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Original Article

The Effect of Urinary Tract Infection on Overall Mortality in Elderly Male Patients

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Abstract

Introduction: Urinary tract infections are the most common bacterial infections in the older population.

Aim: This study aims to determine the impact of the isolated pathogen from urine culture on the estimated survival time of elderly male patients.

Materials and methods: We conducted a retrospective cross-sectional study to evaluate the male patients with pathogenic growth in their urine culture tests. We included in the study only male patients aged 80 years or over with positive urine culture tests for pathogenic growth. Urine samples were collected from either first clean-catch midstream urine or from the urinary catheters. Bacterial growth of $\geq 10^5$ colony-forming units/mL (CFU/mL) in the culture was considered significant. For comparison of the survival time, five groups were created according to the pathogens identified in the urine culture.

Results: Between February 2014 and December 2020, there were 1133 patients that met the study criteria. The most common pathogen was *Escherichia coli* with a rate of 29.5%. The median overall survival time was 4 months. The longest and shortest median overall survival times for the *E. coli* group and the fungi group were 17.4 months and 0.4 months, respectively ($p<0.001$). While being in the ICU is the most important risk factor for mortality in this elderly cohort, the statistical analysis showed that being infected with fungi carries a 1.57-fold increased risk of mortality compared with the *E. coli* infection ($p<0.001$).

Conclusions: The aging of the population requires evaluation of the diseases that are frequently encountered in advanced age. Our study showed that the causative pathogen of the urinary tract infection might have an impact on overall survival time in the senior population.

Keywords

elderly, urinary tract infection, urine culture, survival

INTRODUCTION

Urinary tract infection (UTI) is the most common bacterial infection in the elderly population, and *E. coli* is the most common pathogen in community-dwelling people older than 65 years.[1] Female sex, sexual activity, family history, impaired urinary flow, immunosuppression, and age are the known risk factors for UTIs.[2] On the other hand, the incidence of sepsis and mortality increases with age, and the severity of UTI is high in males.[3-5]

The population is aging, and the related problems are growing. In developed countries, this particular group will have a higher proportion of the population soon. In addition, certain measures will be needed to meet their require-

ments. Consequently, the United Nations took a decision to take action, and the ten years from 2021 to 2030 were declared the United Nations Decade of Healthy Ageing.[6] In the aging male, considerable causes of frailty are impaired urine flow and UTIs. Different risk factors such as urinary incontinence, cognitive impairment, chronic catheter, diabetes mellitus, and the prostatic disease can contribute to the development of UTIs in older males due to aging.[7] Besides the comorbidities, UTIs could be the primary cause of mortality in elderly patients.[8]

AIM

Although there are many reports on urinary tract infections, studies investigating the effect of the causative pathogen on survival in aging men are limited. In this study, we retrospectively reviewed the association between isolated pathogens in urine culture and overall mortality rates in male patients aged ≥80 years.

MATERIALS AND METHODS

A retrospective, cross-sectional study was conducted of the urine cultures carried out by our microbiology department between February 2014 and December 2020. The inclusion criteria of the study were male patients at least 80 years old with urine cultures performed at our laboratory who must have pathogenic growth in their culture results. We excluded cases if there was an anaerobic bacterial infection, polymicrobial growth, growth with non-pathogenic microorganisms, or no growth in urine culture. Demographic features of the patients were collected from hospital records.

Urine samples were obtained from either first clean-catch midstream urine using a sterile wide-mouth container or urinary catheters. A standard loopful of each urine sample (10 µL) was dispensed onto a chromogenic medium and incubated at 37°C for 24 hours. Bacterial growth $\geq 10^5$ CFU/mL was considered significant. A clinical microbiologist evaluated the plates and categorized them according to the Gram stain or as yeast. The bacterial identification and susceptibility tests were performed with the Phoenix automated system (NJ, USA).

