Gaps in Care among Veterans with Urinary Stone Disease

Ryan S. Hsi[1] *and John M. Hollingsworth*[2]

CJASN 14: 1690–1691, 2019. doi: https://doi.org/10.2215/CJN.12131019

Patients who have passed a urinary stone are all able to retell the symptoms and circumstances surrounding it with vivid detail. They will invariably describe the severe, debilitating flank pain, nausea, and emesis during stone passage. Some even suffer AKI and infection. The threat of a recurrent stone can be a powerful motivator for both the patient and the provider who cares for him to identify dietary and medical interventions to reduce recurrence risk.

To guide these interventions, 24-hour urine testing has historically played a central role. The rationale behind this testing is that, by assaying the urine for promoters and inhibitors of stone formation, the provider can better select a diet modification or pharmacologic agent for the patient (1–3). Such a "selective therapy" approach stands in contrast to "empiric therapy," whereby dietary and medical interventions are applied without any urinary chemistry data (4). For instance, it is common practice to recommend increased fluid intake and a low-salt diet to a first-time stone former, even without knowing his urine volume or sodium. How much of urinary stone prevention is selective (versus empirical), and does the 24-hour urine help tailor pharmacologic management? Song *et al.* (5) attempt to address these questions in this issue of *CJASN*.

The context in which 24-hour urine testing is performed is important to consider. Not every first-time stone former will recur. In fact, recurrence rates are only about 20% at 5 years and 31% at 10 years (6). Put differently, most first-time stone formers will not have another symptomatic stone event. Although there is broad agreement that 24-hour urine testing is useful among patients at high risk for recurrence and that it can be skipped in low-risk, first-time stone formers, there is much more controversy on the marginal patients between these two extremes.

At the very least, we should not expect each patient with kidney stones to need 24-hour urine testing. In the study by Song *et al.* (5), prevalence of testing was 13% among a veteran population with stone diagnoses between 2007 and 2013. Is this rate too low? In comparison, among privately insured stone formers considered at high risk for recurrence, the prevalence of testing has been shown to be only 7% (7). Although veterans' rates were higher, it is important to note that the authors did not distinguish between high- and low-risk patients, including all who were free from a stone diagnosis or related procedure in the 2 years before their index encounter.

A key finding from the study by Song *et al.* (5) is that patients who underwent 24-hour urine testing were more likely to be prescribed thiazide diuretics, alkali therapy, and allopurinol than those who did not. Specifically, the authors observed 8%, 15%, and 5% increases in thiazide diuretic, alkali therapy, and allopurinol prescription rates, respectively, before and after 24-hour urine testing. Among those who did not have 24-hour urine testing, these rates were much lower (0.2%, 3%, and 1%, respectively), suggesting the 24-hour urine's utility in helping to select pharmacologic management for stone formers.

However, confounding by disease severity must be taken into consideration when reviewing these results. The two populations compared—those who did and did not undergo 24-hour urine testing—are likely dissimilar. The administrative data analyzed by the authors lacked much of the medical history and stone-specific information used in clinical practice to determine a patient's stone risk, and those veterans who underwent 24-hour urine testing presumably had more severe manifestations of their disease. In other words, the observed increases in the rates of pharmacologic management after 24-hour urine testing could also reflect population risk.

Regardless, the authors' data reveal that 24-hour urine testing helps guide pharmacologic management among those with more severe urine chemistry abnormalities. Note that rates of urine oxalate, citrate, and calcium testing varied (72%, 76%, and 94%, respectively). Thiazides were prescribed more commonly when hypercalciuria was more severe (+21% when urinary calcium was >400 mg daily versus +9% when urinary calcium was 201–400 mg daily). The same was observed with alkali therapy when urinary citrate was lower (+34% when urinary citrate was ≤200 mg daily versus +24% when urinary citrate was 201–400 mg daily).

Another provocative finding is the role of specialists in treating patients with urinary stone disease. Most veterans with stones see only a urologist (57% in this cohort). A nephrologist is the sole provider in 11% of patients, with an additional 11% jointly managed

[1]Department of Urology, Vanderbilt University Medical Center, Nashville, Tennessee; and [2]Dow Division of Health Services Research, Department of Urology, University of Michigan Medical School, Ann Arbor, Michigan

Correspondence: Dr. John M. Hollingsworth, Dow Division of Health Services Research, Department of Urology, University of Michigan Medical School, North Campus Research Complex, 2800 Plymouth Road, Building 16, 1st Floor, Room 112W, Ann Arbor, MI. Email: kinks@med.umich.edu

with a urologist. Patients are more likely to start medical therapy for hypercalciuria when seen by both a nephrologist and a urologist (+24%) followed by a nephrologist only (+17%), a urologist only (+11%), and neither (+4%). This finding raises the possibility of another type of selection bias known as referral bias. In particular, patients who see both nephrologists and urologists may have more severe stone disease and higher recurrence risk. Alternatively, providers without the expertise to interpret 24-hour urine testing may perceive a barrier to initiate pharmacologic management (8).

