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Evaluation of clinical outcomes and risk factors associated with mortality in patients with Stenotrophomonas maltophilia bloodstream infection: a multicenter study

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Abstract

Background *Stenotrophomonas maltophilia*, a pathogen that colonizes medical equipment and causes nosocomial infections due to its ability to form biofilms, has high mortality rates. This study investigated the risk factors related to mortality in patients who were diagnosed with *S. maltophilia* bacteremia.

Methods It is a multi-center, retrospective ad observational cohort study. The demographic characteristics, clinical findings, microbiological data, and risk factors for patients were obtained from the medical records of patients at ten different hospitals between January 1, 2018, and June 30, 2023.

Results The study included a total of 321 patients. The observed thirty-day mortality rate was 46.1%. A central venous catheter (CVC) was present in 276 patients (86%), and in 66 of these patients (23.9%) the CVC was removed. While only 18 patients (5.6%) received appropriate empirical antibiotics, 242 (75.4%) patients received appropriate antibiotics according to antimicrobial susceptibility test (AST) results and treatment revisions. Multivariate analysis revealed that advanced age (hazard ratio [HR] = 1.02; 95% confidence interval [CI]: 1.00- 1.03) was associated with increased mortality, whereas appropriate antibiotic treatment (HR = 0.35; 95% CI: 0.23-0.52) and removal of central venous catheters (HR = 0.31; 95% CI: 0.16-0.60) were significantly related to reduced mortality.

Conclusions *S. maltophilia* is a significant pathogen, and to reduce its high mortality rate, removal of the CVC and switching to appropriate antibiotics should be performed as soon as possible.

Keywords Appropriate antibiotic, Central venous catheter, Mortality, Risk factors, *Stenotrophomonas maltophilia*

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Introduction

Stenotrophomonas maltophilia is a non-fermentative multidrug-resistant Gram-negative bacillus. The bacterium in question is known to thrive in moist environments and is not typically regarded as a component of the human microbiota [1, 2]. This microorganism, which is capable of biofilm formation, colonizes medical equipment in hospital settings and causes opportunistic nosocomial infections in certain patient groups, leading to high morbidity and mortality [3, 4]. Immunosuppression, malignancy, chronic respiratory disease, broad- spectrum antibiotic exposure, prolonged hospital stay, and intensive care unit (ICU) admission are the main risk factors in these patient groups [4–6]. Trimethoprim-sulfamethoxazole (TMP-SMX), levofloxacin, minocycline, tigecycline, and cefiderocol have been reported as options for the therapy of *S. maltophilia* infections [7–11]. The mortality rate of infections caused by *S. maltophilia* varies between 29.6% and 65.1% [6, 10, 12–14]. Intensive care unit admission, septic shock, mechanical ventilation status, central venous catheter use, neutropenia, chronic kidney disease, malignancy and inappropriate antibiotic use are among the factors associated with mortality [12]. Most studies investigating risk factors associated with mortality in *S. maltophilia* bloodstream infections have been single-center studies or have had small sample sizes [1, 6, 14, 15]. This multicenter study aimed to investigate mortality risk factors in *S. maltophilia* bacteremia patients.

Materials and methods

Data collection

This retrospective multicenter investigation included patients aged 18 years and over with *S. maltophilia* growth in blood cultures, collected from ten different hospitals (nine tertiary hospitals and one secondary hospital) in Türkiye between January 1, 2018, and June 30, 2023. These ten hospitals included three hospitals with 500–1000 beds, six hospitals with 1000–1500 beds and one hospital with 2500–3000 beds. During the study period, no outbreak of *S. maltophilia* was reported in any center. Patients who did not have any signs of systemic inflammatory response syndrome (SIRS) at the time of blood culture collection, and who did not have a control blood culture, were excluded from the study. In cases where the same patient had multiple *S. maltophilia* cultures, only the first infectious episode has been taken into account. Basic demographic data, comorbidities, specific risk factors identified, certain laboratory parameters at the date of blood culture, antibiotic treatments administered, dates of hospitalization, discharge or death, and *S. maltophilia* antimicrobial susceptibility test (AST) results were recorded. The BACT/ALERT® automated blood culture system (bioMérieux, USA) was utilized to process the blood samples. The VITEK® 2 Compact system (bioMérieux) was used for identification and susceptibility testing. AST results for *S. maltophilia* were determined at all centers on the basis of the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards.

