Predictive Factors for Spontaneous Stone Passage and the Potential Role of Serum C-Reactive Protein in Patients with 4 to 10 mm Distal Ureteral Stones: A Prospective Clinical Study

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Purpose: We investigated possible predictive factors for spontaneous stone passage and the potential role of serum C-reactive protein and white blood count in patients with 4 to 10 mm distal ureteral stones.

Materials and Methods: A total of 251 patients who presented with renal colic secondary to distal ureteral stone were included in study. Patients were grouped according to spontaneous stone passage. Serum C-reactive protein, white blood count and other possible factors were investigated for their potential predictive value for spontaneous stone passage at a followup of 5 weeks. Potential predictive factors for spontaneous stone passage were evaluated with univariate and multivariate analyses. ROC curve analysis was performed to find an optimal cutoff value for serum C-reactive protein according to spontaneous stone passage. Statistical significance was considered at $p < 0.05$.

Results: Spontaneous stone passage was observed in 135 patients (53.8%) in group 1 while 116 (46.2%) in group 2 did not expel the stone spontaneously. Median stone size was 5.7 mm. Stone size, serum C-reactive protein and white blood count were significantly higher in group 2 than in group 1. The number of patients with hydronephrosis and the number with spontaneous stone passage history were significantly lower in group 2 compared to group 1. The cutoff value of serum C-reactive protein provided by ROC analysis was 0.506 mg/l. Time to spontaneous stone passage was significantly higher in patients with serum C-reactive protein above the threshold and in patients with ureteral stones greater than 6 mm.

Conclusions: Stone size, previous spontaneous passage, hydronephrosis, serum C-reactive protein and white blood count can be used to predict spontaneous stone passage in patients with 4 to 10 mm distal ureteral stones. A serum C-reactive protein level of 0.506 mg/l can serve as a cutoff value to predict spontaneous stone passage.

Key Words: ureter, calculi, C-reactive protein, leukocyte count, prognosis

Abbreviations and Acronyms

BMI = body mass index
CRP = C-reactive protein
CT = computerized tomography
ESWL = extracorporeal shock wave lithotripsy
MET = medical expulsive therapy
SSP = spontaneous stone passage
WBC = white blood count

Accepted for publication April 17, 2015.
Study received institutional ethics committee approval.

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Ureteral stone disease is responsible for 20% of urolithiasis cases and has a prevelance rate of 3% to 5%.[1–3] Renal colic due to ureteral stones may negatively affect patient quality of life and routine daily activities, causing significant pain and discomfort.[1,4] Management of renal colic due

0022-5347/15/1944-1009/0
THE JOURNAL OF UROLOGY®
© 2015 by American Urological Association Education and Research, Inc.
http://dx.doi.org/10.1016/j.juro.2015.04.104
Vol. 194, 1009-1013, October 2015
Printed in U.S.A.

to ureteral stones is controversial. Therapeutic alternatives include conservative treatment, ESWL and ureteroscopy.[1]

MET is widely used as a part of conservative management to promote SSP in patients with distal ureteral stones.[3] Although conservative management is simple and cost-effective, it may possibly cause some problems, including renal function deterioration, urosepsis and continuing renal colic pain.[1,3,5,6] ESWL and ureteroscopy are effective and safe procedures that may be preferred in patients with ureteral stones but even they are not without some complications.[1,3] Furthermore, ureteroscopy and ESWL might possibly cause additional cost and overtreatment in patients with ureteral stones that would most likely pass spontaneously.[1,5,7]

Factors that can be used to predict SSP include stone diameter, duration of pain, pyuria and hydronephrosis.[2,3,8,9] Previously the incidence of SSP for distal ureteral stones was reported to be 71% to 98% for stones 5 mm or less and 25% to 51% for stones greater than 5 mm.[3,8] CRP is an acute phase protein that increases as a result of inflammation.[2,3] The inflammatory response due to ureteral stone can cause an increase in the serum CRP level. Serum CRP was previously used to interpret some urological diseases, including pyelonephritis, vesicoureteral reflux, urinary tract infection and ureteral stones.[3,10–12]

Proper selection of ureteral stone patients who would most likely benefit from conservative treatment, ESWL or ureteroscopy is critical but still controversial. In the current prospective study we aimed to investigate possible predictive factors for SSP and the potential role of serum CRP and WBC in patients with 4 to 10 mm distal ureteral stones.

