JAMA Insights Management of Kidney Stones in 2020

Andrew D. Rule, MD; John C. Lieske, MD; Vernon M. Pais Jr, MD

Kidney stones are common, painful, and frequently recur. Although precise estimates of the incidence of symptomatic kidney stones for the entire US are unavailable, a Minnesota populationbased study reported that between 1984 and 2012, the incidence of symptomatic kidney stones that required treatment increased from 51 to 217 per 100 000 person-years in women and from 145 to 299 per 100 000 person-years in men.¹

Patients with symptomatic stones typically present with unilateral flank pain that may radiate to the ipsilateral abdominal or inguinal areas (ie, renal colic; Figure). Previously, renal colic was commonly managed with opioid analgesics, and opioids are still necessary for severe pain (eg, intravenous morphine). However, given current concerns about opioid prescriptions, there is renewed interest in nonopioid analgesics, including nonsteroidal anti-inflammatory drugs (eg, intravenous ketorolac) in patients without contraindications, such as acute or chronic kidney disease. Intravenous fluids are needed if volume depletion is present, but fluids do not facilitate stone passage. Unless a stone is passed, imaging is needed to confirm the diagnosis. Among imaging methods, computed tomography (CT) most accurately delineates stone size and location and is preferred for initial diagnoses. Ultrasonography facilitates radiation-free assessment and is useful for evaluating frequent recurrences, but small stones may be missed. Plain radiographic film is insufficient for initial evaluation of a suspected kidney stone.

Determining stone size is important because a trial of spontaneous passage is recommended for uncomplicated ureteral stones less than or equal to 10 mm in maximal diameter.² Medical expulsive therapy with a-adrenergic blockers (eg, daily tamsulosin) can result in a 44% higher passage rate of 5 to 10 mm ureteral stones in patients at low risk for hypotension.^{2,3} Surgical procedures should be considered in patients who do not pass a stone after 4 to 6 weeks of outpatient observation; prefer earlier intervention; or have complicating factors, such as fever, uncontrolled pain or nausea, or a solitary functioning kidney. Therapeutic options include shock wave lithotripsy, ureteroscopic stone removal, or percutaneous nephrolithotomy.

Asymptomatic kidney stones typically do not require surgical intervention, but surveillance imaging every 1 or 2 years with kidney ultrasonography or CT can identify patients at risk for symptomatic passage. Specifically, stones larger than 6 mm are less likely to spontaneously pass if they ever migrate into the ureter.⁴ Decisions to perform elective surgical intervention should be based on shared decision-making that considers stone size, composition, and location; patient preferences; lack of access to urgent urological care (eg, planned travel to remote regions); and vocation. For example, the Federal Aviation Administration may disqualify an airplane pilot diagnosed with asymptomatic kidney stones unless the stones have been surgically removed or are stable over time in both size and number.

After the initial episode of a symptomatic kidney stone, recurrences are common. In the first 5 years, 19% of patients will have Figure. Proposed Approach for Diagnosis and Management of Kidney Stones

Patient presentation with renal colic

Imaging to confirm diagnosis of kidney stone Noncontrast computed tomography (CT) scan preferred Ultrasonography an option for patients with frequent kidney stones

Initial management of a kidney stone obstructing the ureter

initiat management of a klancy stone obstructing the arcter	
Kidney stone ≤10 mm maximal diameter with adequate pain control	Kidney stone >10 mm maximal diameter or Kidney stone ≤10 mm maximal diameter • Does not pass after 4-6 wk • Patient preference for early intervention • Complicating factors (eg, fever, uncontrolled nausea or pain, 1 functioning kidney)
 4- to 6-wk trial of spontaneous passage ▶ Straining of urine to capture passing stones 	
	Surgical therapy • Shock wave lithotripsy • Ureteroscopic stone removal • Percutaneous nephrolithotomy
Subsequent management Basic metabolic panel, including serum calcium, with further metabolic evaluations as indicated Assessment for risk of symptomatic recurrence; risk factors for recurrence include younger age, male sex, family history of kidney stones, obesity, and high past or present kidney stone burden 	
Patients at low risk of recurrence	e Patients at high risk of recurrence
 Encourage high fluid intake Follow a low-sodium, moderate protein, normal-calcium diet 	 Metabolic workup including 24 h urine collection for targeted dietary recommendations Possible pharmacologic interventions (eg, potassium citrate or thiazide diuretic) Follow-up CT scan or ultrasonography in 1-2 y

