Original Article

Risk factors for uroseptic shock in hospitalized patients aged over 80 years with urinary tract infection

Chih-Yen Hsiao[1,2], Tsung-Hsien Chen[1], Yi-Chien Lee[3,4], Meng-Chang Hsiao[5], Peir-Haur Hung[1,6], Ming-Cheng Wang[7]

[1]Division of Nephrology, Department of Internal Medicine, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chiayi; [2]Department of Hospital and Health Care Administration, Chia Nan University of Pharmacy and Science, Tainan; [3]Department of Internal Medicine, Fu Jen Catholic University Hospital, Fu Jen Catholic University, New Taipei; [4]School of Medicine, College of Medicine, Fu Jen Catholic University, New Taipei; [5]The Jackson Laboratory for Genomic Medicine, Farmington, CT, USA; [6]Department of Applied Life Science and Health, Chia Nan University of Pharmacy and Science, Tainan; [7]Division of Nephrology, Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan

Contributions: (I) Conception and design: CY Hsiao, MC Wang; (II) Administrative support: MC Wang; (III) Provision of study materials or patients: CY Hsiao; (IV) Collection and assembly of data: CY Hsiao, YC Lee, MC Hsiao; (V) Data analysis and interpretation: TH Chen, PH Hung; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Dr. Ming-Cheng Wang. Division of Nephrology, Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, 1 University Rd., Tainan 70101. Email: tsutsugamushi8901@gmail.com.

Background: The purpose of this study was to compare clinical characteristics and outcomes in individuals of different age groups with urinary tract infection (UTI), and to identify the relationships among advanced age and uroseptic shock.

Methods: This retrospective study compared clinical characteristics and outcomes in patients in different age groups with UTI and identified relationships between advanced age and uroseptic shock among hospitalized patients with UTI in an acute hospital care setting from January 2006 to October 2018. Patients were divided into young (age below 65 years), old (65–80 years), and very old (above 80 years) groups.

Results: Of 1,043 participants, 269 (25.8%) were very old and 200 (19.2%) developed uroseptic shock. Very old age [odds ratio (OR) 1.99, 95% confidence interval (CI): 1.25–3.19, P=0.004], male (OR 1.54, 95% CI: 1.07–2.24, P=0.022), presented flank pain (OR 1.54, 95% CI: 1.05–2.24, P=0.025), congestive heart failure (CHF) (OR 2.54, 95% CI: 1.27–5.06, P=0.008), acute kidney injury (AKI) (OR 4.19, 95% CI: 2.78–6.30, P<0.001), bacteremia (OR 1.78, 95% CI: 1.25–2.53, P=0.001), and multiple drug-resistant (MDR) bacteria (OR 1.43, 95% CI: 1.02–2.00, P=0.039) were associated with an increased risk of uroseptic shock in patients with UTI. In very old patients with UTI, bacteremia (OR 2.54, 95% CI: 1.38–4.69, P=0.003) and AKI (OR 4.37, 95% CI: 2.15–8.90, P<0.001) were independently associated with uroseptic shock.

Conclusions: Very old patients with UTI had a higher risk of developing uroseptic shock than younger patients. Bacteremia was an independent risk factor for uroseptic shock in very old patients with UTI.

Keywords: Urinary tract infection (UTI); very old age; uroseptic shock; bacteremia

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Introduction

The world's population is aging, with the numbers and proportions of older persons increasing in every country. By 2050, the world's elderly population will exceed that of the young for the first time in history (1) and those 80 years and older are the fastest-growing segment of the US population (2). Frail and vulnerable older persons are at particularly high risk for the development of infectious diseases (3). In addition, these individuals are at increased risk of dying from serious infectious diseases, which account for one-third of all deaths among those aged 65 years and older (4). Moreover, the incidence of sepsis increases with age leading to a sharp incidence in people over 80 years of age, and is associated with extremely high mortality rates (5,6). Older persons are also more prone to urinary tract infections (UTIs) (7). At least 20% of women and 10% of men over 80 years of age have bacteriuria (8). UTI is the most common source of bacteremia in the older persons, accounting for 50% of cases of bacteremia in patients aged 80 years or older (9). A previous study predicted that septic shock is an independent risk factor for mortality in patients aged 80 years or over (9). However, few studies have assessed uroseptic shock in older persons with UTI, especially the fastest-growing age population, the very old (aged above 80 years), were lacking. Therefore, this study aimed to investigate how age impacts uroseptic shock in patients with UTI and predict the risk factors of uroseptic shock among very old patients with UTI.

Methods

Study design and population

This retrospective observational study was conducted between January 2006 and October 2018 at Chia-Yi Christian Hospital in southern Taiwan, which consists of 1,077 inpatient beds and an outpatient department serving approximately 4,110 patients per day. We evaluated patients with a clinical and microbiological diagnosis of UTI who required admission to our hospital. The study was conducted after obtaining ethical approval from the Institutional Review Board of Chiayi Christian Hospital (approval No. CYCH-IRB-2019061).

A total of 1,043 consecutive hospitalized patients with UTI without any other concurrent infectious disease was enrolled. The enrolled individuals fulfilled the following criteria: (I) presence of UTI symptoms including pain on urination, lumbago or fever with bacterial isolation of more than 10^5 colony-forming units /mL from a urine specimen; (II) complete image survey such as ultrasonography, intravenous urography, or computed tomography and completion of required laboratory data; and (III) results of antimicrobial susceptibility tests. Patients less than 18 years of age, with concurrent with infections other than UTI, without imaging studies, without complete data, having nosocomial UTI, or receiving regular dialysis therapy were excluded. Urine specimens were collected from clean-catch midstream urine. In patients with long-term indwelling Foley catheter, urine specimens were collected from a newly inserted catheter. Antimicrobial susceptibility was evaluated according to the recommendations of the Clinical and Laboratory Standards Institute. The antibiotics tested included: ampicillin, amoxicillin-clavulanate acid, second-generation cephalosporins, third-generation cephalosporins, carbapenems, aminoglycoside, fluoroquinolones, piperacillin/tazobactam, glycopeptide, and trimethoprim/sulfamethoxazole. The patients were divided into three age groups, young (age between 18 and 64 years), old (65–80 years), or very old (above 80 years).

The clinical characteristics and laboratory data including demographic characteristics (age and gender), comorbidities [diabetes mellitus (DM), hypertension, coronary artery disease (CAD), congestive heart failure (CHF), stroke, cirrhosis, and long-term indwelling Foley catheter], prior history of UTI, vital signs (blood pressure and ear temperature), laboratory results (white blood cell count, platelet count, serum creatinine, and eGFR at baseline and after hospitalization), clinical presentation (pain or burning on urination, flank pain, and fever), existence of urinary tract abnormality (urolithiasis, hydronephrosis, and urogenital cancer), admitted to Intensive Care Unit (ICU), length of hospital stay, antibiotic treatment, causative microorganisms, and antimicrobial resistance pattern were collected in a standard form for further analysis.