Definitions

S. maltophilia bloodstream infection were determined in patients with at least one positive blood culture accompanied by clinical signs of SIRS and isolation of the pathogen in at least two sequential blood cultures taken without initiation of appropriate antibiotic treatment, even in the absence of signs of SIRS. Colonisation/contamination (C/C) was defined as patients who had no signs of SIRS at the time of blood culture collection and no growth in control blood cultures despite not receiving active antibacterial therapy against *S. maltophilia*. The onset of bacteremia was considered the date at which a positive blood culture was obtained. The source of bacteremia was determined clinically on the basis of the presence of an active site of infection, which was determined by reviewing medical records and isolating *S. maltophilia* from other clinical samples concurrent with the bacteremic episode. The removal of the central venous catheter (CVC) was characterized as an action undertaken within five days of the date of a positive blood culture. Polymicrobial bacteremia was defined as bacteremia caused by other pathogens detected 24 h before or after *S. maltophilia*. Hospital-acquired infection was defined as acquired after the 48th hour of hospital admission. Healthcare-associated infection was defined as an infection within 48 h of admission if the patient fulfilled any of the following criteria: (1) Attended a haemodialysis clinic or received intravenous therapy or chemotherapy in a healthcare facility or at home within 30 days prior to infection. (2) Resided in a nursing home or long-term care facility. Community-acquired infection was defined as infections occurred before the 48th hour of hospital admission in patients who did not fulfill the criteria for healthcare-associated infections. Neutropenia was defined as absolute neutrophil count < 500/mm3.

Appropriate antibiotic treatment was defined as the use of at least one of the antibiotics TMP-SMX and levofloxacin with documented in vitro susceptibility to the *S. maltophilia* pathogen. Sequential Organ Failure Assessment (SOFA), Acute Physiology and Chronic Health Evaluation II (APACHE II), and Charlson comorbidity index (CCI) scores were obtained by examining patient data in medical records. Septic shock was defined on the basis of the Sepsis-3 criteria [16]. Mortality was determined as

death from any cause within 30 days following the onset of bacteremia.

Statistical analysis

R version 4.3.2 (R Core Team, 2024) was utilized for the analyses. The study divided patients into two groups: survival and non-survival, and compared their demographic and clinical data. Numeric variables are expressed as means (standard deviation, SD) or medians (interquartile ranges, IQRs), and categorical variables by frequencies and proportions. The t-test was used for comparisons of numerical variables, whereas the chi-square test and Fisher's exact test were used for comparisons of categorical variables. Multivariate analyses were used to examine the effects of various factors on 30-day mortality. Multivariate Cox regression models were used for variables associated with survival. Kaplan Meier survival curves were drawn. A statistical significance level of $P<0.05$ was considered.

Results

Demographic and general information

During the study period, 424 patients with *S. maltophilia* growth in blood cultures were identified. Of these, 69 were excluded from the study according to the exclusion criteria. In 34 of the cases, the isolated pathogen was determined to be C/C. Clinical characteristics and demographic data of 321 patients with *S. maltophilia* bloodstream infection are given in Table 1. The patients had a mean age of 64.6 ± 16.7 years, and 62.3% (200/321) were male. The average CCI score was 4.0 ± 2.9, the APACHE II score was 21.9 ± 10.5, and the SOFA score was 7.7 ± 3.8. The median hospital stay duration until the onset of bacteremia was 16 (5–40) days. Bacteremia was hospital-acquired in 268 patients (83.5%), community-acquired in 34 patients (10.6%), and healthcare-associated in 19 patients (5.9%). Central venous catheters (CVC) were present in 276 patients (86%), and in 66 of these patients (23.9%), the CVC was removed. Eighty-two patients (25.6%) had septic shock at the onset of bacteremia. During their hospital stay, 269 patients (83.8%) required ICU care at some point, 195 patients (60.9%) required mechanical ventilation, and 156 patients (48.6%) required vasopressor support (Table 1).

A total of 292 patients (91%) used at least one empirical antibiotic, with carbapenems being the most frequently used antibiotic ($n=161$, 55.1%). While 5.6% (18/321) of patients received appropriate empirical antibiotic treatment, this proportion increased to 75.4% (242/321) following revisions of therapy based on AST results. The antibiotics used according to the AST results included levofloxacin (111 patients, 45.9%), TMP-SMX (100 patients, 41.3%) and a combination of levofloxacin and TMP-SMX (31 patients, 12.8%) (Table 2).