MATERIALS AND METHODS

The study was approved by the institutional ethics committee. Initially 339 patients admitted to the emergency department or urology outpatient clinic from November 2013 to January 2015 for acute renal colic secondary to distal ureteral stone were included in study. During followup 88 patients were excluded from study, including 12 who could not continue MET due to side effects, 6 with acute pyelonephritis, 11 who required nephrostomy catheter or Double-J® stent insertion, 36 who did not complete followup and 23 who underwent ureteroscopy before 5 weeks due to renal function deterioration or pain despite analgesia use.

The study was designed to be prospective. All patients had a solitary 4 to 10 mm distal ureteral stone and patients older than 17 years were eligible for inclusion in the study. All patients were asked to drink 2 L of water daily. They used an α-blocker and a nonsteroidal anti-inflammatory drug for MET and pain relief. Stone size was noted as the longest diameter. Age, gender, cigarette smoking history, BMI, side of the stone, serum WBC, serum CRP measured before nonsteroidal anti-inflammatory drug use, previous SSP and previous ureteroscopy history were noted. Total blood count, urinalysis, serum CRP and renal function tests were done at presentation. Stone identification was performed by plain abdominal film of the kidneys, ureters and bladder, urinary system ultrasound and noncontrast CT. The degree of renal dilatation on noncontrast CT was noted in all patients according to the SFU (Society for Fetal Urology) Hydronephrosis Classification System.

Patients were followed weekly during 5 weeks with plain abdominal film of the kidneys, ureters and bladder, and ultrasound and noncontrast CT if required for SSP by the same radiologist, who was experienced with urinary system imaging. Patients who failed to expel the ureteral stone spontaneously within 5 weeks of followup underwent ureteroscopy.

All patients were informed about the study and proper treatment alternatives. Patients who required early intervention due to impaired renal function, solitary kidney, severe renal colic pain resistant to medical treatment or hydronephrosis grade 3 or greater and those who preferred active stone removal were not included in analysis. Exclusion criteria were a history of renal colic more than 2 hours before presentation, fever 38C, urinary tract infection, recently diagnosed or active infection of another origin, multiple ureteral stones, chronic renal failure, congenital urinary anomalies, previous open or endoscopic ureteral surgery, malignancy, inflammatory disease, liver failure and pregnancy. Patients receiving medications that could potentially affect serum CRP and WBC, including contraceptives and glucocorticoids, and patients who required insertion of a Double-J stent or percutaneous nephrostomy catheter were also excluded from study.

Patients were grouped according to spontaneous stone passage. Descriptive statistics are presented as the median and range, and mean $\pm$ SD. Patients who did and did not expel the stone spontaneously were compared by age, gender, stone size, degree of hydronephrosis, side of the stone, smoking history, BMI, previous spontaneous stone passage, and serum WBC and CRP on univariate analysis. The Mann-Whitney U test was used to compare the means of numerical variables without a normal distribution. To define risk factors for the outcome variable (spontaneous stone passage) multivariable logistic regression analysis was done. Prior to multivariable logistic regression analysis of the association of each independent variable (age, gender, stone size, CRP, previous SSP and hydronephrosis grade) with the outcome variables a univariate estimate was determined by logistic regression analysis. The OR and 95% CI are shown.

Two groups were compared for the number of patients who had serum CRP greater and less than the cutoff value using the chi-square test. ROC curve analysis was performed to find an optimal cutoff value for serum CRP according to SSP. The cutoff was determined using the Youden index and the maximum value of the index served as a criterion to select the optimum cutoff point. The chi-square test was applied to compare time to stone passage in association with the CRP level and stone size in patients

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