UROLOGYPRACTICE

urologypracticejournal.com

Minimizing the Cost of Treating Asymptomatic Ureterolithiasis

Remy W. Lamberts,* Emily Lines, Simon L. Conti, John T. Leppert† and Christopher S. Elliott

From the Department of Urology, Stanford University School of Medicine (RWL, EL, SLC, JTL, CSE), Stanford, Division of Urology, Veterans Affairs Palo Alto Health Care System (SLC, JTL), Palo Alto and Division of Urology, Santa Clara Valley Medical Center (CSE), San Jose, California

Abstract

Introduction: Treatment of patients with ureterolithiasis who report resolution of their symptoms but do not recall passing the stone presents a clinical challenge. We analyzed the cost of different therapeutic strategies for these patients.

Methods: We performed a cost minimization analysis using published efficacy data and Medicare reimbursement costs. We compared 1) up-front ureteroscopy with planned lithotripsy, 2) followup imaging to determine presence or absence of stone using computerized tomography, abdominal plain film or ultrasound and 3) observation. We performed sensitivity analyses on the factors driving cost, including the probability of stone passage and ultrasound sensitivity.

Results: Observation was associated with the lowest costs for patients likely to spontaneously pass the ureteral stone (greater than 62%). Initial imaging with computerized tomography was the least costly approach for patients with an intermediate probability of stone passage (21% to 62%). When the sensitivity of ultrasound was modeled to be high (greater than 79%), it surpassed computerized tomography as the least costly approach across a wide range of spontaneous passage rates. Ureteroscopy was associated with the lowest costs when the probability of spontaneous stone passage was low (less than 21%).

Conclusions: The probability of spontaneous passage of a ureteral stone can be used to optimize treatment strategies for patients. Observation minimizes costs for patients with stones likely to pass spontaneously, whereas ureteroscopy minimizes costs for stones unlikely to pass. For ureteral stones with an intermediate probability of spontaneous passage computerized tomography to guide treatment is associated with the lowest estimated costs.

Key Words: ureteral calculi, costs and cost analysis, ureteroscopy, ureterolithiasis, diagnostic imaging

Abbreviations and Acronyms

AUA = American Urological Association

CT = computerized tomography

KUB = abdominal plain film

MET = medical expulsive therapy

US = ultrasound

Submitted for publication January 25, 2016.

No direct or indirect commercial incentive associated with publishing this article.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

* Correspondence: Department of Urology, Stanford University Medical Center, 300 Pasteur Dr., Room S-287, Stanford, California 94305 (*e-mail address:* remyl@stanford.edu).

† Financial interest and/or other relationship with Calcula Inc.

2352-0779/18/53-172/0
UROLOGY PRACTICE

https://doi.org/10.1016/j.urpr.2017.03.005
Vol. 5, 172-179, May 2018
Published by Elsevier

It is estimated that 1 in 10 persons in the United States will have urinary stone disease in their lifetime.[1] Data from NHANES (National Health and Nutrition Examination Survey) demonstrate a marked increase in the lifetime prevalence of urinary stone disease since 1976. Consequently urinary stone disease incurs a profound and increasing economic and societal burden, with an estimated financial cost of $3.79 billion in 2014.[2] Moreover, patients presenting with ureteral stones commonly experience significant pain as a symptom of ureteral obstruction.

The AUA guideline for management of ureteral stones smaller than 10 mm suggests that observation to allow for spontaneous passage, followup imaging and ureteroscopy with lithotripsy are all reasonable approaches.[3] However, when passage of stone is suspected or movement of stone may change management, clinicians should offer reimaging. Selecting the appropriate therapy is further complicated when patients report resolution of the presenting symptoms but do not recall passing the stone. MET has been widely adopted but new data question its efficacy.[4] Patients and physicians may be reluctant to repeat imaging studies that require radiation exposure (eg CT) and stones in the ureter may be difficult to visualize with US. Consequently 6% to 10% of ureteroscopic procedures performed for upper tract stones result in a "negative ureteroscopy," where no stone is found.[5,6] To assist in decision-making, we sought to model the costs of each therapeutic approach for patients with asymptomatic ureterolithiasis. We hypothesized that costs could be minimized by selecting a treatment for each patient based on the characteristics of the therapeutic approach and the probability of spontaneous passage of the stone.

