Urinalysis findings are not predictive of positive urine culture in patients with indwelling stents

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POOLI A, COOK G, ISHARWAL S, DESAI V, LAGRANGE C. Urinalysis findings are not predictive of positive urine culture in patients with indwelling stents. *Can J Urol* 2016;23(5):8446-8450.

Introduction: *Indwelling stents produce symptoms and urinalysis findings mimicking urinary tract infection (UTI). In this study, we investigated the correlation of urinalysis findings with urine culture in patients with indwelling ureteral stents.*

Materials and methods: *All patients with ureteral stents who underwent stent removal in urology clinic from July 2013 to January 2015 and had urine culture available immediately prior to stent removal were included in this study. Urine culture results as well as age, gender, duration of indwelling stent, and reason for stent placement were collected.*

Results: *A total of 122 patients were included in this study. The two most common reasons for ureteral stent placement included urolithiasis (65.6%) and renal transplant (22.1%). Red blood cell (RBC), leukocytes and nitrite were positive in 92.9%, 70.2% and 17.9% of urine samples respectively. Only 17 patients (13.9%) had positive urine culture. Although renal transplant patients had significantly longer duration of stent retention, no statistically significant difference was noted in rate of positive urine culture compared to urolithiasis patients (p = 1.0). Among patients with positive urine culture, 62.5% had resistant bacteria to common antibiotic treatments and two patients had yeast in urine culture (12.5%). The duration of stent retention did not correlate with bacterial resistance. Multivariate analysis failed to show significant correlation of gender, reason for stent, stent duration, RBC and nitrite with positive urine culture.*

Conclusions: *Positive findings on urinalysis in patients with indwelling ureteral stent have poor correlation to positive urine culture and therefore the use of urine culture to diagnose UTI is warranted.*

Key Words: indwelling ureteral stent, stent related infection, bacterial resistance

Introduction

Ureteral stents are frequently used in urologic procedures. Lower urinary tract symptoms (LUTS) can be common immediately after and through the duration of stent retention. The discomfort patients experience with ureteral stenting has been well documented, such as dysuria, frequency, urgency, incontinence, suprapubic pain, flank pain and gross hematuria.[1] The difficulty lies in determining the origin of symptoms in these patients, whether it is from a true urinary tract infection (UTI) or simply secondary to stent insertion. Urinalysis, although helpful in diagnosing UTI, may be falsely positive in patients with ureteral stents in place. As expected with introduction of any foreign body, inflammation in the ureter following stent placement in porcine model studies has been described.[2,3] Urine culture may be the only method to differentiate infectious versus irritative stent symptoms in patients with ureteral stents.

Currently the mainstay of work up for acute UTI symptoms in physician office or emergency department settings is urinalysis. With LUTS and positive urinalysis findings (RBC, leukocytes, nitrites), many physicians are inclined to prescribe antibiotics. Undoubtedly, the use of unnecessary antibiotics to treat LUTS increases the risk of UTI's with resistant bacterial species in the future. A study by Kehinde et al revealed a higher incidence of antibiotic resistant bacteria in urine cultures of patients with ureteral stents.[4]

Accepted for publication June 2016

Acknowledgment

The authors would like to express their sincere gratitude to Robin High, MBA, MA who performed the statistical analysis for this study.

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In this prospective study, we hypothesized that urinalysis findings are not predictive of positive urine cultures in patients with indwelling ureteral stents. We also investigated the incidence of bacterial resistance in isolated cultures. With this information we hope to improve practice patterns and patient care by stressing the importance of attaining a urine culture before treating patients with positive urinalysis with an indwelling ureteral stent.

Materials and methods

The authors' Institutional Review Board (IRB) in University of Nebraska Medical Center (202-14-EP) approved the study protocol, and all clinical investigation was conducted according to the principles expressed in the Declaration of Helsinki. The data were obtained prospectively and analyzed anonymously and reported. Therefore, no consent was obtained from study population. All patients who presented to urology clinic for stent removal from July 2013 to January 2015 were considered for inclusion in the study. Patients who were unable to provide a urine sample and patients who received antibiotic treatment other than perioperative prophylaxis were excluded from the study.

