

Acute management of symptomatic nephrolithiasis

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Received: April 23, 2014 Revised: May 23, 2014

Accepted: August 27, 2014

Published online: November 24, 2014

Abstract

Over half a million patients present to emergency departments and nearly 3 million patients visit healthcare providers annually due to problems associated with urolithiasis. Despite updated guidelines from the American Urological Association and European Association of Urology for the evaluation and management of nephrolithiasis, considerable variability still exists regarding treatment for acute symptomatic upper urinary tract stones. Therefore, this article will review the current evaluation and management of acute symptomatic nephrolithiasis. Initial management includes analgesia and antiemetics. Additionally, a urinalysis and creatinine are required laboratory evaluations. Acute imaging with a non-contrast computed tomography (CT) scan is the diagnostic imaging modality of choice. However, concerns over radiation exposure have led towards low-dose and even ultra-low-dose protocols for the detection of urinary calculi. Low-dose non-contrast CT scans are now standard of care for the initial diagnosis of renal colic in patients with a body mass index ≤ 30 . Medical expulsive therapy is recommended for patients with a ureteral calculus < 10 mm and no signs of infection. Emergency urinary decompression is mandatory for a specific subset of patients, especially those with infection. Although limited data exists, emergency ureteroscopy or even shock wave lithotripsy may also be

therapeutic options.

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Key words: Nephrolithiasis; Low-dose computed tomography scan; Medical expulsive therapy; Ureteroscopy; Extracorporeal shockwave lithotripsy

Core tip: Despite updated guidelines from the American Urological Association and European Association of Urology for the evaluation and management of nephrolithiasis, considerable variability still exists regarding treatment for acute symptomatic upper urinary tract stones, especially in regards to imaging modalities used in the emergency department. Acute imaging with a non-contrast computed tomography scan is the diagnostic imaging modality of choice. However, concerns over radiation exposure have led towards low-dose and even ultra-low-dose protocols for the detection of urinary calculi. Low-dose non-contrast computed tomography scans are now standard of care for the initial diagnosis of renal colic in patients with a body mass index ≤ 30 .

Sterling M, Ziemba J, Mucksavage P. Acute management of symptomatic nephrolithiasis. *World J Clin Urol* 2014; 3(3): 161-167 Available from: URL: <http://www.wjgnet.com/2219-2816/full/v3/i3/161.htm> DOI: <http://dx.doi.org/10.5410/wjcu.v3.i3.161>

INTRODUCTION

Over half a million patients present to emergency departments (ED) and nearly 3 million patients visit healthcare providers annually due to problems associated with urolithiasis^[1]. This has led to nearly \$5 billion spent annually in the United States for hospitalizations, procedures, and time lost from work associated with renal/ureteral stone disease^[2]. Despite updated guidelines from the American Urological Association (AUA) and European Associa-

tion of Urology (EAU) for the management of ureteral calculi, considerable variability exists among practitioners. In this review, the acute management of nephrolithiasis will be discussed with a particular emphasis on diagnostic imaging choice, initial medical therapy, and acute surgical interventions.

PRESENTATION

Patients with nephrolithiasis typically present with acute flank pain with or without radiation to the groin. This is referred to as renal colic. The pain is described as colicky in nature because it is intermittent and associated with restlessness, differing from peritonitic pain where patients often remain still. The pain is thought to arise due to obstruction of the ureter with continued peristalsis or spasms of the ureter around the stone. Additionally, obstruction can lead to hydronephrosis and/or hydroureter with pain arising due to distention of the collecting system and renal capsule^[3]. The level of the pain can often give a hint as to its location in the collecting system. For example, stones in the proximal ureter present with classic isolated flank pain, while ureterovesical junction (UVJ) stones often present with groin pain associated with frequency, urgency, and dysuria due to irritation of the bladder^[3]. In addition to renal colic, patients often present with nausea and vomiting. Furthermore, microscopic or gross hematuria can be a presenting sign of nephrolithiasis due to irritation of the mucosa by the stone or a coexisting urinary tract infection (UTI). Close attention needs to be paid to patients presenting with suspected nephrolithiasis and signs and symptoms of a UTI or sepsis as these patients may require emergency surgical intervention.

