Resolution of Hydronephrosis and Pain to Predict Stone Passage for Patients With Acute Renal Colic

Stephen V. Jackman, Avinash Maganty, Allan B. Wolfson, Pamela K. Burrows, Cora MacPherson, Nataly Montano Vargas, Ziya Kirkali, and Andrew C. Meltzer

OBJECTIVE To study patients who presented to the Emergency Department with acute renal colic to determine if resolution of hydronephrosis and pain accurately predicts stone passage on follow-up CT.

MATERIALS AND METHODS This is a secondary analysis of a multicenter prospective randomized clinical trial of patients diagnosed by computed tomography (CT) scan with a symptomatic ureteral stone < 9 mm in diameter. Participants were followed after randomization to evaluate for analgesic use and to assess stone passage and hydronephrosis on a repeat CT scan obtained at 29-36 days.

RESULTS Four-hundred-three patients were randomized in the original study and patients were included in this analysis if they did not have surgery for stone removal and had a CT scan and information on pain medication at follow-up (N = 220). Hydronephrosis was detected in 181 (82%) on initial CT. At follow-up CT, 43 (20%) participants had a persistent ureteral stone. Of these patients, 36 (84%) had no pain, 26 (60%) did not have hydronephrosis, and 23 (53%) had neither pain nor hydronephrosis. Resolution of hydronephrosis was associated with stone passage (RR 4.6, 95% CI 1.9, 11.0), while resolution of pain was not (RR 1.1, 95% CI 0.9, 1.4).

CONCLUSION In patients with urinary stone disease, stone passage is associated with resolution of hydronephrosis but not resolution of pain. In patients with persistent ureteral stones, neither pain nor hydronephrosis are consistently present. These findings have important implications on follow-up imaging of patients with urinary stone disease. UROLOGY 159: 48−52, 2022. © 2021 Elsevier Inc.

More than one million visits annually to UnitedStates Emergency Departments (EDs) are attributed to a stone of the kidney or ureter.[1] While initial treatment of renal colic usually occurs in the ED, follow-up is important to confirm passage of the stone and to assess the need for surgical stone removal.[2] Approximately 10% of patients seen in the ED for stone disease return to the hospital within 30 days of initial visit.[3] Prolonged retention of a ureteral stone may lead to permanent renal or ureteral damage which may require surgical intervention.[4] Currently, there are no definitive guidelines regarding how patients discharged from the ED should be followed or evaluated for stone passage.[5] Patient-reported stone passage and resolution of symptoms have been shown to be inexact measures of retained ureteral stones.[6-8] More commonly, patient symptoms are combined with some form of imaging to determine stone passage, although the optimal type of imaging remains controversial. Follow-up can include a urinalysis and a variety of imaging modalities such as plain X-ray, CT scan or ultrasound (US), or combinations thereof. Physicians balance the risk of missing a persistent stone, with its associated added cost and morbidity, against the time, cost, and potential radiation exposure of further diagnostic modalities, such as CT scan. Hydronephrosis is a secondary finding in stone obstruction that can be detected by US or CT scan. It is unknown whether the resolution of hydronephrosis, either with or without the resolution of pain, is sufficient to predict stone passage. The objective of this study is to determine if stone passage could be predicted by resolution of hydronephrosis or resolution of pain in a multicenter trial on urinary stone disease.

Funding Support: *This study is supported by cooperative agreementU01 DK096037 from the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health.*

ClinicalTrials.gov Identifier: *NCT00382265*

From the Department of Urology, University of Pittsburgh School of Medicine, Pittsburgh, PA; the Department of Emergency Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA; the The George Washington University Biostatistics Center, Rockville, MD; the Department of Emergency Medicine, The George Washington University School of Medicine and Health Sciences, Washington, DC; and the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD

Address correspondence to: Andrew C. Meltzer, M.D., M.S., Department of Emergency Medicine, The George Washington University School of Medicine & Health Sciences, 2120 L Street NW, Suite 450, Washington, DC 20037. E-mail: ameltzer@mfa.gwu.edu

