making.[10]

Table 1: Techniques for stone composition analysis and health consideration [9-11]

Technique	*Application*	*Limitations/Impact*
FTIR spectroscopy	Accurate identification	Equipment cost, requires sample preparation
Raman spectroscopy	*In-vivo* analysis potential	Technical complexity, high cost
LA-ICP-MS	Detailed elemental composition	Highly specialized, not routinely available

- *Mass spectrometry (MS)*

Methods such as laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) allow very sensitive analyzing and detailed characterization of stone composition in chemical terms for the reality of trace elements and minute divergences that may elucidate the stone formation mechanism and individual metabolic signature.[11]

Advancements in Treatment Strategies

The whole concept of treating CaOx stones has been altered by the use of minimal-interventional techniques aimed at maximizing stone-free rates and minimal patient morbidity (Table 2).

Minimally invasive surgical interventions

- *Miniaturized percutaneous nephrolithotomy (PCNL)*

Treatment of large renal stones by PCNL remains the best; advances made include miniaturization of instruments such as mini-PCNL and ultra-mini-PCNL utilizing smaller nephrostomy tracts (≤18 Fr and ≤14 Fr, respectively).[12] Less invasiveness, lesions with lesser bleeding complications, post-op pain, and lesser hospital stay are offset by similar stone-free rates compared with standard PCNL. Some new access techniques are also being tried with robotic assistance and image-guided navigation.[13]

Flexible ureteroscopy (FURS) and laser lithotripsy

FURS has become an important procedure for treating stones anywhere along the ureter and renal collecting system, particularly for lower and mid-pole renal stones and stones in the ureter.
The most recent advancements are:

Better Ureteroscope Engineering

Digital ureteroscopes encompass higher image quality with wide deflection and smaller diameters, aiding in renal anatomical visualization and maneuverability.[14]

Holmium laser advance

Pulse modulation and dusting techniques with Holmium lasers have enhanced stone fragmentation efficiency and led to a significant decrease in retreatment rates. Dusting refers to the procedure whereby a stone is fragmented into very small particles that can be washed out passively without requiring further active retrieval.[15]

Thulium fiber laser (TFL)

TFL represents another promising laser source that is shorter in wavelength and, thus, absorbed more readily in water, possibly leading to better stone ablation with less fiber degradation than Holmium lasers.[16]

Single-use ureteroscopes

Single-use ureteroscopes do not pose a risk of cross-contamination and infection through reuse. Recent improvements enhance the image quality and robustness of single-use scopes, making them more viable, especially in high-risk patients.[17]

Extracorporeal shock wave lithotripsy (ESWL) being optimized

ESWL is a less invasive method; however, the success rates can be variable in the case of CaOx stones, depending on stone size, location, and composition. Efforts have been put forth in the improvements pertaining.

Image-guided targeting

Real-time imaging during ESWL improves targeting of the stones and shockwave delivery, thereby improving fragmentation efficiency.[18]

Optimization of shockwave delivery

There is an ongoing investigation into the possible improvement of fragmentation as well as minimization of renal injury through the modulation of shockwave parameters such as pulse repetition rate and energy level.[19,20]

Patient Selection

Predictive models will help select patients who would benefit from ESWL based on stone characteristics and patient factors to help reduce the burden of treatments that do not bear results.

Robotic and Laparoscopic Stone Surgery

Complex stone cases can still be treated with robotic or laparoscopic techniques despite the increased efficiency that flexible ureteroscopy (FURS) and percutaneous nephrolithotomy (PCNL) have given to stone removal. Such patients benefit most with the operability of robotic or laparoscopic mechanics in their complex anatomy or comorbid renal conditions. In a complex reconstruction and removal of stones in poorly accessible areas, robotic surgery has superior dexterity and visualization.