We created 5 groups: *E. coli*, *Klebsiella*, *Enterococcus*, Fungi, and Others (including *Acinetobacter*, *Citrobacter*, *Enterobacter*, *Proteus*, *Pseudomonas*, *Serratia*, *Staphylococcus*, and *Streptococcus* species) in terms of the isolated pathogen from the urine culture. Risk factors such as the presence of a urethral catheter, hospitalization status, admission to the intensive care unit, having 3 or more comorbidities (hypertension, diabetes mellitus, benign prostate hyperplasia, having any cancer, chronic kidney disease, chronic obstructive pulmonary disease, ischemic heart disease, cerebrovascular event, congestive heart disease, atrial fibrillation, Alzheimer disease, Parkinson disease, anemia, dementia, urethral stricture), and the exitus status was also recorded. For calculation of the estimated survival, we accepted the last positive urine culture date as the starting of the follow-up and the last pathogen in the urine culture was the causative pathogen. All patients received an appropriate antibiotic treatment according to the antibiotic susceptibility test.

Statistical analysis

Distributions were summarized using frequencies. ANOVA tests were used to analyze the association between continuous variables and the mean±standard deviation of the variables was presented. Kaplan-Meier survival analyses were performed to calculate the estimated survival time and the log-rank test was used to compare the survival differences between groups in terms of the causative pathogen. Univariate Cox regression analysis was performed to obtain the effect of pathogen strain and possible confounding factors (department, catheterization status, comorbidities) on overall survival. Any risk factor with a statistically significant impact on overall survival was included in the final multivariate Cox regression analysis to calculate the effect on survival. Any p-value <0.05 was considered statistically significant. Data analysis was performed using SPSS version 21.0 (IBM, Armonk, NY).

This study was conducted following the principles of the Declaration of Helsinki and approved by the University of Health Sciences, Prof. Dr. Cemil Tascioglu City Hospital Ethical Committee (Approval date: 03/Jan/2022, Approval Number: E-48670771-514.9).

RESULTS

A total of 1133 men over 80 years old meeting our inclusion criteria were included in the study. The mean age of the patients was 85.8±4.3 years (range, 80–102). The number of pathogens across the groups and the mean age of the patients in terms of the isolated pathogen are presented in **Table 1**. According to the statistical analysis, there was no difference between groups in terms of age (p=0.10). The most prevalent pathogen was *E. coli* with a 29.5% rate followed by *Enterococcus* with a 21% rate.

The institutionalized and ICU patient rate was 40.6% and 18.4%, respectively. *E. coli* and fungi were the common

Table 1. The percentage and the mean age of the patients according to the groups

Pathogen	N (%)	Mean age ±SD
E. coli	334 (29.5)	86.1±4.3
Klebsiella spp.	194 (17.1)	85.1±4.5
Enterococcus spp.	238 (21)	85.8±4.4
Fungi	224 (19.8)	86.1±4.2
Others	143 (12.6)	85.8±4.4
Total	1133 (100)	85.8±4.3

p=0.10 according to ANOVA test

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pathogens in the institutionalized and ICU patients with a rate of 25.3% and 46.9%, respectively (p<0.001). Of the 1133 patients, 26.9% had a urethral catheter. *E. coli* was the most prevalent microorganism with a rate of 25.2% in catheterized patients (p=0.03). On the other hand, the rate of patients with 3 or more comorbidities was 23.6%, and *Enterococcus* had the highest rate (28.1%) in this group of patients. The overall mortality rate was 73% and the common pathogens in this group were *E. coli*, fungi, and *Enterococcus* with a rate of 24.7%, 23.9%, and 21.4 %, respectively (p<0.001) **(Table 2)**.

The overall median survival time was 4 months in this elderly cohort according to the Kaplan-Meier survival analysis. The highest median survival time was considered in the *E. coli* group with 17.4 months and the lowest time was in the Fungi group with 0.4 months **(Table 3)**. The log rank test showed that the median survival times between groups were statistically significant (p<0.001) **(Fig. 1)**. In univariate Cox regression analysis, the pathogen group, catheterization status, and department of the patient had a statistically significant effect on survival. Therefore, these variables were included in the final multivariate Cox regression analysis. Due to the *E. coli* group and non-institutionalized patients having the highest median survival time in univariate analysis and lack of control group, we designated the *E. coli* group and non-institutionalized patients as the reference groups in multivariate analysis. According to the multivariate Cox regression analysis, being in an ICU unit carried the highest risk for mortality (HR:5.3, p<0.001, 95% CI 4.25–6.72). Regarding the urinary pathogen, being infected by fungi had the highest risk for mortality (HR:1.57, p<0.001, 95% CI 1.25–1.97). However, the *Klebsiella spp.*

