Diagnosis and Management of Kidney Stones Require a Patient-Centered Approach

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The prevalence of kidney stones has been increasing over time. A patient-centered approach to diagnosis and management of kidney stones includes correct interpretation of 24-hour urine samples, selection of dietary and pharmacologic interventions based on their risk/benefit profile, and recognition of rare genetic forms of kidney stones.

Gary C. Curhan, MD, ScD, Brigham and Women's Hospital, Boston, Massachusetts, USA, discussed the epidemiology of kidney stones. He based much of his talk on data derived from 3 large cohort studies, 2 female Nurses' Health Studies (NHS I and II) [Harvard School of Public Health], and the male cohort Health Professionals Follow-Up Study (HPFS) [Harvard School of Public Health].

The lifetime risk of nephrolithiasis in the United States currently approaches 10% to 12% for men and 7% for women. In addition to age and sex, risk factors include diet and systemic conditions such as Crohn disease, hyperparathyroidism, obesity, hypertension, diabetes, chronic kidney disease (CKD), and cardiovascular disease (CVD).

Dietary determinants that increase stone formation include oxalate, sugars, sodium, vitamin C, and calcium supplements. Higher dietary intake of calcium, potassium, magnesium, and beverages such as coffee and tea are associated with reduced risk. The type of dietary calcium (dairy vs nondairy) does not seem to influence stone formation, but a low-calcium diet is associated with a higher risk of stone formation. On the other hand, why supplemental calcium is associated with higher risk is not known. The Dietary Approaches to Stop Hypertension (DASH) diet reduces hypertension [Harrington JM et al. *Am J Hypertens*. 2013], and the DASH score is inversely related to stone risk ($P < .001$) [Taylor EN et al. *J Am Soc Nephrol*. 2009].

Stone formation increases as weight or body mass index increases. However, weight loss and physical activity have not yet been shown to have an effect on the relative risk of stone formation. Diabetes is associated with increased risk of stone formation independent of obesity [Taylor EN et al. *Kidney Int*. 2005].

Nephrolithiasis may increase the risk for CKD and end-stage renal disease, possibly via shared risk factors. The association with CVD appears to occur in women—but not men—in the US cohorts and was higher in women than men in a Canadian study [Alexander RT et al. *Clin J Am Soc Nephrol*. 2013].

Dr Curhan said that the traditional definitions of hypercalciuria and hyperoxaluria are "made up" and arbitrary, as urinary calcium and oxalate excretion linearly increase the risk of stones. With no threshold, even so-called normal concentrations of urine calcium and oxalate are still associated with some risk. In Curhan's studies, uric acid excretion was not associated with increased stone risk; in fact, in some cohorts it was protective. The role of urinary uric acid in promoting calcium stone formation is therefore unclear [Toka HR et al. *PLoS One* 2013].

John R. Asplin, MD, Litholink Corporation, Chicago, Illinois, USA, discussed interpretation of 24-hour urine chemistries to inform clinical practice. The American Urological Association (AUA) Guidelines were recently updated [Pearle MS et al. *J Urol*. 2014] and call for metabolic testing for high-risk or interested first-time stone formers and recurrent stone formers, consisting of 1, or preferably 2, 24-hour urine collections obtained on a random diet and analyzed at minimum for total volume, pH, calcium, oxalate, uric acid, citrate, sodium, potassium, and creatinine. This guideline is based on expert opinion rather than data. Dr Asplin adds chloride, magnesium, phosphorus, urea nitrogen, sulfate, ammonium, and osmolarity to these tests, enabling a supersaturation calculation.

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Table 1. Percentage of Patients With a 25% or 50% Variability Between 2 Consecutive 24-hour Urine Samples

	Patients With 25% Variability, %	Patients With 50% Variability, %
Volume	36	15
Calcium	20	12
Oxalate	20	6
Citrate	24	10
Uric acid	15	3
Any of these	67	36

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Diet, supplements/medications, and location (work vs home) can all affect 24-hour urine collection; by looking at creatinine excretion in paired samples—which should be similar—the reliability of the test is improved and other values can be interpreted. The percentage of patients with a 25% or 50% variability between 2 consecutive 24-hour urine samples (n = 2000 pairs of samples) is shown in Table 1 [Asplin JR. *Semin Nephrol.* 2008].

Follow-up samples should be tested at 6-month or yearly intervals. The cause of any changes, particularly if unexpected, should be investigated. Fluid intake can vary widely, and patients should be encouraged to maintain a high fluid intake. Patient adherence to recommendations can be tracked, and the urine chemistry can be a more reliable indicator of diet than a history.

Supersaturation may be suggestive of the type of stone in the absence of stone analysis. Reduction of supersaturation can decrease stone formation, although it is easier to achieve for uric acid stones than for calcium oxalate stones.

David S. Goldfarb, MD, New York University Langone Medical Center, New York, New York, USA, continued the discussion by presenting approaches to calcium phosphate stones and staghorn calculi. A staghorn calculus is a branched stone that occupies a large portion of the collecting system. It is associated with high urine pH, can cause loss of kidney function, and can be asymptomatic.

Older guidelines suggested surgical management using percutaneous nephrolithotomy monotherapy or in combination with shock wave lithotripsy (SWL). SWL monotherapy or open surgery are no longer appropriate. Nephrectomy should be considered when the involved kidney has negligible function, such as if it provides < 10% of total glomerular filtration rate. Ureteroscopy (URS) is being used more often, particularly by younger practitioners with more skills, which, he speculated, were acquired from video gaming.

AUA guidelines suggest that when a stone is available, clinicians should obtain a stone analysis at least once [Pearle MS et al. *J Urol*. 2014]. Stone composition of uric acid, cystine, or struvite implicates specific metabolic or genetic abnormalities, and knowledge of composition may help direct preventive measures. In type I renal tubular acidosis alkali is beneficial; potassium citrate therapy may prevent recurrent calcium stone formation, as can increased fluid intake.

John C. Lieske, MD, Mayo Clinic, Rochester, Minnesota, USA, described a number of conditions—some rare—that can be associated with nephrolithiasis, including primary hyperparathyroidism, immobilization, Paget disease, and hyperthyroidism. Genetic predispositions to nephrolithiasis have been suggested, because half of first-degree relatives with stones are also affected.

Enteric hyperoxaluria is caused by fat malabsorption, which commonly follows bariatric surgery, and leads to calcium oxalate stones. These stones can be treated with fluids, a low-fat diet, a low-oxalate diet, and a moderate amount of calcium as an oxalate binder.

Rare causes of kidney stones should be suspected in those with a first stone as a preadolescent or in those with acute kidney injury, growth retardation, and a family history of stones, nephrocalcinosis, or unexplained kidney failure. Crystals in the urine may be pathognomonic. Reddish brown, circular crystals are suggestive of adenine phosphoribyltransferase (APRT) deficiency. Other diagnostic tests should include urine protein (low molecular weight proteinuria in younger men plus hypercalciuria suggests Dent disease and should lead to testing for retinol binding protein) and medical imaging (radiolucent stones plus alkaline urine pH suggest APRT deficiency).

Recently identified links between diabetes, obesity, CKD, and hypertension with kidney stones highlight the importance of correctly identifying the cause of an individual patient's stones, initiating proper treatment, and continuing therapy to minimize recurrences.