January 2013

Identification Of Factors Associated With Acute Pyelonephritis Complicated By Ureteral Stones

Warren Perry

Identification of Factors Associated with Acute Pyelonephritis Complicated by Ureteral Stones

A Thesis Submitted to the

Yale University School of Medicine

in Partial Fulfillment of the Requirements for the

Degree of Doctor of Medicine

by

Warren M. Perry, II

2013

ABSTRACT

IDENTIFICATION OF FACTORS ASSOCIATED WITH ACUTE PYELONEPHRITIS COMPLICATED BY URETERAL STONES

Warren M. Perry, II[1], Brock Daniels[1], Annette Molinaro[2], Cary Gross[1], Christopher L. Moore[1]. [1]Yale School of Medicine, New Haven, CT, [2]University of California at San Francisco, San Francisco, CA

In theory, the evaluation of acute pyelonephritis (APN) does not require imaging, but in practice computed tomography (CT) may be ordered because of fear of an obstructing ureteral calculus that may present with similar symptoms. Childbearing age women are susceptible to the radiation exposure of CT imaging and have the highest incidence for APN. It is unknown what combination of clinical signs and point-of-care tests may help identify which patients with APN may require (or be able to avoid) advanced imaging.

We aimed to identify factors associated with ureteral stones in APN patients with the future goal of designing a decision rule that can identify these patients. We hypothesized that a set of clinical characteristics, including identification of hydronephrosis (which may be accomplished with point-of-care bedside ultrasound) would be able to differentiate complicated from uncomplicated APN.

This was a retrospective study of patients at an urban level-1 trauma ED and a freestanding 24-hr suburban ED. All CT-flank pain protocol (CTFPP) scans for renal colic between April 2005 and April 2009 were identified. We identified patients with APN as having >5 WBC/HPF on formal urinalysis in addition to one or more of the following: flank pain, CVA tenderness, chills, fever, nausea, or vomiting.

Clinical data from the medical record were abstracted blinded to CT reports. Classification and regression tree analysis was used to produce decision trees and logistic regression was used to determine odds ratios.

In our study, 250 patients were included. Women composed 68.0% of the sample and the mean age was 41.8 (±15.6). The decision tree produced showed hydronephrosis to be the most predicting factor for a ureteral stones and the logistic regression also found a high statistical significant association with hydronephrosis, OR=29.03.

Our study is the first we are aware of to show that hydronephrosis is a dominant factor for predicting APN complicated by our ureteral stone. Our study also produced 2 clinically relevant decision tree that included hydronephrosis as a key finding for identifying patients with ureteral stones. Ultrasound can be used to detect hydronephrosis but there are few studies about its use in APN. Our findings show us the potential use in APN complicated by ureteral stones and support the further investigation of ultrasound for imaging decisions in cases of APN.

ACKNOWLEDGEMENTS

I would like to thank Dr. Christopher Moore for giving me the guidance and resources I needed to complete this study. In addition to this, I want to thank Dr. Cary Gross, Dr. Brock Daniels, Annette Molinaro, Seth Luty, Christal Esposito and the other members of Dr. Moore's research team who provided their support during the execution of this project. I would also like to thank the Yale School of Medicine's Office of Student Research and the Yale Emergency Medicine department for all of their funding for this project. Finally, I want to thank my family for their endless love and encouraging me to always follow my dreams.

Table of Contents

INTRODUCTION

Acute pyelonephritis (APN) is classically defined as an infection of the upper urinary tract involving the renal parenchyma and pelvis. There are 250,000 cases that present annually in the United States and more than 100,000 of these cases result in hospitalization[1,2]. Acute pyelonephritis normally occurs secondary to a bacterial infection in the lower urinary tract usually involving the bladder or urethra. This infection then ascends to involve the kidneys to cause acute pyelonephritis. The natural flow of urine in the urinary tract is thought to prevent the build up of pathogenic bacteria. In saying this, any obstruction can cause stasis of urine and create conditions suitable for infection. There are a number of conditions that can interrupt the flow of urine and cause this infection to progress to APN. In older men, obstruction is commonly the case when they present with acute pyelonephritis due to the high prevalence of prostatic hypertrophy. Vesicoureteral reflux is a condition in which the valve between the bladder and the ureter is inadequate. This allows the urine to reflux back into the ureters instead of progressing through the urinary system. Vesicourethral reflux presents in approximately 10% of children and is found to be the cause of recurrent urinary tract infections in children. Females are predisposed to urinary tract infections, in general, due to their short urethra[1,2].

The most common bacterial pathogen found in cases of APN is *Escherichia coli.* It is present in urine culture at a prevalence of 82% in women and 73% in men[1]. Other pathogens found in urine culture in cases of APN, but not as often as *E.*

coli, are *Klebsiella pnuemoniae* and *Staphylococcus saprophyticus.* In the elderly population, there is a lower incidence of E. *coli,* 60%, and a greater incidence of *Klebsiella pneumoniae*. Bacterial acute pyelonephritis is the most common form of APN but fungal acute pyelonephritis does present commonly as well. The people at risk the most for fungal acute pyelonephritis are diabetics, immunosuppressed patients, patients with indwelling catheters and patients with urinary obstructions. The most common fungal pathogen is the *Candida albicans* and *Candida tropicalis.* Other less frequently causative fungal pathogens include Aspergeillus sp, Cryptococcus neoformans, Histoplasma capsulatum and Zygomycetes (Rhizopus and Mucor)[3].

Non-pregnant women between the ages of 15-30 are most likely to present with APN[1]. The reason for this is not well known or explained but it is thought that sexual intercourse is higher during this age range in females and, thus, increases their risk for a urinary tract infection. It presents at a rate of 1-2 percent in pregnant women and increases the risk of premature labor and low-birth weights. Of the cases of APN resulting in hospitalization, women are more likely to be hospitalized than men, 11.7 cases per 10,000 in women versus 2.4 cases per 10,000 in men. Contrary to infection, men have a higher mortality rate than females, 16.5 cases per 1,000 versus 7.3 cases per 1,000 respectively[1]. Common risk factors for acquiring APN in women are: sexual intercourse greater than three times a week, stress incontinence in past 30 days, urinary tract infection within the past year, diabetes, spermicide use with contraceptives, new sexual partner within the past year and history of urinary tract infections in the patient's mother's history[1].

In regards to treatment, there is strong support for the use of fluoroquniolones as a first-line drug in APN, as well as Trimethoprim-sulfamethoxazole (TMP-SMX). Fluoroquinolones are commonly used as first-line treatments in APN because they can be given orally due to good gastrointestinal absorption and due to their ability to penetrate the kidney well. There is also low resistance to fluoroquinolones in cases of APN. The arguments for using TMP-SMX as a first-line agent are its lower cost, comparable efficacy rate to fluoroquinolones, and prevention of drug-resistance to fluoroquinolones. One of the drawbacks to TMP-SMX is the risk of an allergic reaction not evident in fluoroquinolones[1,4-6].

While APN can be defined as an infection of the upper urinary tract, there is a lack of consensus on the diagnostic criteria of APN in the medical community. Although there is no agreement on the definitive diagnostic criteria for APN, the literature does report two approaches to the diagnosis of APN. The first one is a clinical diagnosis that is a combination of history and physical exam findings along with laboratory signs. The American Urology Association, American Congress of Obstetricians and Gynecologists, Society for Academic Emergency Medicine, Association of Medical Microbiology and Infectious Diseases- Canada are the main academic communities that are investigating acute pyelonephritis, but these publications focus more on the management and treatment rather than the actual diagnosis of acute pyelonephritis[7]. These academic bodies also focus more on urinary tract infections in women than in men as many of their study samples exclude the male gender. During our literature review we found one set of criteria used by the British Medical Research Council Bacteriuria Committee for the

diagnosis of acute pyelonephritis. They describe bacterial APN as groin pain, tenderness, and pyrexia accompanied by signs of bacterial infection of the kidney, including leukocytosis, pyuria, bacteriuria, and a positive urine culture, sometimes with bacteremia and hematuria[8]. A review article by Hooton on uncomplicated urinary tract infections also reports criteria for acute pyelonephritis but these are only suggested clinical manifestations. These signs and symptoms include flank pain, costovertebral tenderness, fever (>38.0 C), nausea/vomiting, and/or chills[9]. There are other articles that use similar clinical signs but also include abdominal/pelvic pain and signs of a lower urinary tract infection (dysuria and increased frequency)[10-15]. Laboratory findings play an important role in helping physicians understand the clinical signs and symptoms. The recommended labs to request in the case of acute pyelonephritis are: urinalysis, leukocyte esterase test, corrected nitrite test, gram stain of urine and dipstick hematuria. Urinalysis showing >5wbc/hpf has the highest sensitivity of all these test for ruling out pyelonephritis, 72%-95%. A positive leukocyte esterase in combination with a nitrite test has the highest specificity for ruling in urinary infection, 94%-98% and 92%-100% respectively. The clinical approach is advantageous to emergency physicians because it is cost effective but it can only suggest an upper urinary tract infection with APN as a differential diagnosis[7]. The clinical approach cannot determine which level of the urinary tract is infected and our research team found no studies aimed addressing this issue. In saying this, other causes of the patient's presentation should be kept in the differential diagnosis such as, abscess, renal colic, and gynecological pathology for female patients. The lack of a consensus on which

clinical presentations are the most important to use in the diagnosis of APN more likely stems from the variation of APN's presentation.

