



Asymptomatic Renal Stones—to Treat or Not to Treat

Necole M. Streeper¹

Published online: 17 March 2018
© Springer Science+Business Media, LLC, part of Springer Nature 2018

Abstract

Purpose of Review There are no current guidelines on the optimal management of asymptomatic renal stones. This review summarizes the current literature, focusing on more recent studies that have been done to grow the body of evidence on this topic.

Recent Findings Recent studies have found that stone size is a significant predictor of need for future surgical intervention, with > 7 mm for pediatric population and > 4 mm for residual fragments after both PNL and ureteroscopy (URS). The role of URS has been better defined with a recent RCT concluding that URS and SWL had comparable outcomes for an asymptomatic lower pole stone < 1 cm.

Summary The treatment decision for asymptomatic renal stones should take into consideration a variety of relevant patient and stone factors; however, ultimately, a shared decision-making approach should be used. In the properly counseled patient, active surveillance or prophylactic surgical intervention may be appropriate.

Keywords Renal stones · Treatment · Asymptomatic · Observation · Residual fragments

Introduction

Nephrolithiasis affects an estimated 8.8% of American adults with annual medical care costs in the USA exceeding \$2 billion [1, 2]. With the increased utilization of radiologic studies, detection of asymptomatic kidney stones is increasingly prevalent as an incidental finding [2, 3]. We are then faced with the decision to treat or not to treat these asymptomatic stones, which is an ongoing controversy for urologists.

With no clear consensus on the optimal management of asymptomatic renal stones, the decision requires extensive patient counseling. To assist with this, over the years, several studies have attempted to better characterize the natural history of asymptomatic stones. Historically, there is a paucity of literature on this topic with many of the studies retrospective in nature with a small number of

patients followed over a relatively short period of time. Understanding the importance of this topic and a shift in medicine to include shared decision-making with patients, several more recent studies have been done to grow the body of evidence to improve patient outcomes and management of asymptomatic renal stones.

When making the decision to treat or observe asymptomatic renal calculi, one must take into account the likelihood of success for spontaneous stone passage; risk of stone growth; associated morbidity; and possibly most importantly, patient preference. Argument for conservative management or observation is that the stone may never become symptomatic and avoids unnecessary morbidity from surgical interventions. The argument for prophylactic surgical intervention is that in a patient that is medically fit for surgery, treating a stone that will likely require intervention in the future may prevent the morbidity of an acute event and may have more success at achieving stone-free status prior to stone growth. This review article will evaluate the current literature for the management of asymptomatic renal stones, specifically focusing on the natural history, patient and stone factors that should be considered, shared decision-making, active surveillance imaging, surgical modality for intervention, and the natural history of residual fragments after intervention.

This article is part of the Topical Collection on *Endourology*

✉ Necole M. Streeper
nstreeper@pennstatehealth.psu.edu

¹ Division of Urology, Penn State Milton S. Hershey Medical Center, Mail Code H055, 500 University Drive, PO Box 850, Hershey, PA 17033-0850, USA

Natural History of Asymptomatic Renal Calculi

Several studies have described the natural history of asymptomatic renal stones to better define if prophylactic surgical intervention is necessary. These studies provide the basis for counseling patients on the risk of stone progression for those who choose conservative management. Many of the studies have defined stone progression as development of symptoms, stone growth, spontaneous stone passage, and need for surgical intervention.

Most recently, Dropkin et al. in 2015 retrospectively reviewed those with non-obstructing asymptomatic renal stones, identifying 160 stones among 110 patients with an average follow-up of 41 ± 19 months [4•]. Routine surveillance imaging was performed and on follow up, 28% of the stones progressed to causing symptoms, with 3% causing silent obstruction necessitating surgical intervention. The only significant predictor for need for intervention was location, with non-lower pole stones more likely than lower pole stones to become symptomatic (40.6 vs 24.3%, $p = 0.047$) or spontaneously pass (14.5 vs 2.9%, $p = 0.016$). The majority of the patients remained asymptomatic, with 20% requiring surgical intervention for symptomatic progression and 7% spontaneously passing their stone.

