Diabetes mellitus is associated with increased risk of positive qSOFA score but not with increased ICU admission in patients undergoing ureteral stent placement for ureteral stone and suspected infection

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Abstract

Introduction: Patients presenting with an obstructing ureteral stone and urinary tract infection (UTI) are at risk for severe infectious complications. Historically, diabetes mellitus (DM) was considered a risk factor for the development of septic shock in these patients. This study aimed to evaluate DM's impact on risk of septic shock in ureteral stent placement for ureteral stone and presumed UTI.

Methods: An institutional review board-approved, retrospective review was performed at two institutions. All patients who met the following criteria from July 2016 to April 2020 were included in the study: emergency department visit with obstructing ureteral stone, concern for UTI, and ureteral stent placement. The primary outcome of interest was the development of postoperative septic shock defined by sepsis with hypotension requiring vasopressor support for at least one hour.

Results: The study cohort was made up of 187 patients. Median age was 61 (range 16–91). Males represented 40.1% (n=75) of the population, while DM was present in 26.2% (n=49). Thirty-five of 143 patients (18.7%) met the criteria for postoperative septic shock. Quick Sequential Organ Failure Assessment (qSOFA) criteria were met by 11 (22.4%) patients with DM compared to 13 (9.5%) of patients without DM (p=0.026). This difference did not translate into significant differences in use of vasopressors, with DM cohorts requiring pressors in 11 (22.4%), and 241 (17.5%) in non-DM (p=0.523). Purulent urine was more frequently described in patients with DM (22 [44.9%] vs. 342 [4.8%], p=0.011). Intensive care unit (ICU) admissions were similar between DM and non-DM at 13(27.1%) vs. 29 (21.2%), respectively (p=0.543). ICU stay and length of stay were similar between cohorts.

Conclusions: In this multicenter study of patients who underwent ureteral stenting for ureteral stone and presumed UTI, DM was not associated with an increased risk of development of septic shock but was associated with an increased risk of positive qSOFA score.

Introduction

It is estimated that 1% of the United States population between the ages of 18 and 65 will experience a kidney stone event each year — that is, renal colic or other symptoms that prompt the diagnosis of renal or ureteral stone.[1] Of all patients who experience a ureteral stone, roughly 25% will require intervention for that stone; intervention may include a temporizing ureteral stent placement followed by definitive therapy with shockwave lithotripsy, ureteroscopy, or percutaneous nephrolithotomy.[1] Patients who present with an acute obstructing ureteral stone and concomitant pyelonephritis or urinary tract infection (UTI), are at significant risk for infectious complications, including urosepsis, and even mortality, the latter at a rate of 9–19%.[2]

For patients with ureteral stone and ureteral obstruction or presumed UTI, the standard of care is urgent decompression and drainage of the infection either with ureteral stent or with percutaneous nephrostomy and deferral of definitive stone treatment until infectious issues are resolved.[3] Prompt decompression, in addition to intravenous antibiotics, has been demonstrated to reduce mortality by nearly 50% when compared to antibiotics alone;[2] however, among the group of patients who undergo ureteral stent placement for decompression of ureteral stone and concomitant infection, specific risk factors for development of urosepsis and other significant complications are not well understood.

It has been hypothesized that patients with diabetes mellitus (DM) may be at increased risk for UTI due to impairment of immune function associated with poor glycemic control.[4,5] The current study examined a cohort of patients who presented to the emergency department with ureteral stone and UTI and underwent emergent ureteral stent placement, comparing infectious outcomes in patients with and without DM.

Methods

A institutional review board-approved, retrospective review was performed at two institutions. Records of patients admitted from July 2016 to April 2020 were screened for inclusion. Patients presenting to the emergency department (ED) with at least one unilateral obstructing stone and documented concern for concomitant infection, who were taken directly from the ED to the operating room for stent placement, were included. Patients with bilateral obstructing stones, obstructed solitary or transplanted kidneys, obstructions from other etiologies, diagnosed as inpatients, with documented pyelonephritis within the 30 days prior, or those stented for other reasons (such as acute kidney injury) were excluded. Patients already on vasopressor support while in the ED were also excluded. The primary outcome of interest was the development of postoperative septic shock, as defined by the quick Sequential Organ Failure Assessment (qSOFA), with at least two of the following criteria: respiratory rate >22, altered mental status and or systolic blood pressure <100 mmHg, and vasopressor need to maintain mean arterial pressure >65 mmHg.[5]

