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Invited Review

Role of conservative management of stones

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ABSTRACT

Urinary tract stone disease is one of the most common pathologies of the modern era with a rising prevalence owing to incidentally detected renal stones from imaging for other reasons. Although there is consensus on active management of symptomatic and asymptomatic stones in high-risk patient groups, conservative management of stones is still controversial. We have reviewed the literature pertaining to conservative management of 3 groups of stones-asymptomatic calyceal stones, staghorn stones, and ureteric stones-and summarized the findings to provide guidance in the conservative management of stones. In the calyceal stone group, our review showed an average spontaneous stone passage rate of 18% (range, 8%-32%) and an average requirement for surgical intervention of 20% (range, 7%-40%), with 62% of patients remaining safely on surveillance over a mean time of 4 years. In the staghorn group, overall disease-specific mortality was noted to be 16% (range, 0%-30%) and chance of renal deterioration was 21% (range, 0%-34.5%), with a mean incidence of infection of 22%. In case of conservatively managed ureteric stones, the rate of spontaneous passage for stones smaller than 5 mm was 75%, compared with 62% for those larger than 5 mm. Based on the position in the ureter, spontaneous passage rates were 49%, 58%, and 68% for proximal, middle, and distal thirds, respectively. Conservative management may be recommended for asymptomatic patients and those who are deemed unfit for any procedures. However, careful patient selection and thorough counseling about the risks of conservative management could make it a suitable option for an appropriate subset of patients.

Keywords: Calyceal stones; conservative management; kidney stones; staghorn stones; ureteric stones.

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Introduction

Urinary tract stone disease is one of the most common pathologies of the modern era, with varying but globally increasing prevalence rates ranging from 8% to 19% in males and 3% to 5% in females.[1,2] Owing to a rise in renal imaging, a corresponding rise in incidentally detected renal stones has been found in the past few decades. Boyce et al.[3] reviewed 5,047 patients undergoing screening computed tomography (CT) colonography and found the prevalence of asymptomatic renal stones in that population to be 7.8%, with an average stone burden of 2.1 stones per patient.

There is little doubt that the high-risk patient groups such as those with solitary kidneys, abnormal urinary tract anatomy, metabolic or recurrent stone formers, and/or high-risk occupations and children should be encouraged to have early intervention. Active intervention is also recommended by the European Association of Urology guidelines for patients with symptoms (pain or hematuria), obstruction, infection, stone growth, stone size of >15 mm, and/or comorbidities, and those who choose active intervention.[4] However, optimal management of low-risk patients with asymptomatic stones remains a challenge to endourologists, and the supporting evidence is generally varied, contradictory, and of poor-quality, making definitive guidance on this topic very difficult.

Indications and the decision-making process for conservative management of asymptomatic stones depend first and foremost on the position of the stones and the impact on the functioning of the kidney. Other considerations

Table 1. Studies of asymptomatic calyceal stones

Study	Year	Subjects/renal units, n	Average stone size, mm	Average follow-up, months	Intervention, %	Spontaneous stone passage
Hübner and Porpaczy[5]	1990	62	-	88.8	40	16
Glowacki et al.[6]	1992	107	-	31.6	16.8	15
Keeley et al.[7]	2001	99	<15	26.4	21	17
Burgher et al.[8]	2004	300	10.8	39	26	-
Inci et al.[9]	2007	24	8.8	52.3	11.1	12.5
Koh[10]	2012	50	5.7	46	7.1	20
Kang et al.[11]	2012	347	4.4	31	24.5	29.1
Dropkin et al.[12]	2015	110	7.0	41	17	8
Darrad et al.[13]	2018	301	10.8	63	26.6	14.6
Li et al.[14]	2019	297	4.7	50	12.3	32.1

include infection, comorbidities that preclude major surgery, and attitude of patients. For the purpose of this review, we divided stones into 3 groups-asymptomatic calyceal stones, staghorn stones, and ureteric stone-and studied the outcomes in these groups.