Definitions

Uroseptic shock was defined as sepsis-induced hypotension [systolic blood pressure (SBP) <90 mmHg or mean arterial pressure <70 mmHg or a decrease in SBP by >40 mmHg lasting for at least one hour, despite adequate fluid resuscitation and in the absence of other cause of hypotension] (10). AKI was defined as an increase in serum creatinine to ≥2.0 times that of the baseline value according to the KDIGO Clinical Practice Guideline criteria for

serum creatinine value for AKI stages 2 and 3 (11). Long-term urinary catheterization was defined as an indwelling Foley catheter more than 30 days. Afebrile status was defined as a single temperature not rising above 38.3 ℃ (101 ℉) (12). Multiple drug-resistant (MDR) bacteria was defined as isolates not susceptible to at least one agent in three or more antimicrobial categories (13). Inadequate empirical antimicrobial treatment was defined in case the isolated uropathogen was resistant to the first antibiotic administered.

Statistical analysis

The patients were grouped into three age groups. The continuous variables were expressed as means ± SD and categorical variables as numbers (percentage). The data were analyzed using One-way analysis of variance (ANOVA) or Student's *t*-tests for continuous variables and Chi-square tests for categorical variables. Stepwise multivariate logistic regression analyses were performed to identify the factors associated with uroseptic shock in UTI and very old patients with UTI, respectively. P values <0.05 were considered statistically significant. All analyses were performed using PASW Statistics for Windows, version 18.0 (IBM Corp.).

Results

The demographic and clinical characteristics of the 1,043 hospitalized patients with UTI are shown in *Table 1*. The mean age on admission was 67±17 years; 410 (39.3%) patients were younger than 65 years of age, 364 (34.9%) were 65–80 years of age, and 269 (25.8%) were older than 80 years of age. Most patients were female (760, 72.9%). Among UTI patients, 113 were ever admitted to the ICU. There were 266 patients (25.5%) with severe sepsis, 200 patients (19.2%) with uroseptic shock and 151 patients (14.5%) with acute kidney injury (AKI) during hospitalization. The overall mortality rate was 0.67% (7/1,043). The in-hospital mortality rates among young, old, and very old groups were 0%, 0.3%, and 2.2%, respectively. Patients in the old and very old UTI groups had more comorbidities (DM, hypertension, CHF, CAD, and previous stroke, and urogenital cancer) (*Figure 1*); greater mean age; higher serum creatinine concentration on admission; lower platelet count and baseline estimated glomerular filtration rate (eGFR); longer length of hospital stay; higher prevalence of male gender, prior history of UTI, indwelling Foley catheter, inadequate empirical antimicrobial treatment, afebrile during hospitalization, AKI, and all-cause in-hospital mortality; and lower prevalence of presenting with flank pain than patients in the young group (*Tables 1*,*S1*). The isolated uropathogens and antimicrobial resistant pattern are shown in *Tables 2* and *S2*. Patients in the old and very old UTI groups had more *Klebsiella* species, *Enterococcus* species, and *Pseudomonas* species isolated and fewer *Escherichia coli* (*E. coli*) isolated than patients in the young group. In *E. coli* strain isolated, resistance rates to amoxicillin-clavulanate acid, piperacillin/tazobactam, fluoroquinolones, third-generation cephalosporins were higher in the old and very old patients than in the young patients. In *Proteus* species strain isolated, resistance rates to amoxicillin-clavulanate acid, third-generation cephalosporins were higher in the old and very old patients than in the young patients. Characteristics of hospitalized patients with UTI with respect to uroseptic shock are shown in *Tables 3* and *S3*. Patient with uroseptic shock had greater mean age; higher serum creatinine concentration on admission; lower platelet count; longer length of hospital stay; higher prevalence of male gender, CHF, CAD, presenting with flank pain, bacteremia, urolithiasis, hydronephrosis, AKI, admitted to the ICU, all-cause in-hospital mortality, and MDR bacteria isolated; and lower prevalence of afebrile than those without uroseptic shock.

Stepwise multivariate logistic regression analysis revealed that very old [odds ratio (OR) 1.99, 95% confidence interval (95% CI): 1.25–3.19, P=0.004], male (OR 1.54, 95% CI: 1.07–2.24, P=0.022), presenting with flank pain (OR 1.54, 95% CI: 1.05–2.24, P=0.025), CHF (OR 2.54, 95% CI: 1.27–5.06, P=0.008), AKI (OR 4.19, 95% CI: 2.78–6.30, P<0.001), bacteremia (OR 1.78, 95% CI: 1.25–2.53, P=0.001), and MDR (OR 1.43, 95% CI: 1.02–2.00, P=0.039) were independently associated with an increased risk of uroseptic shock, while hypertension (OR 0.64, 95% CI:0.45–0.91, P=0.014) and afebrile status (OR 0.60, 95% CI: 0.41–0.88, P=0.010) were independently associated with a reduced risk of uroseptic shock in patients with UTI (*Table 4*). Bacteremia (OR 2.54, 95% CI: 1.38–4.69, P=0.003) and AKI (OR 4.37, 95% CI: 2.15–8.90, P<0.001) were independently associated with an increased risk of uroseptic shock in the very old patients with UTI (*Table 5*).

Discussion

In patients above 65 years of age, the genitourinary system is the most common site of sepsis (14). In the present