Patient definitions were as follows: prior endourological procedure was considered for all patients who had shockwave lithotripsy, ureteroscopy, and/or percutaneous nephrolithotomy within 30 days prior to admission. Diabetes mellitus was considered in patients who reported having DM, those with evidence in the electronic medical record, or those with prescription for oral or injected anti-diabetic medications. Diabetes control was assessed using most recent Hb1Ac, for which values <7% were considered adequately controlled. Patients with reports or evidence of prior urosepsis at any timepoint prior to admission were considered as positive for history of urosepsis. Recurrent UTI was defined as patients with history or evidence at any time of two episodes in six months or three in 12 months prior to admission. Advanced age was defined as 65 or older.

Data was analyzed using SPSS v25. The Kolmogorov-Smirnov test was used to assess for normality. Parametric testing was performed using Student's t-test or ANOVA, with post-hoc Tukey, with results expressed as means and standard deviations. Nonparametric testing was performed using Mann-Whitney U test or Kruskall-Wallis, and results are expressed as medians and ranges. Qualitative variables are expressed as frequency and percentage, with testing performed through Chi-squared or Fisher's exact test where applicable.

Single and multiple logistic regressions were performed for further analysis. Omnibus test was used to assess the model and Hosmer and Lemeshow test was used to assess data fitness to the model. Testing was done through Enter and Forward Wald's approach. Results are expressed in odds ratio (OR) and adjusted OR. Models with variables whose OR approached infinity were excluded from modelling. P-values under 0.05 were considered statistically significant.

Results

Baseline characteristics

The study cohort was made up of 187 patients from two institutions. Median age was 61 years (range 16–91). Males represented 40.1% (n=75) of the population, while females made up 59.9% (n=112). Patients over 65 years old made up 42.8% (n=80) of included cases. Median body mass index (BMI) was 27 (range 17.33–59), with 34.6% (n=64) of patients having obesity. Diabetes mellitus was reported in 26.3% (n=49), of which 41% (n=16) were inadequately controlled according to Hb1Ac levels. Hypertension was previously diagnosed in 45.4% (n=84) of patients. History of prior UTI was present in 21% (n=39) of patients, while 13% (n=24) had prior history of pyelonephritis or urosepsis. Prior endourological procedures were recorded in 3.3% (n=6) of patients. Multiple stones were present in 7.7% (n=14) of patients; the majority of stones were either middle/proximal (52.7%, n=98) or distal (43%, n=80).

Twenty-two percent (n=42) of patients from the cohort were admitted to the intensive care unit (ICU), while qSOFA criteria was met in 12.8% (n=24) of patients. Vasopressors were used in 18.7% (n=35) of patients. Median vasopressor pressor time was 12.5 hours (range 1–408) and median ICU stay was two days (range 1–24). Median length of stay for the entire cohort was two days (range 0–27). Baseline characteristics are fully summarized in Table 1.

Diabetes mellitus

Patient demographic information, as well as baseline characteristics, are displayed in Table 2. Of note, median age for DM and non-DM patients was 65 years (range 42–92) and 60 (range 16–93), respectively; these were statistically different (p=0.019). The DM cohort had significantly higher median BMI (29.43 [range 18.70–59.05] vs. 24.15 [range 19.22–36.28], p=0.001).

qSOFA criteria was met by 22.4% (n=11) of patients with DM compared to 9.5% (n=13) of patients without DM (p=0.026). This difference did not translate into significant differences in use of vasopressors, with DM cohorts requiring pressors in 22.4% (n=11) as opposed to 17.5% (n=241) in non-DM patients (p=0.523). ICU admissions were also similar between DM and non-DM cohorts, at 27.1% (n=13) and 21.2% (n=29), respectively (p=0.543). ICU stay and length of stay were similar between cohorts. Table 2 summarizes findings from analysis of these cohorts. In diabetic patients, HbA1c means were not different between qSOFA+ (5.12±1.22) and qSOFA– (6.05±0.65) (p=0.848). When comparing diabetic patients with septic shock, HbA1c levels were similar in those with shock (6.12±1.2) vs. those without (6.07±0.89) (p=0.888).