Asymptomatic calyceal stones

A number of studies over the past 30 years have set out to understand the natural history of conservatively managed asymptomatic renal stones (Table 1).[5-14] In one of the first retrospective studies, Hübner and Porpaczy[5] reviewed 62 patients over 88.8 months and found a spontaneous stone passage rate of 16% and a stone growth (progression) rate of 45%. They found very high infection and surgical intervention rates of 68% and 40%, respectively. They concluded that 83% of calyceal stones require intervention within 5 years of diagnosis. This study was followed by one by Glowacki et al,[6] who reviewed 107 patients with asymptomatic stones for a mean period of 31.6 months. They found that 73 patients (68.2%) remained asymptomatic, 16 patients (15%) had spontaneous stone passage, and only 18 patients (16.8%) required surgical intervention in great contrast to the findings of Hübner and Porpaczy[5] They estimated a 5-year probability of a stone-related adverse event of 48.5%. Interestingly, they found a positive correlation between a history of previous stones and the number of stones to symptomatic stone-related events, although this was not statistically significant.

More than a decade later, Burgher et al.[8] conducted a larger study looking at 300 males with asymptomatic stones followed up for 39 months. They found the surgical intervention rate was 26%, which could be considered to be low in view of the significant advancements in endoscopic stone surgery in terms of success rates and patient safety. A disease progression rate (defined as stone growth, pain during follow-up, or need for surgical intervention) of 77% was reported. There was significant disparity between disease progression and the percentage of patients having active stone removal, which could not be explained.

In the only prospective study conducted on this subject, Inci et al.[9] reviewed the outcomes of 24 patients (27 renal units) with conservatively managed asymptomatic lower-pole stones over an average of 52.3 months. They found that 12.5% of patients developed pain and 12.5% required surgical intervention. Stone growth was noticed in 8 patients, and none of them required intervention over 2 years, indicating that stone growth alone was not a definitive factor in active stone removal in the short term. It is important to note the low patient numbers in this study, making definitive conclusions doubtful. A larger study by Dropkin et al.[12] supported these findings when they retrospectively reviewed 160 patients for 41 months and found

Main Points:

- Conservative management may be recommended for a select group of asymptomatic patients. Patients should be counseled about the following consequences:
- Calyceal stones: Stone passage rate is 18%. Requirement for surgical intervention is 20%.
- Staghorn group: Disease-specific mortality is 16%. Renal deterioration is 21%. Incidence of infection is 22%.
- Ureteric stones: Spontaneous passage rates are 75% (stone size <5 mm) and 62% (stone size >5 mm). Passage rates are 49%, 58%, and 68% for proximal, middle, and distal thirds.

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stone growth had no stone-related symptoms. Their definition of stone growth was an increase in stone size greater than 50%, which differs from other studies, making the results not comparable. They also found that patients with middle- and upper-pole stones had a greater chance of spontaneous stone passage, which is not supported by most of the other studies.

Our group has conducted one of the largest cohort studies on asymptomatic calyceal stones in 238 patients (301 renal units) with CT-confirmed stones over a median follow-up of 63 months.[10] The mean stone size was 10.8 mm with an average patient age of 56 years. We found that 58.8% of the patients remained on surveillance at the end of the study, with 26.6% needing surgical intervention and 14.6% having spontaneous stone passage. The 1-, 3-, and 5-year risk of an adverse stone event (defined as either stone symptom and/or need for intervention) was 3.4%, 18.9%, and 30.7%, respectively. In contradiction to the studies by Inci et al.[9] and Dropkin et al.[12], we found that a stone growth velocity of >1 mm/y led to significantly higher stone-related adverse events. We also concluded that patients under the age of 50 years were more likely to suffer significant adverse events compared with older patients. This was theorized to be secondary to younger patients sustaining a more active lifestyle and being more likely to seek intervention for symptoms. Another recent large retrospective study, by Li et al,[14] followed 297 patients over a period of 4.2 years. They reported a relatively low intervention rate of 12.3% with a spontaneous passage rate of 32.1%. However, this may be accounted by the average stone size being 4.7 mm, which was substantially smaller than that in our study. In contradiction to our study, they found older patients (age of >60 years) were more likely to require intervention, and larger lower-pole stones (>5 mm) were less likely to cause symptoms.