Table 2. Distribution of patients by different clinical variables

		Overall N (%)	*E. coli* N (%)	*Klebsiella spp.* N (%)	*Enterococcus spp.* N (%)	Fungi N (%)	Others N (%)	*P*
Department	Non-institutionalized patients	465 (41)	202 (43.4)	93 (20)	88 (18.9)	17 (3.7)	65 (14)	**<0.0018***
	Institutionalized patients	459 (40.6)	116 (25.3)	85 (18.5)	102 (22.2)	109 (23.7)	47 (10.2)	
	ICU Patients	209 (18.4)	16 (7.7)	16 (7.7)	48 (23)	98 (46.9)	31 (14.8)	
Urethral catheter	Yes	305 (26.9)	77 (25.2)	44 (14.4)	66 (21.6)	76 (24.9)	42 (13.8)	**0.03***
	No	827 (73.1)	257 (31.1)	150 (18.1)	172 (20.8)	147 (17.8)	101 (12.2)	
Co-morbidities	≥3	267 (23.6)	58 (21.7)	41 (15.4)	75 (28.1)	54 (20.2)	39 (14.6)	**0.02***
	<3	886 (76.4)	276 (31.9)	153 (17.7)	163 (18.8)	170 (19.6)	104 (12)	
Mortality	Exitus	827 (73)	204 (24.7)	138 (16.7)	177 (21.4)	198 (23.9)	110 (13.3)	**<0.001***
	Alive	306 (27)	130 (42.5)	56 (18.3)	61 (19.9)	26 (8.5)	33 (10.8)	

* Pearson chi-square test

Table 3. Estimated survival time after an UTI with indicated pathogen group

Risk Factor	Median (months)	HR	*p*	95% CI
E. coli	17.4	*Ref*	-	-
Klebsiella spp.	8.9	1.2	0.08	0.98 – 1.51
Enterococcus spp.	5.7	1.16	0.18	0.94 – 1.43
Fungi	0.4	1.57	<0.001*	1.25 – 1.97
Others	3.6	1.42	<0.004*	1.11 – 1.81
Non-institutionalized patients	24	*Ref*	-	-
Institutionalized patients	1.2	2.4	<0.001*	1.99 – 2.79
ICU patients	0.2	5.3	<0.001*	4.25 – 6.72
Catheterized	1.4	1.22	0.011*	1.05 – 1.43
Overall	4			

* Cox Regression analysis; HR: hazard ratio; CI: confidence interval; Ref: *E. coli* group and non-institutionalized patients group were designated as reference group.