The second approach to diagnosing pyelonephritis is pathological and is described as an infection of the kidney usually involving the renal parenchyma and pelvis, as stated above[8]. This definition relies on imaging modalities and/or biopsy, which the latter is rarely done unless a transplant kidney is involved. Computed tomography (CT) is commonly used to image APN because it has a high sensitivity and specificity for detecting other etiologies that mimic APN such as renal stones, renal masses, abscesses and hemorrhage[16]. The CT finding suggesting APN is hypoattenuation of the renal medulla extending into the cortical layer in a wedge-shape fashion[16]. Magnetic resonance imaging (MRI) can also be utilized to look for renal inflammation. Hypoattenuation, perinephric stranding, and renal enlargement are all findings suggesting APN in MRI and are similar to those found on CT imaging. Ultrasound is another imaging modality used in cases of APN. It has a lower sensitivity and specificity than CT and MRI; however, contrast agents can improve its ability to detect poorly perfused areas of the kidney in the case of APN. In the case of uncomplicated acute pyelonephritis there are no major findings seen on ultrasound and the infected kidney appears similar to the uninfected kidney. In 20% of cases of uncomplicated acute pyelonephritis, edema can be seen on ultrasound. This is seen as an enlarged kidney greater than 15cm or 1.5cm greater than the uninfected kidney. Parallel lucent striations can also be a sonographic sign of edema caused by infection in acute pyelonephritis. In cases of fungal infection, gas may be seen in the bladder as some fungi are gas forming. Fungal debris, known

as a bezoar, might also be seen on ultrasound and can possibly lead to obstruction. In general, APN appears as a hypoechoic poorly defined renal parenchyma on ultrasound[3].

The American College of Radiology Appropriateness Criteria for acute pyelonephritis states that imaging is not required for cases of uncomplicated APN unless there is no resolution after 72 hours of antibiotic therapy. If complicated APN is suspected in a patient, imaging is indicated without the 72 hour trial of antibiotic therapy. In both cases of prolonged uncomplicated and suspected complicated APN, computed tomography is the imaging modality of choice[17]. As stated before, CT imaging is superior to MR because it can identify additional findings not suspected on initial assessment and it is less expensive and more convenient. For this reason physicians choose CT as their initial choice of imaging[16].

Acute pyelonephritis has a differential diagnosis including renal stones, abscess, pelvic inflammatory disease, cystitis, and appendicitis. Although all these diagnoses can mimic APN, renal stones have a presentation very similar to APN. Renal stones are stones that form in the kidneys and are composed of calcium oxalate or calcium phosphate in eighty percent of patients. The prevalence of renal stones is 5% with an annual incidence of 1%. Unlike acute pyelonephritis, men are more likely to present with renal stones than women with a peak incidence at 30 years of age. In women there is a bimodal distribution in the prevalence of renal stones with peak incidences at 35 and 55 years of age. The clinical manifestation of renal stones starts to occur when the stone is progressing through the urinary tract. Like acute pyelonephritis many patients experience flank pain that is colicky in

nature and may or may not radiate to the groin. Nausea and/or vomiting are also associated symptoms in renal colic patients. If there is a bacterial predisposition for stone formation, such as a struvite stone, fever and chills can be present, as well. Gross hematuria or microscopic hematuria is a common laboratory finding on urine analysis. Like acute pyelonephritis, the clinical presentation of renal stones varies from patient to patient.

Computed tomography is particularly important when investigating or attempting to tree out cases of complicated APN. Complicated APN occurs when there is a co-existing condition predisposing the patient to the development and progression of APN such as diabetes, pregnancy and autoimmune disorders. In addition to this, any condition that prevents the resolution of APN can complicate the case of APN and lead to urosepsis and death if detection is not made early enough for intervention. These conditions include genitourinary tract abnormalities such as renal and ureteral scarring from chronic vesiculoureteral reflux and obstructing renal or retroperitoneal masses. Renal and ureteral scarring are also harmful sequelae that can result from complicated acute pyelonephritis and place patients at further risk for a urinary tract infection in the future. In addition to this, resistant uropathogens can also complicate a case of acute pyelonephritis[18].

Suspicion of an obstructing ureteral stone is the most common condition causing complicated APN, and suspicion of this may lead a physician to utilize advanced imaging (i.e. CT)[10]. Like APN, renal colic can also present with nausea, vomiting, pyuria, groin pain, flank pain and/or abdominal pain[19]. This presentation, also like acute pyelonephritis, is variable and not consistent amongst all the cases of

renal colic. With this similar presentation it is difficult to determine if APN or renal colic is solely presenting or if they are presenting simultaneously. Computed tomography (CT) is currently the gold standard for imaging ureteral stones and for this reason, physicians may order it during their diagnostic evaluation of APN when they want to tree out a concomitant ureteral stone[20-23].

Though highly specific and sensitive in the detection of ureteral stones, CT studies are expensive and expose patients to radiation[24]. The average effective radiation dose from an abdominal CT is 8mSv and 6mSv for a pelvic CT. One article by Gonzales et al reports that 29,000 future cancers will be caused by computed tomography radiation exposure. Of those 29,000 cases, 14,000 will be from abdominal and pelvic CT scans, and 18,000 (62%) will be in women (who are most susceptible to APN)[25]. These disadvantages are relevant in the midst of the current healthcare reform and due to the significant incidence of APN in childbearing-age women who vulnerable to the harmful effects of radiation[26]. Despite this and the finding of a 5.9 fold increase in the use of computed tomography in emergency department evaluations there are few studies aimed at identifying which cases of APN are more likely to be complicated and require advanced imaging[14,27].

HYPOTHESIS and STATEMENT of PURPOSE

During our extensive literature review we did not find any studies aimed at determining the prevalence of ureteral stones in acute pyelonephritis patients. We are also unaware of any studies addressing the need for identifying acute pyelonephritis patients who may have a concomitant ureteral stone. Most studies in

this area have focused on the clinical diagnosis, imaging and management of acute pyelonephritis[1,2,4,19,22,28-33]. We sought to identify factors in APN associated with co-existing ureteral stones, with the future goal of identifying a decision rule for imaging in acute pyelonephritis patients who may harbor a co-existing ureteral stone. Since the clinical presentation of acute pyelonephritis and renal colic overlaps and varies, we hypothesized that a set of factors (including imaging findings of hydronephrosis, obtainable using point-of-care ultrasound imaging) would prove to be most important in identifying cases of acute pyelonephritis complicated by ureteral stones.

METHODS

Study Setting Description

We conducted a retrospective study in two emergency departments to identify patients at risk for APN complicated by ureteral stones. Yale New Haven Hospital ED is a level 1-trauma facility located in urban New Haven, CT. It receives over 90,000 visits each year. Shoreline Medical Center ED was our second site and is a freestanding suburban facility in Guilford, CT, that receives over 28,000 visits per year. Both sites have 24-hour coverage by board certified emergency physicians and CT availability including a CT Flank Pain Protocol (CTFPP), which is a non-contrast CT of the abdomen and pelvis routinely ordered for suspected ureteral colic. Both ED facilities have identical standard template patient charts and information is recorded in the same manner. All patient data is recorded on the standard templates and scanned into the LYNX medical system (Lynx Medical Systems,

Bellevue WA) where it is retrievable electronically. Radiologic imaging results, laboratory values, and consult notes are reported through Sunrise Clinical Manager (Sunrise Clinical Manager, Eclypsis, Atlanta GA), the electronic medical recording system.

Construction of Study Sample

All CT Flank Pain Protocols performed in the two participating EDs from April 2005-January 2009 were identified using the picture archiving communication system (Synapse, Fujifilm, Tokyo Japan). The patient name, date of birth, medical record number, accession number, date, time, location of study and the full text of the dictated report from the emergency radiologist were included in the results of the query. From the resulting CTFPP studies, we randomly selected 1853 patients to be screened for inclusion into our study. A preliminary chart review was performed to eliminate any patient with a co-existing condition that could complicate APN outside of ureteral stones. The exclusion criteria were any patient with a history of stone procedure or other urological procedure, malignancy, pelvic surgery within 6 weeks of CT imaging or chronic renal disease (CR>1.5). We also excluded any patient under 18 years of age. A secondary partial chart review was performed on the remaining set of patients for inclusion into our study. The inclusion criteria was any patient with >5 WBC/HPF on urine analysis plus one or more of the following: flank pain, costovertebral angle tenderness, chills, fever (subjective or objective, ≥ 100.4° F), nausea or vomiting. We designed our inclusion criteria to be our definition of suspected uncomplicated APN since there is no standard definition. It was derived from peer-reviewed academic journals and medical references[3, 10-14]. Complicated

APN was defined to be a case of uncomplicated APN with coexisting ureteral stones found on CT imaging. A full chart review was performed on all patients meeting our inclusion criteria.

Data Collection

The data extracted from the chart reviews were stored in a database with fixed options for each field to ensure quality data collection. The database was divided into two sections. The first section stored information from the patient's standard ED template charts and EMRs, which consisted of the history, physical exam, and additional information including laboratory results, disposition, and procedures. The second section contained the full CTFPP report from the radiologist and was blindly collected relative to the first section. The CT report was used to categorize the cases of APN as complicated or uncomplicated. In addition to collecting this information, we distinguished small stones from large stones, >5mm, and noted all visits that resulted in a procedure.

