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RESEARCH

Enterococci independently increase the risk for initial antibiotic treatment failure and prolonged hospitalization in adult patients with complicated urinary tract infection: a retrospective cohort study

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Abstract

Objectives We aimed to investigate the impact of enterococci on initial antibiotic treatment (IAT) failure and prolonged hospitalization in complicated urinary tract infection (cUTI) cases, and to identify risk factors for enterococcal cUTI.

Methods Adult cUTI patients were analyzed to compare the differences between the Enterococcus and non-Enterococcus groups. Univariate and multivariate analyses were employed to identify independent risk factors.

Results This study included 419 patients, with the *Enterococcus* group showing significantly higher IAT failure rates and an extended average length of stay by 4.4 days compared to the non-Enterococcus group. Multivariate analysis identified enterococci, hospital-acquired UTIs (HA-UTI), indwelling catheters, and bed rest (bedridden) as independent risk factors for IAT failure. Enterococci were notably linked to prolonged hospitalization, other independent risk factors included IAT failure, prior antimicrobial use, age-adjusted Charlson comorbidity index (ACCI) ≥ 4, hypoalbuminemia, and bed rest. Urological cancer, HA-UTI, indwelling catheters, urinary retention, and urologic surgery were risk factors for enterococcal cUTI.

Conclusion We provide the first evidence that enterococci independently increase the risk for IAT failure and prolonged hospitalization in adults with cUTIs, highlighting the significance of timely identification to optimize measures including antibiotic regimens. Risk factors for enterococcal cUTI have also been identified to aid clinicians in managing this condition.

Keywords *Enterococcus* · Complicated urinary tract infection · Initial antibiotic treatment failure · Prolonged hospitalization · Risk factors

Introduction

Urinary tract infections (UTIs) are among the most prevalent bacterial diseases in both community and hospital settings. For decades, UTIs have been categorized into uncomplicated UTIs and complicated UTIs (cUTIs) to distinguish between benign infections and those with potential for severe progression [1]. This classification is endorsed by recent guidelines from the U.S. Food and Drug Administration (FDA) and European Medicines Agency [2, 3]. According to the 2018 FDA guidance, a cUTI is defined as a UTI with complicating factors that elevate the risk of treatment failure or infection acquisition, such as structural or functional abnormalities in the genitourinary tract or the presence of indwelling urinary catheters [2].

The incidence of cUTI has increased significantly, with data from the U.S. indicating approximately 100,000 hospitalizations annually in the early 2000s. By 2011, this number had risen to 400,000 cases, marking a fourfold increase over a decade and incurring costs of approximately $2.8 billion [4]. By 2018, over 600,000 individuals were hospitalized for cUTIs annually, constituting about 1.8% of total U.S. hospital admissions [5]. Enterococci have become increasingly prevalent in cUTIs, currently ranking second only to *Escherichia coli (E. coli)* [6–8]. They are also the second most prevalent pathogens in UTIs among hospitalized

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patients [9, 10]. A study conducted over a 20-year period in Japan reported isolation rates for *Enterococcus faecalis* (*E. faecalis*) and *Enterococcus faecium* (*E. faecium*) in hospital-acquired cUTIs ranging from 13.3 to 21% and 7.6-10%, respectively [11].Furthermore, *Enterococcus* spp. constituted 13.8% of over 18,000 catheter-associated UTIs in a study by the National Healthcare Safety Network (NHSN), which included data from more than 2,000 U.S. healthcare facilities [12].

Empirical anti-infective therapies for cUTI primarily target gram-negative bacilli (GNB) according to US, European, and Chinese guidelines [2, 3], however, these treatments frequently fall short due to the drug resistance exhibited by enterococci. In fact, inappropriate empiric anti-infective therapy (IEAT) is more prevalent in cases involving enterococcal infections [13], highlighting a critical gap in current therapeutic strategies. The treatment of enterococcal infections presents significant challenges because of the pathogen's inherent and acquired resistance to multiple antibiotics. Enterococci are naturally resistant to a range of antibiotics, including cephalosporins and aminoglycosides. They can also develop acquired resistance to drugs such as ampicillin and levofloxacin. Mechanisms of resistance involve genetic adaptations, altering cell wall precursors, and efflux pumps. In particular, vancomycin-resistant E. faecium (VREfm) has become very prevalent in some countries [14].

Appropriate initial antibiotic treatment (IAT) is crucial for the success of cUTI treatment [15]. Typically, treatment commences prior to obtaining etiological results from urine cultures, making the initial approach largely empirical. IAT failure, which occurs in approximately 10-55% of cUTI cases, can result in prolonged hospitalization, the spread of infection to other organs, and in severe instances, sepsis and death [16–18]. The length of stay (LOS) often reflects the complexity of the patient's recovery process, with extended hospitalization increasing the risk of nosocomial infection and other complications [19].