Microbiological data

Polymicrobial bacteremia was present in 61 patients (19%). The most common pathogens in these polymicrobial bacteremias were *Enterococcus spp.* (21.3%), methicillin-resistant coagulase-negative *Staphylococcus* (19.7%), *Pseudomonas aeruginosa* (14.8%), *Acinetobacter baumannii* (13.1%), *Klebsiella spp.* (11.5%), and *Escherichia coli* (6.6%).

In the included *S. maltophilia* isolates, resistance to levofloxacin was 3.1% (9/290) and resistance to TMP-SMX was 8.8% (28/319). A comparison of the resistance rates between the 2018–2020 and 2021–2023 periods revealed notable differences in the resistance rates of levofloxacin and TMP-SMX. The resistance rates for levofloxacin and TMP-SMX were 7.8% and 1.7%, respectively, during the first three years of the study. In contrast, the rates for these antibiotics during the subsequent three years were 2.1% and 10.4%, respectively. Notably, the increased resistance rates of TMP-SMX antibiotics during the second period were statistically significant ($p=0.033$).

Risk factors associated mortality

All-cause mortality at 30-days was 46.1% (148/321). The average age of the nonsurvivor group was higher than that of the survivor group ($p=0.002$). There were no significant differences in the CCI, SOFA, and APACHE II scores between the two groups. When the underlying diseases were analyzed, only the presence of metastatic solid tumor was higher in the nonsurvivor group ($p=0.038$). Carbapenem exposure in the last month was higher in the nonsurvivor group ($p<0.001$). The presence of CVC was more common in the nonsurvivor group ($p=0.012$). During the hospital stay, cases of septic shock were recorded in the non-survivor group ($p<0.001$). Patients in the nonsurvivor group required more ICU ($p<0.001$) and mechanical ventilation ($p<0.001$). The rates of CVC removal ($p<0.001$) and appropriate antibiotic treatment ($p<0.001$) were significantly higher in the survivor group (Tables 1 and 2).

The Kaplan-Meier estimation curves for the groups that underwent CVC removal and received appropriate antibiotic treatment are presented (Figs. 1 and 2).

A division of patients receiving appropriate antibiotic treatment into two groups, namely monotherapy (regimen containing TMP/SMX or levofloxacin) and combination therapy (regimen containing TMP/SMX + levofloxacin), revealed a mortality rate of 34.6% in the monotherapy group and 38.7% in the combination therapy group. ($p=0.654$). A comparison of patients receiving a levofloxacin and TMP-SMX containing

Table 1 Demographic and clinical characteristics Associated with 30-day mortality