A manual that listed and clearly defined the elements being extracted was used to train all data abstractors and regular meetings for project monitoring were conducted throughout the study, as well. All abstractors, except one, were blinded to the purpose of the study. To assess the reliability of CT categorization we determined an inter-rater agreement *k*-statistic with the assistance of an experienced statistician.

Analysis

The aim of our study was to develop a decision tree that identified cases of acute pyelonephritis complicated by a ureteral stone. To develop the decision trees,

we relied on classification and regression tree analysis (CART) with 10-fold cross validation. This form of binary recursive partitioning is superior to multivariate analysis for this task because it makes no assumptions about the distribution of data in a large dataset. CART has also been used for risk stratifying patients in other areas of medicine, which sets a precedent and justifies its use in our study[13]. We also used univariate logistic regression to calculate odds ratios to determine which factors from the patients chart review were associated with ureteral stone.

RESULTS

From the 1,853 patient charts randomly selected for review, 1603 were excluded. Out of the excluded 1,603, 1,415 did not have greater than 5 white blood cells on formal urine analysis and 21 did not have any of the additional signs and symptoms: flank pain, costovertebral angle tenderness, fever, chills, nausea and/or vomiting. Another 113 patient charts were excluded because they were less than 18 years of age and six more because they had pelvic surgery within six weeks of their emergency department presentation. A history of stone or other urology procedure excluded 27 patients and a urologic anatomical abnormality excluded another five. Eight patients were excluded due to malignancy and eight patients were excluded due to renal disease. Two patient charts did not have a sufficient amount of data and were subsequently excluded as well.

After our exclusion criterion was applied, 250 patients remained in our study. The majority of presentations were at the YNHH ED, 80.1% (n=202). The mean age was 42 ± 15.6 and females composed 68.0% (n=170) of the study sample (Table 1).

Whites made up the majority of our study sample, 57.8% (n=144), followed by Black and Hispanics, 19.6% (n=49) and 18.0% (n=45) respectively. The most common sign or symptom from our definition of acute pyelonephritis was flank pain, 84.6% (n=211) followed by costovertebral angle tenderness, which was present in 63.2% (n=158) of our patients. In regards to the other elements of our definition of pyelonephritis, nausea and/or vomiting was present in 64.8% (n=163), a fever greater than 100.4 F was present in only 10.4% (n=26) and chills were found in 28.0% (n=70) of the study sample. Most patients had between 6 and 10 white blood cells on urine analysis, 39.1% (n=99), followed by 11-30 wbc/hpf, 32.8% (n=83) and greater than 30 wbc/hpf, 26.9% (n= 68).

Table 1: General Characteristics of Study Sample:

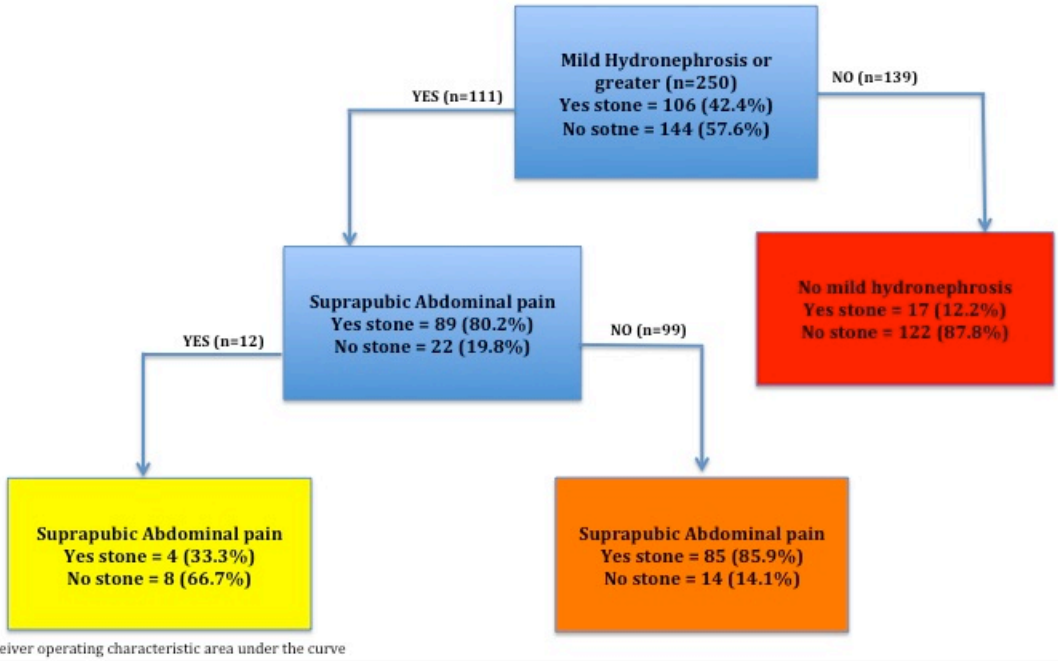
Mean Age (SD)	41.8 (±15.6)
Females %, n:	68.0%, 170
Ethnicity %, n:	
Caucasians	57.8%, 144
African Americans	19.6%, 49
Hispanic	18.0%, 45
Other	4.8%, 12
Formal # WBC UA %, n:	
6.0-10.0	39.1%, 99
11.0-30.0	32.8%, 83
>30 Many	26.9%, 68
APN signs/symptoms %, n:	
Flank Pain	84.6%, 211
CVA tenderness	63.2%, 158
Fever	10.4%, 26
Chills	28.0%, 70
Nausea	30.4%, 76
Nausea and vomiting	34.4%, 87
Target Outcomes %, n:	
Complicated APN: Ureteral stone	42.4%, 106
Complicated APN: Large stone	9.2%, 23
Uncomplicated APN	56.4%, 141

In regards to the methods of data collection and categorizing CT studies, the inter-rater reliability was 80.0% and 81.4% with a kappa of 0.75 and 0.80 respectively. This shows that the data are reliable and the subsequent conclusions are important. In our study, 42.4% (n=106) of acute pyelonephritis cases undergoing CT imaging for suspicion of stone were complicated by a ureteral stone. Within these patients, large stones (>5mm) were found to complicate 9.2% (n=23) of cases of suspected APN. Twelve patients were admitted for procedures with cystoscopy, ureteroscopy, stone extraction and ureteral stent placement being the most common procedures performed. Two out of the twelve procedures were an appendectomy and cholecystectomy. There were three patients whose CT findings required immediate follow-up, not seen in Table 1. The findings were diverticulitis, appendicitis and cholecystitis. The remainder of the study sample had uncomplicated APN, 56.4% (n=141). The inter-rater reliability for the categorization of the CT findings was 80.0% and 81.4% with a kappa of 0.75 and 0.80 respectively.

Salford Systems statistics software (Salford Systems, 2012) was used to perform Classification and Regression Tree analysis with 10-fold cross validation and receiver operating characteristic tests (ROC). Seventy-seven total factors were incorporated into the CART analysis (Table 2) to create 3 decision trees (Figures 1-3). In decision tree 1 (Figure 1), mild hydronephrosis or greater without suprapubic pain was the clinical finding identifying the most APN patients with a ureteral stone. This decision tree had a receiver operator characteristic area under the curve (ROC AUC) of 0.844.

Figure 1: CART retrospective decision tree identifying ureteral stone in patients with suspected APN- All factors included in CART analysis