Submitted: May 30, 2021, accepted (with revisions): September 16, 2021

 https://doi.org/10.1016/j.urology.2021.09.017
0090-4295

MATERIALS AND METHOD

The Study of Tamsulosin for Urolithiasis in the Emergency Department (STONE) was conducted from 2013 to 2016 across six ED recruiting sites.[9] Institutional Review Board (IRB) approval was obtained from each participating recruitment site prior to study initiation. Eligibility criteria have been previously published in detail.[10] Briefly, adults at least 18 years of age were eligible if they presented to the ED with a symptomatic stone determined by CT scan to be less than 9 mm in diameter and located in the ureter. Hydronephrosis was determined by the attending radiologist's review of the CT scan at each of the participating institutions. Study participants were contacted by telephone at regular intervals to assess for stone expulsion and the need for analgesic medication. Participants were also asked to undergo an additional follow-up CT scan at 29-36 days after randomization to determine whether stone passage had occurred and to assess for hydronephrosis. Follow-up CT scans were evaluated by attending radiologists at participating institutions per standard protocol. These physicians were unaware of the participant's symptoms and patient-reported stone status, but may have had access to the initial CT scan. In cases where passage was uncertain, the CT scan results were subject to a central review. Resolution of pain was defined as a patient report of no utilization of analgesic medication on direct telephone inquiry. The analgesia status at the Day 29 contact or the day closest to the follow-up CT scan was used as a surrogate for pain status at follow-up.

Analysis

Participants who were lost to follow-up or in whom surgery was performed were excluded from this analysis. To assess for potential bias, baseline characteristics were compared between the participants who did and did not undergo a follow-up CT scan as part of prior analysis.[11] Among participants who underwent a follow-up CT scan, those who passed a stone were compared to those who did not pass a stone for baseline characteristics, including the presence of hydronephrosis and flank pain. Categorical variables were compared using the chi-square test, and continuous variables using the Wilcoxon test. Finally, a subgroup analysis was performed based on a stone size cut-off of 4mm and 5mm (the size below which most stones are known to pass spontaneously) to determine if the size of stone influenced the predictive value of pain and hydronephrosis. For all outcomes, a nominal p value of less than 0.05 was considered to indicate statistical significance, without adjustment for multiple comparisons. SAS version 9.4 (SAS Institute Inc, Cary, NC) was used in the data analysis.

RESULTS

Of the 403 participants in the trial, 220 did not have surgery for stone removal, obtained a follow-up CT scan 29-36 days after initial presentation, and had information on pain medication collected (Figure 1). Stone passage was confirmed in the majority of participants (177/220, 80%). Participants who did not pass stone were more likely to have a larger median stone size and a more proximal stone on initial CT scan (Table 1). There was no

Table 1. Baseline characteristics of study participants (N = 220)

	Passage (N = 177)	No Passage (N = 43)	*P*-value
Average age	39.4 ± 13.2	41.3 ± 14.4	.435
Female gender	44 (24.9)	10 (23.3)	.827
Non-white race	46/165 (27.9)	9/39 (23.1)	.543
Hispanic	12 (6.8)	5 (11.6)	.337
Past History of urinary stone disease	46 (26.0)	12 (27.9)	.798
Presence of flank pain	147 (83.1)	33 (76.7)	.336
Symptomatic stone in upper ureter	47 (26.6)	27 (62.8)	<.001
Median diameter			<.001
1-2 mm	38 (21.5)	2 (4.7)	
3-4 mm	103 (58.2)	16 (37.2)	
5-6mm	31 (17.5)	22 (51.2)	
7-8mm	5 (2.8)	3 (7.0)	
Hydronephrosis	145 (81.9)	36 (83.7)	.782

Data presented as N (%) or mean ± standard deviation.