Medical Expulsive Therapy (MET)

MET was started for spontaneous stone passage, mainly with small ureteric stones (<10 mm). The principal agents that have played a significant role in improving the yield of stone expulsion and reducing colic episodes are alpha-blockers, particularly tamsulosin. Some advancements in this area are:

Combination therapy

Multiple studies have begun investigating the potential for synergistic effects from combinations of alpha-blockers with other agents, such as phosphodiesterase-5 inhibitors (like tadalafil) or calcium channel blockers (like nifedipine) to further improve ureteral relaxation and stone expulsion.[21]

Targeted delivery systems

Research is going on to develop new drug delivery systems that can be more selectively targeted on ureteral smooth muscle, which may enhance MET efficacy while minimizing systemic side effects.

Chemolysis

Chemolysis, the chemical dissolution of stones, is of much less applicability to CaOx stones compared with uric acid stones. However, research continues into agents that may be able to induce the dissolution of CaOxstones or cessation of further growth under specific clinical conditions, although, at present, it has a limited role in the routine management of CaOx stones.

Progress in Prevention and Reduction of Recurrence

Prevention of recurrence is indeed important in the long-term management of patients with CaOx stones. Advances have been made toward tailoring individualized strategies based on metabolic evaluation, dietary changes, pharmacologic interventions, and new areas like gut microbiome modulation.

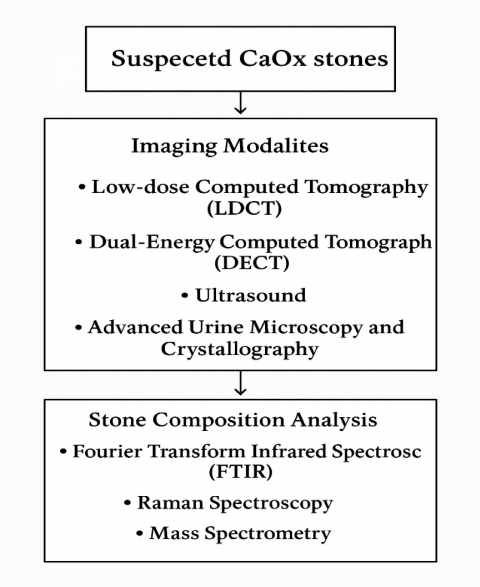

Figure 2: Flowchart of imaging modalities and their detection techniques[4-9]

Table 2: Advanced imaging modalities and their limitations[4-8]

Imaging technique	*Advantages*	*Limitations/health impact*
LDCT	High sensitivity/specificity, reduced radiation	Still involves ionizing radiation exposure
DECT	Material differentiation, stone composition	Expensive, limited availability
Ultrasound	Safe for children/pregnant women, no radiation	Less sensitive than CT, operator-dependent
Contrast-enhanced US	Improved visualization	Requires expertise, may have contrast reactions
Elastography	Assesses stone hardness	Experimental, not widely available

Customized metabolic assessment and dietary modifications

Getting through a complete metabolic evaluation, including 24-hour urine studies, serum biochemistry, and stone analysis, will place metabolic derangements at the core of CaOx stone development. It is suggested that personalized dietary counseling is related to these findings.

New Advancements

Dietary approach

Rather than a generic approach to dietary recommendations, an approach to precise nutrition focuses on metabolic profile, inherited susceptibility, and food habits to give dedicated interventions in reducing urinary calcium and oxalate excretion, increasing urinary citrate, and maintaining adequate hydration.[22]

Digital health solutions for diet compliance

The development of mobile applications and wearable gadgets will enable individuals to have a way of tracking their intake, offering personalized feedback to enhance conformity to diet prescriptions and increase lifestyle change outcomes.[23]

Therapeutic Pharmacological Interventions

Most patients in whom stone formation recurs despite dietary modification or continue to have persistent metabolic abnormalities are probably going to need pharmacological interventions.

Thiazide diuretics

Thiazides remain a cornerstone of medical therapy for hypercalciuria-related CaOx stones. Current research is concentrating on optimizing thiazide dosage and investigating combined therapies with other agents targeted for the improvement of side effects and increased effectivity.[24]

Potassium citrate

Potassium citrate is an effective uriosuppressant that increases urinary pH and citrate excretion. These promote reduced urinary supersaturation with CaOx and inhibit the process of crystal formation. Effervescent preparations and sustained-release formulations would increase compliance and reduce gastrointestinal side effects in patients.