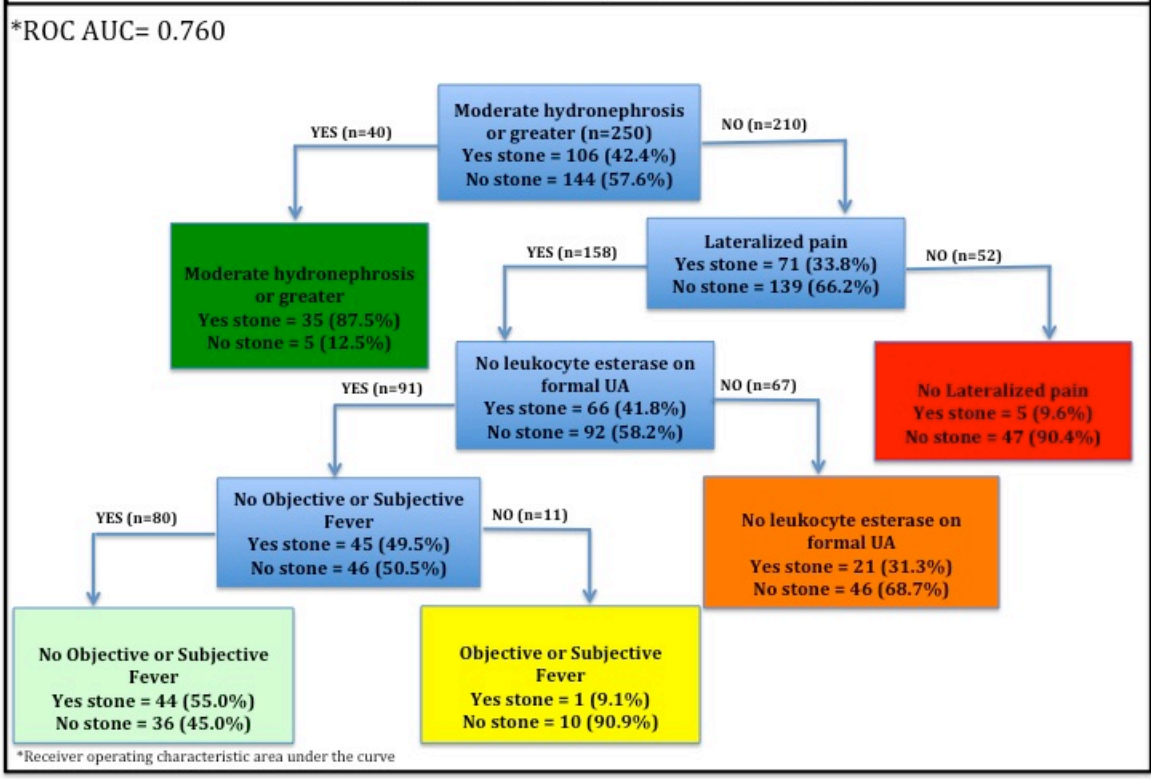
*ROC AUC= 0.844



*Receiver operating characteristic area under the curve

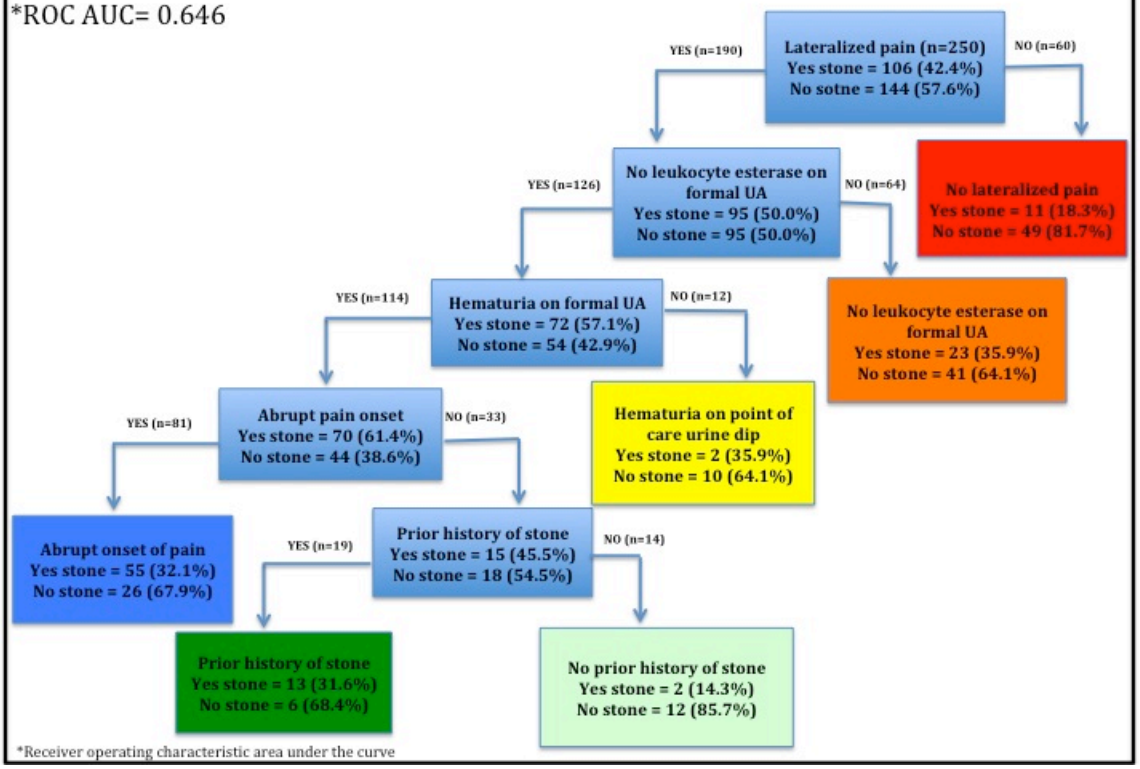
For the second round of CART analysis, we excluded mild or greater hydronephrosis to determine if a decision tree strictly constituting clinical signs and symptoms would be produced. We found that moderate or greater hydronephrosis could identify acute pyelonephritis patients with a ureteral stone (Figure 2). For patients without moderate or greater hydronephrosis, the terminal node identifying the most patients with stone included those presenting with lateralized pain, no leukocyte esterase on urine dip and no objective or subjective fever was identified as having a stone. This decision tree had an ROC AUC of 0.760.

Figure 2: CART retrospective decision tree identifying ureteral stone in patients with suspected APN- Without mild hydronephrosis in CART analysis



The third decision tree produced from our analysis excluded hydronephrosis, both mild and greater and moderate and greater to guarantee that the decision tree generated would constitute clinical elements only. There were six terminal nodes in this decision tree. The one identifying the most APN patients with ureteral stones identified those patients having lateralized pain, no leukocyte esterase on point-of-care urine dip, positive for hematuria on point-of-care urine dip and had an abrupt onset pain (Figure 3). This decision tree had an ROC AUC of 0.646.

Figure 3: CART retrospective decision tree identifying ureteral stone in patients with suspected APN- Without hydronephrosis in CART analysis



Odds ratios were calculated as an adjunct to CART analysis to determine which factors were associated with a ureteral stone (Table 2). The statistically significant odds ratios are listed in Table 2. Like in the classification and regression tree analysis, mild hydronephrosis or greater was found to be the factor most associated with ureteral stones in our sample of acute pyelonephritis patients having an OR=29.03. Mild hydronephrosis was followed by moderate hydronephrosis or greater with an odds ratio of 13.7. Hematuria on POC urine dip was found in 75.4% (n=80) of our patients with ureteral stones and was also found to be highly associated with ureteral stones in our patients having an OR=5.41. The abrupt onset of pain was found in 64.2% (n=68) of patients with ureteral stones and was found to be associated with ureteral stones, OR=2.83. Lateralized pain had an

associated odds ratio of 4.45 with ureteral stones and it presented in 89.6% (n= 95) of patients found to have a stone. The duration of pain was also found to be relevant in regards to factors associated with ureteral stones. Patients who experienced less than six hours of pain was found to have an associated OR=2.96 and it was present in 40.6% (n=43) of APN patients found to have a ureteral stones. Mild to moderate abdominal tenderness was found to be associated with ureteral stones as it had an OR=2.74 and presented in 35.8% (n=38) of patients. The Caucasian race proved to have an associated OR=1.84 and 66.0% (n=70) of patients found to have a ureteral stones were also Caucasian; however it is important to note that this race made up the majority of our study sample. In addition to this, the male gender had an associated OR=2.3 for ureteral stones and 42.5% (n=45) of patients with ureteral stones were male.

Table 2: Factors associated with ureteral stones in APN patients

		Ureteral stone				
Factors from patient charts	**Prevalence of finding**	**Yes**	**No**	**Odds ratio**	**95% C.I.**	**p-value**
White race	144 (57.60%)	70 (66.0%)	74 (51.4%)	1.84	1.10-3.09	0.0275
Male gender	80 (32.00%)	45 (42.4%)	35 (24.3%)	2.3	1.34-3.95	0.0026
Pain Duration <6h	70 (28.00%)	43 (40.6%)	27 (18.8%)	2.96	1.67-5.232	0.0002
Lateralized pain	190 (76.00%)	95 (89.6%)	95 (65.9%)	4.45	2.18-9.09	<0.0001
Abrupt pain onset	127 (60.48%)	68 (64.2%)	59 (41.0%)	2.833	1.57-5.11	0.0004
Point of care urine dip hematuria positive	165 (85.94%)	80 (75.4%)	85 (59.0%)	5.411	1.79-16.33	0.0013
Hydronephrosis Mild or Greater	111 (44.40%)	89 (84.0%)	22 (15.2%)	29.03	14.57-57.85	<0.0001
Hydronephrosis Moderate or Greater	40 (60.0%)	35 (33.0%)	5 (3.47%)	13.7	5.145-36.50	<0.0001

Although this study did not aim to look at the protective factors for ureteral stones, it is important to note them in this paper (Table 3). Suprapubic abdominal pain was found to be protective as it had an OR=.229 and presented in 14.6% (n=21) of patients found to not have ureteral stones on CT imaging. Severe abdominal tenderness had an OR=0.447 and was present in 22.2% (n=32) of patients without a ureteral stones. Chills was also found to be protective with an OR=0.437. Fifty patients presented with chills and had no ureteral stones, which makes up 34.7% of the patients with no ureteral stones found on CT imaging. Diarrhea was another protective factor found in 8.3% of patients with no ureteral stones on imaging and had an OR=0.212. Blacks had a protective OR=0.419 and out of the patients with no ureteral stones, 25% were Black. Finding leukocyte esterase on urine analysis was also protective as it had an OR=0.371 and 85.4 % of the patients without ureteral stones had leukocyte esterase in their urine analysis. Nitrites on urine analysis was also protective against ureteral stones, OR= .443. As the males were found to be associated with ureteral stones, being female was protective. The OR=0.435 and 75.7% of patients without a ureteral stones were female. Presenting with an objective or subjective fever had an OR=0.434 and 30.6% of the patients without ureteral stones had an objective or subjective fever. The gradual onset of pain produced an OR=0.395 and pain with movement produced an OR=.45 making up 37.5% and 31.3%, respectively, of patients who did not have a ureteral stones on CT imaging. Lastly, point of care urine dip for leukocyte esterase and nitrites was found to be protective for ureteral stones with an odds ratio OR=.45 and OR=.443, respectively.