A few studies have also specifically looked at conservatively managed asymptomatic residual stone fragments in patients who have had surgical intervention. This population is a subsection of the asymptomatic stone patients in the studies mentioned earlier rather than an entirely independent group. As most of the studies looking at asymptomatic renal stones have included patients who have had previous intervention, it would be impossible to differentiate residual fragments from new renal stones in these patients. However, El-Nahas et al.[15] reviewed 154 patients with fragments of size <5 mm following shockwave lithotripsy (SWL). Of these patients, 75 patients (49%) either went on to develop recurrent symptoms or required intervention within 3 years. These findings were supported in other studies following post-SWL patients with residual fragments. This suggests that there may be a higher risk of adverse stone-events in patients who have asymptomatic residual stone fragments following surgical intervention compared with patients with untreated asymptomatic stones.[16,17] This correlation was also present in residual fragments in patients who had undergone percutaneous nephrolithotomy (PCNL) or retrograde intrarenal surgery.[18-20]

Keeley et al.[7] conducted a prospective randomized controlled trial evaluating the outcome of prophylactic SWL versus conservative management for small (<15 mm) asymptomatic calyceal stones in 228 patients. They concluded that there was no advantage of treatment in terms of stone-free rates, quality of life, renal function, or hospital admissions. However, some studies have shown a benefit in prevention of renal colic, hematuria, infection, or stone growth following treatment.[21]

In conclusion, the question whether asymptomatic renal stones should be treated is still largely unanswered. More evidence is required in this field to help develop definitive guidelines for clinicians. Our review of long term studies of conservative management shows an average spontaneous stone passage rate of 18% (range 8%-32%) and an average requirement for surgical intervention of 20% (range 7%-40%). Overall, 62% of patients remained safely on surveillance over a mean time of 4 years. It is highly important to involve patients in this decision-making, and these figures are useful for patient counseling. Among patients on surveillance, factors such as development of symptoms (pain or infection) or de novo obstruction should warrant surgical intervention. The role of other factors such as stone location, stone growth, stone size, and age remains inconclusive.

Staghorn calculi

Staghorn calculi are large calculi that occupy multiple calyces in the kidney. They are usually composed of magnesium ammonium phosphate (the so-called triple phosphate stones), which is closely related to urease-producing bacteria.

Traditionally, management of staghorn calculi mostly involved surgical intervention rather than medical or conservative management. This is based on the landmark paper by Blandy and Singh[21] and a previous paper by Singh et al.[22] The authors reviewed autopsy outcomes of 9,000 patients. Nine (0.001%) of these patients had staghorn calculi; the stone was symptomatic and contributed to death in >50% of them.

The authors followed up another 2 cohorts of patients: one cohort was managed surgically and another managed conservatively. The sample size was 185 patients, of which 37 were bilateral. In the surgery cohort (n=145), the rate of mortality was 5%. In the conservative management cohort (n=40), the rate of mortality was 28%. This reduction in mortality has led to recommendation for surgical management of staghorn calculi in all except the high-risk cases. The paper also reported on morbidity

in the form of renal deterioration (23%) and urinary tract infection (40%).

There have been 8 papers since the above study was published. All have documented 1 or more combinations of the following parameters: renal deterioration, dialysis requirement, urinary tract infection (UTI), and mortality.

The largest of these studies was by Koga et al.[23] In this study, the researchers retrospectively analyzed a cohort of 167 patients with staghorn calculi (191 staghorn calculi). A total of 61 (46%) patients were conservatively managed, whereas the remainder were managed with nephrolithotomy (9%), pyelolithotomy (17%), nephrectomy (25%), or partial nephrectomy (3%). Of the conservatively managed patients, 36% developed chronic renal failure, which was more common in patients with bilateral staghorn calculi. Of those who underwent active treatment, chronic renal failure rates were similar in the partial nephrectomy group (33%) but lower in the nephrectomy (21%), pyelolithotomy (11%), and nephrolithotomy (6%) groups. Common pathological findings in the nephrectomy group were chronic pyelonephritis (100%), hydronephrosis (66%), acute pyelonephritis (28%), and abscess (17%).

Teichman et al.[24] retrospectively analyzed the risk factors for renal deterioration in 177 patients who underwent treatment for staghorn calculi. Only 3 of these patients were managed conservatively because they declined treatment. In the treated group, the treatment options were SWL, PCNL, or combination treatment. The renal deterioration rate was not statistically different between the 3 treatment modalities. Significant factors associated with renal deterioration included history of stones, solitary kidney, presence of a complete staghorn calculus, hypertensive disease, neuropathic bladder, and urinary diversion. UTI was not associated with worse renal function. Overall, 20 patients (18%) died, 3 of whom died because of renal deterioration. Importantly, no patient with complete stone clearance died of renal complications, whereas 3% of patients with incomplete clearance did. All 3 patients who declined treatment died, 2 of them because of renal deterioration.