INITIAL DIAGNOSTIC IMAGING

A thorough history and physical examination is the first step in the evaluation of suspected renal colic. This is particularly important given the often non-specific flank or groin pain associated with nephrolithiasis. Once renal colic is suspected, diagnostic imaging should be performed with the choice of modality selected based on patient type. In the adult, non-pregnant patient, the preferred initial imaging modality of choice is a non-contrast computed tomography (NCCT) due to its high sensitivity (Median 98%) and high specificity (Median 97%) for identifying urinary calculi^[4]. This sensitivity and specificity compares favorably to other imaging modalities (Table 1). NCCT scans not only accurately report the presence of stones, but also the size, location, density *via* Hounsfield units, evidence of obstruction, and skin to stone distance, which all help to determine the need for surgical intervention^[5]. Additionally, they also provide information on alternative diagnoses such as appendicitis and diverticulitis.

Although NCCT are valuable in diagnosing urinary calculi, one disadvantage is the delivery of ionizing radiation. Recent investigations have shown an increased

Table 1 Median sensitivity and specificity in detecting nephrolithiasis for various imaging modalities

Imaging modality	Sensitivity ¹	Specificity ¹
Non-contrast CT	98%	97%
Abdominal X-ray	57%	76%
Intravenous pyelogram	70%	95%
Renal/bladder ultrasound	61%	97%
MRI	82%	98%

¹Information from this table obtained from Ref. [4]. MRI: Magnetic resonance imaging; CT: Computed tomography.

risk of a secondary malignancy after just 2-3 computed tomography (CT) scans in a single year, with an estimated 1.5%-2.0% of all cancers in the United States being attributed to the radiation from CT scans^[5-8]. Additionally, nearly 50% of all radiation received by the United States population is a direct result of medical imaging, much of which is related to CT usage^[9]. Furthermore, it has been estimated that the risk of cancer is 1 in 200 for every 100 mSv of radiation received^[10]. This information is critical given the effective dose of radiation for a standard dose NCCT scan is 10 mSv^[11,12].

As a response to the risk of ionizing radiation delivered by standard dose NCCT, low-dose NCCT (LD-NCCT) protocols were developed. This imaging has an effective dose of radiation of 4 mSv^[13] or less. A study by Poletti *et al*^[14] assessed 125 consecutive patients admitted to the emergency department for renal colic with both a standard dose and LD-NCCT scan. LD-NCCT scans had a 97% sensitivity and 96% specificity for the diagnosing of renal colic based on either direct identification of a calculi or *via* indirect signs of a calculi (*i.e.*, hydroureteronephrosis, perinephric stranding, *etc.*)^[14].

When stratified by stone size, a LD-NCCT scan was equivalent to a standard dose NCCT scan for stones ≤ 3 mm in patients with a body mass index (BMI) < 30 ^[14]. In patients with stones < 3 mm, a LD-NCCT scan performed worse with a sensitivity of 83%^[14]. Additionally, LD-NCCT scans resulted in $\pm 20\%$ size variation as compared to standard dose NCCT scan^[14]. Despite these limitations, the authors noted no change in their clinical decision-making^[14]. Furthermore, the majority of stones < 3 mm rarely require urgent urologic procedures and often will pass spontaneously^[14].

When examining the effectiveness of LD-NCCT, BMI also is important. For patients with a BMI ≥ 30 , a standard dose NCCT is still preferred. Poletti *et al*^[14] reported only 50% sensitivity and 89% specificity in patients with BMI ≥ 30 as opposed to 95% sensitivity and 97% specificity for patients with a BMI < 30 . Similar investigations have demonstrated equivalent results^[15,16].

Additional studies have suggested that ultra LD-NCCT scans can be used for patients with a BMI < 30 without significant loss of sensitivity or specificity^[17]. Udayasankar *et al*^[18] investigated the use of ultra-low dose CT scans (mean effective radiation dose of 2.10 mSv)

in 163 patients presenting to the ED with abdominal pain and found a high sensitivity (100%) and specificity (98.5%) for detection of free air, stones, and intestinal obstruction^[18]. Additionally, overall there was a high sensitivity (86%) and specificity (96%) for identifying other sources of abdominal pain with the conclusion that ultra-low dose NCCT scans provide accurate diagnostic information and very low radiation doses^[18] in patients presenting with acute abdominal pain.

The AUA guidelines recommend the use of a LD-NCCT as the preferred initial imaging modality for patients with a BMI ≤ 30 who are presenting with symptoms of renal colic or in those with a prior history of urinary stones. However, in those with a BMI ≥ 30 , LD-NCCT may be used, although the preferred imaging modality would be a standard dose NCCT. At this time, there is not enough data available to recommend an ultra LD-NCCT scan.