Table 1. Frequencies (percentages) and mean (SD) or median (range) from the baseline characteristics and general outcomes of the included cohort

Gender (male)	70 (40.1%)
Age	61 (16–93)*
Geriatrics	80 (42.5%)
BMI	27 (17–53)*
Obesity	64 (34.6%)
DM	49 (26.3%)
HTN	84 (45.4%)
Positive culture within 90 days of admission	8 (6.1%)
History of recurrent UTI	39 (21%)
History of prior pyelonephritis or urosepsis	24 (13%)
Prior endourological procedure	6 (3.3%)
Neuromuscular disorder	10 (5.4%)
Multiple sclerosis	8 (4.3%)
Other	2 (1.1%)
Charlson comorbidity index	
0	35 (24.5%)
1	20 (14%)
2	31 (21.7%)
3	22 (15.4%)
4	14 (9.8%)
5	13 (9.1%)
6	7 (4.9%)
7	0
8	0
9	0
10	1 (0.7%)
Multiple stones	14 (7.5%)
Stone location	
Proximal	8 (4.3%)
Medial	98 (52.7%)
Distal	80 (43%)
Struvite stones	33 (17.7%)
Hydronephrosis	
None	10 (5.3%)
Mild	74 (39.6%)
Moderate	61 (32.6%)
Severe	12 (6.4%)
Operative time	23 (4–58)*
Sepsis	24 (12.8%)
ICU admission	42 (22.6%)
Vasopressors	35 (18.7%)
ICU stay	2 (1–24)*
Length of stay	2 (0–27)*

*Range. BMI: body mass index; DM: diabetes mellitus; HTN: hypertension; ICU: intensive care unit; SD: standard deviation; UTI: urinary tract infection.

Table 2. Findings of comparing baseline and outcomes of patients with DM vs. those without

	DM	No DM	p
Gender (males)	44.9% (22)	38% (52)	0.401
Age	65 (41–92)*	60 (16–93)*	0.019
Geriatric (>65)	53.1% (26)	38.7% (53)	0.093
BMI	29.43 (18.70–59.05)*	24.15 (19.22–36.28)*	0.001
Obesity	55.1% (27)	27.4% (37)	0.001
Hb1Ac	6.95 (1.27)†		
History of recurrent UTI	14.6% (7)	22.6% (31)	0.301
History of pyelonephritis or urosepsis	14.6% (7)	12.4% (17)	0.803
Prior endourological procedure	0% (0)	4.4% (6)	0.341
Stone location			0.496
Proximal	6.1% (3)	3.7% (5)	
Medial	57.1% (28)	51.5% (70)	
Distal	36.7% (18)	44.9% (61)	
Multiple stones	8.2% (4)	9 (6.6%)	0.747
Stone size	7 (3–17)*	5 (3–15)*	0.687
Purulent urine	44.9% (22)	24.8% (34)	0.011
Hydronephrosis			
None	10.2% (5)	3.6% (5)	0.154
Mild	38.85% (19)	40.1% (55)	
Moderate	22.4% (11)	36.5% (50)	
Severe	8.2% (4)	5.8% (8)	
Operative time	22 (10–46)*	32 (6–56)*	0.50
qSOFA	22.4% (11)	9.5% (13)	0.026
ICU admissions	27.1% (13)	21.2% (29)	0.426
Vasopressors used	22.4% (11)	17.5% (24)	0.523
Vasopressor time	39.25 (2–96)*	14 (1–408)*	0.581
ICU stay	2.5 (1–17)*	2 (1–24)*	0.330
Length of stay	10.5 (3–26)*	5 (2–27)*	0.193

*Range. †Standard deviation. BMI: body mass index; DM: diabetes mellitus; HTN: hypertension; ICU: intensive care unit; qSOFA: quick Sequential Organ Failure Assessment; UTI: urinary tract infection.

Table 3. Summarizes single and multiple logistic regressions for target outcomes in relation to DM

	OR	p	AOR	p
qSOFA	3.07 (1.01, 9.36)	0.048	2.90 (1.06, 7.93)	0.038
ICU admission	1.47 (0.62, 3.50)	0.378	–	–
Septic shock	1.49 (0.56, 3.90)	0.417	–	–

AOR: adjusted odds ratio; DM: diabetes mellitus; ICU: intensive care unit; OR: odds ratio; qSOFA: quick Sequential Organ Failure Assessment.

