Predictors of mortality for patients admitted to the intensive care unit with obstructing septic stones

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Abstract

Introduction: Patients diagnosed with septic stone are at significant risk of morbidity and mortality should source control through drainage be delayed, and they are often admitted to intensive care units (ICU) for hemodynamic support. The purpose of this study was to determine patient factors that may predict mortality in patients admitted to ICU with septic stone, particularly whether rural patients at a greater distance from a tertiary care center were at greater risk of mortality given the inherent delay in intervention.
Methods: The Manitoba Intensive Care Unit prospective registry began in 1999 and includes all patients admitted to ICU across Manitoba. Baseline characteristics, such as age, gender, vital signs, creatinine, Charlson comorbidity index (CCI), mortality outcomes, and location of residency were obtained for those admitted to ICU for septic stone. Association between death and clinical/demographic variable was performed with adjusted multivariable logistical regression analysis.
Results: A total of 342 patients admitted to the ICU were analyzed with a mean age of 63.5±15.5 years. Baseline characteristics were similar between groups ($p>0.05$). On multivariable adjusted logistical regression, the presence of acute kidney injury (AKI) ($p<0.001$) and intubation ($p<0.001$) were associated with mortality. There was no difference in mortality attributable to location of residency, vital signs, or CCI.

Conclusions: Among patients admitted to the ICU for septic stones in Manitoba, we demonstrate an association between AKI and intubation with mortality. Other factors, such as whether patients were from a rural region and baseline patient characteristics, were not predictive of mortality.

Introduction

Urosepsis associated with a urinary tract obstructing calculus, or septic stone, is a urological emergency. In addition to antibiotic administration, urgent decompression of the urinary tract with an indwelling ureteric stent or a percutaneous nephrostomy tube is critical. Should these interventions be delayed, patients risk complications including sepsis, septic shock, and disseminated intravascular coagulopathy. These complications may result in admission to an intensive care unit (ICU) for hemodynamic support and may ultimately lead to severe morbidity, and even death.[1-4]

Scant literature concerning outcomes for patients admitted to ICUs with septic stone exists. Previous work has shown that septic stone patients with decreasing platelet counts and serum albumin levels may imminently require ICU admission.[5] Following ICU admission, elective ureteroscopic lithotripsy for definitive treatment has been shown to be safe and efficacious, regardless of the method for emergency decompression that was initially used.[6] However, no study has compared factors of septic stone patients requiring ICU admission at presentation with their subsequent morbidity and mortality.

Our study aimed to investigate predictors of mortality for patients admitted to ICUs with septic stone. We hypothesised that patients with increased age, increased WBC, and increased creatinine (Cr) at presentation would have higher rates of mortality. Additionally, the province of Manitoba has a very large geographic catchment area, with only one major city providing urgent urologic intervention. Given Manitoba's large geographic area, transfer of patients to a tertiary care centre with septic stones is required for urinary tract decompression. Therefore, we hypothesized that rural patients were at greater risk of mortality given the inherent delay in intervention (i.e. hospital transfer).

Methods

The Manitoba Intensive Care Unit prospective registry began in 1999 and includes all patients admitted to ICUs across Manitoba, Canada. Baseline characteristics such as age, gender, creatinine, Charlson comorbidity index (CCI), mortality outcomes, and location of residence were obtained for those admitted to ICU for septic stones from January 1st, 1999, to November 1st, 2019. Vital signs collected and analyzed were at initial patient presentation. Acute kidney injury (AKI) was defined as per Kidney Disease: Improving Global Outcomes (KDIGO) Guidelines for acute kidney injury.

Statistical analysis was performed with SPSS version 24 software for Windows. A p-value <0.05 was considered statistically significant. After determining data distribution, mean ± standard deviation or medians, and interquartile ranges [IQR: 25-75], Student T or U Mann-Whitney tests were used to compare continuous variables between groups. Categorical variables were presented as absolute values and frequencies. They were analyzed with a Chi-square or Fisher's exact test, as indicated. An exploratory analysis comparing patients living in a rural and urban areas was subsequently performed. Urban was defined as postal codes starting with R2, R3, or R4 (urban Winnipeg) and rural was defined as all other postal codes within Manitoba. In the overall population, a univariate and a multivariate-adjusted logistic regression analysis was performed to calculate the risk of mortality using odds ratios (OR) and the 95% confidence interval (95% CI), in accordance with clinical and demographic variables.