Given the unique characteristics of enterococci and the inadequacy of conventional empirical anti-infective treatments in targeting these organisms effectively, we hypothesized that enterococci negatively influence both IAT outcomes and the LOS in cUTI cases. Despite the critical nature of these issues, there is a noticeable lack of studies addressing this hypothesis. Consequently, our research aimed to explore the relationship between enterococcal presence and both IAT failure and prolonged hospitalization, as well as to identify the risk factors for enterococcal cUTI.

Methods

This retrospective cohort study was conducted in compliance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines to ensure high-quality reporting (www.strobe-statement.org) [20].

Design, setting, and patients

This was an observational retrospective cohort study. Inpatients enrolled were from July 2020 to June 2022 at the Second Hospital of Tianjin Medical University, Tianjin, China, a tertiary teaching hospital. The inclusion criteria were as follows: adult patients ($\geq$18 years) with bacterial cUTI as the primary cause of hospitalization or those who developed cUTI during their stay. Patients with mixed infections (more than one species of microorganism being detected in the same urine culture) were excluded to prevent double counting in different statistical analyses. Additionally, patients with concomitant infections at other sites were also excluded to ensure the specificity of antimicrobial therapy for cUTI. cUTI was diagnosed according to the US FDA guidelines. Microbiological criteria for UTI were confirmed by isolating pathogenic bacteria from urine cultures. A urine colony count of $\geq 10^5$ colony-forming units per milliliter (CFU/mL) confirmed the infection [2]. Microbiological identification was performed using the VITEK 2 fully automated system.

Confounders were identified and selected through a comprehensive process that included a review of the relevant literature, consultations with experts in our field, preliminary univariate analyses, and evaluation of the temporal sequence to determine their potential impact on the outcomes [21–23].

Definitions of terms

Hospital-acquired urinary tract infection was defined according to Friedman et al. as occurring 48 h after admission; the remainder were defined as community-acquired UTI [24]. In most previous relevant studies, the cutoff value of the age-adjusted Charlson comorbidity index (ACCI) was 3 to 6 [25]. The mean value of the ACCI in our study was 4.6, and we set the cutoff value at 4. Urological surgery specifically refers to procedures that need to be performed using a transurethral approach. Examples include transurethral resection of the prostate, transurethral resection of bladder tumors for cancer treatment, ureteroscopic lithotripsy, and ureteral stenting for calculi. Open surgeries were excluded.

Initial antibiotic therapy is defined as the administration of antimicrobial agents within 48 h of treatment initiation

[17]. Failure of IAT encompasses the following criteria: (1) persistence or exacerbation of symptoms within 48 h after initiating IAT, specifically including fever (≥ 38.0℃), dysuria, urinary frequency, urgency, suprapubic pain or tenderness, flank pain or tenderness, and perineal pain. Symptoms were assessed by at least two senior clinicians to reduce subjective evaluations; (2) readmission within 30 days of hospital discharge due to a urinary tract infection caused by the same pathogen; (3) adjustment of antibiotic dosage, addition of another antibiotic, or switch to an alternative antibiotic due to lack of significant improvement or worsening of symptoms—note that transitioning from intravenous to oral antibiotics does not constitute failure of IAT; and (4) patient mortality during hospitalization for any reason [17].

Data collection

Clinical, etiological, and laboratory data were collected from the electronic medical records of each patient. Directly collectable data included sex; age; diabetes mellitus, dementia, chronic renal failure, hydronephrosis, prostatic hyperplasia, chronic obstructive pulmonary disease, peptic ulcer, heart failure, liver failure or cirrhosis, hypoalbuminemia, and metastatic cancer; history of ongoing treatment such as active chemotherapy or immunotherapy; and information about urinary retention, urologic cancers, indwelling urinary catheters, urologic surgery, admission to ICU, bed rest, prior antimicrobial use and urine culture results. Data requiring judgment included the ACCI and HA-UTI. Two independent researchers reviewed the cases in this study. In cases of disagreement between the two researchers, a senior expert with over 20 years of experience made the final decision.

Statistical analysis

Categorical variables were analyzed using either the chi-square test or Fisher's exact test (when the expected frequencies in any of the contingency table cells were less than 5). Continuous variables were reported as means ± standard deviations. Two-tailed tests were used to determine statistical significance, with a P-value of < 0.05 was considered significant. Additionally, risk factors were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Variables that reached statistical significance ($P < 0.05$) in the univariate comparisons were entered into a binary logistic regression analysis using the forward stepwise selection method to identify significant independent factors. Data analysis was performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Some analyses and plots were generated using GraphPad Prism 10 (GraphPad Prism, La Jolla, CA).