Table 3: Factors protective against ureteral stones in APN patients

		Ureteral stone				
Factor from patient chart	**Prevalence of finding**	**Yes**	**No**	**Odds ratio**	**95% C.I.**	**p-value**
Suprapubic abdominal pain	25 (10.00%)	4 (3.78%)	21 (14.6%)	0.229	0.076-0.690	0.005
Abdominal tenderness degree Severe	44 (17.60%)	12 (11.3%)	32 (22.2%)	0.447	0.218-0.916	0.029
Abdominal tenderness degree Mild-to-Moderate	75 (63.03%)	38 (35.8%)	37 (25.7%)	2.74	1.22-6.11	0.0135
Chills	70 (28.00%)	20 (18.9%)	50 (34.7%)	0.437	0.241-0.793	0.0067
Diarrhea	14 (5.60%)	2 (1.9%)	12 (8.3%)	0.212	0.0463-0.966	0.0477
African American race	49 (19.60%)	13 (12.3%)	36 (25.0%)	0.419	0.210-0.838	0.0152
Formal UA: nitrite positive	44 (17.67%)	12 (11.3%)	32 (43.1%)	0.443	0.216-0.908	0.0286
Formal UA: leukocyte esterase positive	196 (79.03%)	73 (68.9%)	123 (85.4%)	0.371	0.200-0.700	0.0025
Female gender	170 (68.0%)	61 (57.5%)	109 (75.7%)	0.435	0.253-0.748	0.0026
Objective or Subjective Fever	61 (24.40%)	17 (16.0%)	44 (30.6%)	0.434	0.232-0.814	0.011
Gradual pain onset	77 (36.67%)	23 (21.7%)	54 (37.5%)	0.395	0.218-0.716	0.0024
Pain with movement	63 (25.20%)	18 (17.0%)	45 (31.3%)	0.45	0.242-0.834	0.0121
Point of care urine dip leukocyte esterase positive	80 (41.67%)	26 (24.5%)	54 (37.5%)	0.45	0.246-0.814	0.0084
Point of care urine dip nitrite positive	44 (17.67%)	12 (11.3%)	32 (22.2%)	0.443	0.22-0.91	0.0286

Our study also recorded the characteristics of the ureteral stones found on CT imaging in our study sample. In our study 29.2% (n=31) of patients who presented with a ureteral stone had a stone greater than 5mm. Approximately 70.0% (n=74) of the other patients had a stone 5mm or less. In regards to location in the ureter, the ureterovesical junction was the most common site for stone in our study, 43.4% (n=46). The distal ureter and proximal ureter were other common

locations for stone in our patients, 18.9% (n=20), 17.9% (n=19). Stones were found in the mid ureter in 9.4% (n=10) of cases and 2.8% (n=3) were found in the bladder.

DISCUSSION

To our knowledge, our study is the first to systematically identify factors associated with complicated APN that may help guide imaging decisions. Most prior studies on this topic investigated preconceived factors that were suspected to be associated with ureteral stones. One study by van Nieuwkoop et al investigated the factors associated with imaging in the setting of a urinary tract infection. The study was based on a Dutch population and set out to determine what factors were associated with significant findings on imaging in patients as a way to identify those that would benefit from imaging. The study found that a history of urolithiasis, urine pH ≥ 7.0, and GFR ≤40mL/min/1.73m3 were associated with clinically relevant findings on imaging. Some of these findings were pyonephrosis, ureteropelvic junction stenosis, urologic malignancy, non-obstructive renal stones and enterovesicular fistula. Renal cysts, diverticulitis, choledocholithiasis, and liver metastases were some of the incidental non-urological disorders and clinically irrelevant findings. The researchers of this paper did not determine if the implementation of this tree would prove to decrease healthcare cost on imaging and exposure of radiation to patients with urinary tract infections[34]. Another study by Yoshimura et al looked at the factors associated with urosepsis in the elderly to determine which ones would benefit from emergency drainage. The study was performed on a rural Japanese population and found that patients with a poor

performance status, older than 75 years of age, or of the female gender were at risk for urosepsis[35]. There is only one study that attempts to make a decision tree in the case of acute pyelonephritis in the emergency department. This study used a decisional algorithm to decide whether to discharge female APN patients under the age of 60 directly from the emergency department or from an observation unit. It found that the tree was useful in determining that most women present to the emergency department with uncomplicated pyelonephritis and can be discharged from the emergency department or after a brief stay in an observation unit[36]. However, much like most other studies on APN, this study focuses on the management of acute pyelonephritis and not the identification of complicated cases of acute pyelonephritis.

We found hydronephrosis to be a dominating factor in two out of the three decision trees, figure 1 and figure 2. These two decision trees would prove to have the most clinical use because they involve the presence or absence of one or two signs and symptoms. The last decision tree, figure 3, is not as clinically helpful due to the numerous arms it contains. The decision tree in figure 3 was produced without including hydronephrosis, so its complexity, more than likely, speaks to the variation of signs and symptoms in our study population. The logistic regression analysis found hydronephrosis odds ratios highly associated with a ureteral stone, which further supports its ability to identify APN patients at risk for a ureteral stone. Ultrasound (US) is an imaging modality with sensitivity and specificity for hyrdronephrosis and can potentially be a key tool used to identify APN patients for a coexisting stone. The lack of radiation and low cost add to the advantages of its use

when investigating for a concomitant stone in these patients. Our results are of great importance to the emergency medicine community because it suggests the need for more studies aimed at utilizing ultrasound in patients with acute pyelonephritis suspected of having a ureteral stone.

There is little data on the detection of hydronephrosis on bedside renal US in the setting of APN with obstructing stone. The closest study we found was a study analyzing the role of US in ED patients with clinical signs of APN and no signs of lithiasis on abdominal plain-film. This study found US abnormalities leading to surgical intervention in 5.8% of its patients thus concluding its usefulness in the evaluation of APN for patients who do not respond to antibiotic therapy[37]. An emergency room case report presented a positive finding of hydronephrosis in an APN patient which prompted the order of a CT scan where a distal obstructing ureteral stone was found[15]. Another article investigating the need for US imaging in APN through a review of the Pub Med and Cochrane Collaboration databases concluded that US imaging is useful in the evaluation of APN refractory to antibiotics[37]. The literature also states that minimally trained emergency physicians can accurately diagnose hydronephrosis[11]. All of this supports further studies aimed at determining the US findings in APN patients with coexisting ureteral stones, its ability to select these patients for further CT imaging and the patient outcomes.

While the association with ureteral stones might not be entirely unexpected, hydronephrosis surpassed all clinical signs, symptoms and laboratory values from the database. This finding strongly supports the investigation of using ultrasound

(US) to select patients for further CT imaging. As stated before, the most commonly used studies are CT and ultrasonography. Computed tomography has been noted by the American College of Radiology (ACR) as the best choice in the ACR Appropriateness Criteria for suspected stone disease[38]. In renal colic, CT has a 97% specificity and 96% sensitivity for detecting ureteral stones[11]. Though this test is highly recommended, the radiation exposure in the context of the high incidence of APN in childbearing age women presents a drawback to CT imaging. A population-based epidemiologic analysis of APN found a peak incidence of APN in women age 15-30[26]. These reasons support the investigation of less harmful, inexpensive imaging in the ED patient suspected of APN and co-existing stone.

Though ultrasonography is not superior to CT in detecting obstructing stones or hydronephrosis, the data still supports its use in the detection of hydronephrosis[11,38,39]. The American College of Emergency Physicians (ACEP) issued its first guidelines for ultrasound use in 1991. Since then the use of ultrasound as an imaging tool has been incorporated into the emergency medicine training curriculum. Currently, ACEP indicates bedside US for the detection of hydronephrosis and bladder status. They report a sensitivity of 75-87% and specificity of 82-89% for its indications on bedside renal US[40].

Our findings bring to light the importance of imaging in patients suspected of having APN complicated by a co-existing stone. Future research investigating ultrasound's detection of hydronephrosis in these patients should also investigate low dose radiation CT (LDRCT) scans. The data for the detection of ureteral stones with LDRCT is growing in the literature and reporting promising results. One study

found high accuracy rates in the detection of stones in patients less than 200lbs with a tube current reduced to 100mA. This produced a 25% reduction in radiation for multi-detector row CT (MDCT) scans and 42% reduction for single-detector row CT scans [41]. The drawback to low dose radiation CT scans is the reduced sensitivity and specificity to identify a ureteral stone, but studies have aimed to address this disadvantage. One study performed by Paulson et al artificially added noise to 160mA 16-MDCT to simulate 70mA, 100mA, and 130mA and found acceptable confidence of stone detection as low as 70mA[42]. Prospective studies should not only aim to understand how well LDRCT scans can detect ureteral stones, but they should also investigate their utilization as a follow-up study to point-of-care bedside US.