Results

A total of 342 patients admitted to ICUs were analyzed with a mean age of 63.5 ± 15.5. Of those, 141 (41.2%) were males, 32 (9.4%) had hypothermia (< 36 °C) on admission, 114 (33.3%) were febrile (> 38 °C) on admission, 70 (20.5%) were intubated, and 85 (24.9%) had acute kidney injury (AKI). Patients who died during hospitalization had higher rates of hypothermia on ICU admission [survived: 22 (7.4%) vs. deceased: 10 (23.3%)], worse Glasgow coma scale (GCS; survived: 15 [11 - 15] vs. deceased: 10 [5 - 15]; $p < 0.001$), worse tachycardia ($p = 0.036$), required intubation ($p < 0.001$), and were more likely to have had an AKI ($p < 0.001$) (Table 1).

For the exploratory analysis, 206 patients were included, as information for residential area was obtained in 68 urban residents and 138 rural residents. Clinical and demographic variables between both groups were similar ($p > 0.05$), with no difference in mortality rates (urban = 12 (17.6%) vs. rural 16 (11.6%); $p = 0.233$) (Table 2).

On univariate analysis, hypothermia, AKI, and intubation were significantly associated with increased mortality ($p <0.05$). On multivariate analysis, the presence of AKI (OR = 4.620, 95% CI: 2.103 - 10.150; $p < 0.001$) and intubation ((OR = 5.005, 95% CI: 1.945 - 12.878; $p = 0.001$) were associated with an increased risk of mortality. (Table 3)

Discussion

An obstructing urinary calculus with a concomitant urinary traction infection is a common urological emergency with a reported incidence of 20.1 per 100,000 adults per year,[3] an ICU admission rate of 35%,[6] and a mortality of 0 to 2%.[1,5] While previous literature has demonstrated biochemical factors predictive of ICU admission, we believe that this is the first study to show that septic stone patients presenting with AKI (and hypothermia on univariate analysis) and requiring intubation were at an increased risk of mortality during their hospitalization.

Our results add to the existing literature on clinical factors that may influence mortality in septic stone patients. Patients that required intubation either due to respiratory failure or alternated mental status, had a significant mortality risk (OR = 5.005, $p = 0.001$). These findings are consistent with the literature, suggesting that patients with sepsis, worsening neurologic function,[7,8] and acute respiratory distress syndrome[9] had increased morbidity and mortality. Furthermore, sepsis-associated AKI was a common complication in our cohort (24.9%), and this is a well-known complication associated with high mortality.[10] While neither result is surprising in itself, as a natural course of a patient progressing to intubation or end-organ system failure is concerning for worse outcomes, our findings should alert clinicians to treat these patients more aggressively upon presentation. Two clinical scoring systems (Sequential [Sepsis-related] Organ Failure Assessment (SOFA) and quickSOFA) have been proposed to predict ICU admission and in-hospital mortality in patients with septic stone.[11] These scoring systems include vital parameters and laboratory results. Our findings support the use of serum creatinine and may add credence to include intubation as a disease-specific factor.

Other factors, such as location of residence and baseline patient characteristics, were not predictive of mortality. In the exploratory analysis in which we compare the 68 patients (33%) known to live in urban area against the 138 (67%) patients that reside in rural regions, there was not a significant mortality increase in patients that reside in rural regions (OR = 0.477, 95% CI: 0.183 - 1.244, $p = 0.130$). This study is in line with our previous findings, in which survival among patients with Fournier's gangrene was similar between rural and urban Manitoba residential locations.[12] On the other hand, in other world regions, it has been shown that there is a disparity in sepsis survival among geographical locations, such as rural Midwestern United States, in which rural hospital bypass is independently associated with increased mortality.[13] The similar survival rates among patients with septic stone in ICUs in Manitoba may be explained by how we defined rural and urban regions, the efficacy of a single-tier healthcare system, geographic, political, or socioeconomic factors that are currently unclear. This finding warrants further research.