Factors	Total[1], $n=321$	Survivors[1], $n=173$	Non-survivors[1], $n=148$	P [2]
Age, years	64.6 ± 16.7	61.9 ± 16	67.8 ± 16.9	**0.002**
Gender, Male	200 (62.3%)	105 (60.7%)	95 (64.2%)	0.519
Underlying disease				
Coronary artery disease	115 (35.8%)	63 (36.4%)	52 (35.1%)	0.811
Diabetes mellitus	106 (33.1%)	61 (35.5%)	45 (30.4%)	0.338
Cronic kidney disease	74 (23.1%)	44 (25.4%)	30 (20.3%)	0.274
Cerebrovascular disease	65 (20.3%)	37 (21.4%)	28 (18.9%)	0.583
Chronic lung disease	67 (20.9%)	34 (19.7%)	33 (22.3%)	0.561
Malignancy	91 (28.4%)	44 (25.4%)	47 (31.8%)	0.21
Hematologic malignancy	18 (5.6%)	10 (5.8%)	8 (5.4%)	0.884
Metastatic solid tumor	39 (12.2%)	15 (8.7%)	24 (16.2%)	**0.039**
Charlson Comorbidity Index	4 ± 2.9	3.8 ± 2.6	4.3 ± 3.2	0.14
Source of bacteremia				**0.010**
Central venous catheter-related	88 (27.4%)	57 (33%)	31 (21%)	
Respiratory tract	50 (15.6%)	19 (11%)	31 (21%)	
Urinary tract	4 (1.3%)	1 (0.6%)	3 (2%)	
Intra-abdominal	12 (3.7%)	6 (3.5%)	6 (4.1%)	
Skin and soft tissue	4 (1.3%)	4 (2.3%)	0 (0%)	
Primary/Unknown	163 (50.8%)	86 (49.7%)	77 (52%)	
Acquisition of bacteremia				**0.017**
Hospital-acquired	268 (83.5%)	137 (79.2%)	131 (88.5%)	
Community acquired	34 (10.6%)	20 (11.6%)	14 (9.5%)	
Healthcare-associated	19 (5.9%)	16 (9.3%)	3 (2%)	
Polymicrobial bacteremia	61 (19%)	37 (21.4%)	24 (16.2%)	0.239
SOFA score	7.7 ± 3.8	7.3 ± 3.1	8.1 ± 4.5	0.216
APACHE II score	21.9 ± 10.5	21.1 ± 9	22.6 ± 11.8	0.281
Septic shock	82 (25.6%)	27 (15.6%)	55 (37.2%)	**< 0.001**
ICU admission	269 (83.8%)	129 (74.6%)	140 (94.6%)	**< 0.001**
Duration of hospitalization	38 (22–73)	47 (28–107)	31 (17–49.5)	**< 0.001**
Length of hospital stay until bacteremia onset	16 (5–40)	13 (3–39)	20 (9–41.3)	0.651
CVC	276 (86%)	141 (81.5%)	135 (91.2%)	**0.012**
Mechanical ventilation	195 (60.9%)	83 (48.3%)	112 (75.7%)	**< 0.001**
Urinary catheter	276 (86%)	136 (78.6%)	140 (94.6%)	**< 0.001**
Vasopressor administration	156 (48.6%)	56 (32.4%)	100 (67.6%)	**< 0.001**
Surgery (within 30 days)	50 (15.6%)	27 (15.6%)	23 (15.5%)	> 0.9
Prior chemotherapy	45 (14%)	27 (15.6%)	18 (12.2%)	0.376
Total parenteral nutrition	136 (42.4%)	61 (35.3%)	75 (50.7%)	**0.005**
Glucocorticoid treatment	104 (32.4%)	53 (30.6%)	51 (34.5%)	0.466
CVC removal	66 (66/276, 23.9%)	51 (51/141, 36.2%)	15 (15/135, 11.1%)	**< 0.001**
Carbapenem exposure (within 30 days)	153 (47.7%)	65 (37.6%)	88 (59.5%)	**< 0.001**
TMP-SMX resistance	28 (28/319, 8.8%)	14 (14/173, 8.1%)	14 (14/146, 9.6%)	0.638
Levofloxacin resistance	9 (9/290, 3.1%)	2 (2/155, 1.3%)	7 (7/135, 5.2%)	0.087

CVC central venous catheter, *SD* standard deviation, *IQR* interquartile range, *APACHE II score* Acute Physiology and Chronic Health Evaluation II score, *ICU* intensive care unit, *SOFA* Sequential Organ Failure Assessment

[1] Mean ± SD; Median (IQRs;25–75%) or n (%)

[2] Welch Two Sample t-test or Pearson's Chi-squared test; Fisher's exact test

Table 2 Treatment and laboratory findings associated with 30-day mortality

Factors	Total[1], *n* = 321	Survivors[1], *n* = 173	Non-survivors[1], *n* = 148	*P*[2]
Empirical antibiotic treatment	292 (91%)	158 (91.3%)	134 (90.5%)	0.806
Appropriate empirical antibiotic treatment	18 (5.6%)	9 (5.2%)	9 (6.1%)	0.733
Appropriate antibiotic treatment	242 (75.4%)	157 (90.8%)	85 (57.4%)	**< 0.001**
Laboratory finding				
Hemoglobin, g/dL	10 ± 2.3	10.2 ± 2.3	9.7 ± 2.3	**0.046**
Platelet count, 10^9/L	200.4 ± 133.3	213.8 ± 126.2	184.6 ± 140.1	0.053
White blood cell count, 10^9/L	13.7 ± 16.9	13.4 ± 19.4	14.1 ± 13.3	0.727
Neutrophil count, 10^9/L	10.4 ± 8.6	9.1 ± 5.7	11.9 ± 10.8	**0.006**
Neutropenia	17 (5.3%)	8 (4.6%)	9 (6.1%)	0.561
Lymphocyte count, 10^9/L	1.4 ± 1.3	1.6 ± 1.3	1.2 ± 1.3	**0.017**
Albumin, g/dL	2.8 ± 0.7	3.1 ± 0.7	2.5 ± 0.7	**< 0.001**
Hypoalbuminemia	93 (93/314, 29.6%)	25 (25/170, 14.7%)	68 (68/144, 47.2%)	**< 0.001**
C-reactive protein, mg/L	125 ± 87.7	111.8 ± 75.7	140.8 ± 98	**0.004**
Procalcitonin, µg/L	10.7 ± 21.2	11.5 ± 23	12.3 ± 37.2	0.50

