When (and how) to surgically treat asymptomatic renal stones

Zachariah G. Goldsmith and Michael E. Lipkin

Abstract | Asymptomatic renal stones are identified in 8–10% of screened populations. With the increasing utilization of CT, the number of patients seeking urologic care for incidentally diagnosed renal calculi is likely to increase. Such patients present an important management dilemma: differentiating those to treat surgically from those who can be safely observed. Observational studies have revealed that approximately 50% of asymptomatic stones will progress, but most will not require surgery. Stones >15 mm in diamater and located in the renal pelvis are at highest risk of progression. Although no guidelines exist for the optimal monitoring regimen for asymptomatic stones, follow-up studies may include serum creatinine, plain radiography, ultrasonography, and CT. Shock wave lithotripsy (SWL) does not seem to offer significant benefit over observation for asymptomatic calyceal stones. Percutaneous nephrolithotomy does improve stone-free rates compared to SWL or observation. Additional research is needed to characterize the role of ureteroscopic management of asymptomatic renal stones.

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Introduction

The prevalence of urolithiasis in US populations has been estimated at 5% of women and 10% of men.[1,2] Recent data suggest that prevalence is increasing; analysis of the National Health and Nutrition Examination Survey (NHANES) revealed an increase in prevalence among men and women aged 20–74 years from 3.8% in the 1970s to 5.2% in the 1990s (P <0.05).[3] Similarly, a study of the National Inpatient Sample revealed a 5.7% increase in the number of hospital discharges related to a principal diagnosis of stone disease between 1997 and 2002.[4] In sum, total health-care expenditures for urolithiasis in the US exceeded $2 billion in 2000.[5]

At the same time, the use of imaging is increasing. By one estimate, 72 million CT scans were performed in the US in 2007.[6,7] Given the prevalence of urolithiasis, and concomitant increase in utilization of cross-sectional imaging, a growing number of patients are likely to be diagnosed with an incidentally identified renal calculus. In a series of 5,047 asymptomatic adults who underwent CT colonography screening, urolithiasis was identified in 395 patients (7.8%).[8] A mean of 2.1 stones were found in each affected patient; mean stone size was 3.0 mm. In another study of 1,957 potential kidney donors who underwent screening CT, 9.7% were found to have asymptomatic stones.[9]

The optimum management strategy for patients with asymptomatic urolithiasis is unknown. No consensus exists regarding whether they should be treated or observed, and data on the proportion of patients who are likely to pass the stone spontaneously or ultimately require an intervention are unclear. Simply, what are the goals of care? For this Review we have evaluated the limited body of existing literature in an attempt to inform these decisions. An understanding of the natural history of asymptomatic stones can be obtained from studying the outcomes of not only patients with untreated renal calculi but also those who are found to have residual stone fragments following primary stone intervention, for whom a larger body of research exists. Finally, we discuss data from the small number of randomized clinical trials that have been performed to compare management strategies for asymptomatic stones.

Natural history of asymptomatic stones

A number of studies have characterized the outcomes of patients with asymptomatic renal stones who undergo observation rather than treatment (Table 1). Typical outcomes assessed in these studies are rates of spontaneous passage and overall progression, defined as symptomatic stone events, increase in size on serial imaging, or need for intervention. In a retrospective study of 107 patients with asymptomatic renal stones (mean size not reported) followed for a mean of 31.6 months, the rate of symptomatic events was 31.8%.[10] Kaplan-Meier analysis estimated the risk of experiencing a symptomatic stone event at approximately 10% per year, with a cumulative 5-year probability of 48.5%. Of the 34 patients who developed symptoms, approximately half (n = 16) spontaneously passed the stone, with the remainder (n = 18) requiring intervention in the form of shock wave lithotripsy (SWL), ureteroscopy, or percutaneous nephrolithotomy (PNL).

Competing interests
M. E. Lipkin declares an association with the following company: Boston Scientific. See the article online for full details of the relationship. Z. G. Goldsmith declares no competing interests.