Prior retrospective studies, with varying lengths of follow-up, have found somewhat conflicting progression rates (31.8%–77%) and similar low surgical intervention rates (7.1–26%) [5–8]. In 1992, Glowacki et al. was one of the first to report on the natural history of asymptomatic renal stones [5]. They examined 107 patients with an average follow up of 31.6 months and reported a 31.8% rate of progression to a symptomatic stone event. Of those, 16.8% ultimately required surgical intervention. In one of the largest cohort studies ($N = 347$), Kang et al. reported that approximately half of the patients with asymptomatic renal stones progressed to symptomatic disease or demonstrated stone growth, with 24.5% requiring surgical intervention [6]. Koh et al. found a similar risk of stone progression; 45.9% however reported a lower risk of surgical intervention (7.1%) [7]. On the other hand, Burgher et al. reported a 77% rate of progression and 26% rate of surgical intervention, in a cohort of 300 men, followed for a mean of 3.26 years [8].

Patient Factors to Consider

There is a paucity of supportive literature about patient factors that influence treatment decisions for asymptomatic renal stones. There are certain patient factors in which one may favor prophylactic surgical treatment over active surveillance, and vice versa. See Table 1 for summary of factors to consider for management of asymptomatic renal stones. Patient factors

that are important to consider include age of patient, co-morbidities, pregnancy, renal insufficiency, occupation, and access to medical care.

Consideration should be given for prophylactic surgical intervention in high-risk populations, such as severe renal insufficiency, immunocompromised, female planning future pregnancy, certain occupations (e.g., pilot, military, long-haul truck drivers, business travelers), and in those with poor access to medical care [9]. Anyone that is not willing to or unable to have routine follow-up care with surveillance imaging, possibly secondary to limited access or other social factors, should be considered for prophylactic surgical intervention as well.

There is a role for observation in patients with significant co-morbidities who are not fit for surgery. If progression occurs in this population, less morbid procedures such as stent placement or nephrostomy tube placement may be the most appropriate treatment. However, each patient is evaluated on an individual basis and ultimately requires weighing patient factors with patient preference. Asymptomatic renal stones in pregnant patients should also be observed, as both percutaneous nephrolithotomy (PNL) and shockwave lithotripsy (SWL) are contraindicated, and general anesthesia may put both the patient and fetus at risk.

Previously, there was no evidence on the management of asymptomatic renal stones in the pediatric population. In 2017, Telli et al. performed a retrospective review of 242 pediatric patients with asymptomatic lower pole renal stones < 10 mm in size [10•]. Using a multivariate analysis, they found that children with stone size > 7 mm, renal anomalies, and cystine or struvite composition were statistically significant predictors of need for future surgical intervention. The stone progression rate was high in this population, at 61.2%, which was characterized as the development of pain, infection, obstruction, or stone growth. Similarly, Dos Santos et al. retrospectively reviewed 224 pediatric patients with asymptomatic lower pole stones and found that stone size > 7 mm and stone growth were significant predictors of need for future surgical intervention [11•]. They reported a 53.6% rate of spontaneously passed stones; 25% remained asymptomatic and 21.4% ultimately required surgical intervention after an initial period of observation.

Stone and Anatomical Features to Consider

There are certain stone and anatomical features that are important to consider as they can influence the likelihood of stone progression or need for surgical intervention. Such factors include stone size and location, presence of obstruction, solitary kidney, rate of stone growth, and calyceal diverticular stones (see Table 1).

Table 1 Factors to consider during treatment decision-making for asymptomatic renal stones

Patient factors	Anatomical features	Stone features
<ul style="list-style-type: none"> • Pediatric • Co-morbidities • Renal insufficiency • Pregnancy • Occupation • Access to care 	<ul style="list-style-type: none"> • Solitary kidney • Calyceal diverticulum 	<ul style="list-style-type: none"> • Size • Location (renal pelvis/ lower pole) • Obstruction • Rate of stone growth

The likelihood of spontaneous stone passage correlates with stone size, and the AUA guidelines recommend an initial trial of observation for uncomplicated ureteral stones < 10 mm [12]. Previously discussed retrospective studies on the natural history of asymptomatic renal stones in adults concluded that larger stone size (≥ 4 mm) was predictive of stone progression and in children, stone size > 7 mm was predictive of need for future surgical intervention [8, 10, 11]. Therefore, stone size plays a role when counseling patients about the prophylactic treatment for asymptomatic renal stones.

As stones progress in size up to 10 mm and the likelihood of spontaneously sequentially decreases, prophylactic treatment may be preferred secondary to the higher probability of needing surgical intervention eventually. Prophylactic treatment in these instances may avoid the experience of an acute episode with need for urgent treatment. Although not well studied, the rate of stone growth may also be an important factor. For example, continued observation of a stone that took 10 years to grow 1 mm may be more appropriate vs 1 mm growth in 6 months, despite similar overall stone size.