Table 1 Characteristics of patients with urinary tract infections

Characteristic	All (n=1,043)	Age group			P value	Post hoc tests (LSD)
		Young (<65 years) (n=410)	Old (65–80 years) (n=364)	Very old (>80 years) (n=269)		
Age (years)	67±17	49±12	73±4	85±4	<0.001*	V > O > Y
Gender (male)	283 (27.1)	82 (20.0)	119 (32.7)	82 (30.5)	<0.001¥	
Diabetes mellitus	452 (43.3)	136 (33.2)	205 (56.3)	111 (41.3)	<0.001¥	
Hypertension	549 (52.6)	134 (32.7)	232 (63.7)	183 (68.0)	<0.001¥	
Congestive heart failure	45 (4.3)	7 (1.7)	16 (4.4)	22 (8.2)	<0.001¥	
Coronary artery disease	111 (10.6)	15 (3.7)	53 (14.6)	43 (16.0)	<0.001¥	
Cirrhosis	63 (6.0)	17 (4.1)	29 (8.0)	17 (6.3)	0.082¥	
Stroke	230 (22.1)	36 (8.8)	106 (29.1)	88 (32.7)	<0.001¥	
Prior history of urinary tract infection					<0.001¥	
None	684 (65.6)	323 (78.8)	211 (58.0)	150 (55.8)		
Once	204 (19.6)	57 (13.9)	84 (23.1)	63 (23.4)		
Twice	86 (8.2)	20 (4.9)	36 (9.9)	30 (11.2)		
Thrice or more	69 (6.6)	10 (2.4)	33 (9.1)	26 (9.7)		
Indwelling Foley catheter	70 (6.7)	11 (2.7)	26 (7.1)	33 (12.3)	<0.001¥	
Temperature (℃)	38.1±1.4	38.2±1.4	38.1±1.4	37.9±1.4	0.070*	
Afebrile	395 (37.9)	113 (27.6)	150 (41.2)	132 (49.1)	<0.001¥	
Flank pain	461 (44.2)	271 (66.1)	130 (35.7)	60 (22.3)	<0.001¥	
Bacteremia	480 (46.0)	183 (44.6)	176 (48.4)	121 (45.0)	0.541¥	
Urinary tract abnormality	273 (26.2)	105 (25.6)	98 (26.9)	70 (26.0)	0.916¥	
Urolithiasis	184 (17.6)	79 (19.3)	64 (17.6)	41 (15.2)	0.404¥	
Hydronephrosis	148 (14.2)	61 (14.9)	55 (15.1)	32 (11.9)	0.455¥	
Urogenital cancer	45 (4.3)	9 (2.2)	16 (4.4)	20 (7.4)	0.004¥	
Inadequate empirical antimicrobial treatment	275 (26.4)	89 (21.7)	103 (28.3)	80 (29.7)	0.032¥	
Inadequate empirical antimicrobial treatment for multiple drug resistance bacteria (N=362)	185 (51.1)	61 (45.9)	68 (51.9)	56 (57.1)	0.232¥	
Length of hospital stay (days)	9±5	8±4	10±6	10±5	<0.001*	V = O > Y
Admitted to the Intensive Care Unit	113 (11.4)	37 (9.2)	46 (13.8)	30 (11.9)	0.136¥	
Uroseptic shock	200 (19.2)	66 (16.1)	73 (20.1)	61 (22.7)	0.090¥	
Acute kidney injury	151 (14.5)	42 (10.2)	67 (18.4)	42 (15.6)	0.005¥	
All-cause in-hospital mortality	7 (0.7)	0 (0.0)	1 (0.3)	6 (2.2)	0.001¥	
Multiple drug resistance bacteria	362 (34.7)	133 (32.4)	131 (36.0)	98 (36.4)	0.461¥	
White blood cell (10^3/uL)	13.19±6.08	13.41±5.69	13.47±6.16	12.47±6.50	0.076*	
Platelets (10^3/μL)	203±112	215±135	196±93	196±93	0.024*	Y > O = V
Serum creatinine on admission (mg/dL)	1.60±1.60	1.32±1.62	1.83±1.57	1.72±1.54	<0.001*	V = O > Y
Baseline eGFR (mL/min/1.73 m^2)	75.21±30.00	93.10±28.63	65.48±25.75	61.13±23.08	<0.001*	Y > O > V

Data are expressed as mean ± SD or number (percentage) *, one-way analysis of variance (ANOVA); ¥, Chi-square test. eGFR, estimated glomerular filtration rate; V, very old (>80 years) ; O, old (65–80 years); Y, young (<65 years).

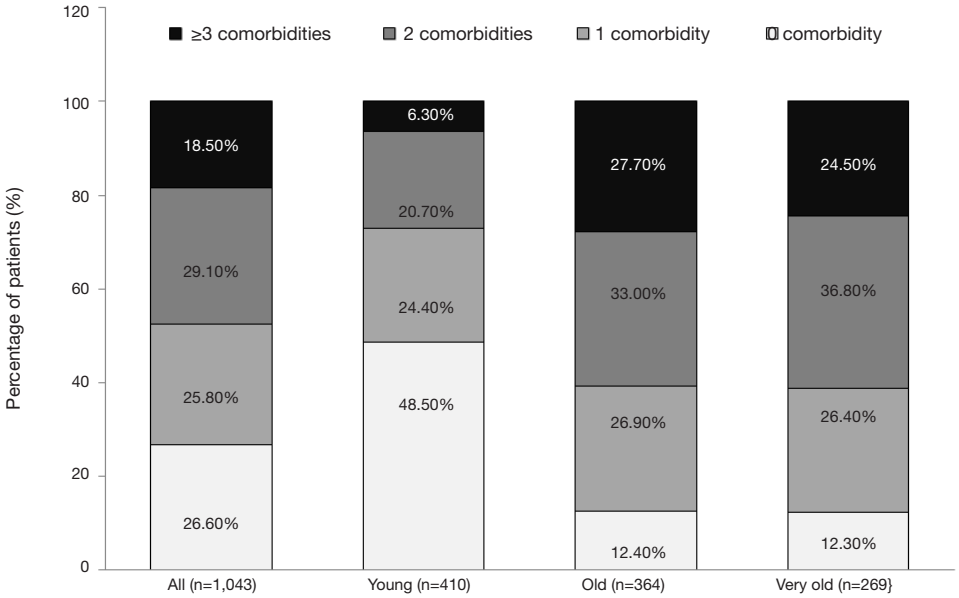

Figure 1 Percentage of comorbidities stratified by age. Comorbidity: diabetes mellitus, hypertension, congestive heart failure, coronary artery disease, and stroke. Young: <65 years; old: 65–80 years; very old: >80 years.

study, patients in the old and very old groups had distinct clinical manifestations of male sex, multiple comorbidities, afebrile status during hospitalization, more deteriorated renal function, and increased *Klebsiella* species, *Enterococcus* species, and *Pseudomonas* species isolating and decreased *E. coli* isolating compared with those in the young age group. Increased age is a risk factor for sudden deterioration in sepsis to severe sepsis and septic shock (1,15). The results of our study demonstrated that very old patients with UTI were more predisposed to developing uroseptic shock than the young patients with UTI. Bacteremia and AKI were independently associated with uroseptic shock in the very old patients with UTI.

UTIs are more common in older persons: both in patients above 65 years versus those younger (15-17) and in patients above 80 years than in those aged 60–80 years (9,18). The older persons are predisposed to UTIs due to urinary incontinence, impaired emptying with residual urine, urethral catheters and instrumentation, and obstructive uropathy from prostatic disease in older man and declining estrogen levels that alter the vaginal flora promoting the colonization of the vagina with uropathogens in older woman (19,20). Population-based prospective follow-up study of 86-year-old persons found that a history of UTI between the age of 85 and 86 years, cognitive impairment, activities of daily living disability and urine incontinence are independent predictors of developing UTI (21). UTI can be either asymptomatic or symptomatic, characterized by a wide spectrum of symptoms ranging from mild irritative voiding to bacteremia, sepsis, uroseptic shock, and cause sudden deterioration of renal function or even death. Previous studies showed that older patients with UTI less experiencing of lower urinary tract symptoms, flank pain and lumbar tenderness compared to their non-older counterparts (22,23). In current study, the very old patient with UTI had a lower frequency of flank pain compared to those young and old counterparts. Complicated UTI is the most frequent cause of sepsis in adults above 65 years of age (24). The incidence of severe sepsis increases with age and septic patients have a mean age of around 65 years (25). Among patients with community-acquired bloodstream infection, those aged above 85 years have an increased tendency to develop septic shock compared to those aged 65–84 years (15) Previous studies showed that the rate of developing uroseptic shock in older patients with UTI can range from 15.6% to 26% based on different underlying conditions (26,27). In the current study, the incidence of uroseptic shock among the old and very old patients with UTI was 20.1% and 22.7%, respectively. Aged is a risk of severe sepsis or uroseptic shock for patients with UTI has been observed in some study (28) but not in others (29,30). In current study, very old patients with UTI