Our group (Deutsch and Subramonian[25]) followed up a prospective cohort of 22 patients with unilateral or bilateral staghorn calculi who were managed conservatively. Reasons for conservative management were comorbidities, patient choice, or poor access/anatomy. The primary outcome measures were UTI, renal deterioration, and mortality. The rate of UTI was 50%, whereas the rate of renal deterioration was 14%. Disease-specific mortality was 9%, much lower than the rate initially reported by Blandy and Singh.[21] Furthermore, we reported a dialysis dependence rate of 9%, and the rate of hospital attendances attributable to stone-related morbidity was 27%. A comparison of outcome measures between unilateral and bilateral staghorn stones showed statistically significant differences in disease-specific mortality (0% vs 40%) and morbidity (12% vs 80%) in favor of the unilateral group. Although there was a lower incidence of UTIs (41% vs 80%), renal deterioration (6% vs 40%), and dialysis requirement (6% vs 20%) in the unilateral group, these findings were not statistically significant.

These findings were corroborated by Morgan et al,[26] who reported on 29 patients with staghorn calculi managed conservatively. Renal deterioration in this cohort was higher, at 35%. There was 1 disease-specific death. Other studies by Rous and Turner[27] Vargas et al.[28] Burchard[29] and Flamm and Forstik[30] have quoted disease-specific mortality rates ranging from 0% to 30% and renal deterioration ranging from 0% to 28.5%. The data from the studies are summarized in Table 2.

In summary, conservative management of staghorn calculi for patients who are unfit for surgery or who decline intervention is perhaps not as unsafe as previously thought. Based on long term studies of conservative management of 20 or more patients with a mean follow-up of 6.4 years, the overall disease-specific mortality is 16% (range, 0%-30%) and chance of renal deterioration is 21% (range, 0%-34.5%). The incidence of infection varied between 0% and 50% with a mean of 22%. Careful patient selection (i.e., patients with asymptomatic unilateral stones, patients who are unfit for surgical intervention) and thorough patient counseling about the risks of conservative management could make it a suitable option for an appropriate subset of patients.

Ureteric stones

Small ureteric stones are ideally suited for conservative management. Initial trial of conservative management is preferred in this group, provided they have no complications (infection, refractory pain, or deterioration of kidney function).

The largest systematic review on this subject, by Yallappa et al,[31] analyzed 6,600 patients with ureteric stones managed conservatively. From the analysis of 70 studies, they concluded that the rate of spontaneous passage for stones smaller than 5 mm was 75%, compared with 62% for those larger than 5 mm, irrespective of their position in the ureter at the time of presentation. Stones discovered in the distal third of the ureter had a spontaneous passage rate of 68%, whereas those in the middle third had a rate of 58%, and those in the proximal third had a rate of 49%.

Conservative management of ureteric stones requires assessment of factors that help in the decision-making. The most important predictors of spontaneous passage rate for ureteric stones are size and location.[32] Other predictors of spontaneous

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Table 2. Summary of studies of conservative management of staghorn stones

Study	Year	Sample size managed conservatively	Mean follow-up, y	Disease-specific mortality, %	Renal deterioration, %	Urinary infection, %
Singh et al.[22]	1973	54	NA	24	14	NA
Blandy and Singh[21]	1976	40	NA	28	22.5	40
Rous and Turner[27]	1977	30	NA	30	NA	NA
Vargas et al.[28]	1982	21	6	9.5	28.5	19
Burchard[29]	1982	20	7	0	0	NA
Flamm and Forstik[30]	1987	24	NA	25	NA	NA
Koga et al.[23]	1991	61	7.8	11.4	36	1.6
Teichman et al.[24]	1995	3	7.7	66.7	100	NA
Deutsch and Subramonian[25]	2016	22	8.1	9.1	13.6	50
Morgan et al.[26]	2018	29	2	3.4	34.5	0

NA: Not applicable.

passage rate have been reported, including duration of symptoms before presentation, hydronephrosis,[33] maximum ureteric stone area,[34] C-reactive protein levels, leukocyte count,[35] neutrophil-to-lymphocyte ratio,[36] and peri-calculus ureteral thickness.[37] Our review studied a novel factor called proximal to distal ureteric ratio in predicting the stone passage with high diagnostic accuracy.[38]

In conclusion, conservative management is a well-recognized treatment option for the management of asymptomatic stones. Provision for conservative management of asymptomatic stones has been proposed in the guidelines by the European Association of Urology,[4] British Association of Urological Surgeons,[39] and American Urology Association.[40] Careful selection of patients, counseling regarding the possible complications, and appropriate monitoring are the cornerstones of conservative management.

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