Neutropenia: absolute neutrophil count < 500/mm^3, hypoalbuminemia: albumin < 2,5 g/dL

SD standard deviation, *IQR* interquartile range

[1] Mean ± SD; Median (IQRs;25–75%) or n (%)

[2] Welch Two Sample t-test or Pearson's Chi-squared test; Fisher's exact test

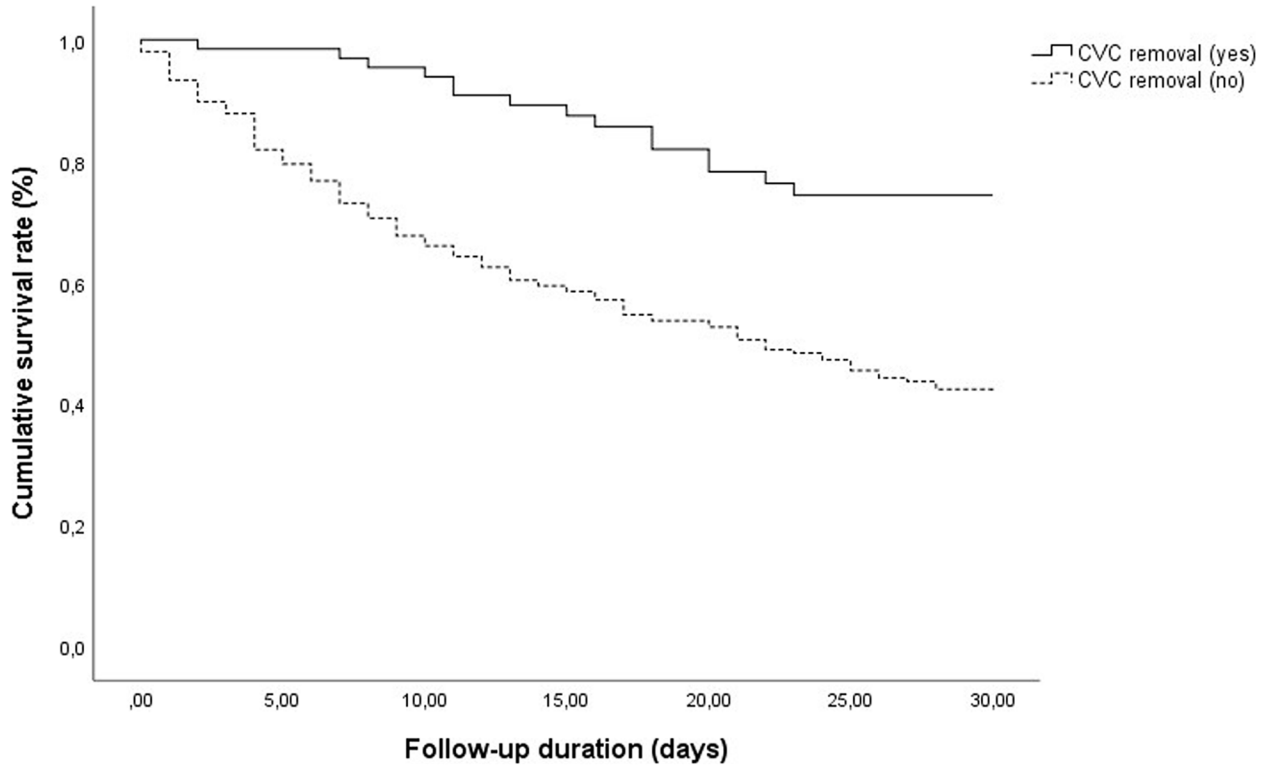

Fig. 1 Kaplan-Meier survival curves for 30-day mortality according to central venous catheter removal in patients with *S. maltophilia* bacteremia