To be complete it is important to discuss all other forms of imaging in the setting of acute pyelonephritis. Radiographic plain films were the routine study for evaluation of pyelonephritis and ureteral colic before the implementation of computed tomography. Radiographs were used primarily to detect gas suggesting emphysematous pyelonephritis. It was also used to identify an obstructing stone. Plain films have its drawbacks in that it can only detect stones that contain calcium. This makes plain films unreliable in the case of struvite stones or cysteine stones. In addition to this X-rays are not able to distinguish bowel gas from gas in the kidney in some scenarios[43]. Intravenous pyelogram (IVP) is another form of imaging that can be utilized in the case of acute pyelonephritis or ureteral colic. It allows for a complete view of the urinary tract from the kidneys down to the bladder. Signs of renal infection on an intravenous pyelogram include renal enlargement, delayed

nephrogram and striations on nephrogram. IVP has its drawbacks in that it cannot provide detailed imaging of the renal parenchyma, it cannot characterize masses and it relies on a functioning kidney to work. Magnetic resonance imaging is another form of imaging that his is effective in the detection of surgical and medical renal diseases. It is preferred over computed tomography due to the fact that it does not use radiation. It also does not utilize iodinated-contrast, which can be harmful in patients with a history of renal failure or diabetes, a risk factor for stone formation. MRI has also been proven to be helpful in the diagnosis of acute pyelonephritis in the pediatric population. One of the drawbacks to using MRI is its high cost. One article reports the cost of an MRI scan to the patient as $1,329.00 which is expensive compared to other forms such as ultrasound and computed tomography. There is also a need for sedation in MRI in some patients who is experience claustrophobia[44].

In our study we had a set of patients who presented with hydronephrosis but was found to not have a ureteral stones on imaging with computed tomography. Of the 144 patients found not to have a ureteral stone on CT imaging, 20.8% (n=22) of them were found to have mild or greater hydronephrosis. None of these patients had a significant finding on CT imaging that was suspected to cause the hydronephrosis. There is no clear understanding why dilation of the collecting system is present in acute pyelonephritis but it is an image finding that has been reported in the literature. It is thought that during the ascending infection in acute pyelonephritis endotoxins of the pathogen disrupt the naturally occurring peristaltic motion of the ureter thus causing hydroureter and hydronephrosis. The

constant flow of urine is also one mechanism thought to prevent infection, so the stasis of urine can also exacerbate the renal infection. We found no studies investigating the prevalence of hydronephrosis in cases of isolated acute pyelonephritis nor did we find any studies comparing its prevalence to cases of acute pyelonephritis complicated by a ureteral stone.

In this study we also aimed to identify the associated factors of ureteral stones to determine if acute pyelonephritis altered the presentation of ureteral stones in emergency department patients. Many of our factors associated with ureteral stones were shared in other studies and reviews on renal colic[45,46]. One review article reports hematuria as a common laboratory finding in renal colic; however, it can be absent in 10-30% of cases. As mentioned in the results, 75.4% of patients with ureteral stones had hematuria but 18.9% of patients with ureteral stones had no hematuria, which falls in line with the current literature. The onset of abrupt pain is another presenting factor we found associated with ureteral stones in our study sample. This finding is also consistent with the literature in regards to presenting factors of ureteral stones[45,47]. In addition to an abrupt onset of pain, we also found lateralized pain to be associated with ureteral stones. There were no specific reports or mentioning of lateralized pain as a sign suggesting ureteral stones in the literature. In saying this, it makes sense that pain manifested by a ureteral stones would be lateralized pain since bilateral ureteral stones is more rare than unilateral stones. There are no reports on the prevalence of bilateral ureteral stones in the general population. An article by Lorenz et al aimed to determine the factors associated with asymptomatic renal stones found the prevalence of bilateral

stones was higher in patients with a history of past symptomatic stones[48]. The literature also reports that the male gender has a higher incidence of ureteral stones than females[48,49]. We also found the male gender to be associated with ureteral stones and found the female gender to be a protective factor. Lastly whites had a higher association with ureteral stones in our study sample and blacks were protective. This is also consistent with literature as Caucasians have been shown to have a higher prevalence of ureteral stones than African Americans[50]. Other factors associated with a ureteral stone found in the literature that we did not find in our study were old age, hypertension, obesity, and metabolic syndrome. The coinciding of our factors associated with ureteral stones with those found in the literature suggests that the same guidelines used to assess risk for stone in patients solely presenting with signs of renal/ureteral colic and can possibly be used to assess risk of ureteral colic in acute pyelonephritis patients.

Infection can predispose ureteral stones as in the case of struvite stones produced in the presence of urea-splitting organisms such as *Proteus, Klebsiella, Pseudomonas, Staphylococcus* and *Mycoplasma.* Infection can also be secondary to an obstructing ureteral stone so it is important to address the characteristics of ureteral stones found in our study. As stated before, the ureterovesical junction was found to be the most common location for ureteral stones, 43.4% (n=74). This is a significant find because the literature reports that most stones found in this location pass without intervention. A study investigating the relationship between size and location of ureteral stone with spontaneous passage found passage rates for distal and UVJ stones to be 75% and 79%, respectively. We also recorded the size of each

stone found on CT imaging and found that 70.0% of stones were 5mm or less and 29.2% were greater than 5mm. This is important to note because the study by Coll et al also found stones 1mm, 2-4mm, and 5-7mm had spontaneous passing rates of 87%, 75%, and 60%, respectively[51]. From these studies, it is plausible to conclude that our patients having distal stones, 18.9%, or UVJ stones, 43.4%, and/or stones less than 5mm, 70.0%, should have passed their stone spontaneously thus resolving any obstruction and complication to their APN.

The presentation of acute pyelonephritis complicated by ureteral stones to the emergency department has long been seen as an indication for hospitalization[2]. Our results, however, question this practice and suggest that these patients may be safely discharged home. Although this study was not designed or aimed to address this issue, our results show that the ureteral stones are presenting in a similar fashion to isolated cases of ureteral colic. Our data also shows that these patients have stones most commonly in places where they are likely to spontaneously pass them. Though the patient population in these studies supporting the above conclusion were renal colic patients and not APN patients with ureteral stone, it is still relevant to draw conclusions from their results because ureteral stone is the complication of APN in our population.

STUDY STRENGTHS AND LIMITATIONS

This study had three major strengths. First, the decision tree and factors found to be associated with ureteral stones were derived, a posteriori. In the study by van Nieuwkoop et al, the researchers selected their potential predictors from

known risk factors associated with negative outcomes in patients with a urinary tract infection: history of ureteral stones, pH > 7, GFR< 40ml/min/1.73m^3, diabetes mellitus, male sex, history of a urinary tract disorder and failure of prior treatment with antibiotics[34]. Though these preconceived risk factors were supported by the literature, the exclusive use of them apriori biases the study by excluding factors exogenous to the model. Second, the study was designed to mitigate common limitations found in retrospective studies involving chart reviews. These limitations were reported by Gilbert et al to be training of abstractors, protocol for case selection and exclusion, definition of variables, standard forms for data collection, monitoring of data abstraction, blinding abstractors to the hypothesis and purpose of the study and determining a reliable inter-rater agreement[52]. More importantly, our study used classification and regression tree analysis to identify our patients for ureteral stone.

One limitation to this study was the small study sample size. It is important to reiterate, however, that this is the largest study of its kind to date based off our literature review. In our study, we determined hydronephrosis through computed tomography and not by ultrasound. In saying this, ultrasound is a user dependent method of imaging and the hydronephrosis found in our study by CT imaging may not be detected on ultrasound as its sensitivity and specificity is lower for this. Another major limitation to our study was the lack of agreement to the diagnostic criteria for acute pyelonephritis. We developed our definition using a reliable source of medical journals and references[2,16,21,53-55]. In the end, we decided to err on the side of inclusion versus exclusion.

The limitations to our study bring to light some important topics for future research. First, the lack of standard criteria for acute pyelonephritis makes its diagnosis difficult and subjective. Not only is there a need for more studies investigating the diagnostic criteria of acute pyelonephritis through signs, symptoms, and laboratory markers, the emergency medicine community should also be investigating the criteria emergency physicians are currently using to distinguish pyelonephritis from other pathology in the differential diagnosis. The implications of studies like this might not lead to a concrete diagnosis criterion for pyelonephritis, however, it would enlighten the medical community to the general practice of assessing, diagnosing, managing and treating APN in the emergency department. By looking at patient outcomes, the emergency medicine community can comment on how appropriate the current evaluation of acute pyelonephritis is in the emergency department.

The lower sensitivity and specificity of ultrasound to detect hydronephrosis than computed tomography supports a need for more studies as well. There are currently studies on this topic but most of them involve renal colic patients and not patients who have acute pyelonephritis complicated by a stones obstruction. The investigation of ultrasound in these APN patients is also important because we found literature stating that uncomplicated acute pyelonephritis patients can also have a baseline hydronephrosis. It would be interesting to compare the prevalence of hydronephrosis in patients with uncomplicated acute pyelonephritis to those with APN complicated by a ureteral stone. These studies should have a large sample size so that accurate and appropriate generalizations can be applicable. It should

also include tertiary academic medical centers as well as small suburban/rural hospitals to determine how useful ultrasound could potentially be in emergency departments with no access to computed tomography.