Clean catch urine sample was obtained for urinalysis and urine culture prior to stent removal. Positive urine culture was defined as growth of more than 10,000 colonies/unit of single bacteria in urine culture sample. In case of growth of three or more types of bacteria in urine sample, urine culture was determined as contaminated. Results for urine cultures (positive, negative, contaminated), bacterial resistance (no resistance, resistant, yeast), and urinalysis results (leukocyte, nitrite, RBC) were recorded. In case of positive urine cultures, patients were treated with appropriate antibiotics based on culture sensitivity. Demographic information including age, gender, stent duration, and reason for stent placement were recorded in a data sheet. All statistical results and graphical displays were produced with SAS/STAT and SAS/SG software, Version 9.4 (2002-2012) of the SAS System for Windows (Cary, NC, USA).

TABLE 1. **Indications for ureteral stent placement**

Indication for stent placement	**Number of patients (n)**
Urolithiasis	80
Renal transplant	27
Other*	16

*indications: metastatic pancreatic cancer, pyeloplasty, ureteral reimplantation, retroperitoneal lymph node dissection, iatrogenic ureteral injury during ob/gyn sugery, ureterolysis for retroperitoneal fibrosis, bladder cancer and renal trauma

Results

From July 2013 to January 2015, a total of 188 patients presented to urology clinic for cystoscopy and stent removal. Of those, 65 patients were excluded due to inability to provide a urine sample, inadequate urine sample, or failure to collect a urine sample in clinic. One patient was excluded from the study due to considerably long duration of stent (290 days, missed to follow up) and receiving several antibiotic treatments for reasons other than UTI (pneumonia, abscess). One hundred and twenty two patients were included in the study. The study consisted of 56 females and 66 males. The two most common reasons for ureteral stent placement included urolithiasis (N: 80, 65.6%) and renal transplant (N: 27, 22.1%). Other reasons for stent placement included metastatic pancreatic cancer, pyeloplasty, ureteral reimplantation, retroperitoneal lymph node dissection, iatrogenic ureteral injury during gynecologic surgery, ureterolysis for retroperitoneal fibrosis, bladder cancer and renal trauma, Table 1. Eighty-four patients had urinalysis available in addition to urine culture. Of those, RBC and leukocytes were positive in 92.9% and 70.2% of urine samples respectively. Nitrite showed a much smaller positive response rate of 17.9%. In 15.5% of the patients, both nitrite and leukocytes were positive in urine sample. However 72.6% of patients had positive leukocyte or nitrite in urine.

Positive and negative predictive values of urinalysis findings (nitrite, leukocyte, RBC, individually and in combination) were calculated for having a positive urine culture. Results are summarized in Table 2a. Positive predictive value of RBC, leukocyte, nitrite and nitrite/leukocyte (nitrite or leukocyte) were 12.8%, 16.9%, 20% and 16.4%, respectively. Negative predictive value of RBC, leukocyte, nitrite and nitrite/leukocyte (nitrite or leukocyte) calculated to be 100%, 96%, 79.7% and 95.7% respectively. In addition, sensitivity/specificity of RBC, leukocyte, nitrite and leukocyte/nitrite in the urine sample for positive urine culture were also calculated to be 100%/8.1%, 100%/33.8%, 30%/83.8% and 100%/31.1%.