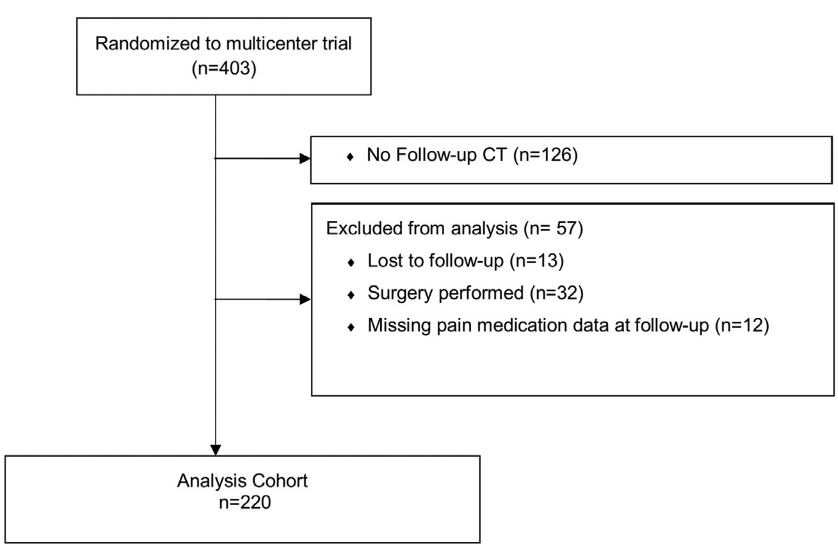

Figure 1. Flow diagram.

Table 2. Hydronephrosis and pain status at follow-up

	All N = 220	Passed Stone N = 177	Persistent Stone N = 43
No hydronephrosis or pain	179	156 (88%)	23 (53%)
No hydronephrosis, but pain	20	17 (10%)	3 (7%)
No pain, but hydronephrosis	15	2 (1%)	13 (30%)
Both hydronephrosis and pain	6	2 (1%)	4 (9%)

Table 2a. Hydronephrosis and pain status at follow-up **(stone < 4mm)**

	All N = 96	Passed Stone N = 88	Persistent Stone N = 8
No hydronephrosis or pain	83	77 (88%)	6 (75%)
No hydronephrosis, but pain	8	8 (9%)	0
No pain, but hydronephrosis	3	2 (2%)	1 (13%)
Both hydronephrosis and pain	2	1 (1%)	1 (13%)

Table 2b. Hydronephrosis and pain status at follow-up **(stone ≥ 4mm)**

	All N = 124	Passed Stone N = 89	Persistent Stone N = 35
No hydronephrosis or pain	96	79 (89%)	17 (49%)
No hydronephrosis, but pain	12	9 (10%)	3 (9%)
No pain, but hydronephrosis	12	0	12 (34%)
Both hydronephrosis and pain	4	1 (1%)	3 (9%)

Table 2c. Hydronephrosis and pain status at follow-up **(stone < 5mm)**

	All N = 159	Passed Stone N = 141	Persistent Stone N = 18
No hydronephrosis or pain	134	124 (88%)	10 (56%)
No hydronephrosis, but pain	15	13 (9%)	2 (11%)
No pain, but hydronephrosis	6	2 (1%)	4 (22%)
Both hydronephrosis and pain	4	2 (1%)	2 (11%)

Table 2d. Hydronephrosis and pain status at follow-up **(stone ≥ 5mm)**

	All N = 61	Passed Stone N = 36	Persistent Stone N = 25
No hydronephrosis or pain	45	32 (89%)	13 (52%)
No hydronephrosis, but pain	5	4 (11%)	1 (4%)
No pain, but hydronephrosis	9	0	9 (36%)
Both hydronephrosis and pain	2	0	2 (8%)

difference in the rate of hydronephrosis on initial CT scan between those who passed a stone (145/177, 82%) and those who did not (36/43, 84%). Likewise, there was no difference in the presence of flank pain at baseline for participants who passed (147/177, 83%) versus those who did not pass a stone (33/43, 77%). At the baseline CT scan, 82% (181/220) of participants had hydronephrosis, compared to only 7% (15/220) on the follow-up scan. For participants who passed their stone, the rate of hydronephrosis at follow-up was very low (2/177, 1%) compared to subjects with a retained stone (13/43, 30%) (Table 2). Rates of hydronephrosis were reported by stone size to try to identify more accurate cut-offs (Table 2a-2d). Two participants with a persistent stone had no hydronephrosis at baseline but developed hydronephrosis at follow-up. The absence of hydronephrosis on the follow-up CT was significantly associated with stone passage (RR 4.6, 95% CI 1.9, 11.0, P <0.01), with a sensitivity of 98% and a specificity of 40% (Table 3). Regarding pain, more participants reported flank pain at baseline (180/220, 82%) than at follow-up (20/220, 9%). At follow-up, pain was reported at the same rate whether patients had passed their stone (17/177, 10%) or had a retained stone (3/43, 7%). Finally, persistent stones were still evident when hydronephrosis had resolved even when stratified by stone size (Tables 2a, 2b, 2c, 2d). In patients with resolution of hydronephrosis, 93% of patients with stone size less than 5mm passed their stone versus only 71% of those with stone size 5 mm or greater.