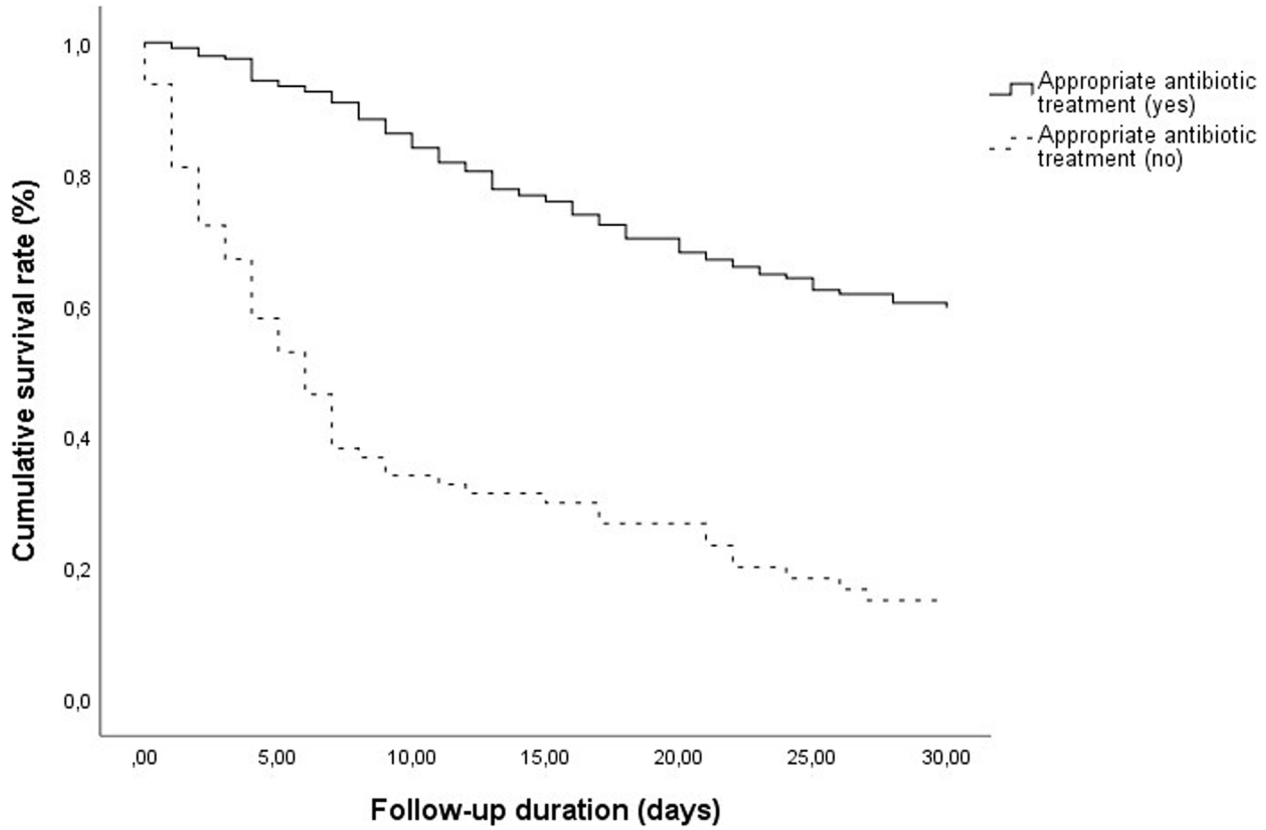

Fig. 2 Kaplan-Meier survival curves for 30-day mortality according to appropriate antibiotic treatment in patients with *S. maltophilia* bacteremia

Table 3 Multivariate Cox regression analysis of factors associated with 30-day mortality in patients with *S. maltophilia* bacteremia

Factor	HR[1]	95% CI[1]	*p*
Age	1.02	1.00, 1.03	**0.02**
CVC	1.24	0.60, 2.56	0.558
CVC removal	0.31	0.16, 0.60	**0.001**
APACHE II score	1.00	0.98, 1.02	> 0.9
Septic shock	1.28	0.84, 1.95	0.246
Charlson Comorbidity Index	1.00	0.91, 1.10	> 0.9
Mechanical ventilation	0.87	0.52, 1.50	0.606
Metastatic solid tumor	2.17	0.90, 5.22	0.084
Total parenteral nutrition	1.39	0.89, 2.17	0.153
Appropriate antibiotic treatment	0.35	0.23, 0.52	**< 0.001**

[1] *HR* Hazard Ratio, *CI* Confidence Interval, *CVC* central venous catheter, *APACHE II score* Acute Physiology and Chronic Health Evaluation II score

regimens revealed that 36.9% of those receiving levofloxacin and 32% of those receiving TMP-SMX died ($p = 0.452$).

The multivariable Cox regression model is presented in Table 3. Variables that could be associated with a fatal outcome were included in the model. When other variables were controlled for, advanced age (hazard ratio [HR] = 1.02; 95% confidence interval [CI]: 1.00– 1.03; $p = 0.02$) was related to an increased risk of death, whereas CVC removal (HR = 0.31; 95% CI: 0.16–0.60; $p = 0.001$) and appropriate antibiotic treatment (HR = 0.35; 95% CI: 0.23–0.52; $p < 0.001$) were correlated with a decreased risk of death.