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Key points

- The prevalence of asymptomatic stones identified in screened populations is 8–10%, and is likely to grow with increased CT utilization
- Outcomes of asymptomatic stones <10 mm in diamater include a symptomatic stone event (13–32%), spontaneous passage (13–20%), size increase (30–46%) and intervention (7–26%)
- Asymptomatic stones located in the renal pelvis and >15 mm are at high risk of progression, defined as increase in size, symptomatic stone event, or need for intervention
- Shockwave lithotripsy does not improve stone-free rates or quality of life compared to observation for asymptomatic calyceal stones <15 mm
- Percutaneous nephrolithotomy improves stone-free rates compared to shockwave lithotriposy and observation for asymptomatic lower pole stones
- Randomized trials are needed to define the role of ureteroscopy in the management of asymptomatic renal stones

In a large retrospective series of 300 men with asymptomatic stones (mean stone size 10.8 mm),[11] followed up for a mean of approximately 3 years, there was a 77% rate of overall progression, defined as development of pain, stone growth on serial imaging, or need for intervention. Kaplan-Meier analysis revealed a 50% risk of intervention at 7.25 years. Although statistical analysis was limited, this study also reports the effects of stone size and location on outcome. A larger size and location within the renal pelvis (as opposed to the calyces) was positively associated with risk of progression; 100% of patients with stones >15 mm located in the renal pelvis experienced progression, suggesting they might be poor candidates for observation. Although the effects of stone location on symptom severity have yet to be fully characterized in the literature, it is interesting to note that the majority of asymptomatic stones in this series were identified in the lower pole (44%). A retrospective study of 50 patients with smaller asymptomatic stones (mean size 5.7 mm in a total of 85 stones) reported rates of spontaneous passage, size increase, and intervention of 20%, 46%, and 7%, respectively.[12]

A single prospective study has been performed in patients with asymptomatic lower pole stones, who were followed with observation for a mean of 52.3 months.[13] 24 patients (27 affected renal units) with a mean stone size of 8.8 mm were followed prospectively, 12.5% of whom developed pain, and 12.5% required intervention. An increase in size was observed in eight stones. However, none of the patients who experienced stone growth required intervention over the 2-year follow-up period, suggesting that increasing stone size alone does not indicate a need for intervention in the short term. An additional three patients passed their stones spontaneously. Taken together, these data suggest that approximately half of patients with asymptomatic renal stones will progress, but most will not require surgery.

Residual postoperative stones

Although stone fragments that remain after primary treatment have a pathogenesis that is distinct from primary asymptomatic stones, some additional insights can be gleaned by reviewing the larger body of literature on this population. Furthermore, the observation that up to 40% of patients with asymptomatic stones have a prior history of stone formation[13] suggests that the populations overlap.

In a retrospective review of 11 patients with residual stone fragments (<4 mm) after SWL treatment, fragment growth was demonstrated in six individuals.[14] Similarly, 49% (75/154) of patients with <5 mm fragments after SWL went on to develop pain or require intervention in another retrospective review with 3-year follow-up.[15] A prospective study of 160 patients with post-SWL fragments (<4 mm) reported that 43% had a symptomatic episode or required intervention during a mean follow-up of 2 years.[16] At 5 years, Kaplan-Meier estimation revealed

Table 1 | Observation of asymptomatic or residual stones

Study	*n*	Mean stone size (mm)	Outcome (%)				
			Overall progression	Stone passage	Symptoms	Size increase	Intervention
Asymptomatic							
Glowacki *et al*. (1992)[10]	107	NR	NR	15	32	NR	17
Burgher *et al*. (2004)[11]	300	10.8	77	NR	NR	NR	26
Koh *et al*. (2011)[12]	50	5.7	NR	20	NR	46	7
Inci *et al*. (2007)[13]*	24	8.8	NR	13	13	30	13
After SWL							
Fine *et al*. (1995)[14]	11	NR	NR	NR	NR	55	NR
El-Nahas *et al*. (2006)[15]	154	NR	49	NR	15	34	34
Streem *et al*. (1996)[16]*	160	NR	43	NR	26	18	28
After PNL							
Raman *et al*. (2009)[17]	42	NR	43	NR	NR	NR	26
Ganpule *et al*. (2009)[18]	187	NR	NR	45	NR	NR	NR
After URS							
Rebuck *et al*. (2011)[19]	46	NR	NR	22	20	NR	NR

*Prospective studies. Abbreviations: NR, not reported; PNL, percutaneous nephrolithotomy; SWL, shock wave lithotripsy; URS, ureteroscopy.

a probability of 71% of developing symptoms or requiring intervention in this population. These results suggest higher rates of overall progression and intervention in patients with stone fragments after SWL than in those with *de novo* asymptomatic stones.