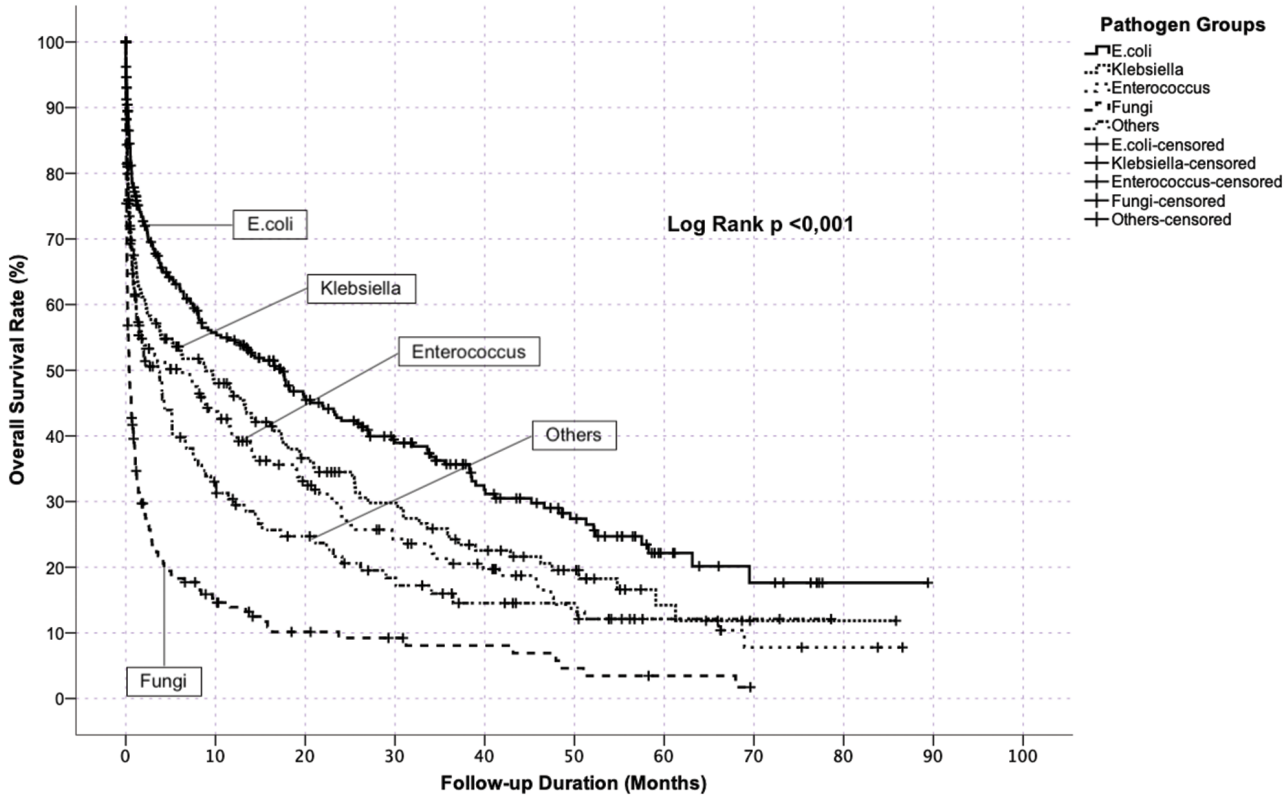

Figure 1. The overall survival rate of patients according to the pathogen group.

and *Enterococcus spp*. groups did not show a statistically significant difference despite the elevated risk for mortality compared with the *E. coli* group **(Table 3)**.

DISCUSSION

This study, including a large cohort of male patients aged ≥80 years and over, has shown that isolated pathogens from urine culture have an effect on the overall mortality in this cohort. The common pathogen in the cohort was *E. coli*; moreover, the overall survival time was better in patients infected with *E. coli*. On the other hand, the worst-case scenario for these patients was a fungal infection with an almost 1.57-fold increase in overall mortality risk. The median survival time after a fungal infection in male patients aged ≥80 years were calculated at 0.4 months.

The aging population and related issues are growing across the world. As a result, the United Nations (UN) declared the ten years between 2021 and 2030 as the United Nations Decade of Healthy Ageing.[6] According to a UN report, the number of people aged ≥80 increased almost 3-fold between 1990 and 2019, from 54 million to 143 million, globally. The calculated projections also proved the increase for 2050 that the ≥80-year-old population will rise to 426 million.[9] One of the key areas for the action indicated by the UN report is to improve evidence of clinical data interested in the elder population.[10] With the motivation of the United Nations Decade of Healthy Ageing plan, we retrospectively evaluated the urine cultures of male patients ≥80 years old which is a growing problem for urological service providers. Our results highlighted the fact that the different pathogens might affect the overall survival of aging males.

In elderly patients, altered physiology in the urinary tract, immobility, use of urinary catheters, hospitalization, and age-related deficiencies are responsible for urinary bacterial outgrowth and can lead to bacteremia, hospitalization, urosepsis, and even death.[7,11] It has been shown that the male sex is an independent risk factor associated with mortality in older patients with UTIs.[12] Also, in men without urinary catheters, the UTI is a rare condition amongst men younger than 60 years. However, the incidence increases considerably in men over 60 years old.[13,14] According to literature, the incidence of UTI in men younger than 55 years is 0.9 to 2.4 cases per 1000 men, which increases to 7.7 cases per 1000 men when the patient's age is 85 years or above.[15,16] In older men, the common cause of bacteremia is UTI; however, it is rarely responsible for the death.[17] Our initial hypothesis was that the pathogens causing a UTI in male patients aged ≥80 years would affect the survival time of the patients due to frailty. The mean age of our cohort was 85.8 years and there was no statistical difference between groups in terms of age. The commonly isolated pathogen was *E. coli* as usual. However, the estimated survival was better in the *E. coli* group with a median of 17.4 months than in the other groups. Our results were unable to suggest a cause-and-effect connection between

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the variables.