Results

Patients and distribution of isolated pathogens

In this study, a total of 419 patients were finally included in the analyses. Of the total cases, 239 (57%) were GNB and 180 (43%) were gram-positive bacilli (GPB). The most common pathogenic bacteria identified were *E. coli* (129 patients, 30.8%), *E. faecium* (70 patients, 16.7%), *E. faecalis* (66 patients, 15.8%), and *Klebsiella* spp. (26 patients, 6.2%) (Fig. 1).

Baseline data and the impact of enterococci on IAT and LOS

The average age of the 419 eligible patients was 70.7 ± 14.7 years, with 232 (55.4%) were male. The mean LOS for all patients was 14.5 ± 11.63 days, with 136 patients (32.5%) having an extended LOS compared to the mean. IAT failed in 153 patients, representing 36.5% of cases. Patients were divided into two groups: *Enterococcus* (136 patients, 32.5%) and non- *Enterococcus* (283 patients, 67.5%) to assess the impact of enterococci on IAT and LOS.

The proportion of IAT failures was significantly higher in the *Enterococcus* group compared to the non-*Enterococcus* group (52.9% vs. 28.6%, $P = 0.001$). Additionally, the mean LOS was 17.5 days in the Enterococcus group, significantly longer than the 13.1 days in the non-*Enterococcus* group ($P = 0.002$). This resulted in a mean LOS prolongation of 4.4 days in the *Enterococcus* group (Table 1; Fig. 2). Significant differences were also observed in HA-UTI, urologic cancer, and urologic surgery between the two groups (Table 1). Given these differences, we aimed to investigate whether enterococcal infection was an independent risk factor for IAT failure and prolonged hospitalisation.

Risk factors for IAT failure and prolonged hospitalization

Univariate and multivariate analyses were conducted to confirm the role of enterococci in IAT failure and prolonged hospitalization and identify other independent risk factors affecting both. The IAT failure group had a higher proportion of enterococci (47.1% vs. 24.1%, $P < 0.001$), HA-UTI (54.9% vs. 36.1%, $P < 0.001$), bed rest (bedridden) (9.8% vs. 3%, $P = 0.003$), and indwelling urinary catheters (66% vs. 53.4%, $P = 0.012$) compared to the IAT success group (Table 2). Multivariate analysis revealed enterococci (OR 2.51; 95% CI 1.62–3.88; $P < 0.001$), HA-UTI (OR 2.03; 95% CI 1.33–3.09; $P = 0.001$), indwelling urinary catheter (OR 1.57; 95% CI 1.02–2.43; $P = 0.042$), and bed rest (OR