CONCLUSION

This study is the first that we are aware of to quantify the association of hydronpehrosis, along with other factors, as predictors of ureteral stone in ED patients suspected of having APN. The implications of our results suggest that ultrasound could potentially be used as a tool to identify hydronephrosis in these patients and select them for further imaging with CT to tree out co-existing ureteral stone. The literature on US and hydronephrosis further supports its use as an imaging tool, however, there are few studies on its use in the setting of APN with coexisting ureteral stones. Our findings support future studies investigating the US findings in APN patients, its implementation in the emergency department, and larger prospective studies identifying factors to help guide imaging decisions in patients with suspected acute pyelonephritis patients.

REFERENCE

1. Colgan R, Williams M, Johnson JR. Diagnosis and treatment of acute pyelonephritis in women. Am Fam Physician 2011;84:519-26.

2. Ramakrishnan K, Scheid DC. Diagnosis and management of acute pyelonephritis in adults. Am Fam Physician 2005;71:933-42.

3. Vourganti S, Agarwal PK, Bodner DR, Dogra VS. Ultrasonographic Evaluation of Renal Infections. Radiol Clin North Am 2006;44:763-75.

4. Fihn SD. Acute Uncomplicated Urinary Tract Infection in Women. N Engl J Med 2003;349:259-66.

5. Montini G, Tullus K, Hewitt I. Febrile Urinary Tract Infections in Children. N Engl J Med 2011;365:239-50.

6. Ramakrishnan K, Scheid DC. Diagnosis and management of acute pyelonephritis in adults. Am Fam Physician 2005;71:933-42.

7. Piccoli G, Consiglio V, Deagostini M, et al. The clinical and imaging presentation of acute "non complicated" pyelonephritis: A new profile for an ancient disease. BMC Nephrol 2011;12:68.

8. Talner LB, Davidson AJ, Lebowitz RL, Dalla Palma L, Goldman SM. Acute pyelonephritis: can we agree on terminology? Radiology 1994;192:297-305.

9. Hooton TM. Uncomplicated Urinary Tract Infection. N Engl J Med 2012;366:1028-37.

10. Urology AUAaEAo. The Management of Ureteral Stones: Diagnosis and Treatment Recomendations. In: Clincal Practice Guidelines; 2007:33.

11. Noble VE, Brown DFM. Renal ultrasound. Emerg Med Clin North Am 2004;22:641-59.

12. Talner LB, Davidson AJ, Lebowitz RL, Dalla Palma L, Goldman SM. Acute pyelonephritis: can we agree on terminology? Radiology 1994;192:297-305.

13. Piccoli GB, Consiglio V, Colla L, et al. Antibiotic treatment for acute 'uncomplicated' or 'primary' pyelonephritis: a systematic, 'semantic revision'. Int J Antimicrob Agents 2006;S28:S49-S63.

14. Lichtenberger P, Hooton TM. Complicated urinary tract infections. Curr Infect Dis Report 2008;10:499-504.

15. Carnell J, Fischer J, Nagdev A. Ultrasound detection of obstructive pyelonephritis due to urolithiasis in the ED. Am J Emerg Med 2011;29:843.e1-3.

16. Stunell H, Buckley O, Feeney J, Geoghegan T, Browne RFJ, Torreggiani WC. Imaging of acute pyelonephritis in the adult. Eur Radiol 2007;17:1820-8.

17. Radiology ACo. Acute Pyelonephritis. In: ACR Appropriateness Critera®; 2012.

18. Nicolle L. Complicated pyelonephritis: Unresolved issues. Curr Infect Dis Report 2007;9:501-7.

19. Hooton TM. Acute complicated cystitis and pyelonephritis. In: Basow D, ed. UpToDate. Waltham MA: UpToDate; 2012.

20. Heptinstall RH. Pyelonephritis: pathologic features. Pathology of the kidney 1992;4:1489-561.

21. Kawashima A, Sandler CM, Goldman SM. Current roles and controversies in the imaging evaluation of acute renal infection. World J Urol 1998;16:9-17.

22. Hooton TM, Stamm WE. Diagnosis and treatment of uncomplicated urinary tract infection. Infect Dis Clin North Am 1997;11:551-81.

23. Talner L, Vaughan M. Nonobstructive renal causes of flank pain: findings on noncontrast helical CT (CT KUB). Abdom Imaging 2003;28:210-6.

24. Springhart WP, Preminger GM. Advanced imaging in stone management. Curr Opin Urol 2004;14:95-8.

25. Berrington De Gonzalez A, Mahesh M, Kim KP, et al. Projected Cancer Risks from Computed Tomographic Scans Performed in the United States in 2007. Arch Intern Med 2009;169:2071-7.

26. Czaja CA, Scholes D, Hooton TM, Stamm WE. Population-based epidemiologic analysis of acute pyelonephritis. Clin Infect Dis 2007;45:273-80.

27. Larson DB, Johnson LW, Schnell BM, Salisbury SR, Forman HP. National Trends in CT Use in the Emergency Department: 1995-2007. Radiology 2011;258:164-73.

28. Berger RE. Risk factors associated with acute pyelonephritis in healthy women. J Urol 2005;174:1841.

29. Bergeron MG. Treatment of pyelonephritis in adults. Med Clin North Am 1995;79:619-49.

30. Bjerklund Johansen TE. Diagnosis and imaging in urinary tract infections. Curr Opin Urol 2002;12:39-43.

31. Bjerklund Johansen TE. The role of imaging in urinary tract infections. World J Urol 2004;22:392-8.

32. Browne RF, Zwirewich C, Torreggiani WC. Imaging of urinary tract infection in the adult. Eur Radiol 2004;14:S168-S83.

33. Chen K-C, Hung S-W, Seow V-K, et al. The role of emergency ultrasound for evaluating acute pyelonephritis in the ED. Am J Emerg Med 2011;29:721-4.

34. van Nieuwkoop C, Hoppe BP, Bonten TN, et al. Predicting the need for radiologic imaging in adults with febrile urinary tract infection. Clin Infect Dis 2010;51:1266-72.

35. Yoshimura K, Utsunomiya N, Ichioka K, Ueda N, Matsui Y, Terai A. EMERGENCY DRAINAGE FOR UROSEPSIS ASSOCIATED WITH UPPER URINARY TRACT STONES. J Urol 2005;173:458-62.

36. Elkharrat D CC, Boudiaf M, Le Corre A, Raskine L, Caulin C. Relevance in the emergency department of a decisional algorithm for outpatient care of women with acute pyelonephritis. Eur J Emerg Med 1999;6:15-20.

37. Lujan Galan M, Paez Borda A, Fernandez Gonzalez I, et al. [Usefulness of ultrasonography in the assessment of acute pyelonephritis]. Arch Esp Urol 1997;50:46-50.

38. Radiology ACo. Radiologic Management of Urinary Tract Obstruction. . In: ACR Appropriateness Critera®.

39. Mostbeck G, Zontsich T, Turetschek K. Ultrasound of the kidney: obstruction and medical diseases. Eur Radiol 2001;11:1878-89.

40. Emergency Ultrasound Guidelines. Ann Emerg Med 2009;53:550-70.

41. Jin DH, Lamberton GR, Broome DR, et al. Effect of Reduced Radiation CT Protocols on the Detection of Renal Stones1. Radiology 2010;255:100-7.

42. Thiemich M. Uber die eitrigen Erkrankungen der Nieren und Harnwege im Sauglingsalter. Jahr Kinderheilkd 1910;72:243.

43. Craig WD, Wagner BJ, Travis MD. Pyelonephritis: Radiologic-Pathologic Review1. RadioGraphics 2008;28:255-76.

44. Weiser AC, Amukele SA, Leonidas JC, Palmer LS. The Role of Gadolinium Enhanced Magnetic Resonance Imaging for Children With Suspected Acute Pyelonephritis. J Urol 2003;169:2308-11.

45. Shokeir A. Renal colic: new concepts related to pathophysiology, diagnosis and treatment. Curr Opin Urol 2002;12:263-9.

46. Curhan G. Diagnosis and acute management of suspected nephrolithiasis in adults. In: Basow D, ed. UpToDate Waltham, MA: UpToDate; 2012.

47. Radiology ACo. Acute onset of Flank Pain. In: ACR Appropriateness Critera®; 2012.

48. Lorenz EC, Lieske JC, Vrtiska TJ, et al. Clinical characteristics of potential kidney donors with asymptomatic kidney stones. Nephrol Dial Transplant 2011.

49. Pietrow PKM. Medical Management of Common Urinary Stones. Am Fam Physician 2006;74:86-94.

50. Akoudad S, Szklo M, McAdams MA, et al. Correlates of kidney stone disease differ by race in a multi-ethnic middle-aged population: The ARIC study. Prev Med 2010;51:416-20.

51. Coll DM, Varanelli MJ, Smith RC. Relationship of Spontaneous Passage of Ureteral Stones to Stone Size and Location as Revealed by Unenhanced Helical CT. Am J Roentgenol 2002;178:101-3.

52. Gilbert EH, Lowenstein SR, Koziol-McLain J, Barta DC, Steiner J. Chart Reviews In Emergency Medicine Research: Where Are The Methods? Ann Emerg Med 1996;27:305-8.

53. Stamm WE. Urinary Tract Infections, Pyelonephritis, and Prostatitis. In: Fauci ASea, ed. Harrison's Principles of Internal Medicine. 17 ed. New York McGraw-Hill; 2008:1822.