FOLLOW-UP DIAGNOSTIC IMAGING

A recent review of the National Hospital Ambulatory Medical Care Survey estimated that approximately 5%-10% of visits to the ED for nephrolithiasis were return visits^[19]. While LD-NCCT is the imaging modality of choice during the initial presentation, Goldstone and Bushnell reported that repeat CT imaging of known nephrolithiasis changed the diagnosis in only a small percentage of patients^[11]. Therefore, the AUA recommends that initial imaging should include a renal ultrasound (RUS) and KUB in patients presenting with a known radio-opaque ureteral/kidney stone and persistent symptoms^[4]. If no hydronephrosis or stone is identified on KUB or RUS and the patient is still symptomatic, then a LD-NCCT scan is recommended^[4]. In those with radio-lucent stones and persistent symptoms, RUS can be used to assess for hydronephrosis with a clinical decision made whether to repeat a NCCT based on the RUS results^[4].

INITIAL MANAGEMENT

The initial management for renal colic is supportive care with analgesia and anti-emetics. The mainstay of pain control for renal colic includes non-steroidal anti-inflammation drugs (NSAIDs) and narcotic medications. NSAIDs have been shown to provide improved pain relief *vs* narcotics without the added side effects of nausea or vomiting^[3]. Therefore, an oral or intravenous NSAID is first line therapy^[3]. Narcotic medications can be added for additional relief. Furthermore, antiemetic medication can be utilized as needed for nausea and/or vomiting often associated with renal colic. There is no evidence supporting increased fluid intake for acutely symptomatic stones to help with spontaneous passage; however, increased fluid intake may help prevent future stones. Patients being treated conservatively should strain their urine for confirmation of passage and for analysis^[3].

INITIAL LABORATORY AND URINE EVALUATION

According to the EAU guidelines, all patients presenting with acute symptomatic nephrolithiasis should have a urine dipstick to assess for blood in the urine, leukocytes for signs of inflammation, and nitrite to assess for specific bacteria and thus infected urine^[20]. If the urine dipstick is suspicious for infection, a urine culture should be sent^[20]. Additionally, all patients should have a creatinine level to assess for acute kidney injury and the possibility of an obstructive process^[20]. In patients with a fever, evaluation should also include a complete blood count [for analysis of a patient's white blood cell (WBC) count for evidence of inflammation or infection] and C-reactive protein^[20]. Additional studies can include a basic metabolic panel for analysis of sodium and potassium levels in those with nausea and vomiting^[20].

INDICATIONS FOR CONSULTATION

Many patients with an acute episode of nephrolithiasis initially present to their primary care physician or the ED. At our institution we recommend consulting urology if pain is intractable, the patient is unable to tolerate an oral diet due to persistent nausea or vomiting, there is evidence of obstructive uropathy, concurrent UTI is suspected, or in any patient with a solitary or transplant kidney. If the patient is to be discharged from a primary care physician or ED, we generally recommend urology outpatient follow up in 1-2 wk in all cases of nephrolithiasis.

EMERGENCY DECOMPRESSION

The majority of patients (83%) presenting with nephrolithiasis will pass their stone without any need for intervention^[21]. Furthermore, 95% of these patients will pass their stone within 6 wk^[21]. While most patients will eventually pass small ureteral stones, clear indications for decompression in the acute management of ureteral stones includes the presence of infection, intractable pain or vomiting, obstruction in a solitary or transplant kidney, bilateral obstructing stones, or relief of ureteral calculi obstruction in pregnant females pending definitive management post-partum^[20]. Randomized controlled trials (RCTs) have shown ureteral stenting and percutaneous nephrostomy (PCN) tubes are equally effective for emergency decompression of the urinary system^[22]. A small RCT of 42 patients by Pearle *et al*^[22] investigated ureteral stent *vs* PCN tube for obstructive ureteral stones and signs of infection, reporting equal times to normalization of fever and WBC count with a trend towards longer hospital stays in those following PCN placement. Another small trial assessed 40 patients with a ureteral stone and hydronephrosis, with or without signs of infection, and did not demonstrate a difference in outcomes between ureteral stent and PCN tube placement^[23]. A recent retrospective study by Goldsmith

et al^[24] investigated patients with obstructive stones identified on CT scan and systemic inflammatory response syndrome at the time of diagnosis to determine differences in outcomes between ureteral stent and PCN tube placement. A total of 130 patients met inclusion criteria. Patients selected for PCN tube placement had larger stones (10 mm *vs* 7 mm), were more ill based on their APACHE score, and had a higher proportion of surgically altered urinary tract anatomy^[24]. After resolution of the patient's sepsis, those undergoing ureteral stent were more likely to be treated with ureteroscopy (65% *vs* 40%, $P = 0.004$) and those undergoing PCN tube placement were more likely to be treated with percutaneous nephrolithotomy (38% *vs* 6%, $P = 0.001$)^[24]. Time from initial septic event to definitive treatment and rate of spontaneous stone passage was similar between the PCN tube and ureteral stent group^[24]. Intensive care unit admission rates were higher for the PCN tube group (42% *vs* 20%, $P = 0.006$), likely due to more ill patients being selected for PCN tube placement^[24].