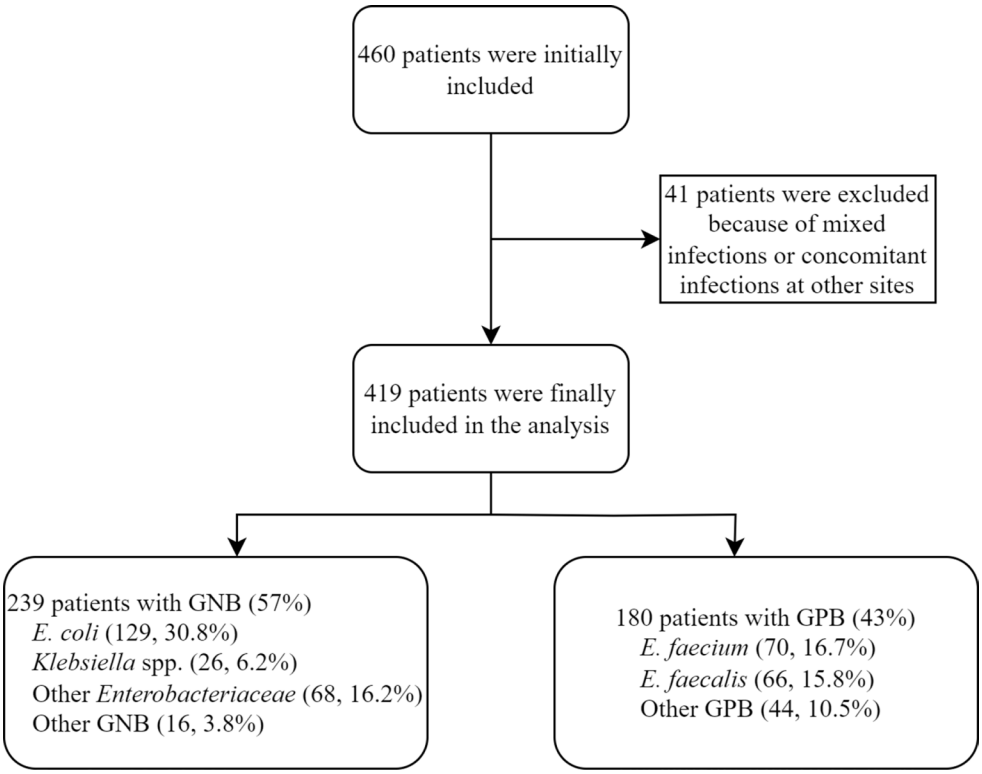

Fig. 1 Flow chart for inclusion of 419 patients and distribution of causative organisms. *GNB* gram-negative bacilli, *E. coli Escherichia coli*, *GPB* gram-positive bacilli, *E. faecium Enterococcus faecium*, *E. faecalis Enterococcus faecalis*

2.58; 95% CI 1.02–6.51; $P=0.046$) as independent risk factors for IAT failure (Fig. 3).

Univariate analysis showed that the longer LOS group had a higher proportion of age ≥ 65 years, enterococci, IAT failure, bed rest, indwelling urinary catheter, prior antimicrobial use, ACCI ≥ 4, and hypoalbuminemia (all P-values < 0.05) (Table 2). Multivariate analysis identified enterococci (OR 1.92; 95% CI 1.16–3.15; $P=0.011$), IAT failure (OR 2.34; 95% CI 1.43–3.82; $P=0.001$), prior antimicrobial use (OR 1.97; 95% CI 1.22–3.18; $P=0.005$), ACCI ≥ 4 (OR 2.92 ; 95% CI 1.63–5.20; $P<0.001$), hypoalbuminemia (OR 2.79 ; 95% CI 1.69–4.61; $P<0.001$), and bed rest (OR 9.12 ; 95% CI 2.47–33.69; $P=0.001$) were independent risk factors for prolonged hospitalization (Fig. 3).

Risk factors for enterococcal cUTI

As shown in the above results, enterococci are an independent risk factor for both IAT failure and prolonged hospitalization, highlighting the significance of early identification of enterococcal cUTI and timely administration of targeted measures. Therefore, we further investigated the risk factors leading to enterococcal cUTI. All factors with $P<0.05$ in Table 1 were included in a binary logistic regression model. The independent risk factors for enterococcal cUTI were urologic cancer (OR 2.29; 95% CI 1.38–3.78; $P=0.001$), HA-UTI (OR 1.72; 95% CI 1.11–2.67; $P=0.015$), indwelling urinary catheter (OR 1.67; 95% CI 1.06–2.63; $P=0.027$), urinary retention (OR 2.71; 95% CI 1.04–7.03; $P=0.042$), and urologic surgery (OR 4.30; 95% CI 2.17–8.52; $P<0.001$). The results are presented in Fig. 4.

Discussion

This study is among the first to establish enterococci as an independent risk factor for both IAT failure and prolonged hospitalization in patients with cUTI. The high proportion of IAT failures for enterococcal cUTI may be due to commonly used antimicrobials in empirical anti-infective therapy. These antimicrobials are insufficiently effective against enterococci. The first line of empirical anti-infective therapy for cUTI, as stated in US, European, and Chinese guidelines, is mainly directed at GNB rather than enterococci [2, 3]. Esparcia et al. found that inappropriate empirical anti-infective therapy (IEAT) was more likely to occur in enterococcal infections [13]. Enterococci prolong LOS perhaps due to their higher adaptability, biofilm formation and relatively high drug resistance. Enterococci possess remarkable adaptability and resilience, allowing them to survive harsh conditions and persist in healthcare environments [26]. Enterococci have the ability to form biofilms, particularly on the surface of indwelling medical devices, which enhances their virulence and persistence [27]. Additionally, they are intrinsically resistant to various common antibiotics, including cephalosporins and aminoglycosides