Table 3. Accuracy of no hydronephrosis or no pain for predicting passed stone at 29-36-day follow-up CT scan 3a) No hydronephrosis 3b) No pain 3c) No hydronephrosis and no pain

Sensitivity	173/177 (98%)
Specificity	17/43 (40%)
Likelihood ratio +	1.6
Relative Risk & 95% CI	4.6 (1.9, 11.0)
Sensitivity	158/177 (89%)
Specificity	7/43 (16%)
Likelihood ratio +	1.1
Relative Risk & 95% CI	1.1 (0.9, 1.4)
Sensitivity	156/177 (88%)
Specificity	20/43 (47%)
Likelihood ratio +	1.7
Relative Risk & 95% CI	1.7 (1.3, 2.3)

COMMENT

Persistent stones are important to diagnose because they may lead to silent obstruction and permanent renal damage. In this secondary analysis of a multicenter study of ED patients with symptomatic ureteral stones, stone passage was associated with the resolution of hydronephrosis but not the resolution of pain. For patients with retained stones, resolution of pain and resolution of hydronephrosis may still occur. Based on this study, if clinicians relied on the resolution of pain only, 84% of patients with persistent stones would be missed. If clinicians relied on the presence of hydronephrosis only to detect persistent stones, 60% of patients with persistent stones would be missed. If clinicians relied on either pain or hydronephrosis, 53% of persistent stones would be missed. While persistent stones can be missed in the absence of pain or hydronephrosis, pain and hydronephrosis retain predictive utility. Among all patients with hydronephrosis, 81% had a persistent stone. Among all patients without hydronephrosis, 13% had a persistent stone.

While CT scan was used in this study for initial and follow-up evaluation, the results of this study directly relate to the use of US as an imaging choice for follow-up. US is a commonly used imaging modality due to low cost and lack of radiation exposure.[12,13] US is sensitive in detecting significant hydronephrosis and less sensitive at detecting the stone itself.[14] Since this study calls into question the accuracy of hydronephrosis on follow-up for detecting persistent stones, it also questions the utility of US as a follow-up modality. Other modalities such as ultra-low-dose CT may be better for confirming stone passage.[15]

Multiple studies have shown that pain cessation is not accurate in predicting stone passage. One study showed that cessation of pain for greater than 3 days would still miss 26% of patients with persistent stone.[4] In addition, patient-reported stone passage has limitations in predicting actual passage.[7]

Our study has several strengths. First, patients were recruited from multiple EDs where all participants first presented with symptomatic ureterolithiasis. Second, the diverse sample population and the lack of limitation on stone location make our findings more generalizable. Third, there was a high-rate of patient response, with 97% of patients contacted to assess for analgesic use. Finally, all participants had both an initial CT scan and a follow-up CT scan that was interpreted for the presence of hydronephrosis. The follow-up CT is more accurate than the imaging used in prior studies, in which either US, plain X-Ray, or both were used to confirm stone passage.[16]

Our findings must also be considered in the context of several limitations. First, the reported use of analgesia was employed as a surrogate for having pain. Second, additional data that may be available to clinicians, such as history, physical exam, and urinalysis, was not included in this analysis. Third, the radiologist who interpreted the second CT scan was not blinded to the results of the first CT scan. Fourth, we did not incorporate microscopic hematuria and do not know whether this additional information would change prediction of stone passage. Finally, since CT scan was required prior to randomization and only those patients who underwent follow-up CT scanning were included in this analysis, there may have been a selection bias for patients in whom ordering physicians were less concerned about radiation exposure.

CONCLUSION

In summary, patients who do not report stone passage after being discharged from the ED may still have a retained ureteral stone despite lack of pain and lack of hydronephrosis. This implies that if a patient is evaluated using renal ultrasound to confirm passage, the clinician may miss persistent ureteral stones. Based on our findings, a certain percentage of stones will be missed if another marker besides CT is used to assess passage. Therefore, urologists and primary providers need to have a relatively high index of suspicion for retained stones and carefully follow the patient with additional diagnostic studies as appropriate.