Table 2 Isolated uropathogens and antimicrobial resistance profiles

Characteristic	All (n=1,043)	Age group			P value
		Young (<65 years) (n=410)	Old (65–80 years) (n=364)	Very old (>80 years) (n=269)	
Escherichia coli	809 (77.6)	348 (84.9)	269 (73.9)	192 (71.4)	<0.001*
Amoxicillin-clavulanate acid	210 (26.0)	74 (21.3)	75 (27.9)	61 (31.8)	0.019*
Piperacillin/tazobactam	26 (3.2)	4 (1.1)	8 (3.0)	14 (7.3)	0.001*
Trimethoprim/sulfamethoxazole	397 (49.1)	166 (47.7)	127 (47.2)	104 (54.2)	0.269*
Aminoglycoside	190 (23.5)	74 (21.3)	64 (23.8)	52 (27.1)	0.308*
Fluoroquinolones	185 (22.9)	62 (17.8)	66 (24.5)	57 (29.7)	0.005*
Carbapenems	3 (0.4)	0 (0.0)	1 (0.4)	2 (1.0)	0.163*
Second-generation cephalosporins	136 (16.8)	48 (13.8)	46 (17.1)	42 (21.9)	0.055*
Third-generation cephalosporins	135 (16.7)	46 (13.2)	47 (17.5)	42 (21.9)	0.033*
Proteus species	34 (3.3)	8 (2.0)	17 (4.7)	9 (3.3)	0.104*
Amoxicillin-clavulanate acid	6 (17.6)	0 (0.0)	2 (11.8)	4 (44.4)	0.038*
Piperacillin/tazobactam	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Trimethoprim/sulfamethoxazole	13 (38.2)	2 (25.0)	6 (35.3)	5 (55.6)	0.407*
Aminoglycoside	8 (23.5)	0 (0.0)	4 (23.5)	4 (44.4)	0.098*
Fluoroquinolones	8 (23.5)	0 (0.0)	4 (23.5)	4 (44.4)	0.098*
Carbapenems	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Second-generation cephalosporins	3 (8.8)	0 (0.0)	1 (5.9)	2 (22.2)	0.227*
Third-generation cephalosporins	3 (8.8)	0 (0.0)	0 (0.0)	3 (33.3)	0.010*
Klebsiella species	79 (7.6)	20 (4.9)	29 (8.0)	30 (11.2)	0.010*
Amoxicillin-clavulanate acid	12 (15.2)	2 (10.0)	6 (20.7)	4 (13.3)	0.555*
Piperacillin/tazobactam	7 (8.9)	2 (10.0)	3 (10.3)	2 (6.7)	0.865*
Trimethoprim/sulfamethoxazole	23 (29.1)	7 (35)	8 (27.6)	8 (26.7)	0.796*
Aminoglycoside	9 (11.4)	2 (10.0)	2 (6.9)	5 (16.7)	0.485*
Fluoroquinolones	14 (17.7)	5 (25.0)	4 (13.8)	5 (16.7)	0.590*
Carbapenems	4 (5.1)	0 (0.0)	3 (10.3)	1 (3.3)	0.230*
Second-generation cephalosporins	16 (20.3)	4 (20.0)	8 (27.6)	4 (13.3)	0.395*
Third-generation cephalosporins	13 (16.5)	4 (20.0)	6 (20.7)	3 (10.0)	0.479*

Table 2 (*continued*)

Table 2 (*continued*)

Characteristic	All (n=1,043)	Age group			P value
		Young (<65 years) (n=410)	Old (65–80 years) (n=364)	Very old (>80 years) (n=269)	
Enterococcus species	38 (3.6)	7 (1.7)	14 (3.8)	17 (6.3)	0.007*
Ampicillin	6 (15.8)	2 (28.6)	3 (21.4)	1 (5.9)	0.294*
Piperacillin/tazobactam	1 (2.6)	0 (0.0)	1 (7.1)	0 (0.0)	0.415*
Glycopeptide	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Pseudomonas species	53 (5.1)	11 (2.7)	25 (6.9)	17 (6.3)	0.017*
Amoxicillin-clavulanate acid	1 (1.9)	0 (0.0)	1 (4.0)	0 (0.0)	0.565*
Piperacillin/tazobactam	2 (3.8)	0 (0.0)	1 (4.0)	1 (5.9)	0.725*
Trimethoprim/ sulfamethoxazole	6 (11.3)	0 (0.0)	4 (16.0)	2 (11.8)	0.377*
Aminoglycoside	8 (15.1)	2 (18.2)	3 (12.0)	3 (17.6)	0.837*
Fluoroquinolones	12 (22.6)	0 (0.0)	7 (28.0)	5 (29.4)	0.130*
Carbapenems	2 (3.8)	0 (0.0)	1 (4.0)	1 (5.9)	0.725*
Second-generation cephalosporins	1 (1.9)	1 (9.1)	0 (0.0)	0 (0.0)	0.143*
Third-generation cephalosporins	3 (5.7)	1 (9.1)	2 (8.0)	0 (0.0)	0.468*

*, Student *t*-test.

were more predisposed to developing uroseptic shock than young patients with UTI. Our study showed that very old patients with uroseptic shock had several poor outcomes, including longer length of hospital stay (13 *vs.* 9 days), higher incidences of AKI (34.4% *vs.* 10.1%) and in hospital mortality (8.2% *vs.*0.5%), compared to those without uroseptic shock. The mortality rate in older patients with UTI can range from 0% to 33% based on different underlying conditions (22,23,26,27,31-33). UTI have been known to be a low risk source of bacteremia-associated mortality (34). The all-cause in-hospital mortality in older male adults with febrile UTIs was 4.3% (22). However, functional dependence is associated with urosepsis related mortality (31). Tal *et al.* reported that 87.4% of geriatric patients with UTI were functionally dependent, their in-hospital mortality rate was up to 33% (32). Older patients with severe sepsis and septic shock have increased mortality compared to their younger counterparts (35,36). In addition, sepsis patients 80 years or over have higher hospital mortality rates than patients aged 65–79 years (37). Uroseptic shock is a risk factor for in-hospital mortality in older patients with UTI (38,39). On the contrary, severe UTI with bacteremia has been shown not associated with a worse prognosis in elderly patients with pyelonephritis or urinary sepsis (40). In a multicenter study reported by Yamamichi *et al.* showed that among 77 uroseptic shock patients (aged 25–104 years, median 73) bacteremia was seen in 74 cases (96%) and no cases leading to death (41). In our hospital, patients with UTI were diagnosed properly at earlier stage with appropriate resuscitation and treatment, which resulted in overall low mortality rate in the presence of a higher rate of uroseptic shock in our study. However, very old patients with UTI had an in-hospital mortality rate of 2.2%, which was higher compared to those young and old counterparts. For very old patients identifying uroseptic shock, more vigilance fluid resuscitation and administration of effective intravenous antibiotics within an hour is critical according to the recommendation of Surviving Sepsis Campaign guidelines (42).