Materials and Methods

Decision Model

We performed a cost minimization analysis using published efficacy data and direct medical costs derived from reported Medicare reimbursement rates. We compared the cost of initial treatment approaches consisting of 1) up-front ureteroscopy with planned lithotripsy, 2) followup imaging to determine the presence or absence of stone using nonenhanced CT, abdominal plain film or US and 3) continued observation (fig. 1). We included branch points based on the likelihood of success or failure of each initial approach. In addition, we performed sensitivity analyses of relevant inputs to assess how varying the threshold values affected cost. Our model was developed and analyzed with Pro Healthcare 2015 (TreeAge Software, Inc., Williamstown, Massachusetts).

Base Case

We defined the base case as a normal weight, nongravid, otherwise healthy patient with a unilateral radiodense ureteral stone diagnosed on CT. The base case presents for consultation after a 4-week trial of MET with no current pain but no noted stone passage event.

Model Description

We assigned the probability of spontaneous passage of the ureteral stone in the prior 4-week observation period by stone size (2 to 4 mm and 5 to 7 mm) from data published by Coll et al (see table).[7] We used these data as they were the most contemporary data relying on CT for diagnosis and determination of stone passage. We then averaged these rates of spontaneous passage to determine rates of passage for the 2 stone size groups.

We evaluated 4 possible outcomes for each model arm consisting of 1) a true-negative test confirming stone passage, 2) a false-negative test leading to recurrent renal colic, 3) a true-positive test leading to ureteroscopy with laser lithotripsy and 4) a false-positive test leading to a "negative ureteroscopy" with no stone found during surgery. For observation we included spontaneous stone passage or recurrent renal colic as a possible outcome.

We estimated the sensitivity and specificity of each imaging modality using published data. CT was modeled to have the highest sensitivity (97%) and specificity (98%) and was considered the gold standard imaging modality.[8–10] We used studies that compared KUB and US with concurrent CT to estimate their performance. In the case of KUB we used a weighted average of sensitivity and specificity values from 2 studies.[11,12] We defined the sensitivity and specificity of US based on its ability to directly visualize the stone and not on other surrogate measures such as hydronephrosis (see table).[13]

We performed 1-way sensitivity analyses in which each variable was adjusted spanning a range of realistic values while keeping all other model variables constant. We varied the probability of stone passage to determine the threshold rates of stone passage at which a treatment approach became cost dominant. We varied US sensitivity using a wide range of estimates to determine when it would become the least costly imaging approach.[12–16] Lastly we performed 2-way analyses varying the rate of spontaneous stone passage and the sensitivity of US.

Cost

We calculated direct costs in 2015 United States dollars using Medicare fee-for-service payment data. All procedures