Allopurinol

Usually reserved for uric acid stones, allopurinol may help a select group of CaOx stone formers with hyperuricosuria, especially when associated with hyperoxaluria.[25]

New Pharmacological Targets

Researchers delve into unique pharmacological targets that prevent the emergence of CaOx stones by inhibiting intestinal oxalate absorption (e.g., with oxalate-degrading enzymes, calcium binders) or modulating calcium handling into the kidney (e.g., calcium receptor agonists). Target crystal nucleation and growth (e.g., osteopontinmimetics).

New interest in gut microbiome modulation

Recent findings highlight the important role of the gut microbiome in controlling oxalate metabolism. Examined in this study are supplementation of oxalobacterformigenes bacteria degrading oxalate and other probiotic approaches as preventive approaches to hyperoxaluria and CaOx stone formation.[26]

CONCLUSION

Recently, because of advancements in technology and understanding of the pathogenesis of stones, there have been considerable changes in the treatment of CaOx stones. From improved diagnostic imaging and stone analysis to minimally invasive surgical techniques and personalized preventative strategies, it has made significant progress in improving patient outcomes and reducing stone recurrence. However, there are some limitations to these techniques, like procedural cost, accessibility, and potential health impacts, so it is quietly challenging to maintain a balance between cost-effectiveness and reduction of health impacts.

Future Directions

Improving diagnostic techniques

Development of more accurate, non-invasive, and cost-effective imaging modalities and stone analysis techniques, including AI-driven image interpretation and point-of-care diagnostics.

Optimizing treatment strategies

Further refinement in minimally invasive surgical techniques, development of new laser technologies, and targeted drug delivery systems for MET and chemolysis.

Personalized prevention

Bring together multi-omics data (genomics, metabolomics, microbiomics) to develop highly personalized preventive strategies, including precision nutrition and microbiome-based therapies.

Translational research

Speed up the translation of promising nanotechnology-based approaches from bench to bedside for both diagnostic and therapeutic applications. Continued research and innovation in these areas hold immense promise for further improving the management of CaOx stones, reducing the burden of this prevalent condition, and enhancing the quality of life for affected individuals.

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

REFERENCES

1. Turney BW. The global burden of urolithiasis. Nat Rev Urol. 2012;9(8):405-6.
2. Coe FL, Evan AP, Worcester EM. Kidney stone disease. J Clin Invest. 2005;115(10):2598-608.
3. Khan SR, Pearle MS, Robertson WG, Gambaro G, Canales BK, Trinchieri A, et al. Kidney stones. Nat Rev Dis Primers. 2016;2:16008.
4. Fink HA, Akbarnia A, Pritchett NR, Koerner JS, Funk MJ, MacDonald R, et al. Medical management to prevent recurrent nephrolithiasis in adults: a systematic review for an American College of Physicians Clinical Guideline. Ann Intern Med. 2013;158(7):535-43.
5. Smith-Bindman R, Aubin C, Bailitz J, Bengiamin R, Brown B, Guru K, et al. Ultrasonography versus computed tomography for suspected nephrolithiasis. N Engl J Med. 2014;371(12):1100-8.