Our study was limited by biases inherent in a retrospective review of a database. Although our reported mortality was high (12.6%), it is important to emphasize that our cohort only included patients that required ICU admission. Additionally, we classified location by rural and urban, rather than distance from nearest hospital. In Manitoba, there is large heterogeneity in rural settings, where some communities are supplied by a primary or secondary level hospital with reasonable land transport access, whereas other communities are only supplied by nursing stations with requirements for air transport for access. Accounting for these differences more in-depth may have provided a result more consistent with our hypothesis and existing literature. Additionally, our study did not account for patients who had initially presented to a rural hospital and were then transferred to a tertiary care hospital, as opposed to patients who presented directly to a tertiary care hospital. Furthermore, while we did not study the association of indwelling ureteric stents versus percutaneous nephrostomy tubes on our outcome, previous studies have shown similar rates of success (98-100%) and of patients requiring ICU admission post intervention (3-9%).[14-18] However, more randomized clinical trials with adequate power are needed to help elucidate the optimum management for these patients. Finally, our study did not differentiate patients based on the variable of time (i.e. time from symptom onset to decompression); however, a recent study did show that a delay in treatment was associated with worse outcomes. [19]

Conclusions

In summary, intubation and AKI are associated with higher rates of mortality in septic stone patients requiring ICU admission. This information offers clinicians a greater understanding of their patient trajectories. It is also reassuring to note that we did not find any differences in mortality for patients from urban or rural areas, suggesting that equitable quality of care is maintained within our single-tier healthcare system, as it concerns septic stone patients' emergent management, ICU admission, and mortality. Further work is needed to study potential geographic differences on our outcomes.

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Figures and Tables

Table 1. Comparison of clinical and demographic variables between patients that survived a septic stone episode and those who did not

Variable	Overall n=342 (100%)	Survived n=299 (87.4%)	Deceased n=43 (12.6%)	p
Age in years	63.5±15.5	63.3±15.2	64.6±17.3	0.618
Sex				
Male	141 (41.2%)	118 (39.5%)	23 (53.5%)	
Female	201 (58.8%)	181 (60.5%)	20 (46.5%)	0.081
Temperature (°C)	37.4 (36.5-38.4)	37.5 (36.5-38.4)	37.2 (36-38.4)	0.117
Temperature codified				
<36 °C	32 (9.4%)	22 (7.4%)	10 (23.3%)	
36–38 °C	196 (57.3%)	176 (58.9%)	20 (46.5%)	
>38 °C	114 (33.3%)	101 (33.8%)	13 (30.2%)	**0.004**
SBP (mmHg)	80 (70–90)	80 (70–91)	77 (68–88)	0.183
DBP (mmHg)	46 (40–51)	46 (40–52)	45 (40–50)	0.354
HR (bpm)	120 (105–138)	119 (104–135)	127 (111–146)	**0.036**
Total GCS	15 (10–15)	15 (11–15)	10 (5–15)	**<0.001**
Intubated status				
Not intubated	272 (79.5%)	249 (83.3%)	23 (53.5%)	
Intubated	70 (20.5%)	50 (16.75)	20 (46.5%)	**<0.001**
WBC	19.8 (13.3–28.5)	20.4 (13.6–29)	17.1 (9.8–23.3)	**0.022**
Creatinine (µmol/L)	176 (113.8–265.3)	173 (112–252)	224 (132–406)	**0.029**
AKI				
No AKI	257 (75.1%)	238 (79.6%)	19 (44.2%)	
AKI	85 (24.9%)	61 (20.4%)	24 (55.8%)	**<0.001**
Charlson score	2 (0–3)	2 (0–3)	2 (1–5)	0.121
LOS (in days)	3.8 (1.9–7.6)	3.8 (2 –7.6)	3.8 (1.6–8.9)	0.825
Location				
Urban	68 (19.9%)	56 (18.7%)	12 (27.9%)	
Rural	138 (40.4%)	122 (40.8%)	16 (37.2%)	
Not reported	136 (39.8%)	121 (40.5%)	15 (34.9%)	0.366

AKI: acute kidney injury; DBP: diastolic blood pressure (mmHg); GCS: Glasgow coma scale; HR: heart rate (bpm); LOS: length of stay in the ICU (days); SBP: systolic blood pressure (mmHg); WBC: white blood cells; mean ± standard deviation; median (interquartile range 25–75).