Fever, the most common sign associated with sepsis (43), is an adaptive response to aid in defense against the invading organisms (44). However, approximately 30–50% of older persons with infection are afebrile (43). In the current study, fever was absent in 49.1% of the very old patients

Table 3 Characteristics of patients with urinary tract infections

Characteristic	All (n=1,043)	Uroseptic shock		P value
		Non (n=843)	Yes (n=200)	
Age (years)	67±17	66±18	70±16	0.009¥
Age group				0.090¥
Youth	410 (39.3)	344 (40.8)	66 (33.0)	
Old	364 (34.9)	291 (34.5)	73 (36.5)	
Very old	269 (25.8)	208 (24.7)	61 (30.5)	
Sex (male)	283 (27.1)	216 (25.6)	67 (33.5)	0.024¥
Diabetes mellitus	452 (43.3)	373 (44.2)	79 (39.5)	0.223¥
Hypertension	549 (52.6)	449 (53.3)	100 (50.0)	0.406¥
Congestive heart failure	45 (4.3)	28 (3.3)	17 (8.5)	0.001¥
Coronary artery disease	111 (10.6)	82 (9.7)	29 (14.5)	0.049¥
Cirrhosis	63 (6.0)	49 (5.8)	14 (7.0)	0.526¥
Stroke	230 (22.1)	178 (21.1)	52 (26.0)	0.134¥
Prior history of urinary tract infection				0.333¥
None	684 (65.6)	546 (64.8)	138 (69.0)	
Once	204 (19.6)	173 (20.5)	31 (15.5)	
Twice	86 (8.2)	71 (8.4)	15 (7.5)	
Thrice or more	69 (6.6)	53 (6.3)	16 (8.0)	
Indwelling Foley catheter	70 (6.7)	56 (6.6)	14 (7.0)	0.856¥
Temperature (℃)	38.1±1.4	38.0±1.3	38.2±1.6	0.263*
Afebrile	395 (37.9)	337 (40.0)	58 (29.0)	0.004¥
Flank pain	461 (44.2)	353 (41.9)	108 (54.0)	0.002¥
Bacteremia	480 (46.0)	355 (42.1)	125 (62.5)	<0.001¥
Urinary tract abnormality	273 (26.2)	204 (24.2)	69 (34.5)	0.003¥
Urolithiasis	184 (17.6)	130 (15.4)	54 (27.0)	<0.001¥
Hydronephrosis	148 (14.2)	108 (12.8)	40 (20.0)	0.009¥
Urogenital cancer	45 (4.3)	38 (4.5)	7 (3.5)	0.528¥
Inadequate empirical antimicrobial treatment	272 (26.1)	214 (25.4)	58 (29.0)	0.295¥
Inadequate empirical antimicrobial treatment for multiple drug resistance bacteria (N=362)	185 (51.1)	144 (51.8)	41 (48.8)	0.631¥
Length of hospital stay (days)	10±5	9±5	12.0±7.0	<0.001*
Admitted to the Intensive Care Unit	113 (11.4)	41 (5.1)	72 (37.7)	<0.001¥
Acute kidney injury	151 (14.5)	83 (9.8)	68 (34.0)	<0.001¥
All-cause in-hospital mortality	7 (0.7)	1 (0.1)	6 (3.0)	<0.001¥
Multiple drug resistance bacteria	362 (34.7)	278 (33.0)	84 (42.0)	0.016¥

Table 3 (*continued*)

Table 3 (*continued*)

Characteristic	All (n=1,043)	Uroseptic shock		P value
		Non (n=843)	Yes (n=200)	
White blood cell (10^3/uL)	13.2±6.1	13.0±5.7	14.0±7.5	0.238*
Platelets (10^3/μL)	203.9±112.0	208.4±115.5	184.9±93.9	0.008*
Serum creatinine on admission (mg/dL)	1.6±1.6	1.5±1.5	2.0±1.9	<0.001*
Baseline eGFR (mL/min/1.73 m^2)	75.2±30.0	75.4±30.5	74.6±28.1	0.728*
Escherichia coli	809 (77.6)	654 (77.6)	155 (77.5)	0.981¥
Proteus spp.	34 (3.3)	26 (3.1)	8 (4.0)	0.512¥
Klebsiella spp.	79 (7.6)	66 (7.8)	13 (6.5)	0.523¥
Enterococcus spp.	38 (3.6)	27 (3.2)	11 (5.5)	0.119¥
Pseudomonas spp.	53 (5.1)	46 (5.5)	7 (3.5)	0.257¥

Data are expressed as mean ± SD or number (percentage). *, Student *t*-test or Mann-Whitney U-test; ¥, Chi-Square test or Fisher's exact test. eGFR, estimated glomerular filtration rate.

Table 4 Stepwise multivariate logistic regression model for factors related to uroseptic shock

Covariate	Uroseptic shock		
	β	OR (95% CI)	P value
Age group (ref: youth)			
Old	0.35	1.42 (0.93–2.19)	0.105
Very old	0.69	1.99 (1.25–3.19)	0.004
Sex (male)	0.43	1.54 (1.07–2.24)	0.022
Hypertension	–0.45	0.64 (0.45–0.91)	0.014
Congestive heart failure	0.93	2.54 (1.27–5.06)	0.008
Afebrile	–0.51	0.60 (0.41–0.88)	0.01
Flank pain	0.43	1.54 (1.05–2.24)	0.025
Bacteremia	0.58	1.78 (1.25–2.53)	0.001
Acute kidney injury	1.43	4.19 (2.78–6.30)	<0.001
Multiple drug resistance bacteria	0.36	1.43 (1.02–2.00)	0.039

The stepwise multivariate logistic regression model was adjusted for age group, mean white blood cell, platelets, sex, diabetes mellitus, hypertension, congestive heart failure, coronary artery disease, liver cirrhosis, stroke, prior history of UTI, afebrile, flank pain, acute kidney injury, inadequate empirical antimicrobial treatment, bacteremia, urolithiasis, hydronephrosis, urogenital cancer, and multiple drug-resistant pathogen.