Table 1 Epidemiological and clinical characteristics of the inpatients

	Enterococcus*n* = 136	Non-Enterococcusn = 283	*P*
Sex (male), n (%)	82 (60.3)	150 (53)	0.160
*Age ≥ 65 years, n (%)	105 (77.2)	190 (67.1)	0.035
*IAT failure, n (%)	72 (52.9)	81 (28.6)	< 0.001
*Longer than mean LOS, n (%)	64 (47.1)	72 (25.4)	< 0.001
*HA-UTI, n (%)	68 (50.0)	112 (39.6)	0.044
*ACCI ≥ 4, n (%)	103 (75.7)	177 (62.5)	0.007
*Urologic cancer, n (%)	44 (32.4)	48 (17.0)	< 0.001
*Indwelling urinary catheter, n (%)	89 (65.4)	154 (54.4)	0.032
*Urologic surgery, n (%)	28 (20.6)	16 (5.7)	< 0.001
*Urinary retention, n (%)	10 (7.4)	8 (2.8)	0.032
*Bed rest, n (%)	12 (8.8)	11 (3.9)	0.038
Prior antimicrobial use, n (%)	69 (50.7)	130 (45.9)	0.357
Diabetes, n (%)	45 (33.1)	91 (32.2)	0.849
Dementia, n (%)	2 (1.5)	2 (0.7)	0.598
Chronic renal failure, n (%)	9 (6.6)	20 (7.1)	0.865
Cerebral infarction, n (%)	44 (32.4)	76 (26.9)	0.244
Hydronephrosis, n (%)	15 (11.0)	39 (13.8)	0.431
Prostatic hyperplasia, n (%)	49 (36.0)	97 (34.3)	0.724
Chronic obstructive pulmonary disease, n (%)	2 (1.5)	5 (1.8)	1.000
Peptic ulcer, n (%)	8 (5.9)	10 (3.5)	0.267
Chemotherapy, n (%)	7 (5.1)	8 (2.8)	0.231
Immunotherapy, n (%)	3 (2.2)	3 (1.1)	0.395
Heart failure, n (%)	14 (10.3)	32 (11.3)	0.756
Liver failure or cirrhosis, n (%)	9 (6.6)	12 (4.2)	0.340
Metastatic cancer, n (%)	6 (4.4)	7 (2.5)	0.284
Hypoalbuminemia, n (%)	43 (31.6)	75 (26.5)	0.267
ICU, n (%)	2 (1.5)	12 (4.2)	0.243

IAT initial antibiotic therapy, *LOS* length of stay, *HA-UTI* hospital-acquired urinary tract infection, *ACCI* age-adjusted Charlson comorbidity index, *ICU* intensive care unit, * represents $P < 0.05$

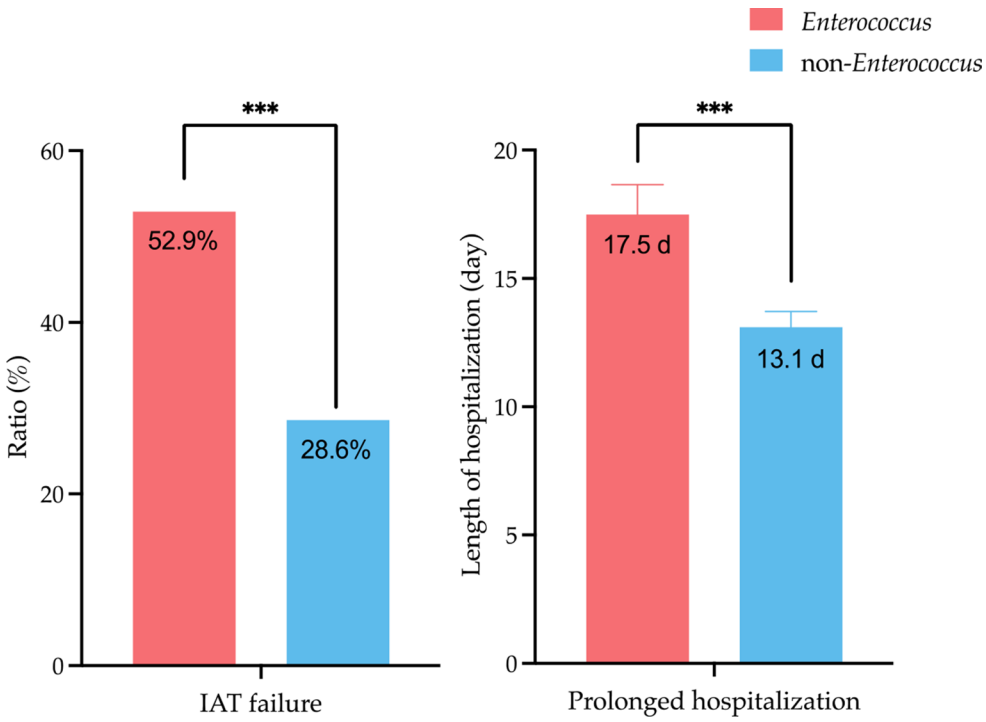

Fig. 2 Comparisons of IAT failures and length of hospitalization. *IAT* initial antibiotic treatment, *** means $P < 0.001$