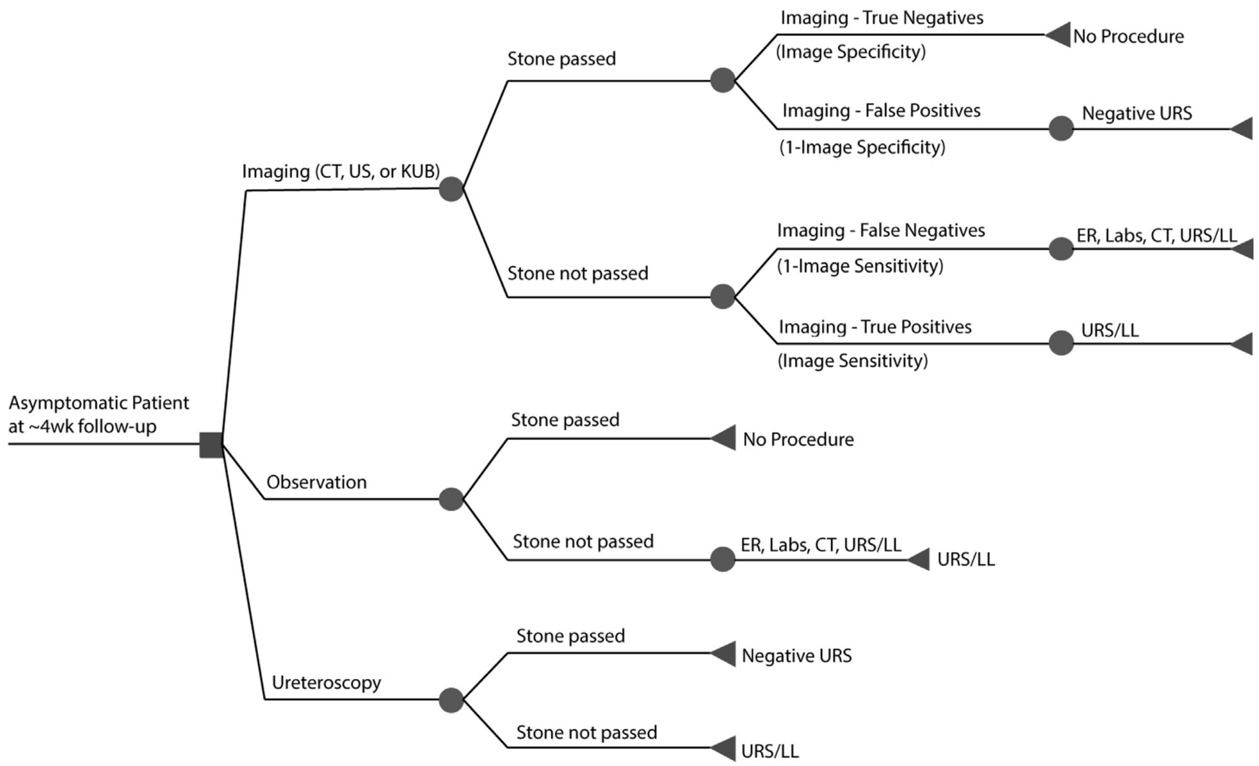

Figure 1. Decision tree model for nonobese, nongravid, otherwise healthy patient with unilateral radiopaque asymptomatic ureteral stone. Model evaluates outcomes for each imaging study in case ureteral stone has passed or remains. If stone has not passed, patient will have false-negative or true-positive, which can be estimated using imaging sensitivity. True-positive will have added cost of ureteroscopy (*URS*) with laser lithotripsy (*LL*), while false-negative will have added cost of repeat emergency department visit, CT, laboratory costs and ureteroscopy/laser lithotripsy.

Table.
Imaging performance characteristics, procedure codes and Medicare costs used to model costs for patients with asymptomatic ureterolithiasis

References		CPT Code	Base Case
Miller,[8] Fielding,[9] Smith[10] et al	Noncontrast CT:		
	Sensitivity		0.97
	Specificity		0.98
Levine[11] and Hamm[12] et al	KUB:		
	Sensitivity		0.52
	Specificity		0.72
Coll et al[7]	Renal/bladder US:		
	Sensitivity		0.57
	Specificity		0.98
Centers for Medicare and Medicaid Services[17]	Cost:		
	Noncontrast CT	74176	$455.61
	KUB	74000	$68.68
	US	76770	$269.46
	Ureteroscopy with laser lithotripsy	52353	$3,512.59
	Ureteroscopy	52351	$2,392.74
	Emergency department visit, level V	99285	$666.33
	Urology followup visit	99214	$79.12
Kanno et al[13]	Tamsulosin (1 mo supply)		$139.23
	Hydrocodone/acetaminophen (1 mo supply)		$75.04
Centers for Medicare and Medicaid Services[17]	Laboratory evaluation:		$34.26
	Urinalysis	81005	
	Urine culture	87086	
	Complete blood count	80048	
	Basic metabolic panel	85027	
Kreshover et al[5]	Probability of spontaneous stone passage:		
	2−4 mm		0.76
	5−7 mm		0.6

and imaging tests were modeled as outpatient procedures, and all fees and modifiers were determined based on CPT codes. The total cost of each intervention included the facility cost, physician fee and Medicare conversion factor for January to March 2015.[17] Geographic practice cost index modifiers were omitted from the physician fee calculation to provide a cost independent of location. The cost of observation included a 1-month supply of tamsulosin.[18] In cases of recurrent renal colic we modeled costs to include an emergency room visit, a diagnostic CT, laboratory evaluation, subsequent urology followup and a scheduled ureteroscopy (fig. 1).