54. Sakarya, Arslan, Erkoç, Bozkurt, Atilla. The role of power Doppler ultrasonography in the diagnosis of acute pyelonephritis. BJU Int 1998;81:360-3.

55. Hooton TM. Clinical manifestations; diagnosis; and treatment of acute pyelonephritis. In: Basow D, ed. UpToDate. Waltham, MA: UpToDate; 2012.

APPENDIX

Table A: Odds ratios for factors associated with ureteral stone in patients suspected of APN:

	Prevalence of finding	Ureteral Stone			
Factors from patient chart	n (%)	Yes (n = 106)	No (n = 144)	Odds Ratio	95% C.I.
Left lower quadrant abdominal pain	70 (28%)	32 (30.2%)	38 (26.4%)	0.946	0.541-1.66
Left upper quadrant abdominal pain	28 (11.2)	9 (8.5%)	19 (13.2%)	1.956	0.883-4.33
Midline abdominal pain	7 (2.80%)	1 (.94%)	6 (4.2%)	1.02	0.223-4.65
Right lower quadrant Abdominal pain	63 (25.20%)	21 (19.8%)	42 (29.2%)	1.327	0.748-2.36
Right upper quadrant Abdominal pain	31 (12.40%)	9 (8.5%)	22 (15.3%)	0.84	0.389-1.82
Suprapubic Abdominal pain	25 (10.00%)	4 (3.78%)	21 (14.6%)	0.229	.076-.690
Any Abdominal pain	145 (58.00%)	57 (53.8%)	88 (61.1%)	1.11	0.666-1.84
Abdominal distension	5 (2.00%)	2 (1.9%)	3 (2.8%)	0.904	0.148-5.51
Any Abdominal tenderness	142 (56.80)	60 (56.6%)	82 (56.9%)	0.986	0.594-1.64
Severe abdominal tenderness	44 (17.60%)	12 (11.3%)	32 (22.2%)	0.447	0.218-.916
Mild to moderate abdominal tenderness	75 (63.03%)	38 (35.8%)	37 (25.7%)	2.74	1.23-6.12
Back pain	62 (24.80%)	26 (24.5%)	36 (25%)	1.16	0.651-2.07
Chief complaint abdominal pain	51 (20.40%)	21 (19.8%)	30 (20.8%)	0.764	0.406-1.44
Chief complaint flank pain	91 (36.40%)	35 (33.0%)	56 (38.9%)	1.38	0.82-2.35
Chief complaint groin	2 (0.80%)	1 (.94%)	1 (.70%)	0	N/A
Chief complaint hematuria	14 (5.60%)	5 (4.7%)	9 (3.60%)	0.743	0.242-2.283
Chief complaint dysuria	4 (1.60%)	3 (2.8%)	1 (.40%)	1.36	0.189-9.85
Chief complaint back pain	10 (4.00%)	3 (2.8%)	7 (4.9%)	0.327	0.068-1.57
Any CVA flank tenderness	158 (63.20%)	64 (60.4%)	94 (65.3%)	1.33	0.786-2.25
Chills	70 (28.00%)	20 (18.9%)	50 (34.7%)	0.437	.241-.793
Diarrhea	14 (5.60%)	2 (1.9%)	12 (8.3%)	0.212	0.0463-0.966
Dysuria	82 (32.80%)	28 (26.4%)	54 (37.5%)	1.37	0.189-9.85
White race	144 (57.60%)	70 (66.0%)	74 (51.4%)	1.84	1.10-3.09
African American race	49 (19.60%)	13 (12.3%)	36 (25.0%)	0.419	0.210-.838
Hispanic race	45 (18.00%)	17 (16.0%)	28 (19.4%)	1.24	0.646-2.36
Race other	12 (4.80%)	6 (5.7%)	6 (4.1%)	1.97	0.61-6.37
Family history of stones	15 (6.00%)	9 (8.5%)	6 (4.1%)	2.13	0.734-6.19

Flank pain any	211 (84.40%)	94 (88.7%)	117 (81.25%)	0.944	0.473-1.88
Flank pain or CVA tenderness	227 (90.80%)	99 (93.4%)	128 (88.9%)	0.953	0.401-2.26
Formal UA: Nitrite	44 (17.67%)	12 (11.3%)	32 (43.1%)	0.443	0.216-0.908
Formal UA: Few Bacteria	118 (47.20%)	56 (52.8%)	62 (%)	1.08	0.65-1.8
Formal UA: Moderate Bacteria	72 (29.51%)	25 (23.6%)	47 (32.6%)	0.969	0.554-1.69
Formal UA: Many Bacteria	45 (18.0%)	16 (15.1%)	29 (20.1%)	0.798	0.41-1.55
Formal UA: Leukocyte esterase	196 (79.03%)	73 (68.9%)	123 (85.4%)	0.371	0.200-0.700
Female gender	170 (68.0%)	61 (57.5%)	109 (75.7%)	0.435	0.253-0.748
Male gender	80 (32.00%)	45 (42.4%)	35 (24.3%)	2.3	1.34-3.95
General appearance: Severe	10 (4.00%)	6 (5.7%)	4 (2.8%)	0.902	0.25-3.28
General appearance: Mild	69 (27.94%)	24 (22.6%)	45 (31.25%)	0.83	0.471-1.46
General appearance: Moderate	44 (17.81%)	24 (22.6%)	20 (13.9%)	2.275	1.17-4.42
General appearance: within normal limits	124 (50.20%)	51 (48.1%)	73 (50.7%)	0.693	0.42-1.15
Objective or subjective fever	61 (24.40%)	17 (16.0%)	44 (30.6%)	0.434	0.232-.814
Nausea or vomiting	168 (65.20%)	75 (70.8%)	88 (83.0%)	1.54	0.90-2.63
Pain course: decreasing	10 (4.00%)	6 (5.7%)	4 (2.8%)	2.1	0.578-7.64
Pain course: increasing	73 (29.20%)	30 (28.3%)	43 (29.9%)	0.927	0.533-1.61
No pain	8 (2.53%)	1 (.94%)	5 (3.5%)	0	N/A
Pain Course: resolved	3 (1.20%)	1 (.94%)	2 (1.4%)	0.676	0.061-7.56
Pain Duration <6h	70 (28.00%)	43 (40.6%)	27 (18.8%)	2.96	1.67-5.232
Pain Duration >1w	27 (10.80%)	8 (7.5%)	19 (13.2%)	0.537	0.23-1.28
Lateralized pain	190 (76.00%)	95 (89.6%)	95 (65.9%)	4.45	2.18-9.09
Abrupt pain onset	127 (60.48%)	68 (64.2%)	59 (41.0%)	2.833	1.57-5.11
Gradual pain onset	77 (36.67%)	23 (21.7%)	54 (37.5%)	0.395	0.218-0.716
Pain with movement	63 (25.20%)	18 (17.0%)	45 (31.3%)	0.45	0.242-0.834
Past medical history gallstones	1 (.4%)	0	1 (.70%)	0	N/A
Past medical history GERD/PUD	12 (4.80%)	5 (4.7%)	7 (4.9%)	0.97	0.29-3.14
Past medical history pancreatitis	2 (0.80%)	1 (.94%)	1 (.70%)	1.36	0.0842-22.02
Past medical history vascular disease	66 (26.40%)	31 (29.2%)	35 (24.3%)	1.29	0.731-2.26
Prior history of ureteral/renal stones	96 (38.40%)	46 (43.4%)	50 (47.2%)	1.44	0.86-2.41
Past surgical history abdominal aortic aneurysm	0	0	0	N/A	N/A
Past surgical history	9 (3.60%)	5 (4.7%)	4 (2.8%)	1.73	0.453-6.61

Appendectomy					
Past surgical history Bowel/Laparatomy	3 (1.20%)	1 (.94%)	2 (1.4%)	0.67	0.06-7.56
Past surgical history Cholecystectomy	14 (5.60%)	3 (2.8%)	11 (7.6%)	0.35	0.096-1.30
Past surgical history Pelvic Surgery	25 (10.00%)	10 (9.4%)	15 (10.4%)	0.9	0.386-2.081
Past surgical history PTCA/CABG/Stent	2 (0.80%)	0	2 (1.4%)	0	N/A
Radiation of pain	115 (54.00%)	50 (47.2%)	65 (45.1%)	1.09	0.656-1.79
Radiation of pain to groin	60 (24.00%)	25 (23.6%)	35 (24.3%)	1.08	0.589-1.99
Point of care urine dip hematuria positive	165 (85.94%)	80 (75.4%)	85 (59.0%)	5.411	1.79-16.33
Point of care urine dip leukocyte esterase positive	80 (41.67%)	26 (24.5%)	54 (37.5%)	0.45	0.246-0.814
Point of care urine dip nitrite positive	44 (17.67%)	12 (11.3%)	32 (22.2%)	0.443	.22-.91
Increased urinary frequency	46 (18.40%)	17 (16.0%)	29 (20.1%)	0.76	0.39-1.46
Hydronephrosis Mild or Greater	111 (44.40%)	89 (84.0%%)	22 (15.2%)	29.03	14.57-57.85
Hydronephrosis Moderate or Greater	40 (60.0%)	35 (33.0%)	5 (3.47%)	13.7	5.145-36.50