References

1. Foster G (Social & Scientific Systems, Inc.), Stocks C (AHRQ), and Borofsky MS (New York University). Emergency Department Visits and Hospital Admissions for Kidney Stone Disease, 2009. HCUP Statistical Brief #139. July 2012. Agency for Healthcare Research and Quality, Rockville, MD. Available at http://www.hcup-us.ahrq.gov/reports/statbriefs/sb139.pdf. Accessed November 4, 2021.
2. Hyams ES, Matlaga B, Korley F. Practice patterns in the emergency care of kidney stone patients: an analysis of the national hospital ambulatory medical care survey (NHAMCS). *Can J Urol.* 2012;19:6351–6359.
3. Scales CD, Lin L, Saigal CS, et al. Emergency department revisits for patients with kidney stones in california. *Acad Emerg Med.* 2015;22:468–474. https://doi.org/10.1111/acem.12632.
4. Wimpissinger F, Türk C, Kheyfets O, Stackl W. The silence of the stones: asymptomatic ureteral calculi. *J Urol.* 2007;178:1341–1344. https://doi.org/10.1016/j.juro.2007.05.128.
5. Fulgham PF, Assimos DG, Pearle MS, Preminger GM. Clinical effectiveness protocols for imaging in the management of ureteral calculous disease: AUA technology assessment. *J Urol.* 2013;189:1203–1213. https://doi.org/10.1016/j.juro.2012.10.031.

6. Hernandez N, Mozafarpour S, Song Y, Eisner BH. Cessation of ureteral colic does not necessarily mean that a ureteral stone has been expelled. *J Urol*. 2018;199:1011–1014. https://doi.org/10.1016/j.juro.2017.10.032.
7. Meltzer AC, Burrows PK, Kirkali Z, et al. Accuracy of patient reported stone passage for patients with acute renal colic treated in the emergency department. *Urology*. 2020;136:70–74. https://doi.org/10.1016/j.urology.2019.10.010.
8. McLarty R, Assmus M, Senthilselvan A, Schuler T, Wollin T, De S. Patient reported outcomes predicting spontaneous stone passage may not have acceptable accuracy. *J Urol*. 2020;204:524–530. https://doi.org/10.1097/JU.0000000000001030.
9. Meltzer AC, Burrows PK, Wolfson AB, et al. Effect of tamsulosin on passage of symptomatic ureteral stones: a randomized clinical trial. *JAMA Intern Med*. 2018;178:1051–1057. https://doi.org/10.1001/jamainternmed.2018.2259.
10. Burrows PK, Hollander JE, Wolfson AB, et al. Design and challenges of a randomized clinical trial of medical expulsive therapy (tamsulosin) for urolithiasis in the emergency department. *Contemp Clin Trials*. 2016;52:91–94. https://doi.org/10.1016/j.cct.2016.11.010.
11. Meltzer AC, Wolfson AB, Mufarrij P, et al. Analgesic and opioid use for patients discharged from the emergency department with ureteral stones. *J Endourol*. 2020. https://doi.org/10.1089/end.2020.0835.
12. Nicolau C, Claudon M, Derchi L, et al. Imaging patients with renal colic—consider ultrasound first. *Insights Imaging*. 2015;6:441–447. https://doi.org/10.1007/s13244-015-0396-y.
13. Smith-Bindman R, Aubin C, Bailitz J, et al. Ultrasonography versus computed tomography for suspected nephrolithiasis. *N Engl J Med*. 2014;371:1100–1110. https://doi.org/10.1056/NEJMoa1404446.
14. Ganesan V, De S, Greene D, Torricelli FCM, Monga M. Accuracy of ultrasonography for renal stone detection and size determination: is it good enough for management decisions? *BJU Int*. 2017;119:464–469. https://doi.org/10.1111/bju.13605.
15. Cheng RZ, Shkolyar E, Chang TC, et al. Ultra-low-dose CT: an effective follow-up imaging modality for ureterolithiasis. *J Endourol*. 2020;34:139–144. https://doi.org/10.1089/end.2019.0574.
16. Brisbane W, Bailey MR, Sorensen MD. An overview of kidney stone imaging techniques. *Nat Rev Urol*. 2016;13:654–662. https://doi.org/10.1038/nrurol.2016.154.