Results

Base Case

Using our base case assumptions, the least costly followup approach was dependent on stone size and the corresponding probability of spontaneous passage (fig. 2). Using established probabilities of spontaneous stone passage by stone size, observation was associated with the lowest cost ($1,158) and ureteroscopy with the highest cost ($2,662) for ureteral stones 2 to 4 mm (76% rate of spontaneous passage). In this size group all imaging modalities were associated with slightly higher estimated total costs than observation (ranging from an additional $135 for US to $414 for KUB).

For 5 to 7 mm ureteral stones imaging with CT was the least costly approach ($1,905). In this group the difference in cost between the imaging modalities and observation was small ($25 more for observation compared to CT). When comparing the 3 imaging modalities (CT, KUB and US) across the stone sizes modeled, KUB was always the most expensive approach.

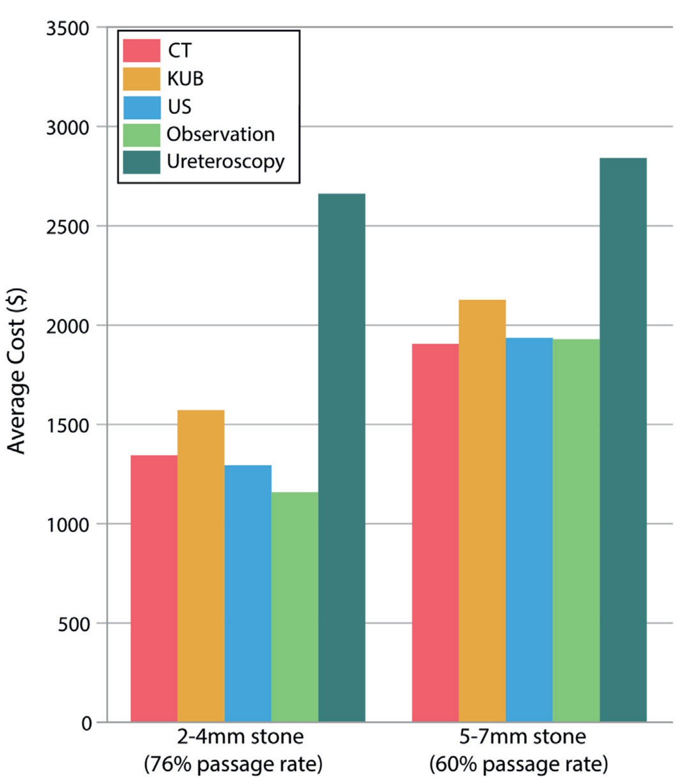

Figure 2. Associated costs of different treatment approaches for our base case. Costs are stratified by stone size for 2 to 4 mm stone (76% chance of spontaneous passage) and 5 to 7 mm stone (60% chance of spontaneous passage).

Sensitivity Analyses

The 1-way sensitivity analysis varying the probability of spontaneous passage is shown in figure 3. Ureteroscopy is the least costly management approach when the probability of spontaneous passage is less than 21%. As the spontaneous passage rate increases (from 22% up to 62%), initial use of CT with subsequent treatment as necessary becomes the least costly management method. Once the probability of spontaneous passage exceeds 62%, observation is the least costly management strategy.

Given the wide range of published sensitivity and specificity values for US, we specifically investigated the costs of US as an initial management strategy at followup for the intermediate size stone group (5 to 7 mm, estimated 60% probability of stone passage, fig. 4). When the sensitivity of US to detect the ureteral stone is greater than 63%, it becomes the least costly approach to followup for this group.