Discussion

Patients with *S. maltophilia* bacteremia had a 30-day mortality rate of 46.1%. The study revealed that advanced age was an independent risk factor associated with high mortality, whereas CVC removal and appropriate antibiotic treatment were associated with low mortality. The mortality rate ranges from 29.6% to 65.1% in *S. maltophilia* infections [6, 10, 12–14]. Given the high mortality rates, it is necessary to assess the risk factors that affect mortality.

One of the most important virulence factors of *S. maltophilia* is the formation of biofilms. This biofilm allows *S. maltophilia* to adhere tightly to abiotic, inanimate surfaces such as catheters and ventilation tubes [3]. Therefore, the presence of a CVC and mechanical ventilation status are among the main risk factors for bacteremia.

Studies investigating *S. maltophilia* bacteremias have reported the presence of CVC (66.9–94.3%) and mechanical ventilation (23.9–85.7%) at varying rates [5, 15, 17]. In our study, the presence of CVC was observed at a rate of 86% and mechanical ventilation was observed at a rate of 60.9%. It is known that relapses occur in patients with *S. maltophilia*-related bacteremia where the CVC is not removed [18]. Studies have shown that the removal of CVC has a protective effect on mortality [5, 15, 19]. Our study also revealed that early removal of CVC was a factor in reducing mortality. According to the data, CVC removal should be considered an important procedure in the treatment for patients with *S. maltophilia* bacteremia.

Studies have reported rates of polymicrobial bacteremia ranging from 16.9 to 42.9% [1, 13, 14]. A recent meta-analysis reported as 35.6% [12]. In our study, the rate of polymicrobial bacteremia was 19%. The adhesive property of the biofilm structure formed by *S. maltophilia* also causes other bacteria to adhere to this area, leading to polymicrobial infections of varying frequency [20]. The coexistence of other bacteria in *S. maltophilia* infections should be kept in mind.

In our study, an analysis of the underlying diseases revealed that the presence of metastatic solid tumor was a risk factor for mortality. A recent meta-analysis indicated that hematologic malignancy and chronic kidney disease are associated with mortality [12]. Our study did not identify these diseases as risk factors. Additionally, the neutropenia was not found to be associated with mortality, which differs from the results of the meta-analysis [12]. The reason why neutropenia was not associated with mortality in our study may be due to the small number of patients with haematological malignancies and the small number of neutropenic patients. The presence of hypoalbuminemia was associated with increased mortality in our study, in a manner similar to that reported by Kim et al. [13].

An increased mortality rate was observed in patients exposed to carbapenems within the previous 30 days. A similar result was observed in the study conducted by Garazi et al. [21]. Patients with *S. maltophilia* bacteremia are typically individuals who have previously been hospitalized and who have other medical comorbidities. These patients are often susceptible to broad-spectrum antibiotics such as carbapenems. It is possible that mortality may be increased due to underlying medical conditions.

In our study, TMP-SMX and levofloxacin resistance rates for *S. maltophilia* isolates were 8.8% and 3.1%, respectively, according to AST results using the automated VITEK® 2 system. In a study, the VITEK® 2 categorical agreement for TMP-SMX and levofloxacin was 77.1% and 85.3%, respectively. The major error (false resistance) rate was 25.1% for TMP-SMX and 2.6% for levofloxacin [22]. The reason for the high TMP-SMX resistance in our study may be that the AST results were obtained using the VITEK® 2 system. Therefore, it should be considered that high resistance rates may be observed when using automated systems for *S. maltophilia* AST results.

Consistent with the literature, our multiple survival analysis revealed that appropriate antibiotic treatment was associated with low mortality [5, 15, 23]. In the guidelines "Treatment of Antimicrobial Resistant Gram-Negative Infections" published by Tama PD et al., it is recommended to prefer combination therapy to increase the probability of using at least one active drug in the empirical antimicrobial therapy of *S. maltophilia* infections [24]. A multicenter retrospective study investigating *S. maltophilia* infections revealed no significant difference in mortality between the use of levofloxacin and TMP-SMX, showing that either antibiotic can be chosen based on AST results [9]. In a recent meta-analysis, inappropriate treatment was reported to increase mortality, and no significant difference in mortality was observed between TMP-SMX and fluoroquinolones in antimicrobial treatment [12]. The findings of our study indicate no statistically significant difference in mortality rates between patients receiving monotherapy and those receiving combination therapy. Furthermore, no notable differences in mortality were observed when levofloxacin-based therapy was compared with TMP-SMX-based therapy. These data show that the use of at least one of the antibiotics TMP-SMX and levofloxacin in the empirical treatment of *S. maltophilia* infections is the most appropriate approach.