The catheterized patients rate was 26.9% at the time of collecting the urine for a culture test. In the presence of a urinary catheter, despite *E. coli* being the common pathogen that was isolated, the second common pathogen was fungi, with 24.9% of all catheterized patients. This rate was calculated at 3.7% in community-acquired urinary tract infection patients without catheterization. Also, ICU patients had the highest fungal infection rate. Fungal infections can easily be lethal, especially in older patients. Older patients with a urinary catheter have an increased mortality risk according to Gong et al.[18] In our cohort, the fungal infection group had the lowest estimated survival time, and had a 1.57-fold increased mortality risk compared to the *E. coli* infected patients. All other infection groups had worse survival outcomes compared to the *E. coli* group.

In elderly patients, comorbidities should be considered in the management of infections.[7] In this study group, 23.6% of the patients had at least 3 or more comorbidities. Interestingly, the *Enterococcus* group had the highest proportion of pathogens in patients with 3 or more comorbidities. The distribution of the pathogens in different clinical variables is shown in **Table 2**.

There are several limitations to our study. The retrospective design without a control group is limiting the interpretation of the results. Also, some patients at this age could be transferred to ICU several times during the hospitalization, but we assigned them according to the urine sampling time. The grouping of the pathogens was decided with the frequency of the pathogens with the consideration of microbiology taxonomy. However, our grouping is not a universal system. There could be an interference in the survival time for patients registered in 2020 due to the coronavirus pandemics. Since the follow-up time was accepted as the duration after the last UTI to death or the last registry at our hospital, our results were consistent to offer perspective.

CONCLUSIONS

There is limited data in the literature about the aging male population and the effect of UTIs on several outcomes such as cost or survival. In this study, we presented our results about the effect of isolated pathogens from urine culture on survival in a large cohort with a broad timespan. In the face of the fact that society is aging rapidly, further studies are needed to investigate UTIs in the senior population.

Author contributions

Study concept and design: C.B.; data acquisition: C.B., A.T.A., V.S., A.B., and Ç.A.; data analysis: C.B., Ç.A., and A.Ö.; drafting of manuscript: C.B. and E.C.P.; critical revision of the manuscript: Ç.A., E.C.P., and A.Ö.

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Competing Interests

The authors have declared that no competing interests exist.

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Влияние инфекции мочевыводящих путей на общую смертность мужчин пожилого возраста

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Резюме

Введение: Инфекции мочевыводящих путей являются наиболее распространёнными бактериальными инфекциями у пожилых людей. Это исследование направлено на определение влияния выделенного возбудителя из мочи на расчётное время выживания пожилых пациентов мужского пола.

Материалы и методы: Мы провели ретроспективное поперечное исследование, чтобы оценить пациентов мужского пола с патогенным ростом в их посевах мочи. Мы включили в исследование только пациентов мужского пола в возрасте 80 лет и старше с положительными посевами мочи на патогенный рост. Образцы мочи собирали либо из первой чистой мочи средней порции, либо из мочевых катетеров. Бактериальный рост ≥105 колониеобразующих единиц/ mL (CFU/mL) в культуре считался значительным. Для сравнения времени выживания было создано пять групп в соответствии с возбудителями, идентифицированными в посевах мочи.

Результаты: С февраля 2014 г. по декабрь 2020 г. 1133 пациента соответствовали критериям исследования. Наиболее частым возбудителем была *Escherichia coli* с частотой 29.5 %. Медиана общей продолжительности жизни составила 4 месяца. Самая длинная и самая короткая медиана общего времени выживания для группы *E. coli* и группы грибковых инфекций составила 17.4 месяца и 0.4 месяца соответственно (p<0.001). Хотя пребывание в отделении интенсивной терапии является наиболее важным фактором риска смертности в этой пожилой когорте, статистический анализ показал, что инфицирование грибковыми инфекциями сопряжено с 1.57-кратным увеличением риска смертности по сравнению с инфекцией *E. coli* (p<0.001).

Заключение: Старение населения требует оценки заболеваний, часто встречающихся в пожилом возрасте. Наше исследование показало, что возбудитель инфекции мочевыводящих путей может влиять на общую продолжительность жизни пожилых людей.

Ключевые слова

пожилой возраст, инфекции мочевыводящих путей, посев мочи, выживаемость