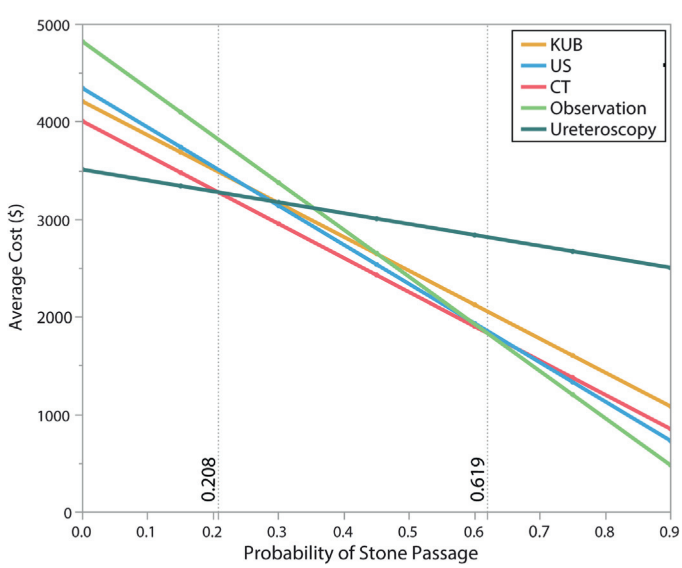

Figure 3. One-way sensitivity analysis reveals costs for different followup modalities for stones with varying probabilities of spontaneous passage (0% to 90%). Dotted lines denote threshold values (20.8% and 61.9%) at which different modality becomes cost dominant.

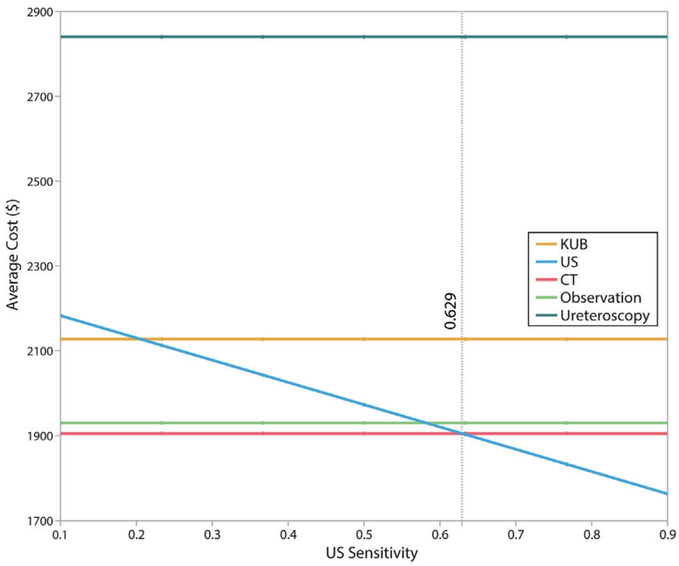

Figure 4. One-way sensitivity analysis demonstrates costs for different treatments for range of ultrasound sensitivities (0% to 90%) for patients with 5 to 7 mm stones (60% chance of spontaneous passage). Dotted line indicates sensitivity threshold value (62.9%) at which US becomes least costly treatment.

In our 2-way sensitivity analysis, where the probability of spontaneous passage and the sensitivity of US are varied (fig. 5), we find that for stones with less than a 16.3% chance of passage ureteroscopy is always associated with the lowest cost irrespective of the sensitivity of US imaging. Conversely for any stone with a greater than 73.5% chance of passage observation is always associated with the lowest cost. Between these threshold values the management approach with the lowest cost depends on US sensitivity. If US sensitivity exceeds 79.3%, it is the least costly approach for stones in these ranges. However, below a US threshold sensitivity of 62.9% CT is cost dominant for the majority of these cases.

Discussion

We sought to determine the least costly treatment strategy for patients with ureteral stones that are asymptomatic after a 4-week trial of MET. This analysis has several significant findings. First, our study suggests that the likelihood of spontaneous passage of a ureteral stone can be used to select treatment when the goal is to reduce costs. When stone passage is unlikely (less than 21%), ureteroscopy is the least costly approach as it avoids return emergency department visits and additional testing/imaging. This finding is in contrast to the current AUA guideline on imaging of calculous disease, which does not recommend ureteroscopy in an asymptomatic patient until failure of progression or hydronephrosis is observed on imaging.[19] Additionally while our model suggests that there is a point at which proceeding directly to ureteroscopy minimizes cost, the potential for a "negative ureteroscopy"—where no stone is found at surgery—must be considered. Negative ureteroscopy has been described as occurring in 6% to 10% of all ureteroscopy procedures but is thought to be less common for patients with larger stones (0.8% for 10 mm stones).[5,6] It is unclear if there is an acceptable negative ureteroscopy rate from a cost containment perspective.