Table 5 Stepwise multivariate logistic regression model for factors related to uroseptic shock in very old people

Covariate	Uroseptic shock		
	β	OR (95% CI)	P value
Acute kidney injury	1.48	4.37 (2.15–8.90)	<0.001
Bacteremia	0.93	2.54 (1.38–4.69)	0.003

The stepwise multivariate logistic regression model was adjusted for mean white blood cell, platelets, sex, diabetes mellitus, hypertension, congestive heart failure, coronary artery disease, liver cirrhosis, stroke, prior history of UTI, afebrile, flank pain, acute kidney injury, inadequate empirical antimicrobial treatment, bacteremia, urolithiasis, hydronephrosis, urogenital cancer, and multiple drug-resistant pathogen.

with UTI. The very old patients had a lower incidence of fever episodes (50.9%) than the old (58.8%) and young (72.4%) patients. In addition, the very old bacteremic patients had a higher prevalence of afebrile status (28.9%) than the old (24.5%) and young (19.7%) counterparts. The baseline body temperature changes with age and can be 0.6–0.8 ℃ lower in older adults than that in younger adults (45). In addition, decreased cytokine production, decreased sensitivity of the hypothalamus to cytokines, and poor peripheral thermoregulation in older persons results in decreased temperature response to infection (46). This blunted temperature response suggest that shaking chills and elevated temperature during physical examination may serve as good predictors of sepsis in the older persons (47). The older persons, especially those older than 80 years of age, frequently display non-specific signs and symptoms of sepsis (48), while later presentation may be very severe with rapid progression to septic shock (1). Early identification of "atypical" infection signs like confusion, falls, malaise, incontinence, immobility, and changes in temperature and timely administration of effective fluid resuscitation and broad-spectrum antimicrobials are important in very old patients.

Multiple factors including comorbid illnesses, immunosenescence, malnutrition, instrumentation, and institutionalization make older persons prone to have bacteremia (49). UTI is the most frequent origin of community-acquired bacteremia and sepsis in the older persons (31,32). A previous study showed that UTI was the source in 30–40% of cases of community-acquired bacteremia and that 40–57% of bacteremic older persons had UTIs (27). In patients with UTI aged 80 years or over, the urinary tract was the source for 50% of episodes of bacteremia (9). Bacteremia is present in 15–25% of patients with complicated UTIs (50), and is more frequent in older persons with UTI, with incidence rates just over 40% (27,40). In the current study, the prevalence of bacteremia among the young, old, and very old patients with UTI was 44.6%, 48.4%, and 45.0%, respectively. A previous study showed that 39% of bacteremic patients aged above 85 years presented with septic shock (15); in our study, the incidence rate of uroseptic shock among very old patients with UTI and bacteremia was 32.2% (39/121) and bacteremia was independently associated with uroseptic shock in the very old patients with UTI. The older persons are more susceptible to gram-negative bacilli (GNB) due to changes in the immune system (51). Older adults are approximately 1.3 times more likely to have gram-negative pathogens than younger populations (35) and *Escherichia coli* is the most common pathogen in community-acquired bloodstream infections the older persons (52). *E. coli* is also the most common microorganism in UTIs (53). *E. coli* accounted for 60.2–61.8% of bacterial isolates in patients with UTI aged 65 years and over (33) and 46.1% of those aged 75–105 years (31). In the current study, the five most common bacterial species isolated in the very old group were *E. coli* (71.4%), *Klebsiella* species (11.2%), *Pseudomonas* species (6.3%), *Enterococcus* species (6.3%), and *Proteus* species (3.3%). Compared to the young patients, the very old patients with UTI had more isolates of *Klebsiella*, *Enterococcus*, and *Pseudomonas* species but fewer *E. coli* isolates. Our study did not show statistical difference of MDR bacteria among young, old, and very old patients with UTI. Several factors could not be analyzed for no significant difference in the prevalence of MDR bacteria between older and non-older patients due to the study limitations. No inappropriate management of asymptomatic bacteriuria or less broad-spectrum antibiotic therapy may be the reason for no significant difference in the prevalence of MDR bacteria between older and non-older patients with community-acquired UTI. However, our study showed that MDR bacteria are an independent risk factor for uroseptic shock in patients with UTI. Bacteremia is considered a marker of severe infection (54,55), therefore, the Surviving Sepsis Campaign Guidelines recommend routine microbiologic culture (including blood) before starting antimicrobial therapy in patients with UTI with suspected sepsis or septic shock (42).

Up to 60% of patients with sepsis have AKI and patients with sepsis complicated by AKI have significantly increased mortality than that in those without AKI (56). AKI is the most frequent complication in patients with septic shock (57) and older age is a risk factor for AKI in patients with septic shock (58). The results of our study showed that 14.5% of patients with UTI were complicated with AKI. The old and very old patients with UTI had higher incidences of AKI than young patients with UTI. In addition, very old patients with uroseptic shock had a higher incidence rate of AKI than patients without uroseptic shock and AKI was associated with an increased risk of uroseptic shock in very old patients. The risks of premature death, chronic kidney disease, and end-stage renal disease increase after AKI in the older persons (59). Early detection, aggressive resuscitation, and appropriate antibiotics treatment are necessary for very old uroseptic shock patients at risk of AKI.

Our study has several limitations. First, this is a

retrospective study, although we comprehensively collected data using a standard form to overcome bias. However, unavoidable bias, confounding data, and missing data such as comorbidity of dementia, age-adjusted Charlson comorbidity index score, prior antimicrobial therapy, risk factors contributing to the development of MDR bacteria, health-care associated UTI, are to be expected; in particular, the signs of atypical infections or the lower urinary tract symptoms were not fully evaluated or recorded. Second, this single-center study included only hospitalized patients with UTI, which limits the generalizability of the results. A multicentric prospective randomized study is warranted to confirm our findings. Third, due to the study limitation, the information about risk factors contributing to the development of MDR bacteria was incomplete. In addition, our study did not routinely screen for extended-spectrum β-lactamase (ESBL)/AmpC and carbapenemase-producing Enterobacteriaceae. Further study with complete information of risk factors contributing to the development of MDR bacteria and investigating for ESBL/AmpC and carbapenemase-producing Enterobacteriaceae will be needed to find the different mechanisms of antimicrobial resistance between older and non-older patients. Fourth, this is a 12-year study; the majorities of clinical data collection were performed before 2016. Uroseptic shock was not defined according to The Third International Consensus Definitions for Sepsis and Septic Shock. Further study according to The Third International Consensus Definitions for Sepsis and Septic Shock is warranted to find the risk factor of uroseptic shock in older persons.

Herein, very old patients with UTI had a higher risk of developing uroseptic shock than younger patients. Moreover, bacteremia was an independent risk factor for the development of uroseptic shock in very old patients with UTI. Early diagnosis, timely and effective fluid resuscitation, and initial administration of intravenous antimicrobials are critical for these patients.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm.2020.03.95). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study protocol was approved by the Research Ethics Committee of Ditmanson Medical Foundation Chia-Yi Christian Hospital (CYCH-IRB-2019061).