Table 2. Exploratory analysis comparing clinical and demographic variables between patients that live in urban vs. rural areas

Variable	Urban n=68 (33%)	Rural n=138 (67%)	p
Age in years	61 ± 15.6	62.1 ± 16.1	0.661
Sex			
Male	29 (42.6%)	59 (42.8%)	
Female	39 (57.4%)	79 (57.2%)	0.988
Temperature (°C)	37.3 (36.5–38.4)	37.2 (36.4–38.1)	0.355
Temperature codified			
<36 °C	3 (4.4%)	16 (11.6%)	
36–38 °C	45 (66.2%)	87 (63%)	
>38 °C	20 (29.4%)	35 (25.4%)	0.235
SBP (mmHg)	80 (70–93)	79 (69.8–89.3)	0.394
DBP (mmHg)	46 (40.3–50)	47 (40–52)	0.655
HR (bpm)	119 (104.5–140)	116 (100.8–132)	0.292
Total GCS	14 (10–15)	14 (9–15)	0.385
Intubated status			
Not intubated	45 (66.2%)	92 (66.7%)	
Intubated	23 (33.8%)	46 (33.3%)	0.944
WBC	19.4 (14.3–28.1)	18.9 (11.8–26)	0.425
Creatinine (μmol/L)	197 (120.3–262.8)	163 (104.3–284)	0.338
AKI			
No AKI	50 (73.5%)	98 (71%)	
AKI	18 (26.5%)	40 (29%)	0.706
Charlson score	2 (0–3.8)	2 (0.8–3)	0.791
LOS (in days)	3.3 (1.2–6.1)	3.8 (1.7–7.2)	0.141
Mortality			
Alive	56 (82.4%)	122 (88.4%)	
Death	12 (17.6%)	16 (11.6%)	0.233

AKI: acute kidney injury; DBP: diastolic blood pressure (mm Hg); GCS: Glasgow coma scale; HR: heart rate (bpm); LOS: length of stay in the ICU (days); SBP: systolic blood pressure (mm Hg); WBC: white blood cells; mean ± standard deviation; median (interquartile range 25–75).

Table 3. Univariate and multivariate-adjusted logistical regression for the outcome of mortality in the overall population						
	Univariable			**Multivariable**		
Variable	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Age (1 year)	1.005	0.984–1.027	0.617	0.999	0.974–1.024	0.908
Sex						
Male	1			1		
Female	0.567	0.298–1.078	0.083	0.495	0.231–1.061	0.071
Temperature codified						
36–38 °C	1			1		
<36 °C	4.000	1.661–9.634	**0.002**	2.357	0.820–6.778	0.111
>38 °C	1.133	0.540–2.374	0.741	0.843	0.352–2.018	0.701
SBP (1 mmHg)	0.996	0.984–1.009	0.561	1.000	0.987–1.013	0.963
HR (1 bpm)	1.009	0.998–1.020	0.097	1.009	0.997–1.021	0.138
Intubated status						
Not intubated	1			1		
Intubated	4.330	2.212–8.478	**<0.001**	5.005	1.945–12.878	**0.001**
WBC (g/L)	0.973	0.945–1.002	0.069	0.971	0.943–0.9999	0.0497
AKI						
No AKI	1			1		
AKI	4.928	2.536–9.577	**<0.001**	4.620	2.103–10.150	**<0.001**
CCI	1.103	0.965–1.261	0.151	1.076	0.915–1.267	0.375
LOS (1 day)	1.008	0.995–1.022	0.207	1.003	0.989–1.018	0.668
Location						
Urban	1			1		
Rural	0.612	0.272–1.379	0.236	0.477	0.183–1.244	0.130
Not reported	0.579	0.254–1.317	0.192	1.228	0.407–3.701	0.716

AKI: acute kidney injury; CI: confidence interval; HR: heart rate (bpm); LOS: length of stay in the ICU (days); OR: odds ratio; SBP: systolic blood pressure (mmHg); WBC: white blood cells.