For patients with an intermediate probability of stone passage (22% to 62%) our modeling suggests that reimaging with CT to guide treatment decisions is the approach most likely to minimize costs. However, it is noteworthy that the differences in cost between the various imaging modalities (CT, KUB and US) appear to be small. These results are congruent with the lack of preference in the AUA guideline for a particular imaging modality and affirm that clinicians can use their choice of imaging at followup with minimal impact on cost.[3] It is also noteworthy that KUB alone was never associated with the lowest cost in our model. This finding is likely attributable to the reported low sensitivity and specificity of KUB in detecting ureteral stones. However, there are data to suggest that the sensitivity of KUB for ureteral stones previously seen on the scout images of a CT would be close to 100%.[20] Thus, clinician judgment should be used in determining followup approach, and KUB imaging alone may be useful for some patients.

When the probability of stone passage is high (greater than 63%), our model suggests that observation is the least costly approach. However, our model does not account for the possibility of a patient experiencing silent hydronephrosis and subsequent loss of kidney function. Based on these concerns, a recent AUA panel recommended imaging (KUB or US) to confirm that a ureteral stone has passed.[19] However, the rate of silent obstruction in general is not known, and we could not model this scenario accurately. Thus, our findings on observation as an appropriate management arm may have limitations, and we are not suggesting that observation be widely implemented even if it is a less costly approach.

Improvements in the ability to image and treat ureteral stones will likely alter the costs of treating patients with asymptomatic ureterolithiasis. Our analysis suggests that US could become the least costly approach for many stones (those with probability of passage ranging from 16.3% to 73.5%) if the sensitivity were to exceed 79.3%. For intermediate sized stones (5 to 7 mm, estimated 60% probability of stone passage) the sensitivity of US would need to improve to 63% to minimize costs. New features such as the "twinkle artifact," which has been reported to increase the sensitivity of ureteral stone detection to more than 65%, may establish US as a preferred imaging modality for ureteral stones.[21,22] Similarly the costs of emerging low dose and ultralow dose

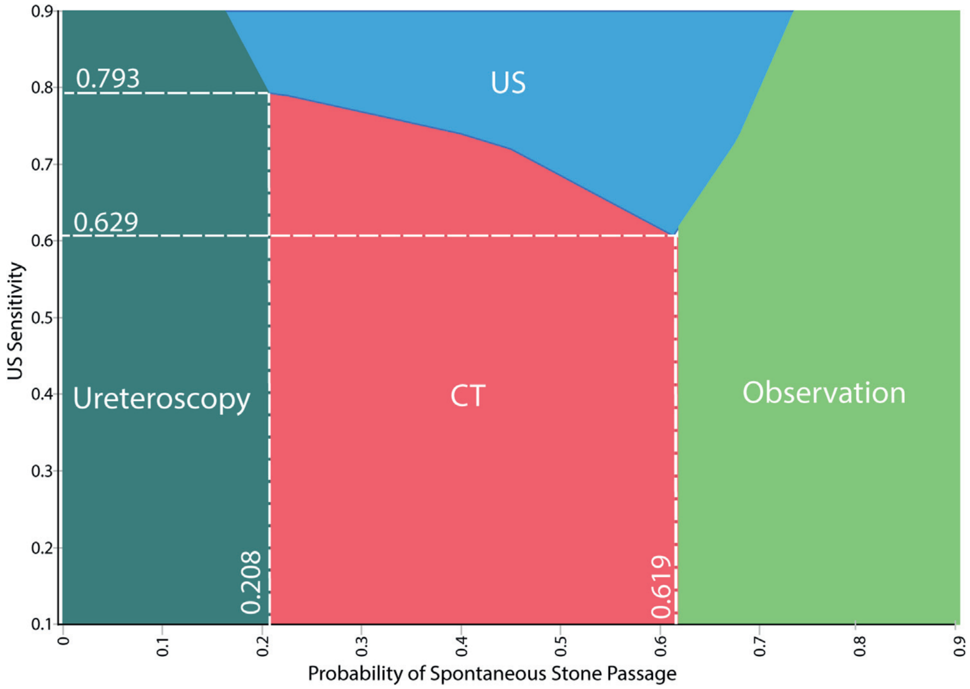

Figure 5. Two-way sensitivity analysis, which varies probability of spontaneous stone passage and sensitivity of US imaging. Modality shown at any given coordinates on graph designates cheapest modality for that specific point. In our model KUB was never cheapest approach and, therefore, is not represented. Dashed lines denote threshold values for points at which different treatment modality becomes cost dominant.