The authors raise an important question in their conclusion. Why are the vast majority of stone formers not prescribed medications that are known to reduce recurrence risk? This presumes that the presence of a urine chemistry abnormality would motivate providers to prescribe a medication and that patients would be willing to adhere to it.

Not captured in the authors' data are the factors weighing patient and provider decision making when choosing among different dietary and medical interventions, especially when considering that these interventions are often lifelong. There is a growing interest in understanding patient perspectives and health-related quality of life as they relate to decision making around urinary stone disease prevention (9,10). These factors certainly need to be factored into future evaluations of the effectiveness of different prevention strategies in the real world.

We must also keep in mind that the most important outcome is whether these strategies result in meaningful reductions in stone recurrence. Long-term adherence rates to dietary and medical interventions among stone formers require further study. Future research should examine the role of 24-hour urine testing for initial diagnosis and treatment monitoring and how the results from 24-hour urine testing can translate into personalized care.

Disclosures

Dr. Hollingsworth and Dr. Hsi have nothing to disclose.

Funding

Dr. Hollingsworth is supported by a grant from Agency for Healthcare Research and Quality.

References

1. Pearle MS, Goldfarb DS, Assimos DG, Curhan G, Denu-Ciocca CJ, Matlaga BR, Monga M, Penniston KL, Preminger GM, Turk TM, White JR; American Urological Assocation: Medical management of kidney stones: AUA guideline. *J Urol* 192: 316–324, 2014
2. Gambaro G, Croppi E, Coe F, Lingeman J, Moe O, Worcester E, Buchholz N, Bushinsky D, Curhan GC, Ferraro PM, Fuster D, Goldfarb DS, Heilberg IP, Hess B, Lieske J, Marangella M, Milliner D, Preminger GM, Reis Santos JM, Sakhaee K, Sarica K, Siener R, Strazzullo P, Williams JC; Consensus Conference Group: Metabolic diagnosis and medical prevention of calcium nephrolithiasis and its systemic manifestations: A consensus statement. *J Nephrol* 29: 715–734, 2016
3. Türk C, Petřík A, Sarica K, Seitz C, Skolarikos A, Straub M, Knoll T: EAU guidelines on diagnosis and conservative management of urolithiasis. *Eur Urol* 69: 468–474, 2016
4. Goldfarb DS: Empiric therapy for kidney stones. *Urolithiasis* 47: 107–113, 2019
5. Song S, Thomas I-C, Ganesan C, Sohlberg E, Chertow GM, Liao JC, Conti SL, Elliott CS, Pao AC, Leppert JT: Twenty-four hour urine testing and prescriptions for urinary stone disease-related medications in veterans. *Clin J Am Soc Nephrol* 14: 1773–1780, 2019
6. Rule AD, Lieske JC, Li X, Melton LJ 3rd, Krambeck AE, Bergstralh EJ: The ROKS nomogram for predicting a second symptomatic stone episode. *J Am Soc Nephrol* 25: 2878–2886, 2014
7. Milose JC, Kaufman SR, Hollenbeck BK, Wolf JS Jr., Hollingsworth JM: Prevalence of 24-hour urine collection in high risk stone formers. *J Urol* 191: 376–380, 2014
8. Hsi RS, Sanford T, Goldfarb DS, Stoller ML: The role of the 24-hour urine collection in the prevention of kidney stone recurrence. *J Urol* 197: 1084–1089, 2017
9. Penniston KL, Sninsky BC, Nakada SY: Preliminary evidence of decreased disease-specific health-related quality of life in asymptomatic stone patients. *J Endourol* 30[Suppl 1]: S42–S45, 2016
10. Raffin EP, Penniston KL, Antonelli JA, Viprakasit DP, Averch TD, Bird VG, Chew BH, Sivalingam S, Sur RL, Nakada SY, Pais VM Jr.: The effect of thiazide and potassium citrate use on the health related quality of life of patients with urolithiasis. *J Urol* 200: 1290–1294, 2018

Published online ahead of print. Publication date available at www.cjasn.org.

See related article, "Twenty-Four Hour Urine Testing and Prescriptions for Urinary Stone Disease–Related Medications in Veterans," on pages 1773–1780.