In summary, indications for emergency urinary tract decompression include intractable pain, nausea/vomiting, evidence of obstructive uropathy, symptoms or signs of infection, and calculi in a solitary or transplant kidney. The preferred method of decompression (ureteral stent or PCN) is likely equivalent, and should therefore be based on stone size, stability of the patient, available hospital resources, and anticipated future method of definitive treatment.

URGENT URETEROSCOPY

In the acute management of stones, patients are typically discharged without the need for a procedure. If, however, a procedure is indicated, then palliation with a ureteral stent or PCN is often performed. Despite this common practice, recent investigations have assessed emergency ureteroscopy. Proponents of this practice cite that immediate stone removal can relieve pain, and prevent multiple trips to the operating or emergency room. Sarica *et al*^[25] published a prospective study on 145 patients presenting to the ED with obstructing ureteral stones. Stones were located in the distal ureter in 67.6% and proximal ureter in 32%^[25]. Patients were split into either ureteroscopy within 24 h of first colic attack or medical expulsive therapy (MET) for > 7 d followed by ureteroscopy within 7-21 d^[25]. There was no difference in intraoperative complications or stone location^[25]. Ureteral stents were placed in 24.6% of those on MET *vs* 0% in those undergoing immediately ureteroscopy ($P = 0.001$)^[25]. There was no difference in the need for additional procedures^[25]. Stone free rate was 87.9% in the MET first group and 90.8% in the emergency ureteroscopy group^[25]. Readmission rates were higher in the MET first group, with 3.03 mean readmission to the ED^[25].

Al-Ghazo *et al*^[26] examined 244 patients treated with emergency ureteroscopy (within 24 h of admission) for acutely symptomatic ureteral stones. Overall success rate,

defined as complete absence of stone fragments at 4 wk post-operatively, was 90.6%^[26]. Proximal ureter, mid ureter, and distal ureter stones had 69.4%, 94.8%, and 96.6% success rates, respectively ($P < 0.001$)^[26]. Overall complication rate was 13.1%, decreasing to 2.5% when excluding stones 10 mm or greater, consistent with prior studies^[27-30]. The success rate of ureteroscopy is due in part to improving optics and advances in intracorporeal lithotripters such as the holmium yttrium-aluminum-garnet laser, allowing for safe and effective lithotripsy and stone removal^[31]. Another advantage to ureteroscopy is that it does not require thromboprophylaxis following surgery, except in high risk patients^[32].

Although limited data exists on this topic, ureteroscopy within 24 h of initial presentation may be a viable option, especially for patients with a symptomatic, obstructing mid to distal ureteral stone without evidence of infection. However, further investigation is necessary prior to widespread adoption.

EMERGENCY EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY

Since its introduction in the 1980s, emergency extracorporeal shockwave lithotripsy (ESWL) is a minimally invasive method to treat both kidney and ureteral stones. According to the EAU guidelines, ESWL and ureteroscopy are both first line treatments for proximal ureteral stones^[20]. A recent meta-analysis by Picozzi *et al*^[33] assessed 7 studies with a total of 570 patients who underwent urgent ESWL for the treatment of a symptomatic stone. Stone free rates and complication rates did not differ statistically from those reported in the most recent AUA or EAU guidelines for elective ESWL; however, subsequent surgery was required in 15.8% of patients to completely remove the stone^[33]. ESWL is thus an option to emergently treat stones, although further investigation is needed. One must be careful in performing ESWL in patients with a known bleeding diathesis or on blood thinning medications. Appropriate bridging therapy should be utilized in patients on warfarin and patients on antiplatelet therapy should discontinue these medications prior to ESWL as severe complications have been reported^[32,34,35]. These patients tend to undergo ureteroscopy as it is safer from a bleeding standpoint. This should be taken into account when deciding the best treatment method, especially if emergency surgery is being considered.

MEDICAL EXPULSIVE THERAPY

The majority of patients (83%) presenting with nephrolithiasis will pass their stone without any need for intervention^[21]. Therefore, the EAU guidelines recommend for ureteral stones < 10 mm with minimal to moderate hydronephrosis and no evidence of renal damage, observation with or without MET is standard of care^[20]. MET

has been shown to improve the rate of stone passage^[20]. Calcium channel blockers, steroids, and alpha-blockers have all demonstrated improved stone passage rates^[20]. Steroids are usually avoided because of the numerous systemic effects. In a meta-analysis of available RCTs comparing MET to placebo, calcium channel blockers showed an absolute increase in stone passage of 9% and alpha-blockers shown an absolute increase in stone passage of 29%^[20]. Therefore, alpha-blockers are the preferred agent for MET.