CT protocols that provide a high sensitivity imaging modality with decreased radiation exposure will also need to be considered in future analyses.[23,24] Moreover, efforts to educate patients on the importance of straining urine to detect stone passage could also lead to a reduction in costs.

This analysis has several strengths. To our knowledge, it is the first attempt to address the issue of cost minimization for an increasingly common and challenging clinical scenario. We analyzed a wide range of inputs to determine the drivers of overall costs. To further increase the generalizability of this model, we used Medicare cost data, which are transparent and widely applicable among older patients in the United States population.

The limitations of this analysis are based primarily on the data available to construct our model. Our model uses cost data from Medicare and may not reflect costs in private health systems or the true costs borne by the patients or society. Additionally the true sensitivity and specificity of imaging to detect ureteral stones remain elusive. To address this issue, we modeled US and KUB sensitivity and specificity using studies with concurrent CT as a gold standard. However, it is noteworthy that our modeling of US sensitivity and specificity values was for direct visualization of the ureteral stone in question as opposed to imaging for surrogate findings like hydronephrosis. While hydronephrosis is not known to be a reliable predictor of the degree of obstruction in patients with ureteral stones,[19] its finding could help inform the treatment of asymptomatic ureterolithiasis. Thus, the true usefulness of US may be underestimated in our study. We included a wide range of sensitivity and specificity values for US in our sensitivity analysis to account for this uncertainty.

Our model is also sensitive to the probability of spontaneous stone passage, which is dependent on the location of the stone in the ureter. This factor was not accounted for in our model.[5,7]

Lastly, as in any cost model, there are inherent limitations as to what can be included because of the lack of literature or good published data. Our model could have been more robust if we had been able to include factors such as patient specific characteristics, history of stone passage, prior or secondary procedures, complications such as urinary tract infection and ureteral strictures, quality of life data, time lost from work, stent pain costs, stone location and patient preferences. Although there was inadequate literature to include these factors, we were fortunate enough to build our model based on excellent literature on spontaneous rates of passage, costs, and imaging sensitivity and specificity.

Conclusions

The least costly approach to treating patients with asymptomatic ureterolithiasis is determined by the probability of spontaneous stone passage. Primary management with observation minimizes up-front costs for individuals with stones likely to pass spontaneously, while ureteroscopy minimizes costs for stones unlikely to pass. For ureteral stones with an intermediate probability of spontaneous passage repeat imaging with CT may minimize costs.