Table 2 Univariate analysis of IAT failure and prolonged hospitalization

	IAT success $n=266$	IAT failure $n=153$	*P*	≤mean LOS $n=283$	> mean LOS $n=136$	*P*
Sex (male), n (%)	143 (53.8)	89 (58.2)	0.382	159 (56.2)	73 (53.7)	0.629
*Age ≥ 65, n (%)	181 (68)	114 (74.5)	0.163	181 (64)	114 (83.8)	<0.001
**Enterococcus*, n (%)	64 (24.1)	72 (47.1)	<0.001	72 (25.4)	64 (47.1)	<0.001
*IAT failure, n (%)	-	-	-	33 (22.9)	21 (39.6)	0.002
*HA-UTI, n (%)	96 (36.1)	84 (54.9)	<0.001	116 (41)	64 (47.1)	0.24
*Bed rest, n (%)	8 (3)	15 (9.8)	0.003	3 (1.1)	20 (14.7)	<0.001
*Indwelling urinary catheter, n (%)	142 (53.4)	101 (66)	0.012	154 (54.4)	89 (65.4)	0.032
Urologic surgery, n (%)	25 (9.4)	19 (12.4)	0.332	31 (11)	13 (9.6)	0.663
*Prior antimicrobial use, n (%)	119 (44.7)	80 (52.3)	0.136	112 (39.6)	87 (64)	<0.001
*ACCI ≥ 4, n (%)	172 (64.7)	108 (70.6)	0.215	163 (57.6)	117 (86)	<0.001
Urologic cancer, n (%)	58 (21.8)	34 (22.2)	0.921	59 (20.8)	33 (24.3)	0.429
*Cerebral infarction, n (%)	68 (25.6)	52 (34)	0.066	60 (21.2)	60 (44.1)	<0.001
*Peptic ulcer, n (%)	8 (3)	10 (6.5)	0.086	8 (2.8)	10 (7.4)	0.032
*Hypoalbuminemia, n (%)	67 (25.2)	51 (33.3)	0.074	56 (19.8)	62 (45.6)	<0.001
*ICU, n (%)	13 (4.9)	1 (0.7)	0.022	12 (4.2)	2 (1.5)	0.14

IAT initial antibiotic therapy, *LOS* length of stay, *HA-UTI* hospital-acquired urinary tract infection, *ACCI* age-adjusted Charlson comorbidity index, *ICU* intensive care unit, * represents $P<0.05$