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Supplementary

Table S1 Characteristics of patients with urinary tract infections

Characteristic	All (n=1,043)	Age group			F value or Person χ^2 value	P value	Post hoc tests (LSD)
		Young (<65 years) (n=410)	Old (65–80 years) (n=364)	Very old (>80 years) (n=269)			
Age (years)	67±17	49±12	73±4	85±4	1,684.18	<0.001*	V > O > Y
Gender (male)	283 (27.1)	82 (20.0)	119 (32.7)	82 (30.5)	17.77	<0.001¥	
Diabetes mellitus	452 (43.3)	136 (33.2)	205 (56.3)	111 (41.3)	42.71	<0.001¥	
Hypertension	549 (52.6)	134 (32.7)	232 (63.7)	183 (68.0)	109.03	<0.001¥	
Congestive heart failure	45 (4.3)	7 (1.7)	16 (4.4)	22 (8.2)	16.49	<0.001¥	
Coronary artery disease	111 (10.6)	15 (3.7)	53 (14.6)	43 (16.0)	34.98	<0.001¥	
Cirrhosis	63 (6.0)	17 (4.1)	29 (8.0)	17 (6.3)	5.01	0.082¥	
Stroke	230 (22.1)	36 (8.8)	106 (29.1)	88 (32.7)	70.38	<0.001¥	
Prior history of urinary tract infection					56.61	<0.001¥	
None	684 (65.6)	323 (78.8)	211 (58.0)	150 (55.8)			
Once	204 (19.6)	57 (13.9)	84 (23.1)	63 (23.4)			
Twice	86 (8.2)	20 (4.9)	36 (9.9)	30 (11.2)			
Thrice or more	69 (6.6)	10 (2.4)	33 (9.1)	26 (9.7)			
Indwelling Foley catheter	70 (6.7)	11 (2.7)	26 (7.1)	33 (12.3)	24.00	<0.001¥	
Temperature (℃)	38.1±1.4	38.2±1.4	38.1±1.4	37.9±1.4	2.66	0.070*	
Afebrile	395 (37.9)	113 (27.6)	150 (41.2)	132 (49.1)	34.59	<0.001¥	
Flank pain	461 (44.2)	271 (66.1)	130 (35.7)	60 (22.3)	142.63	<0.001¥	
Bacteremia	480 (46.0)	183 (44.6)	176 (48.4)	121 (45.0)	1.23	0.541¥	
Urinary tract abnormality	273 (26.2)	105 (25.6)	98 (26.9)	70 (26.0)	0.18	0.916¥	
Urolithiasis	184 (17.6)	79 (19.3)	64 (17.6)	41 (15.2)	1.81	0.404¥	
Hydronephrosis	148 (14.2)	61 (14.9)	55 (15.1)	32 (11.9)	1.58	0.455¥	
Urogenital cancer	45 (4.3)	9 (2.2)	16 (4.4)	20 (7.4)	10.81	0.004¥	
Inadequate empirical antimicrobial treatment	275 (26.4)	89 (21.7)	103 (28.3)	80 (29.7)	6.86	0.032¥	
Inadequate empirical antimicrobial treatment for multiple drug resistance bacteria (N=362)	185 (51.1)	61 (45.9)	68 (51.9)	56 (57.1)	2.93	0.232¥	
Length of hospital stay (days)	9±5	8±4	10±6	10±5	13.68	<0.001*	V = O > Y
Admitted to the Intensive Care Unit	113 (11.4)	37 (9.2)	46 (13.8)	30 (11.9)	3.99	0.136¥	
Uroseptic shock	200 (19.2)	66 (16.1)	73 (20.1)	61 (22.7)	4.82	0.090¥	
Acute kidney injury	151 (14.5)	42 (10.2)	67 (18.4)	42 (15.6)	10.75	0.005¥	
All-cause in-hospital mortality	7 (0.7)	0 (0.0)	1 (0.3)	6 (2.2)	13.44	0.001¥	
Multiple drug resistance bacteria	362 (34.7)	133 (32.4)	131 (36.0)	98 (36.4)	1.55	0.461¥	
White blood cell (10^3/μL)	13.19±6.08	13.41±5.69	13.47±6.16	12.47±6.50	2.58	0.076*	
Platelets (10^3/μL)	203±112	215±135	196±93	196±93	3.74	0.024*	Y > O = V
Serum creatinine on admission (mg/dL)	1.60±1.60	1.32±1.62	1.83±1.57	1.72±1.54	11.43	<0.001*	V = O > Y
Baseline eGFR (mL/min/1.73 m^2)	75.21±30.00	93.10±28.63	65.48±25.75	61.13±23.08	158.46	<0.001*	Y > O> V

Data are expressed as mean ± SD or number (percentage). *, one-way analysis of variance (ANOVA); ¥, Chi-square test. eGFR, estimated glomerular filtration rate; V, very old (>80 years); O, old (65–80 years); Y, young (<65 years).

Table S2 Isolated uropathogens and antimicrobial resistance profiles

Characteristic	All (n=1,043)	Age group			Person χ^2 value	P value
		Young (<65 years) (n=410)	Old (65–80 years) (n=364)	Very old (>80 years) (n=269)		
Escherichia coli	809 (77.6)	348 (84.9)	269 (73.9)	192 (71.4)	21.33	<0.001*
Amoxicillin-clavulanate acid	210 (26.0)	74 (21.3)	75 (27.9)	61 (31.8)	7.88	0.019*
Piperacillin/tazobactam	26 (3.2)	4 (1.1)	8 (3.0)	14 (7.3)	15.08	0.001*
Trimethoprim/sulfamethoxazole	397 (49.1)	166 (47.7)	127 (47.2)	104 (54.2)	2.63	0.269*
Aminoglycoside	190 (23.5)	74 (21.3)	64 (23.8)	52 (27.1)	2.35	0.308*
Fluoroquinolones	185 (22.9)	62 (17.8)	66 (24.5)	57 (29.7)	10.52	0.005*
Carbapenems	3 (0.4)	0 (0.0)	1 (0.4)	2 (1.0)	3.63	0.163*
Second-generation cephalosporins	136 (16.8)	48 (13.8)	46 (17.1)	42 (21.9)	5.80	0.055*
Third-generation cephalosporins	135 (16.7)	46 (13.2)	47 (17.5)	42 (21.9)	6.85	0.033*
Proteus species	34 (3.3)	8 (2.0)	17 (4.7)	9 (3.3)	4.53	0.104*
Amoxicillin-clavulanate acid	6 (17.6)	0 (0.0)	2 (11.8)	4 (44.4)	6.57	0.038*
Piperacillin/tazobactam	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Trimethoprim/sulfamethoxazole	13 (38.2)	2 (25.0)	6 (35.3)	5 (55.6)	1.80	0.407*
Aminoglycoside	8 (23.5)	0 (0.0)	4 (23.5)	4 (44.4)	4.65	0.098*
Fluoroquinolones	8 (23.5)	0 (0.0)	4 (23.5)	4 (44.4)	4.65	0.098*
Carbapenems	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Second-generation cephalosporins	3 (8.8)	0 (0.0)	1 (5.9)	2 (22.2)	2.97	0.227*
Third-generation cephalosporins	3 (8.8)	0 (0.0)	0 (0.0)	3 (33.3)	9.14	0.010*
Klebsiella species	79 (7.6)	20 (4.9)	29 (8.0)	30 (11.2)	9.26	0.010*
Amoxicillin-clavulanate acid	12 (15.2)	2 (10.0)	6 (20.7)	4 (13.3)	1.18	0.555*
Piperacillin/tazobactam	7 (8.9)	2 (10.0)	3 (10.3)	2 (6.7)	0.29	0.865*
Trimethoprim/sulfamethoxazole	23 (29.1)	7 (35)	8 (27.6)	8 (26.7)	0.46	0.796*
Aminoglycoside	9 (11.4)	2 (10.0)	2 (6.9)	5 (16.7)	1.45	0.485*
Fluoroquinolones	14 (17.7)	5 (25.0)	4 (13.8)	5 (16.7)	1.06	0.590*
Carbapenems	4 (5.1)	0 (0.0)	3 (10.3)	1 (3.3)	2.94	0.230*
Second-generation cephalosporins	16 (20.3)	4 (20.0)	8 (27.6)	4 (13.3)	1.86	0.395*
Third-generation cephalosporins	13 (16.5)	4 (20.0)	6 (20.7)	3 (10.0)	1.47	0.479*
Enterococcus species	38 (3.6)	7 (1.7)	14 (3.8)	17 (6.3)	9.91	0.007*
Ampicillin	6 (15.8)	2 (28.6)	3 (21.4)	1 (5.9)	2.45	0.294*
Piperacillin/tazobactam	1 (2.6)	0 (0.0)	1 (7.1)	0 (0.0)	1.76	0.415*
Glycopeptide	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Pseudomonas species	53 (5.1)	11 (2.7)	25 (6.9)	17 (6.3)	8.15	0.017*
Amoxicillin-clavulanate acid	1 (1.9)	0 (0.0)	1 (4.0)	0 (0.0)	1.14	0.565*
Piperacillin/tazobactam	2 (3.8)	0 (0.0)	1 (4.0)	1 (5.9)	0.64	0.725*
Trimethoprim/sulfamethoxazole	6 (11.3)	0 (0.0)	4 (16.0)	2 (11.8)	1.95	0.377*
Aminoglycoside	8 (15.1)	2 (18.2)	3 (12.0)	3 (17.6)	0.36	0.837*
Fluoroquinolones	12 (22.6)	0 (0.0)	7 (28.0)	5 (29.4)	4.07	0.130*
Carbapenems	2 (3.8)	0 (0.0)	1 (4.0)	1 (5.9)	0.64	0.725*
Second-generation cephalosporins	1 (1.9)	1 (9.1)	0 (0.0)	0 (0.0)	3.89	0.143*
Third-generation cephalosporins	3 (5.7)	1 (9.1)	2 (8.0)	0 (0.0)	1.52	0.468*