6. Patel U, Gupta P, Beddy P, Sabharwal T, Dikaios N, Nair R, et al. Diagnostic accuracy of low-dose computed tomography for adult renal colic: systematic review and meta-analysis. ClinRadiol. 2016;71(4):383-92.
7. Primak AN, Ramirez G, Kumar S, Kambadakone AR. Dual-energy CT: principles, clinical applications, and pitfalls. Radiographics. 2009;29(7):1903-23.
8. Manglaviti G, Arellano RS, Raman SS, Sahani DV. Dual-energy CT in urolithiasis: current applications and future directions. Abdom Imaging. 2012;37(6):875-83.
9. Pak CY. Medical management of nephrolithiasis. J Urol. 1998;160(3 Pt 1):676-82; discussion 682-3.
10. Hoppe B. An update on primary hyperoxaluria. Nat Rev Nephrol. 2016;12(8):467-77.
11. Hesse A, Tiselius HG, Siener R. Urinary stones: diagnosis, treatment, and prevention of recurrence. EndocrMetab Immune Disord Drug Targets. 2005;5(4):349-61.
12. Curhan GC, Willett WC, Knight EL, Stampfer MJ. Dietary factors and the risk of incident kidney stones in younger women: Nurses' Health Study II. Arch Intern Med. 2004;164(8):885-91.
13. Siener R, Hesse A. Importance of dietary oxalates for hyperoxaluria and calcium oxalate stone risk. World J Urol. 2005;23(6):307-13.
14. Ticinesi A, Nouvenne A, Meschi T, Guerra A, Allegri F, CosimoPelà G, et al. Gut microbiome and kidney stones: a systematic review. Urol Int. 2018;100(3):267-279.
15. Preminger GM, Tiselius HG, Assimos DG, Alken P, Buck C, Gallucci M, et al. 2007 guideline for the management of ureteral calculi. J Urol. 2007;178(6):2418-34.
16. Furyk JS, Chu K, Dalton A, Banks R, Greenslade J, Ballard DW. Distal ureteric stones and tamsulosin: a systematic review and meta-analysis of randomised trials. Emerg Med Australas. 2016;28(1):38-48.
17. Campschroer T, Zhu Y, Vernooij RW, Lock MT. Alpha-blockers as medical expulsive therapy for ureteral stones. Cochrane Database Syst Rev. 2018;4:CD008509.
18. Lieske JC, Goldfarb DS, De Simone C, Regnier C. Use of Oxalobacterformigenes to reduce urinary oxalate in subjects with enteric hyperoxaluria. Kidney Int. 2005;68(3):1244-9.
19. Ettinger B, Pak CY, Citron JT, Skurla C, Adrogue HE, Schwille PO. Potassium-magnesium citrate: a new drug for potassium citrate-resistant hypocitraturic calcium nephrolithiasis. J ClinEndocrinolMetab. 1997;82(1):69-72.
20. Eisner BH, Porten SP, Bearelly PA, Stoller ML. Selective estrogen receptor modulator therapy and the risk of urinary stone formation. Urology. 2005;66(5):989-92.
21. Turk C, Petřík A, Sarica K, Seitz C, Skolarikos A, Straub M, et al. EAU Guidelines on Interventional Treatment for Urolithiasis. Eur Urol. 2016;69(3):475-82.
22. Traxer O, Thomas A. Prospective evaluation and classification of intrarenal anatomy using flexible ureterorenoscopy. J Urol. 2002;167(4):1389-93.
23. Bader MJ, Pongratz T, Khullar M, Tilki D, Janetschek G, Rassweiler JJ, et al. Holmium:YAG laser lithotripsy: impact of pulse frequency and energy settings on stone fragmentation, ablation, and dusting. J Endourol. 2010;24(11):1793-8.
24. Aboumarzouk OM, Dreger NM, Ismail S, El-Karamani E, MacLennan G, Wilcox DT, et al. Flexible ureteroscopy and laser lithotripsy for nephrolithiasis: a systematic review and meta-analysis.J Endourol 2012;26(10):1257-63.
25. Lin CH, Lin YC, Chiang HC, et al. Totally tubeless single access tract mini-percutaneous nephrolithotripsy in treatment of large burden >2-cm and/or complex renal stones: a case series of 62 patients. *BMC Urol.* 2022;22(61):1-8. doi:10.1186/s12894-022-01012-9.
26. Agrawal MS, Agarwal K, Jindal T, Sharma M, et al. Ultra-mini-percutaneous nephrolithotomy: A minimally-invasive option for percutaneous stone removal. *BMC Urol.* 2022;22(61):1-8.

HOW TO CITE THIS ARTICLE: Kamdi D, Dudhe AR, Dudhe R. Recent Advancements in the Management of Calcium Oxalate Stones: A Comprehensive Review. *J Adv Sci Res*. 2025;16(05): 1-5 **DOI:** 10.55218/JASR.2025160501