References

1. Scales CD, Smith AC, Hanley JM et al: Urologic Diseases in America Project: Prevalence of kidney stones in the United States. Eur Urol 2012; **62:** 160.
2. Antonelli JA, Maalouf NM, Pearle MS et al: Use of the National Health and Nutrition Examination Survey to calculate the impact of obesity and diabetes on cost and prevalence of urolithiasis in 2030. Eur Urol 2014; **66:** 724.
3. Assimos D, Krambeck A, Miller NL et al: Surgical management of stones: American Urological Association/Endourological Society guideline, part I. J Urol 2016; **196:** 1153.
4. Pickard R, Starr K, MacLennan G et al: Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. Lancet 2015; **386:** 341.
5. Kreshover JE, Dickstein RJ, Rowe C et al: Predictors for negative ureteroscopy in the management of upper urinary tract stone disease. Urology 2011; **78:** 748.
6. Lamberts RW, Conti SL, Leppert JT et al: Defining the rate of negative ureteroscopy in the general population treated for upper tract urinary stone disease. J Endourol 2017; **31:** 266.
7. Coll DM, Varanelli MJ and Smith RC: Relationship of spontaneous passage of ureteral calculi to stone size and location as revealed by unenhanced helical CT. AJR Am J Roentgenol 2002; **178:** 101.
8. Miller OF, Rineer SK, Reichard SR et al: Prospective comparison of unenhanced spiral computed tomography and intravenous urogram in the evaluation of acute flank pain. Urology 1998; **52:** 982.
9. Fielding JR, Steele G, Fox LA et al: Spiral computerized tomography in the evaluation of acute flank pain: a replacement for excretory urography. J Urol 1997; **157:** 2071.
10. Smith RC, Verga M, McCarthy S et al: Diagnosis of acute flank pain: value of unenhanced helical CT. AJR Am J Roentgenol 1996; **166:** 97.
11. Levine JA, Neitlich J, Verga M et al: Ureteral calculi in patients with flank pain: correlation of plain radiography with unenhanced helical CT. Radiology 1997; **204:** 27.
12. Hamm M, Wawroschek F, Weckermann D et al: Unenhanced helical computed tomography in the evaluation of acute flank pain. Eur Urol 2001; **39:** 460.
13. Kanno T, Kubota M, Sakamoto H et al: Determining the efficacy of ultrasonography for the detection of ureteral stone. Urology 2014; **84:** 533.
14. Haddad MC, Sharif HS, Shahed MS et al: Renal colic: diagnosis and outcome. Radiology 1992; **184:** 83.
15. Sinclair D, Wilson S, Toi A et al: The evaluation of suspected renal colic: ultrasound scan versus excretory urography. Ann Emerg Med 1989; **18:** 556.
16. Kuuliala IK, Niemi LK and Ala-Opas MY: Ultrasonography for diagnosis of obstructing ureteral calculus. Scand J Urol Nephrol 1988; **22:** 275.
17. Centers for Medicare and Medicaid Services: Medicare. Available at https://www.cms.gov/Medicare/Medicare.html. Accessed January 5, 2016.
18. Epocrates Online. 2015. Available at https://online.epocrates.com/. Accessed January 5, 2016.
19. Fulgham PF, Assimos DG, Pearle MS et al: Clinical effectiveness protocols for imaging in the management of ureteral calculous disease: AUA technology assessment. J Urol 2013; **189:** 1203.
20. Johnston R, Lin A, Du J et al: Comparison of kidney-ureter-bladder abdominal radiography and computed tomography scout films for identifying renal calculi. BJU Int 2009; **104:** 670.
21. Moesbergen TC, de Ryke RJ, Dunbar S et al: Distal ureteral calculi: US follow-up. Radiology 2011; **260:** 575.
22. Abdel-Gawad M, Kadasne R, Anjikar C et al: Value of color Doppler ultrasound, KUB and urinalysis in diagnosis of renal colic due to ureteral stones. Int Braz J Urol 2014; **40:** 513.
23. Kim BS, Hwang IK, Choi YW et al: Low-dose and standard-dose unenhanced helical computed tomography for the assessment of acute renal colic: prospective comparative study. Acta Radiol 2005; **46:** 756.
24. Hur J, Park SB, Lee JB et al: CT for evaluation of urolithiasis: image quality of ultralow-dose (Sub mSv) CT with knowledge-based iterative reconstruction and diagnostic performance of low-dose CT with statistical iterative reconstruction. Abdom Imaging 2015; **40:** 2432.

Editorial Commentary

The authors make a valiant attempt to apply a cost analysis model to decision-making regarding asymptomatic ureterolithiasis. While the methods they use are sound and literature based, I am still wary of applying hypotheticals to patient care. These models do not take into account variables such as complication costs, location of stones, patient factors such as anatomy (ability to pass large stones), pain tolerance and access to medical care/facilities, and finally patient-physician relationships. Most practitioners stratify and individualize their approach to this problem and will be aggressive with larger, more proximal stones and more conservative with smaller distal stones. Also, most urologists are aware of the overuse of CT and attempt to minimize patient exposure to this modality. However, when faced with the potential of silent obstruction, nephron loss and possible nephrectomy for a nonfunctioning kidney, we need to be thorough in our evaluation of the patient whose symptoms have changed when there is no proof of stone passage. I have a hard time convincing patients to undergo ureteroscopy when they are having no symptoms and they know that a third party will pay for followup imaging.

We need studies like this and the excellent resources provided. However, to determine best practice, we truly need randomized controlled studies. I congratulate the authors on a well thought out and nicely done project. I would like to see more clinical data with patient factors and better controlled variables.

Brad Schwartz
Department of Urology
Southern Illinois University School of Medicine
Springfield, Illinois