Stone location is another important factor to consider. The majority of asymptomatic stones are in the lower pole, and as previously discussed, lower pole stones are less likely to become symptomatic or spontaneously pass [4, 8]. In the only prospective study, Inci et al. evaluated a smaller cohort of 24 patients with asymptomatic lower pole renal stones, mean size 8.8 mm and mean follow-up of 52.3 months [13]. There was a progression rate of 33% with only one-third of those requiring surgical intervention (overall 11%). Another study performed a literature review for best management of lower pole calculi, concluding that lower pole stone less than 1 cm may be observed with equal morbidity outcomes as shock wave lithotripsy and ureteroscopy [14]. On the other hand, stones located in the renal pelvis have been found to have higher risk of stone progression and are not good candidates for observation [8].

The majority of asymptomatic stones are non-obstructing. If obstruction is present, one should strongly consider surgical intervention since there is a risk of permanent renal damage if obstruction persists. One exception to this may be in the case of a chronically obstructed non-functioning kidney that is otherwise asymptomatic. Counseling about risk of infection is

necessary; however, in the properly selected patient, conservative management may be favorable.

Anatomical features should also factor into the decision process. Prophylactic surgical intervention should be strongly considered in the case of a solitary kidney. There is a higher risk of renal failure in this population with obstruction during spontaneous stone passage. Asymptomatic calyceal diverticular stones is a case were conservative management may be appropriate. There is no literature evaluating the role for observation in asymptomatic calyceal diverticular stones; however, with no risk of spontaneous passage, this is certainly an option.

Shared Decision-Making

In recent years, the patient-physician relationship has evolved with an increased emphasis on patient involvement through shared decision-making. This becomes exceedingly important for asymptomatic renal stones in which more than one suitable management strategy often exists. The process involves adequately informing patients about the risks and benefits of each management strategy. With this paradigm shift, there is an increased emphasis on the assessment of patients' preferences and allows patients to take an active role in the management of their stone disease. However, it is important to note that patients often look to their physicians to make treatment decisions [15].

One study performed a survey to better understand patient decision-making for asymptomatic renal stones [16]. Patients were given a hypothetical scenario of an asymptomatic 8-mm lower pole renal stone and were informed of the risks and benefits for observation, SWL, and ureteroscopy (URS). They found that patients were more likely to prophylactically treat their asymptomatic stone with surgical intervention compared to observation (77 vs 23%), with the majority choosing SWL (61.5%). Patients were more likely to choose procedures that they have previously experienced. Despite patients wanting to play an active role in their stone management, they found that 56.4% of patients prefer to defer treatment decisions to their urologist.

Not to Treat—Active Surveillance Imaging

Review of the literature suggests that conservative management with observation is appropriate as long as patients are appropriately counseled. Both the AUA and EAU guidelines state that active surveillance is an option for asymptomatic, non-obstructing renal stones, citing evidence level grade C [12, 17]. However, a proper surveillance imaging protocol is necessary to monitor for stone growth or new stone formation. Typically, alternating between KUB and renal ultrasound with low-dose CT imaging is largely dependent on physician preference. There are no guidelines on the optimal modality or frequency of surveillance imaging; however, CT scan may be the preferred modality for patients that are morbidly obese, those with a stone with low HU density or known to be radiolucent and small stone size (< 3 mm) that may be more difficult to visualize by KUB or ultrasound. Timing of this should typically be at 6 months or annually, depending on the size of stone and likelihood of progression [18].

In addition to active surveillance imaging, patients should be offered metabolic evaluation to direct preventative strategies, such as dietary modification and/or medical therapy [19]. This may help prevent further stone growth and reduce the need for future surgical intervention. Furthermore, this strategy provides patients with an active role in preventing the progression of their stone disease, rather than being passive observers.

To Treat—Deciding on Modality of Surgical Treatment

In addition to the decision to treat or not to treat, there is no consensus on the appropriate timing or surgical modality if treatment is elected. It is extremely important to consider the morbidity of these procedures in an otherwise asymptomatic patient, and the risks and benefits should be carefully weighed. However, with proper patient counseling, prophylactic surgical intervention may be an appropriate decision.