Tamsulosin is the most widely studied alpha-blocker used for MET. Fan *et al*^[36] performed a meta-analysis of 20 RCTs across 10 countries including 799 patients in the tamsulosin arm and 794 patients in the control arm. Expulsion rates for lower and upper ureteral stones were significantly higher in the tamsulosin arm (lower ureteral stones: RR = 1.55, $P < 0.00001$; upper ureteral stones: RR = 1.28; $P = 0.02$)^[36]. Additionally, expulsion time was improved in the tamsulosin group by an average of 2.63 d^[36]. These patients also had fewer colic episodes and underwent fewer auxiliary procedures. In a RCT, Al-Ansari *et al*^[37] studied 100 patients with lower ureteral stones and compared placebo to tamsulosin and found spontaneous passage rate to be 82% in the tamsulosin group *vs* 61% in the placebo group. Expulsion time was also shorter^[37]. Yencilek *et al*^[38] showed improved passage rates in those receiving tamsulosin *vs* placebo for ureteral stones < 5 mm (passage rate 71.4% *vs* 50%).

In summary, for ureteral calculi < 10 mm without signs of infection or acute renal failure, a trial of MET should be initiated. Alpha-blockers are considered first line for MET due to the familiarity with the drugs, improved rates of spontaneous passage, decreased time to stone passage, and fewer colic episodes. While tamsulosin is the most studied medication for MET, other alpha-blockers should have similar outcomes. For those with documented spontaneous passage of their stone, repeat imaging is not necessary. If the patient is persistently symptomatic after passage, Fulgham *et al*^[41] recommend a follow up RUS with a NCCT if the patient has hydronephrosis. While the optimal length of time of MET before intervention is controversial, common practice is for 4-6 wk^[39].

PREGNANT PATIENTS

Nephrolithiasis affects about 1 in 500 pregnancies^[40-42] and often becomes symptomatic in the second or third trimester^[43-45]. Fortunately 70%-80% of these patients will pass their stone spontaneously with conservative management^[45]. A RUS is universally accepted as the first line study in pregnant patients presenting with suspected nephrolithiasis with a sensitivity of 34% and specificity of 86%^[46]. If a RUS fails to identify nephrolithiasis or alternative diagnoses, the EAU recommends either a transvaginal ultrasound to assess for UVJ or bladder stones or an MR Urography (MRU), which avoids ionizing radiation^[20]. MRU has limited capacity to identify

small calculi, is costly, and is often unavailable; however, it avoids ionizing radiation, which may increase the risk of secondary malignancies^[47-49]. Additionally, MRU should not be used in the first trimester due to unknown risks to the developing fetus^[47,50]. Some have advocated the use of LD-NCCT scans in complicated cases where no other diagnosis has been identified, but this requires ionizing radiation and patients must be counseled extensively about the risks and benefits to the mother and fetus. Most notably, a single pelvic CT may increase the risk of childhood cancer in the exposed fetus by 2 times; however, due to the low absolute risk of childhood cancer (1 in 2000), the increase in absolute risk is extremely low^[51]. The American Congress of Obstetricians and Gynecologists guidelines for diagnostic imaging during pregnancy report that exposure to less than 5 rad (which is the case for a NCCT of the abdomen and pelvis) has not been associated with an increase in fetal anomalies or pregnancy loss and that a single diagnostic X-ray procedure does not result in harmful fetal effects^[52].

Pregnant patients should be treated similarly to non-pregnant patients with fluids and analgesia^[20]. Additionally, urinary diversion with a ureteral stent or PCN may be required in the emergent setting when meeting the same criteria as the non-pregnant patient. These should be placed using ultrasound guidance or with limited fluoroscopic radiation as possible. Ureteral stents or PCN tubes need to be exchanged every 4-8 wk during pregnancy *vs* every 3 mo in non-pregnant patients due to an increased risk of encrustation^[20]. Ureteroscopy, using laser lithotripsy, is increasing being employed in this population as experience has increased^[20].

CONCLUSION

Nephrolithiasis is common and is often treated by urologist and non-urologists alike. While the AUA and EAU currently have guidelines for the evaluation and management of nephrolithiasis, these are directed at urologists. To our knowledge no national or universal guidelines exist for the acute management of stone disease in the ED. Therefore, we hope that this review will assist physicians to evaluate and manage nephrolithiasis in the acute care setting.

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