Only 17 patients (13.9%) had positive urine culture. When comparing positive urine culture incidence between renal transplant patients (14.8%), urolithiasis patients (13.8%) and ureteral stent placement for reasons other than renal transplant and urolithiasis (13.3%), no

TABLE 2. **A) Sensitivity and specificity of urinalysis findings for positive urine culture in this study. B) Sensitivity and specificity of urinalysis findings for positive urine culture reported in other studies[7,8]**

A	**RBC (%)**	**Leukocytes (%)**	**Nitrites (%)**	**Nitrites or leukocytes (%)**
Sensitivity	100	100	30	100
Specificity	8.1	33.8	80.3	31.1
PPV	12.8	16.9	20	16.4
NPV	100	96	79.7	95.7
B	**RBC (%)**	**Leukocytes (%)**	**Nitrites (%)**	**Nitrites or leukocytes (%)**
Sensitivity	18-44	90-96	19-48	X
Specificity	88-89	47-50	92-100	100
PPV	27	56-59	50-83	100
NPV	82	83-95	70-88	X

RBC = red blood cell; PPV = positive predictive values; NPV = negative predictive values

statistically significant difference was noted (p = 1.0), Figure 1. However, the duration of stent retention was considerably longer for the transplant patients (median: 42 days) compared to urolithiasis patients (median: 12 days) (hazard ratio 9.6% (0.050-0.174, 95% confidence interval, p < .001), Figure 2 and Table 3.

The patients who needed ureteral stents for reasons other than kidney transplant and urolithiasis had significantly higher rates of contaminated urine culture (p value: 0.016 and 0.42). Of those patients with positive urine culture, 10 patients (62.5%) had resistant bacteria to common antibiotic treatments (fluoroquinolones, trimethoprim-sulfamethoxazole) and two patients had yeast in urine culture (12.5%). Antibiogram was not available for one of the positive urine cultures.

The median duration of stent retention was 16 days and 20 days for patients with negative and positive urine culture, respectively. The chi-square test did not indicate a statistically significant difference in stent duration and positive urine culture (p = 0.86). In addition, the duration of stent retention did not correlate with bacterial resistance when assessing patients with positive urine culture, Figure 3. The median stent duration in bacterial resistant group and non-bacterial resistant group was 21 and 18 days, respectively. The chi-square test did not indicate a different in stent duration based on the culture result (p = 0.33). The exact chi-square test failed to show a significant difference in the reason for stent and bacterial resistance (p = 0.55), though the sample size of 16 did not allow for a test of sufficient power to detect a difference. Multivariate analysis to evaluate results with bacterial resistance was not of practical value and in most cases could not be estimated (e.g., with the urinalysis results). However, gender had a pattern of interest with 100% bacterial resistance/yeast in males and 55.5% bacterial resistance/yeast in females in case of positive urine culture (p = 0.088). Exact methods did not show a significant effect of age (p = 0.24) or stent duration (p = 0.40) on incidence of bacterial resistance/yeast.

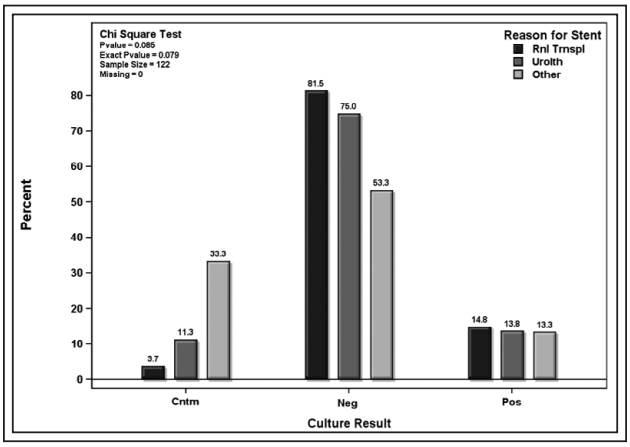

Figure 1. Reason for stent by culture result.