In 2010, Yuruk et al. performed a three-armed randomized controlled trial (RCT), comparing PNL, SWL, and observation for asymptomatic lower pole renal stones < 2 cm in diameter [20]. The 3 month stone-free rate was 97% for PNL, 55% for SWL, and 0% for observation which was statistically significant. They also showed that PNL, in comparison to SWL, had less renal scarring (3 vs 16%) and lower rate of additional procedures (0 vs 10%) at a mean follow-up of 19.3 months. The observation group had a rate of 22% for future surgical intervention, concluding that if prophylactic treatment for an asymptomatic lower pole renal stone is chosen, both PNL and SWL are acceptable modalities with PNL providing better stone clearance and less renal scarring. In 2001, Keely et al. performed an RCT to compare active surveillance with SWL in patients with asymptomatic renal

stones < 15 mm ($N=228$); there were no differences in stone-free rates, need for secondary procedures, or quality of life during follow-up of 2 years [21].

Previously, there were no RCTs evaluating the role of ureteroscopy for asymptomatic renal stones. Sener et al. have recently attempted to address this by performing a three-armed RCT, randomizing patients with asymptomatic single lower pole stones < 1 cm to URS, SWL, and observation [22•]. The stone-free rate for URS was 92 and 90% for SWL after an average of 1.48 ± 0.65 sessions. During the 2-year follow-up period, the observation group had a 12% rate of developing symptoms or stone growth, concluding that each treatment option is suitable.

Asymptomatic Residual Fragments after Surgical Treatment

Patients should be informed that there is a risk of residual stone fragments after any surgical intervention. Recent literature has evaluated the natural history of asymptomatic residual fragments following both PNL and URS. In 2016, Olvera-Posada et al. evaluated the natural history of residual fragments after PNL and found that residual fragments > 4 mm, and struvite or apatite composition, were associated with higher likelihood to require surgical intervention during mean follow-up of 57.9 months [23•].

Similar results have been shown for residual fragments after ureteroscopy. In 2016, Chew et al. performed a multicenter retrospective review of the natural history of asymptomatic residual fragments following ureteroscopy ($N=232$) [24•]. They reported that 56% of patients remained asymptomatic with a mean follow-up of 16.8 months. Of the patients, 29% required a secondary procedure. In addition, they concluded that residual fragment size > 4 mm after ureteroscopy was associated with significantly higher rate of stone growth and need for re-intervention. Previously, in 2011, Rebeck et al. evaluated the natural history of residual fragments < 4 mm after ureteroscopy ($N=51$) and found that nine patients (19.6%) had a subsequent stone event over a mean follow-up of 2.2 years [25]. Six of those patients (11.8%) required re-intervention for development of symptomatic disease; 21.7% of the patients spontaneously passed their stone within the same timeframe.

Conclusions

The treatment decision for asymptomatic renal stones should take into consideration a variety of relevant patient and stone factors; however, ultimately, a shared decision-making approach should be adopted to tailor the best treatment plan to each individual patient. In the properly counseled patient,

conservative management with active surveillance imaging is an appropriate initial treatment strategy for asymptomatic renal stones. Although approximately 50% of asymptomatic renal stones will progress to symptomatic disease, the majority of patients will not require surgical intervention. However, risk stratification is essential to identifying high-risk patients who may benefit from prophylactic surgical intervention.

Table 2 provides a summary of the recently added literature for the optimal management of asymptomatic renal stones. The first studies on the natural history of asymptomatic renal stones in the pediatric population show that stone size > 7 mm is a significant predictor of need for future surgical intervention. Secondly, recent studies have suggested that residual fragments > 4 mm after both PNL and URS are associated with higher likelihood for re-intervention. Finally, and perhaps

most importantly, the role of URS in the management of these patients has been better defined with a recent three-armed RCT comparing URS, SWL, and observation for an asymptomatic lower pole renal stone < 1 cm. Both URS and SWL had comparable outcomes, and the observation group had a low rate of developing symptoms, concluding that each is a suitable treatment option.

As we continue to make advances on the optimal management of asymptomatic renal stones, continued emphasis should be placed on improving the shared decision-making process. With increased focus in contemporary medicine on patient-reported outcomes such as patient satisfaction and health-related quality of life, future work may be necessary to evaluate the impact shared decision-making for the management of asymptomatic renal stones has on both.