Regression analysis

Single and multiple logistic regression analyses analyzing the effect of DM diagnosis on qSOFA criteria fulfillment, ICU admission, and septic shock adjusted for age, gender, weight, prior history of endourological procedures, recurrent UTI, and urosepsis were performed. These revealed significant odds of positive qSOFA score in patients with DM (OR 3.07 [1.01, 9.36], p=0.038) but not for ICU admission (OR 1.47 [0.62, 3.50], p=0.378) or septic shock (OR 1.49 [0.56, 3.90], p=0.417). Models are summarized in Table 3 and Figure 1.

Discussion

Urosepsis refers to a clinical syndrome characterized by excessive, dysregulated host inflammatory response to an

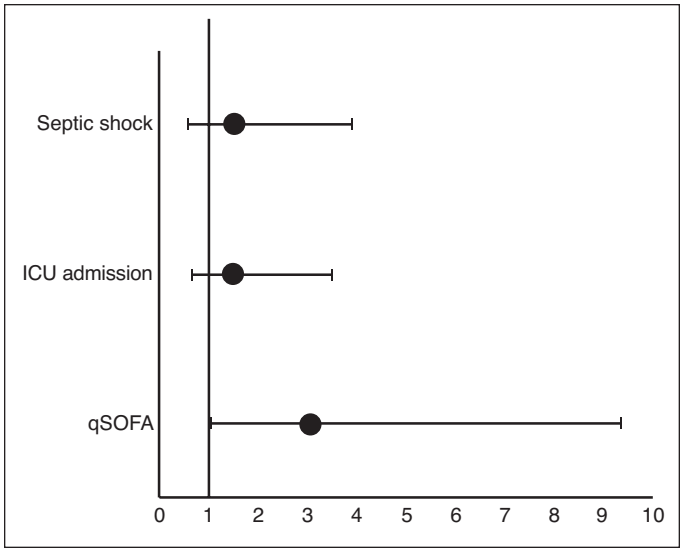

Figure 1. Displays forest plot of regression analysis of the impact of diabetes mellitus on measured outcomes. ICU: intensive care unit; qSOFA: quick Sequential Organ Failure Assessment.

infection arising from the genitourinary tract.[6] The third international consensus definitions for sepsis and septic shock define septic shock as a lactate level >2 mmol/L and necessity for vasopressor support to maintain a mean arterial pressure of 65 mmHg in the absence of hypovolemia.[6] Worldwide, the overall prevalence trends to an increase, and while improvements in management stemming from better understanding has led to a decrease in mortality, it remains high in urosepsis at an estimated 40%.[7,8] This high morbidity and mortality has led multidisciplinary teams to seek a better understanding of the underlying risk factors and their impact on risk. Various studies have attempted to determine and stratify factors associated with sepsis in urological pathologies and procedures.[9-11] Diabetes mellitus' role in susceptibility to infection and sepsis has been previously described in both urological and non-urological procedures.[4,5]

Prior studies in cohorts with UTIs, urolithiasis (even when non-obstructing), DM, acute kidney injury, and heart failure were identified as an important risk factor for progression to septic shock in patients with UTIs.[9-14] While patients with DM in this study were not at increased risk for septic shock, multivariate regression demonstrated a nearly threefold risk for DM patients to have a positive qSOFA score when compared with non-diabetic patients. qSOFA is an assessment score that was designed to evaluate patients for risk of sepsis, and a recent consensus conference put forth qSOFA criteria as superior to Systemic Inflammatory Response Syndrome (SIRS) criteria for the prediction of infectious complications in medicine in general. Few studies have evaluated this in the urologic literature.[6] This finding underscores the concept that these predictive scoring systems (e.g., qSOFA, SIRS) may demonstrate false-positives in terms of their ability to predict septic shock as a clinical endpoint for patients with stone disease and concomitant UTI.

In the current study, it did not appear that DM was associated with increased risk of septic shock in patients who presented with obstructing ureteral stones and concomitant UTI who underwent ureteral stent placement. For this entire cohort, the rate of admission to the ICU, the rate of prolonged vasopressor use, and the duration of ICU stay were the same for patients with and without DM. In our study, the ICU admission rate was above 20% for patients presenting with the aforementioned clinical scenario. It is important to note that in our study, patients without DM appear to experience the infectious complications that we defined as our endpoints as often as those with DM.