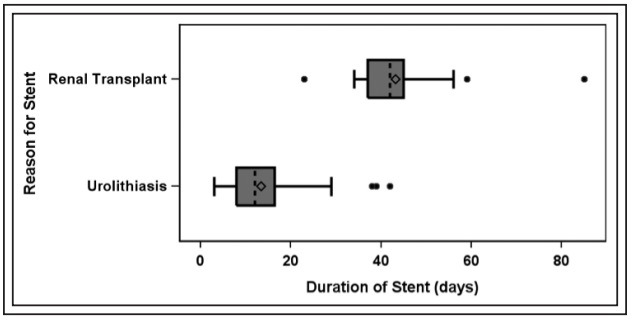

Figure 2. Duration of stent by transplant/urolithiasis.

TABLE 3. **Duration of stent by reasons for stent placement**

Reason for stent	Duration of Stent (days)			
	N	Min	Median	Max
Renal transplant	27	23	42	85
Urolithiasis	80	3	12	42
Other	15	7	29	59

The urine cultures were contaminated in 15 patients, 14 of them were females. The odds ratio was 21.7 for females to have contaminated urine culture compared to males ($p < 0.0001$).

Multivariate analysis for age, gender, reason for stent, stent duration, and urinalysis findings failed to show significant correlation of gender, reason for stent, stent duration, RBC, nitrite. However, age (in units of 5 years) had significant odds ratio of 1.242 (1.034 to 1.527), which meant that for each 5 year increase in a subject's age, the chance of a positive culture result increased. In addition, positive leukocytes on urinalysis provided an exact odds ratio of 6.84 with confidence interval 1.34-infinity, $p = 0.046$. The exact odds ratio for nitrite/leukocyte (nitrite or leukocyte) was 6.05 with confidence interval 1.18-infinity, $p = 0.065$. In both cases a positive test for leukocyte was associated with a positive culture result.

Discussion

Discomfort and symptoms resulting from indwelling ureteral stents affect up to 80% of patients.[5] LUTS from ureteral stents has been well researched. A review article by Miyaoko et al, highlighted the incidence of specific symptoms such as frequency (50%-60%), urgency (57%-60%), dysuria (40%), incomplete emptying (76%), flank pain (19%-32%), suprapubic pain (30%), and hematuria (25%). In addition, the potential etiology of each of these LUTS was defined.[6] With the rate of LUTS being so high among this unique population, many of these patients may present to providers other than their urologist, such as primary care physicians, acute care, or emergency departments, for care. Standard management of patients that present with LUTS in these settings commonly involves the use of urinalysis to either help rule in or rule out UTI. In most cases if a patient is symptomatic and urinalysis shows evidence of infection (positive for leukocyte esterase, nitrites, or RBC's), the reflex management is empiric antibiotics. In this study, we did not evaluate the LUTS but we checked the urine culture and urinalysis findings in patients with indwelling ureteral stents.

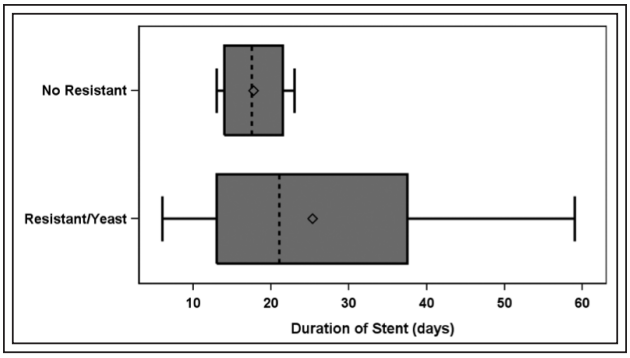

Figure 3. Duration of stent by bacteria resistance.

A review article by the American Academy of Family Physicians cites a sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV) for leukocytes of 90%-96%, 47%-50%, 56%-59%, and 83%-95%, respectively. RBC's on urinalysis are cited at 18%-44%, 88%-89%, 27% and 82% respectively. Similarly for abnormal nitrites sensitivity, specificity, PPV, and NPV are cited at 19%-48%, 92%-100%, 50%-83%, and 70%-88%, respectively.[7] The combination of leukocytes on urinalysis and nitrite positivity has been shown to have a specificity of 100% and PPV of 100% in a study done by Leman.[8] Although NPV seen for each of the respective urinalysis findings are at or above 79%, the PPV seen in our study compared to other studies is much lower. The comparison of our results to figures seen in other reviews and studies, Table 2b, calls into question the reliability of urine dipstick and urinalysis to predict urine culture positive UTI in patients with ureteral stents.