Progression patterns of similar stone fragments resulting from PNL treatment have been characterized in a number of studies. In a retrospective review of 42 patients with small post-PNL fragments (mean size 2 mm), 43% progressed to a symptomatic event, and 26% required intervention.[17] An additional large retrospective review of 2,469 patients focused on stone passage rates of residual post-PNL fragments. Residual stones with a mean size of 39 mm^2 were identified in 187 patients, 84 of which passed spontaneously within a mean follow-up period of 2 years.[18]

A single study has examined the outcomes of residual fragments following ureteroscopy.[19] In 46 patients with residual stones <4 mm, a symptomatic event rate of 20% was observed. 22% of patients experienced stone passage, and the remainder retained the fragments and remained asymptomatic throughout the 19-month follow-up period.

Taken together, these data suggest that residual stones following primary intervention (particularly PNL and SWL) are more likely to progress than those discovered incidentally. Notably, studies of residual stones also revealed that patients receiving targeted medical treatment, following comprehensive metabolic evaluation, had significantly attenuated fragment growth after both SWL[14] and PNL.[20] These studies[14,20] included patients with a variety of stone compositions (including calcium, uric acid, and cysteine), but did not stratify the efficacy of the targeted metabolic therapy by type of stone. Targeted metabolic treatment has not been studied in patients with *de novo* asymptomatic stones.

When to treat asymptomatic stones

Stone characteristics (size and location) might influence how likely an asymptomatic stone is to progress or require intervention (Box 1). In a survey of 167 practicing urologists, stone size was reported a primary factor in determining management trends. The majority of respondents (61%) indicated that they would recommend SWL rather than observation (25%) for asymptomatic renal stones sized 5–10 mm.[21] For calculi >20 mm, most interviewees (72%) indicated that PNL was their recommended treatment option.

In a large retrospective study of patients with asymptomatic renal stones who were kept under observation, stones >4 mm were 26% more likely to progress than stones <4 mm ($P = 0.012$).[11] For stones >15 mm, a 100% rate of progression (defined as symptomatic stone pain, size increase, or intervention) was observed. Therefore, 15 mm seems a reasonable threshold for asymptomatic renal stones. In a recent review, Skolarikos and colleagues[22] suggested 10 mm as a cut-off for intervention of lower pole stones. Furthermore, stones located in the pelvis had a higher rate of progression than those in the calyces,[11] suggesting that patients with pelvic stones are poor candidates for observation.

Box 1 | Characterstics of high-risk asymptomatic stones

Stone characteristics
- Located in renal pelvis
- Size >15 mm

Patient characteristics
- Solitary kidney
- Urinary tract reconstruction
- Immunodeficiency
- Children
- High-risk occupation
- Poor access or compliance

Although not well-characterized in the literature, patient-related factors can also identify asymptomatic stones at high risk of progression. These factors are listed in Box 1. Patients with asymptomatic stones in a solitary kidney or with renal insufficiency are considered high risk.[23] Such patients experience higher rates of surgical complications following intervention. In a retrospective multicenter review, significantly lower stone-free rates and higher rates of transfusion were reported in 189 patients with solitary kidneys who underwent PNL compared with the bilateral kidney cohort.[24] In this high-risk population, the risks and benefits of observation versus surgical intervention need to be considered and discussed with each patient to determine the appropriate course of action.

Although not well-studied, asymptomatic stones in patients with urinary tract reconstruction, specifically those who have undergone ureteroneocystostomy, ureteroureterostomy, ileal interposition, or enteral bladder reconstruction, are considered high risk. An anterograde percutaneous approach is usually recommended for first-line therapy in these patients. However, in one series of 15 patients who had previously undergone urinary diversion with Bricker ureteroenteric anastomoses, retrograde flexible ureteroscopy was successful in 73% of patients with an ileal conduit, 33% with an Indiana pouch, and 90% with a neobladder.[25] In this series, a flexible cystoscope was used to place the guide wire in patients with conduits or Indiana pouches. An additional retrospective review of 24 patients who were treated for nephrolithiasis following ureteroneocystostomy stratified patients according to whether they received Glenn-Anderson advancement or Cohen cross-trigonal reimplantation.[26] Patients with Glenn-Anderson advancement had higher success rates with both ureteroscopy (100%) and SWL (50%), while all patients with Cohen reimplantation failed treatments with ureteroscopy (100%) and SWL (100%). PNL treatment was successful in all patients.