*, Student *t*-test.

Table S3 Characteristics of patients with urinary tract infections

Characteristic	All (n=1,043)	Uroseptic shock		*t*-value, Person χ^2 value or Z-value	P value
		Non (n=843)	Yes (n=200)		
Age (years)	67±17	66±18	70±16	2.62	0.009¥
Age group				4.82	0.090¥
Youth	410 (39.3)	344 (40.8)	66 (33.0)		
Old	364 (34.9)	291 (34.5)	73 (36.5)		
Very old	269 (25.8)	208 (24.7)	61 (30.5)		
Sex (male)	283 (27.1)	216 (25.6)	67 (33.5)	5.07	0.024¥
Diabetes mellitus	452 (43.3)	373 (44.2)	79 (39.5)	1.48	0.223¥
Hypertension	549 (52.6)	449 (53.3)	100 (50.0)	0.69	0.406¥
Congestive heart failure	45 (4.3)	28 (3.3)	17 (8.5)	10.50	0.001¥
Coronary artery disease	111 (10.6)	82 (9.7)	29 (14.5)	3.87	0.049¥
Cirrhosis	63 (6.0)	49 (5.8)	14 (7.0)	0.40	0.526¥
Stroke	230 (22.1)	178 (21.1)	52 (26.0)	2.24	0.134¥
Prior history of urinary tract infection				3.41	0.333¥
None	684 (65.6)	546 (64.8)	138 (69.0)		
Once	204 (19.6)	173 (20.5)	31 (15.5)		
Twice	86 (8.2)	71 (8.4)	15 (7.5)		
Thrice or more	69 (6.6)	53 (6.3)	16 (8.0)		
Indwelling Foley catheter	70 (6.7)	56 (6.6)	14 (7.0)	0.03	0.856¥
Temperature (℃)	38.1±1.4	38.0±1.3	38.2±1.6	1.14	0.263*
Afebrile	395 (37.9)	337 (40.0)	58 (29.0)	8.28	0.004¥
Flank pain	461 (44.2)	353 (41.9)	108 (54.0)	9.64	0.002¥
Bacteremia	480 (46.0)	355 (42.1)	125 (62.5)	27.05	<0.001¥
Urinary tract abnormality	273 (26.2)	204 (24.2)	69 (34.5)	8.88	0.003¥
Urolithiasis	184 (17.6)	130 (15.4)	54 (27.0)	14.92	<0.001¥
Hydronephrosis	148 (14.2)	108 (12.8)	40 (20.0)	6.86	0.009¥
Urogenital cancer	45 (4.3)	38 (4.5)	7 (3.5)	0.40	0.528¥
Inadequate empirical antimicrobial treatment	272 (26.1)	214 (25.4)	58 (29.0)	1.10	0.295¥
Inadequate empirical antimicrobial treatment for multiple drug resistance bacteria (N=362)	185 (51.1)	144 (51.8)	41 (48.8)	0.23	0.631¥
Length of hospital stay (days)	10±5	9±5	12.0±7.0	7.57	<0.001*
Admitted to the Intensive Care Unit	113 (11.4)	41 (5.1)	72 (37.7)	161.43	<0.001¥
Acute kidney injury	151 (14.5)	83 (9.8)	68 (34.0)	76.17	<0.001¥
All-cause in-hospital mortality	7 (0.7)	1 (0.1)	6 (3.0)	20.13	<0.001¥
Multiple drug resistance bacteria	362 (34.7)	278 (33)	84 (42.0)	5.81	0.016¥
White blood cell (10^3/μL)	13.2±6.1	13.0±5.7	14.0±7.5	1.18	0.238*
Platelets (10^3/μL)	203.9±112.0	208.4±115.5	184.9±93.9	2.68	0.008*
Serum creatinine on admission (mg/dL)	1.6±1.6	1.5±1.5	2.0±1.9	4.78	<0.001*
Baseline eGFR (mL/min/1.73 m^2)	75.2±30.0	75.4±30.5	74.6±28.1	0.35	0.728*
Escherichia coli	809 (77.6)	654 (77.6)	155 (77.5)	0.001	0.981¥
Proteus spp.	34 (3.3)	26 (3.1)	8 (4.0)	0.43	0.512¥
Klebsiella spp.	79 (7.6)	66 (7.8)	13 (6.5)	0.41	0.523¥
Enterococcus spp.	38 (3.6)	27 (3.2)	11 (5.5)	2.43	0.119¥
Pseudomonas spp.	53 (5.1)	46 (5.5)	7 (3.5)	1.28	0.257¥

Data are expressed as mean ± SD or number (percentage). *, Student *t*-test or Mann-Whitney U-test; ¥, Chi-Square test or Fisher's exact test. eGFR, estimated glomerular filtration rate.