another symptomatic episode requiring clinical care, while an additional 11% will self-manage a symptomatic episode.⁵ At the time of the initial symptomatic kidney stone episode, 50% of patients will have at least 1 concurrent asymptomatic kidney stone that does not pass. Half of these patients will pass a retained stone within 5 years and, of these patients, half will have a symptomatic episode with a retained stone's passage.⁵

Approximately 94% of stones in patients presenting with an initial symptomatic episode contain some combination of calcium oxalate monohydrate, calcium oxalate dihydrate, and/or hydroxyapatite (referred to as a *common calcium stone*).⁶ An additional 5% of first-time stones contain uric acid, while any other composition is rare (<1%).⁶ Because some stone compositions, including uric acid, struvite, or cystine stones, may prompt specific therapies, patients attempting spontaneous passage should strain their urine for up to 4 to 6 weeks to capture the stone. As a general principal, the less common the stone composition, the higher the recurrence rate.⁶ Hydroxyapatite stones occur at a higher urine pH (>6.3) and are more common in younger women, whereas uric acid stones occur at a lower urine pH (<5.5) and are more common in older adults.⁶

jama.com

inflammatory bowel disease or those who underwent bowel resections or bariatric surgery, are at increased risk for calcium oxalate and uric stones due to enteric hyperoxaluria, fluid and base loss, or both due to diarrhea. Patients with calcium stones require further diagnostic evaluations if they have hypercalcemia, including serum parathyroid hormone testing to detect hyperparathyroidism.

Patients with a larger number of prior episodes of symptomatic kidney stones have a higher incidence of subsequent symptomatic kidney stones.⁷ Even a previously suspected episode (no stone confirmed) or a past incidental asymptomatic kidney stone is associated with increased risk for symptomatic recurrence. Other risk factors for recurrence include younger age, male sex, family history of kidney stones, obesity, and pregnancy. Larger stones and a greater number of asymptomatic stones detected on imaging are associated with higher rates of future symptomatic recurrence.^{7,8} Rates of recurrence are highest during the first year after an episode, and then decline over time. Attempts to develop predictive models for recurrence based on these risk factors have been disappointing,^{7,8} in part because of asymptomatic or selfmanaged stone passage that goes unrecognized.⁵ Individuals with recurrent symptomatic stones are at a 2-fold higher risk for kidney failure, and it is unknown if preventive treatments for kidney stones reduce the risk of this complication.9

Dietary and drug treatments for stone prevention should consider both risk for recurrence and patient preferences. Diet changes can be effective, and medications can be effective if dietary interventions alone fail. After the stone is passed or removed, a 24-hour urine

evaluation can help guide preventive therapy. A lower urine volume (<2L) can be managed with increased fluid intake, such that the urine output exceeds 2 L per 24 hours. Higher sodium intake increases urine sodium (>100 mmol/24 h), which leads to higher urine calcium (>250 mg/24 h). Therefore, increased urine calcium can be managed with a low-sodium diet (1500-2000 mg/24 h). Higher urine calcium can also be lowered with a thiazide diuretic (eg, chlorthalidone 25 mg daily). Lower urine citrate (<300 mg/24 h; a crystallization inhibitor) or a lower urine pH (<6.5 for uric acid stones) can both be managed with potassium citrate (eg, 20 to 30 mEq twice daily). Although randomized trials have shown that thiazide diuretics and potassium citrate prevent recurrent stones, they have not determined whether assessing stone composition or a 24-hour urine evaluation to tailor the treatment choice is beneficial. Because of this, the American College of Physicians does not recommend routine testing of stone composition or 24-hour urine chemistries.¹⁰ Their guidelines instead support empirical treatment with potassium citrate or thiazide diuretics to prevent kidney stones that recur after attempting increased fluid intake. In contrast, guidelines by urological societies recommend stone composition and 24-hour urine testing with more targeted treatment strategies.^{2,4} This is based on the rationale that treatment should target the presumed pathogenic mechanisms of the stone formation that are specific to each patient.