For pediatric stone formers, the high rates of underlying metabolic abnormalities and atypical symptomatology in these patients[27] suggest that treatment of asymptomatic stones is a reasonable option. SWL is the treatment of choice for nonstruvite stones in this population,[28] but ureteroscopy and PNL have also been reported as suitable treatment options in a number of centers.[29] Pediatric or adult patients with spinal cord injury and neurogenic bladder may also warrant prompt treatment

of asymptomatic stones, particularly those with severe debilitation that would increase the morbidity associated with stone progression. Struvite stones diagnosed in the setting of UTI in such patients warrant prompt treatment.[30] UTI, vesicoureteral reflux, pelviectasis, renal scarring, urinary tract reconstruction, and thoracic-level lesions have all been identified as risk factors for stone formation in patients with neural tube defects.[30]

Nephrolithiasis in transplanted allograft kidneys is rare, with an estimated incidence of <1% (including both *de novo* stone formation and donor-gifted allograft lithiasis).[31] Allograft nephrolithiasis does not usually result in pain, probably owing to denervation during explant; stones are often identified during workup for allograft dysfunction.[32] PNL and SWL are the typical treatment options described for asymptomatic stones in transplant allografts.[31,33] In addition, although there is a paucity of literature, immunocompromised patients with asymptomatic stones should be deemed at a lower threshold for intervention, given concerns for severe morbidity from infectious sequelae that may result from stone progression and obstruction.

The roles of socioeconomic disparities in health-care access and delivery in urologic care are becoming better characterized, specifically with regard to prostate cancer.[34] However, the role of such factors in the management of urolithiasis remains poorly described. Patients with limited access to health-care resources or other barriers to care may be good candidates for intervention, particularly if compliance with observation protocols is likely to be problematic. In addition, it seems prudent to offer prompt intervention to patients with specific high-risk occupations, including pilots, business travelers, long-haul truckers, and members of the military. Speculation exists regarding whether patients with recurrent urolithiasis and prior symptomatic stone events are more likely to develop further episodes of renal colic, and this has not been directly addressed in the existing literature.

Although the importance of these factors may guide intervention in individual patients, the utility and cost-effectiveness of this approach certainly requires further investigation.

Active surveillance protocols

Once a patient has been deemed suitable for observation, the choice of follow-up method must be made. The goals of serial imaging are to identify increase in stone size, change in location, stone passage, or hydroureteronephrosis. Notably, no guidelines have been established for the optimum modality and frequency of imaging for evaluating patients with urolithiasis. Given the increasing awareness of exposure to ionizing radiation from medical imaging,[7,35] it is important to recognize that stone formers are at high risk for significant radiation exposure from the number of imaging procedures performed during the acute stone event, treatment, and follow-up.[36] Low-dose CT has emerged as an effective modality for detection of urolithiasis as well as hydroureteronephrosis.[37] With continued development, novel low-radiation alternatives, such as digital tomosynthesis,[38] are likely to emerge as options for following patients with asymptomatic renal stones.

A surveillance regimen used in one prospective study involving asymptomatic stones included abdominal plain film radiography, serum creatinine measurement, and urine culture on an annual basis.[39] Another trial followed asymptomatic patients with plain film radiography, serum creatinine measurement, and urine culture every 3 months.[40] In yet another trial, patients were assessed every 6 months with abdominal film radiography, serum creatinine level, and urinalysis, and obtained annual CT and ultrasonography in alternate years. Skolarikos *et al.*[22] recommend annual CT for 2–3 years for active surveillance of asymptomatic renal stones. Longer term follow-up plans are not described in the literature. Furthermore, the authors recommend alternating annual CT and ultrasonography for lower pole stones <10 mm. For the majority of patients with radio-opaque non-uric-acid stones, it is currently our practice to perform annual plain radiography and urinalysis. A CT scan is obtained if patients report pain or if there is suspicion for obstruction.

How to treat asymptomatic renal stones

The majority of asymptomatic stones are localized in the lower pole,[11] allowing some insight to be gleaned from trials comparing the efficacy of SWL, PNL, and ureteroscopy for symptomatic lower pole stones. In a multicenter trial of 128 patients with symptomatic lower pole stones (mean size ~14 mm) randomized to SWL or PNL, stone-free rates were significantly higher in the PNL group (95%) than in the cohort who received SWL (37%; $P<0.001$).[41] In addition, stone-free rates with PNL were independent of stone burden, while SWL resulted in lower stone-free rates for larger stones. Thus, PNL offers superior stone-free rates compared to SWL for symptomatic lower pole stones.