In our study the rate of positive clean catch urine culture prior to stent removal was 13.9%. This rate of positive urine culture is in accordance with rates found by Kehinde et al (16.8%),[9] but other studies have shown higher 26.1%,[10] 21%[11] rates of positive urine culture. Comparing our data to data of similar studies, it was interesting to observe that our positive urine culture rates were lower than that of other studies, especially considering that that 22.1% of our patients had ureteral stent placement after renal transplantation and were immunosuppressed. In fact, although the renal transplant patients were under immunosuppressive therapy and had significantly longer duration of stent compared to stone patients ($p < .001$), the rates of positive urine culture between the groups was not statistically significant ($p = 1.0$).

Of the patients in our study with positive urine culture, the prevalence of antibiotic resistance to ciprofloxacin or TMP-SMX (two commonly used UTI treatments) was 62.5%. A much higher rate of antibiotic

resistance to ciprofloxacin and TMP-SMX is seen when comparing the patients of our study to the antibiogram for hospital wide UTIs at our institution. When incorporating the presence of yeast on two positive cultures, a treatment failure rate of up to 75% could be expected based on results from our study. These findings are indicative of higher antibiotic resistance among patients with ureteral stents in place compared to other patients being assessed and managed for UTI, likely due to prior antibiotic exposure in these surgical patients.

No correlation between duration of stent placement and rate of positive urine culture was found in our study ($p = 0.86$), which is in concordance with Lifshitz et al who found no correlation between stent dwelling time and bacteriuria.[12] Numerous other studies have found a statistical significance when comparing ureteral stent duration to positive urine culture.[10,13] This difference however may be due to our overall low duration of stent retention. The average duration of stent in patients with positive and negative urine culture was 16 and 20 days, respectively. Studies highlighted above by Klis et al and Farsi et al that showed a significant correlation between stent duration and positive urine culture compared groups with stent duration of 20-30 days, 30-90 days, and greater than 90 days. However, much lower rates of positive urine culture, 7.1%[10] and 15.4%,[13] respectively, were seen in the 20-30 day group.

Contamination rates were significantly higher in females compared to males (p value < 0.0001). This is in concordance with other studies that have shown females to have higher rates of urine contamination as compared to males, which may or may not be related to collection technique.[14,15]

Multivariate analysis for numerous factors found age had positive correlation with positive urine culture. Increasing age was a risk factor for positive urine culture (odds ratio: 1.242). The prevalence of bacteriuria has been shown to have a J-shaped distribution, with a higher frequency among the very young and a gradual increase with age in both men and women.[16] This is in concordance with our study that for each 5 year increase in a subject's age, the chance of a positive culture result increased.

Conclusion

The lack of reliability of urinalysis findings to differentiate infectious versus irritative LUTS, as well as the higher incidence of bacterial resistance among patients with indwelling ureteral stents, can lead to the use of unnecessary antibiotics in this patient population. Positive findings on urinalysis in this population have poor correlation to positive urine culture and therefore the use of urine culture to diagnose UTI is warranted. Possible exceptions would be in patients appearing toxic, septic, febrile, or pregnant. Utilization of urine culture in patients with ureteral stents can eliminate unwarranted use of antibiotics as well as give guidance for appropriate antibiotic selection in this population at higher risk for antibiotic resistant UTI's.

Although this study confirms a common concept among urologists, many of the patients with indwelling ureteral stents may be seen by other health care professionals who are not as familiar with taking care of these patients.

That would be interesting to look at the pattern of antibiotic prescription and health care costs in patients with indwelling ureteral stents. □

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