Kidney stones range from an asymptomatic condition to one with substantial morbidity, including chronic pain or even kidney failure.⁹ Accurate and timely diagnosis, appropriate treatment, and preventive therapies can optimize care (Figure).

ARTICLE INFORMATION

Author Affiliations: Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota (Rule, Lieske); Division of Epidemiology, Mayo Clinic, Rochester, Minnesota (Rule); Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota (Lieske); Division of Urology, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire (Pais).

Corresponding Author: Andrew D. Rule, MD, MSc, Division of Nephrology and Hypertension, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (rule.andrew@mayo.edu).

Published Online: March 19, 2020. doi:10.1001/jama.2020.0662

Conflict of Interest Disclosures: Dr Lieske reported receiving grants from the National Institutes of Health and the Mayo Foundation during the conduct of the study and grants and personal fees from Alnylam, Dicerna, and Allena; grants from Retrophin and OxThera; and personal fees from Orphan outside the submitted work. Dr Pais reported receiving grants from the American Urological Association and having financial investments and equity in Sonomotion, a lithotripsy company that is developing machines to move kidney stones using ultrasonography, outside the submitted work. No other disclosures were reported.

REFERENCES

 Kittanamongkolchai W, Vaughan LE, Enders FT, et al. The changing incidence and presentation of urinary stones over 3 decades. *Mayo Clin Proc*. 2018;93(3):291-299. doi:10.1016/j.mayocp.2017.11. 018

2. Assimos D, Krambeck A, Miller NL, et al. Surgical management of stones: American Urological Association/Endourological Society guideline, part II. *J Urol*. 2016;196(4):1161-1169. doi:10.1016/j.juro. 2016.05.091

3. Cui Y, Chen J, Zeng F, et al. Tamsulosin as a medical expulsive therapy for ureteral stones: a systematic review and meta-analysis of randomized controlled trials. *J Urol*. 2019;201(5): 950-955. doi:10.1097/JU.00000000000029

 Türk C, Petřík A, Sarica K, et al. EAU guidelines on diagnosis and conservative management of urolithiasis. *Eur Urol.* 2016;69(3):468-474. doi:10. 1016/j.eururo.2015.07.040

5. D'Costa MR, Haley WE, Mara KC, et al. Symptomatic and radiographic manifestations of kidney stone recurrence and their prediction by risk factors: a prospective cohort study. *J Am Soc Nephrol.* 2019;30(7):1251-1260. doi:10.1681/ASN.2018121241 **6**. Singh P, Enders FT, Vaughan LE, et al. Stone composition among first-time symptomatic kidney stone formers in the community. *Mayo Clin Proc.* 2015;90(10):1356-1365. doi:10.1016/j.mayocp.2015. 07.016

7. Vaughan LE, Enders FT, Lieske JC, et al. Predictors of symptomatic kidney stone recurrence after the first and subsequent episodes. *Mayo Clin Proc.* 2019;94(2):202-210. doi:10.1016/j.mayocp. 2018.09.016

8. Rule AD, Lieske JC, Li X, Melton LJ III, Krambeck AE, Bergstralh EJ. The ROKS nomogram for predicting a second symptomatic stone episode. *J Am Soc Nephrol*. 2014;25(12):2878-2886. doi:10. 1681/ASN.2013091011

9. Dhondup T, Kittanamongkolchai W, Vaughan LE, et al. Risk of ESRD and mortality in kidney and bladder stone formers. *Am J Kidney Dis*. 2018;72(6): 790-797. doi:10.1053/j.ajkd.2018.06.012

10. Qaseem A, Dallas P, Forciea MA, Starkey M, Denberg TD; Clinical Guidelines Committee of the American College of Physicians. Dietary and pharmacologic management to prevent recurrent nephrolithiasis in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2014;161(9):659-667. doi:10.7326/M13-2908