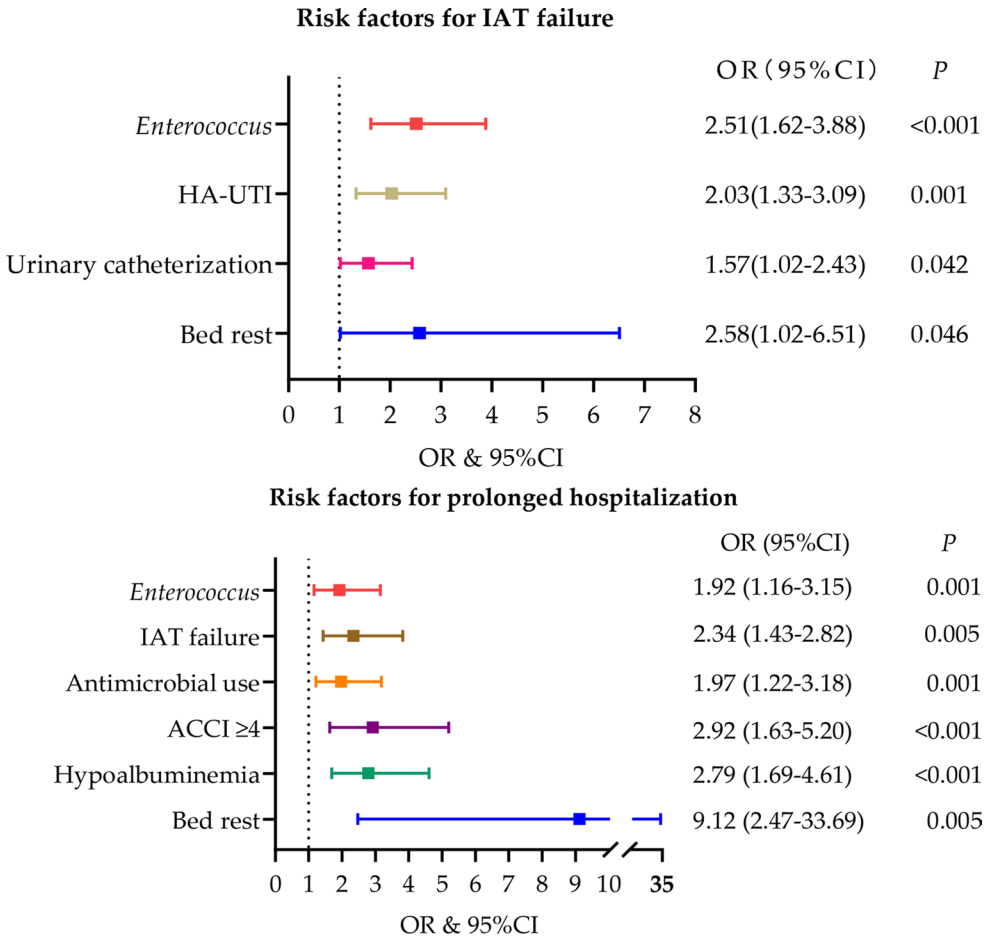

Fig. 3 Forest plot of multivariate analysis of IAT failure and prolonged hospitalization in cUTI inpatients. *IAT* initial antibiotic therapy, *HA-UTI* hospital-acquired urinary tract infection; *ACCI* age-adjusted Charlson comorbidity index; *OR* odds ratio, *CI* confidence interval

[28]. Besides (1) enterococci (OR 1.92; 95% CI 1.16–3.15), (2) bed rest (OR 2.58, 95% CI 1.02–6.51), (3) HA-UTI (OR 2.03, 95% CI 1.33–3.09), and (4) indwelling catheter (OR 1.57, 95% CI 1.02–2.43) were also independent risk factors for cUTI IAT failure in our study. Another retrospective multinational and multicenter study by Eliakim-Raz et al. also identified bed rest and indwelling catheters as independent risk factors for IAT failure in cUTI. Additionally, their

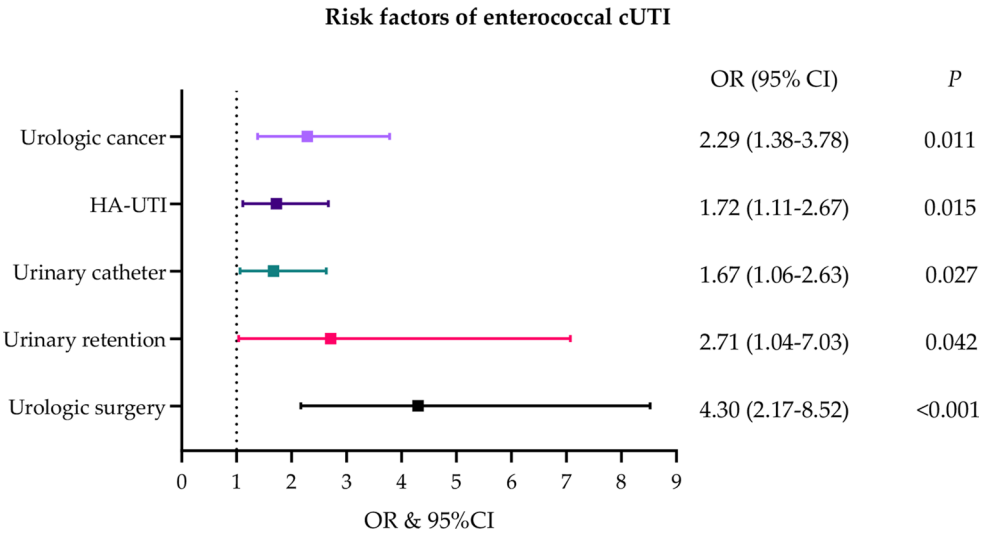

Fig. 4 Forest plot of risk factors for enterococcal urinary tract infection. *HA-UTI* hospital-acquired urinary tract infection, *OR* odds ratio; *CI* confidence interval

study found other risk factors such as age and ICU admission [16].

Our study recognized that independent risk factors for prolonged hospital stay included (1) IAT failure (OR 2.34; 95% CI 1.43–3.82), (2) prior antibacterial use (OR 1.97; 95% CI 1.22–3.18), (3) ACCI ≥ 4 (OR 2. 92; 95% CI 1.63–5.20), (4) hypoalbuminemia (OR 2.79; 95% CI 1.69–4.61), and (5) bed rest (OR 9.12; 95% CI 2.47–33.69), in addition to (6) enterococci (OR 1.92; 95% CI 1.16–3.15). Hence, pathogens, host conditions, and treatments could all significantly affect patient recovery time. Zilberberg et al. retrospectively examined data on patients hospitalized with cUTI in the USA. They found that IEAT and multidrug-resistant pathogens resulted in prolonged hospital stays [29]. Zhu et al. conducted a study in China involving 213 patients diagnosed with cUTI. They reported several independent risk factors for prolonged hospitalization, including IEAT, ACCI ≥ 2, lung disease, and heart disease [19]. Although Moses et al. reported patients with enterococcal bacteremia in the ICU had longer hospital stays [30], our study is the first to show that enterococci are an independent risk factor for prolonged hospital stays in cUTI. Recent research underscores the challenging prognosis of complicated urinary tract infections (cUTIs) involving drug-resistant bacteria such as carbapenem-resistant *E. coli* (CRE) [31] and vancomycin-resistant enterococci (VRE) [32]. Studies reveal an increase in resistance among these pathogens, significantly complicating treatment options and patient outcomes. In our study, only a single strain of VRE was identified, and no cases of CRE were detected.