Table 2 Summary of recent literature for the management of asymptomatic renal stones

Study	Year	Number	Mean FU (months)	Mean stone size	Study design	Summary of results
Sarkissian et al.	2013	101	NA	NA	Survey	Patients were given a hypothetical scenario of asymptomatic 8-mm lower pole stone. Of those, 22.8% chose observation, 29.7% URS, and 47.5% SWL. Patients' past experience with stone pain and surgical procedures significantly influenced their treatment choice. Of the patients, 56.4% prefer to defer treatment decisions to their physician.
Kang et al. [19]	2013	347	31.0	4.4 mm	Retrospective	Approximately half of patients with asymptomatic renal stones progressed to symptomatic disease or demonstrated stone growth, with 24.5% requiring surgical intervention.
Sener et al. [17]	2015	150	21.2	8.0 mm	RCT	URS, SWL, and observation were compared a for single lower pole renal stone < 1 cm. Stone-free rates were 92% for URS and 90% for SWL (no. of sessions 1.48 ± 0.65). Observation group had a 12% rate of stone progression over 2-year follow-up.
Dropkin et al. [7]	2015	110	41.0	7.0 mm	Retrospective	Natural history of asymptomatic renal stones was evaluated, finding 72% remained asymptomatic. Lower pole stones were less likely to become symptomatic or spontaneously pass.
Olvera-Posada et al.	2016	44	57.9	5.5 mm	Retrospective	Natural history of residual fragments after PNL was evaluated. Residual fragments > 4 mm, and struvite or apatite composition, were associated with higher likelihood to require surgical intervention.
Chew et al.	2016	232	16.8	NA	Multicenter/ retrospective	Natural history of asymptomatic residual fragments following ureteroscopy was reviewed. Of the patients, 56% remained asymptomatic and 29% required a secondary procedure. Residual fragment size > 4 mm after ureteroscopy was associated with significantly higher rate of stone growth and need for re-intervention.
Dos Santos et al.	2016	224	28.5	5.0 mm	Retrospective	Pediatric study evaluating asymptomatic lower pole renal stones. Of those, 53.6% spontaneously passed, 25% remained asymptomatic, and 21.4% ultimately required surgical intervention.
Telli et al.	2017	242	40.8	7.4 mm	Retrospective	Pediatric study evaluating asymptomatic lower pole renal stones < 10 mm. Estimated stone progression rate of 61.2%. Stone size > 7 mm, renal anomalies, and cystine or struvite composition were statistically significant predictors of need for future surgical intervention.