In the context of our study, we observed that the effect of resistant strains on mortality was not influenced by either TMP-SMX or levofloxacin resistance. This finding contrasts with the conclusions of the study conducted by Kim et al., who reported an increased mortality risk associated with quinolone-resistant strains [13].

Although it was not one of the principal outcome variables of our study, we deemed it pertinent to highlight this subanalysis, given the increasing concerns surrounding antibiotic resistance rates. A comparison of antibiotic resistance rates between the initial three-year period and the subsequent three-year period revealed that the TMP-SMX resistance rates were higher during the latter period. Furthermore, the intrinsic resistance of *S. maltophilia* to numerous antibiotics presents a significant challenge for effective treatment. The increase in resistance rates to TMP-SMX, a first-line antibiotic, over time is of particular concern.

A recent multicenter report showed that *S. maltophilia* was the most commonly occurring cause of carbapenem-resistant Gram-negative bacteremia [25]. Our

study observed that 90.7% of patients received empirical antimicrobial therapy, more than half of which were carbapenem group antibiotics. Empirical therapy appropriateness was found in only 18 patients (5.6%). These findings suggest that *S. maltophilia*, owing to its intrinsic resistance to broad-spectrum agents, could be overlooked in initial antimicrobial therapies [20]. It is crucial to be aware of risk factors for *S. maltophilia* infection when choosing empirical treatments. Contrary to studies suggesting that appropriate empirical antibiotics reduce mortality in bloodstream infections [26, 27], this factor was not related to mortality in our investigation. One reason could be the small number of patients receiving empirical antibiotics included in our study, preventing statistically significant results regarding mortality.

The strongest aspect of our investigation is the high number of patients included and the fact that the data were collected from different centers. To our knowledge, this is the multicenter report with the highest number of patients in the literature examining mortality rates and factors related to death in patients with bloodstream infection caused by *S. maltophilia*. We believe that this study will contribute to reducing mortality rates by eliminating these risk factors and will guide the selection of appropriate empirical antimicrobial treatments by revealing the resistance pattern of *S. maltophilia*.

The retrospective cohort nature of our study design is a limitation, complicating the distinction between true infections and C/C of *S. maltophilia* isolates. Another limitation of the study was that AST results of *S. maltophilia* isolates were taken by automated systems. Studies using gold standard methods such as broth microdilution are needed to more accurately presentation the resistance rates. Additionally, some healthcare quality factors that could affect mortality were not measurable. Reliable determination of these factors requires multicenter, prospective controlled studies.

Conclusions

In conclusion, the observed increases in TMP-SMX resistance rates over time are cause for concern and highlight the need for a greater emphasis on antimicrobial stewardship. In our study, the presence of resistant strains did not affect mortality. We believe that the use of TMP-SMX and levofloxacin as monotherapy or combination therapy for the treatment of *S. maltophilia* bacteremia with in vitro susceptibility to TMP-SMX and levofloxacin does not affect mortality. However, this issue requires further clarification through the conduct of prospective studies.

Patients with *S. maltophilia* bacteremia have high mortality, and to reduce these rates, removal of the CVC and switching to appropriate antibiotics should be performed as soon as possible.

Abbreviations

CVC	Central venous catheter
AST	Antimicrobial susceptibility test
ICU	Intensive care unit
TMP-SMX	Trimethoprim-sulfamethoxazole
CCI	Charlson comorbidity index
C/C	Colonisation/contamination
SIRS	Systemic inflammatory response syndrome

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Clinical trial number

Not applicable.

Authors' contributions

Data collection was performed by all authors. Data analysis was performed by YG, MRT, AT. YG wrote the original draft of the manuscript. All authors contributed to the conception, design and writing of the study. All authors read and approved the final version of the manuscript.

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Data availability

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from Karatay University Faculty of Medicine, Non-interventional Clinical Trials Ethics Committee (approval date/number: 17.11.2023/2023/017). Since the study was retrospective and did not involve patient interaction, informed consent to participate was waived by the Karatay University Faculty of Medicine, Non-interventional Clinical Trials Ethics Committee. As part of the consent process, general consent was obtained for the use of medical records in research.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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