Limitations

Our study has various limitations. It is a retrospective study and is subject to the inherent biases of a non-prospective study. Also, sample size was small (<200 patients), which may have affected accurate statistical analysis of our findings; however, ICU admission rates were not negligible, which perhaps adds strength to the findings. In addition, DM was analyzed as a binary factor and our analysis did not include possible modifying and confounding factors related to the management and control. For example, length of DM diagnosis, current management regimes, and type of DM are unaccounted and unadjusted for. In addition, our pool of identified diabetes patients had a relatively well-managed DM and further studies need to analyze the impact of management on studied outcomes. Another factor to consider as potential limitation is related to the management each patient received in the ED prior to stenting, which was non-protocolized, per se, and may have been dependent on the patient's perceived condition and possibility of deterioration, thus introducing heterogeneity. Further prospective studies are important to examine these findings and to better understand the pathophysiology and risk factors for sepsis in these kidney stone patients.

Conclusions

In this multicenter study of patients who underwent ureteral stenting for ureteral stone and presumed UTI, DM was not associated with an increased risk of septic shock. This information may be useful when evaluating patients with ureteral stones and presumed infection.

Competing interests: Dr. Borofsky has been a consultant for Auris Health and Boston Scientific. Dr. Eisner has been a consultant for Ambu, Auris Health, Boston Scientific, Calyxo, Cook, Dr. Arnie's LLC, Olympus, and Sonomotion. The remaining authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

References

1. Saigal CS, Joyce G, Timilsina AR. Urologic Diseases in America project. Direct and indirect costs of nephrolithiasis in an employed population: Opportunity for disease management? *Kidney Int* 2005;68:1808-14. https://doi.org/10.1111/j.1523-1755.2005.00599.x
2. Borofsky MS, Walter D, Shah O, et al. Surgical decompression is associated with decreased mortality in patients with sepsis and ureteral calculi. *J Urol* 2013;189:946-51. https://doi.org/10.1016/j.juro.2012.09.088
3. Assimos, D, Krambeck, A, Miller, NL, et al. Surgical management of stones: American Urological Association/Endourological Society guideline, part I. *J Urol* 2016;196:1153-60. https://doi.org/10.1016/j.juro.2016.05.090
4. Kamei J, Yamamoto S. Complicated urinary tract infections with diabetes mellitus. *J Infect Chemother* 2021;27:1131-6. https://doi.org/10.1016/j.jiac.2021.05.012
5. Frydrych LM, Fattahi F, He K, et al. Diabetes and sepsis: Risk, recurrence, and ruination. *Front Endocrinol (Lausanne)* 2017;8:271. https://doi.org/10.3389/fendo.2017.00271
6. Singer M, Deutschman CS, Seymour CW, et al. The 3rd international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016;315:801-10. https://doi.org/10.1001/jama.2016.0287
7. Gaieski DF, Edwards JM, Kallan Mj, et al. Benchmarking the incidence and mortality of severe sepsis in the United States. *Crit Care Med* 2013;41:1167-74. https://doi.org/10.1097/CCM.0b013e31827c09f8
8. Mayr FB, Yende S, Angus DC. Epidemiology of severe sepsis. *Virulence* 2014;5:4-11. https://doi.org/10.4161/viru.27372
9. Yamamoto Y, Fujita K, Nakazawa S, et al. Clinical characteristics and risk factors for septic shock in patients receiving emergency drainage for acute pyelonephritis with upper urinary tract calculi. *BMC Urol* 2012;12:4. https://doi.org/10.1186/1471-2490-12-4
10. Hsiao CY, Chen TH, Lee YC, et al. Urolithiasis is a risk factor for uroseptic shock and acute kidney injury in patients with urinary tract infection. *Front Med (Lausanne)* 2019;6:288. https://doi.org/10.3389/fmed.2019.00288
11. Tambo M, Okegawa T, Shishido T, et al Predictors of septic shock in obstructive acute pyelonephritis. *World J Urol* 2014;32:803-11. https://doi.org/10.1007/s00345-013-1166-4
12. AC, Karvetski CH. Urinary obstruction is an important complicating factor in patients with septic shock due to urinary infection. *Am J Emerg Med* 2016;34:694-6. https://doi.org/10.1016/j.ajem.2015.12.068
13. Kakinoki H, Tobu S, Kakinoki Y, et al. Risk factors for uroseptic shock in patients with urolithiasis-related acute pyelonephritis. *Urol Int* 2018;100:37-42. https://doi.org/10.1159/000481801
14. Shigemura K, Tanaka K, Osawa K, et al Clinical factors associated with shock in bacteremic UTI. *Int Urol Nephrol* 2013;45:653-7. https://doi.org/10.1007/s11255-013-0449-4

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