A comparison of SWL and ureteroscopy for symptomatic lower pole stones has also been performed in a randomized multicenter clinical trial.[42] 78 patients with lower pole stones <10 mm were randomized to receive either SWL or ureteroscopy, and equivocal stone-free rates were reported at 3 months (35% for SWL, 50% for ureteroscopy; $P=0.92$). However, patient-derived quality of life measures were significantly better in the SWL group, including number of days until the patient was able to drive, or able to return to work, and the number of patients who would choose to undergo the same procedure again.

Two randomized clinical trials have focused specifically on patients with asymptomatic stones. In one trial of 228 patients with asymptomatic calyceal stones (<15 mm), patients were randomized to SWL or active surveillance.[39] End points included stone-free rates, requirement for additional treatment (including analgesics, antibiotics, or a procedure), development of symptoms, quality of life, and renal function. Mean follow-up was 2.2 years. There was no significant difference in stone-free rates between patients randomized to SWL or observation (28% versus 17%, $P=0.06$). Similarly, no difference in overall rates of additional treatments was observed between SWL and observation groups (15% versus 21%, $P=0.27$). Quality of

life outcomes were also similar, with no significant differences reported regarding the impact of kidney stones on everyday life, or absence from the workplace. Serum creatinine at the time of last follow-up was also equivalent in each group. However, it is important to note that patients in the observation group did require a greater number of interventions than those in the SWL group, suggesting the importance of risk-stratification to guide management of patients with asymptomatic stones <15 mm.

An additional trial of patients with asymptomatic stones also included a PNL arm.[40] 94 patients with asymptomatic lower pole stones were randomized to observation, SWL, or PNL. Mean stone size was identical in the observation, SWL, and PNL groups (137 mm^2, 139 mm^2, and 153 mm^2, respectively). At 3-month and 12-month follow-up, stone-free rate in the PNL group was higher than both the SWL and observation groups (96.7% versus 54.8% and 0%, respectively; P <0.001). Adverse events in the PNL group included fever (3.2%), and blood loss requiring transfusion (3.2%). In the observation group, seven patients (18.7%) required intervention during 12 months of follow-up. Spontaneous passage was observed in one patient (3.1%). No quality of life assessments were included in this analysis; however, renal scintigraphy with DMSA scans revealed evidence of renal scarring in 16.1% patients who underwent SWL, 3.2% of those who received PNL, and 0% of patients under observation. The long-term sequelae of this finding are not clear.

Ureteroscopic intervention for asymptomatic stones has not been evaluated in a prospective randomized trial. However, higher stone-free rates for lower pole stones treated with ureteroscopy compared to SWL,[41] and the minimally invasive nature of ureteroscopy, suggest that it is a reasonable management option for patients with asymptomatic lower pole stones. Flexible ureteroscopy with holmium laser lithotripsy to address asymptomatic ipsilateral renal stones at the time of intervention for ureteral stones has been described.[43] Negotiating a laser fiber into a lower pole calyx has been identified as a factor that makes these procedures challenging. Laser fragmentation of lower pole calculi can be facilitated by first manipulating the stone into the pelvis using a Nitinol basket device.[44] Randomized clinical trials are needed to investigate the role of ureteroscopy in the management of asymptomatic renal stones.

Conclusions

Patients with asymptomatic stones should be counseled that although approximately 50% will progress, most of these will not progress so far as to require surgery. Stones >15 mm in diameter and those located in the renal pelvis are at an increased risk of progression. SWL does not offer improved stone-free rates or quality of life over observation in patients with asymptomatic calyceal stones <15 mm. PNL does improve stone-free rates compared to SWL and observation for asymptomatic lower pole stones. Future studies are warranted to determine the role of ureteroscopy in management of these patients. Additionally, novel low-radiation alternatives are needed to monitor for progression in these patients.

Review criteria

Articles were selected by searching the PubMed database, using the following search terms: "asymptomatic renal stones", "lower pole renal stones", and "high risk stones". Only full-text, English language articles were selected. Articles from 1975 to the time of the search (January 2012) were included. The reference lists of relevant papers were search to identify additional citations.

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Author contributions

Z. G. Goldsmith and M. E. Lipkin contributed equally to researching data for the article, discussion of content and reviewing the manuscript before submission. Z. G. Goldsmith wrote the article.