Our study highlights the significance of early recognition of enterococcal cUTI. But investigations on risk factors for enterococcal cUTI are still limited in recent years [21–23]. Indwelling urinary catheterization and previous urinary instrumentation were identified as risk factors for *E. faecalis* UTI [22]. Another study displayed male sex, individuals aged between 55 and 75 years, catheter-associated UTI, and urinary retention as contributing factors to enterococcal cUTI [23]. Moreover, male sex, obstructive uropathy, nosocomial infection, cancers of the urinary system, and prior antimicrobial therapy emerged as independent predictors within a study investigating bacteremic UTI [21]. Our findings revealed that the independent risk factors for enterococcal UTI were (1) urologic cancer (OR 2.29; 95% CI 1.38–3.78), (2) HA-UTI (OR 1.72; 95% CI 1.11–2.67), (3) indwelling urinary catheter (OR 1.67; 95% CI 1.06–2.63), (4) urinary retention (OR 2.71; 95% CI 1.04–7.03), and (5) urologic surgery (OR 4.30; 95% CI 2.17–8.52). Our study and others underline the crucial role of urinary tract procedures (indwelling catheters and urologic surgery) and urologic diseases (urologic cancers, urinary tract obstruction, and urinary retention) in enterococcal cUTI. In comparison to other bacteria, urinary tract procedures are more likely to result in enterococcal cUTI. This increased risk may be attributed to several factors. First, enterococci possess a superior ability to form biofilms, which enhances their capacity to colonize and persist in the urinary tract [33]. Additionally, prophylactic antibiotic regimens in urologic surgery primarily target GNB. This targeting may have a relatively limited impact on enterococci and may potentially increase the probability of enterococcal infections [34]. Furthermore, enterococci exhibit robust resistance to environmental stresses, allowing them to survive and proliferate in conditions that might inhibit other bacterial species [14]. Timely and appropriate prediction of enterococcal cUTI may improve patient management and prognosis. As a retrospective study, our research inherently faces challenges such as selection bias and recall bias. Additionally, the single-center nature of our study may limit the generalizability of our findings. Although we made efforts to minimize

subjective assessments by having several senior clinicians evaluate patient conditions, some degree of subjectivity may still be present. Furthermore, despite our attempts to identify and account for confounders, there may still be residual confounding factors that were not addressed. We look forward to larger and multicenter studies conducted by other research teams to further validate our findings.

A recently published reference standard on UTIs, formed by an international panel of experts, places emphasis on key symptoms such as new-onset dysuria, urinary frequency, and urgency, while excluding non-specific symptoms in older patients. This consensus revised bacteriuria threshold and focused on pyuria quantification to improve diagnostic precision [35]. We believe that this consensus will enhance research consistency, particularly in the context of rising antimicrobial resistance.

Conclusions

To the best of our knowledge, we provide the first evidence that enterococci independently increase the risk for IAT failure and prolonged hospitalization in adults with cUTIs. This highlighs the significance of timely identification to optimize measures including antibiotic regimens. Moreover, we have identified and elucidated risk factors associated with enterococcal cUTI, thereby aiding clinicians in managing this condition. Notably, as a retrospective cohort study, potential limitations may include selection bias and information bias.

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Author contributions Y.W. designed the study. Z.Z., W.D., Y.Z. and Y.Y. contributed to data acquisition. Z.Z. and W.D. conducted research and statistical analyses. Z. Z. and W.D. wrote the first draft of the manuscript. Y.W. and J.F. provided critical revisions. All the authors have read and agreed to the published version of the manuscript.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Institutional review board statement This study was approved by the Ethical Review Committee of the Second Hospital of Tianjin Medical University, Tianjin, China, ethic approval number: KY2023K194. All experiments were performed in accordance with the guidelines of the ethics review committee. The Ethical Review Committee waived the need for informed consent because the study's non-intrusive design, patient anonymity, and use of only de-identified data made it unnecessary to obtain written consent.

Informed consent The requirement for written informed consent was waived, given the research's non-intrusive nature and patient anonymity.

Competing interests The authors declare no competing interests.

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