Compliance with Ethical Standards

Conflict of Interest Necole M. Streeper declares no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by the author.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Scales CD, Smith AC, Hanley JM, Saigal CS. Urologic diseases in America project. Prevalence of kidney stones in the United States. *Eur Urol.* 2012;62(1):160–5.
2. Pearle MS, Calhoun EA, Curhan GC. Urologic diseases in America project: urolithiasis. *J Urol.* 2005;173:848–57.
3. Boyce CJ, Pickhardt PJ, Lawrence EM, Kim DH, Bruce RJ. Prevalence of urolithiasis in asymptomatic adults: objective determination using low dose noncontrast computerized tomography. *J Urol.* 2010;183:1017–21.
- 4.• Dropkin BM, Moses RA, Devang S, Pais VM Jr. The natural history of nonobstructing asymptomatic renal stones managed with active surveillance. *J Urol.* 2015;193:1265–9. **Retrospective review of 110 patients with 160 renal stones, 72% remained asymptomatic with average follow up of over 3 years**
5. Glowacki LS, Beecroft ML, Cook RJ, Pahl D, Churchill DN. The natural history of asymptomatic urolithiasis. *J Urol.* 1992;147(2):319–21.
6. Kang HW, Lee SK, Kim WT, Kim YJ, Yun SJ, Lee SC, et al. Natural history of asymptomatic renal stones and prediction of stone related events. *J Urol.* 2013;189(50):1740–6.
7. Koh LT, Ng FC, Ng KK. Outcomes of long-term follow-up of patients with conservative management of asymptomatic renal calculi. *BJU Int.* 2012;109:622–5.
8. Burgher A, Beman M, Holtzman JL, Monga M. Progression of nephrolithiasis: long-term outcomes with observation of asymptomatic calculi. *J Endourol.* 2004;18:534–9.
9. Goldsmith ZG, Lipkin ME. When (and how) to surgically treat asymptomatic renal stones. *Nat Rev Urol.* 2012;9:315–20.
- 10.• Telli O, Hamidi N, Bagci U, Demirbas A, Hascicek AM, Soygur T, et al. What happens to asymptomatic lower pole kidney stones smaller than 10 mm in children during watchful waiting? *Pediatr Nephrol.* 2017;32(5):853–7. **Retrospective review of 242 pediatric patients with asymptomatic lower pole renal stones < 10 mm in size, estimated stone progression rate of 61.2%. Stone size > 7mm, renal anomalies, and cystine or struvite composition were statistically significant predictors of need for future surgical intervention**
- 11.• Dos Santos J, Lopes RI, Veloso AO, Harvey E, Farhat WA, Papanikolaou F. Outcome analysis of asymptomatic lower pole stones in children. *J Urol.* 2016;195:1289–93. **Retrospective review of 224 pediatric patients, reported a 53.6% rate of spontaneously passed stones, 25% remained asymptomatic and 21.4% ultimately required surgical intervention**
12. Assimos D, Krambeck A, Miller NL, Monga M, Murad MH, Nelson CP, et al. Surgical management of stones: American Urological Association/Endourological Society guideline. *J Urol.* 2016;196(4):1153–69.
13. Inci K, Sahin A, Islamoglu E, Eren MT, Bakkaloglu M, Ozen H. Prospective long-term followup of patients with asymptomatic lower pole caliceal stones. *J Urol.* 2007;177:2189–92.
14. Raman JD, Pearle MS. Management options for lower pole renal calculi. *Curr Opin Urol.* 2008;18(2):214–9.
15. Omar M, Tarplin S, Brown R, Sivalingam S, Monga M. Shared decision making: why do patients choose ureteroscopy? *Urolithiasis.* 2016;44(2):167–72.
16. Sarkissian C, Noble M, Li J, Monga M. Patient decision making for asymptomatic renal calculi: balancing benefit and risk. *Urology.* 2013;81:236–40.
17. Turk C, Petrik A, Sarica K, Seitz C, Skolarikos A, Straub M, et al. EAU guidelines on diagnosis and conservative management of urolithiasis. *Eur Urol.* 2016;69(3):468–74.
18. Skolarikos A, Laguna MP, Alivizatos G, Kural AR, de la Rosette JJ. The role for active monitoring in urinary stones: a systematic review. *J Endourol.* 2010;24(6):923–30.
19. Pearle MS, Goldfarb DS, Assimos DG, Curhan G, Denu-Ciocca CJ, Matlaga BR, et al. Medical management of kidney stones: AUA guideline. *J Urol.* 2014;192:316–24.
20. Yuruk E, Binbay M, Sari E, Akman T, Altinyay E, Baykal M, et al. A prospective randomized trial of management for asymptomatic lower pole calculi. *J Urol.* 2010;183(4):1424–8.
21. Keely FX Jr, Tilling K, Elves A, Menezes P, Wills M, Rao N, et al. Preliminary results of a randomized controlled trial of prophylactic shock wave lithotripsy for small asymptomatic renal calyceal stones. *BJU Int* 2001; 87 (1): 1–8.
- 22.•• Sener NC, Bas O, Sener E, Zengin K, Ozturk U, Altunkol A, et al. Asymptomatic lower pole small renal stones: shock wave lithotripsy, flexible ureteroscopy or observation? A prospective randomized trial. *Urology.* 2015;85:33–7. **RCT randomizing patients with asymptomatic single lower pole stones <1cm to ureteroscopy, shockwave lithotripsy, and observation. The stone free rate for URS was 92% and 90% for SWL after an average of 1.48±0.65 sessions. Observation group had a 12% rate of stone progression over 2 year follow-up**
- 23.• Olvera-Posada D, Ali SN, Dion M, Alenezi H, Denstedt JD, Razvi H. Natural history of residual fragments after percutaneous nephrolithotomy: evaluation of factors related to clinical events and intervention. *Urology.* 2016;97:46–50. **Retrospective review of 44 out of 781 patients with residual fragments after PNL. Residual fragments > 4mm, and struvite or apatite composition, were associated with higher likelihood to require surgical intervention during mean follow up of 57.9 months**
- 24.• Chew BH, Brotherhood HL, Sur RL, Wang AQ, Knudsen BE, Yong C, et al. Natural history, complications, and re-intervention rates of asymptomatic residual stone fragments after ureteroscopy: a report from the EDGE Research Consortium. *J Urol.* 2016;195:982–6. **A multicenter retrospective review of the natural history of asymptomatic residual fragments following ureteroscopy, including 232 patients. They reported that 56% of patients remained asymptomatic with a mean follow up of 16.8 months. 29% of patients required a secondary procedure. In addition, they concluded that residual fragment size > 4mm after ureteroscopy was associated with significantly higher rate of stone growth and need for re-intervention**
25. Rebeck DA, Macejko A, Bhalani V, Ramos P, Nadler RB. The natural history of renal stone fragments following ureteroscopy. *Urology.* 2011;77(3):564–8.