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Risk Factors and Outcome in Patients with Bacteraemia Secondary to Ventilator-Associated Pneumonia Due to *Acinetobacter baumannii*

Acinetobacter baumannii Etkeniyle Gelişen Ventilatör İlişkili Pnömoniye Sekonder Bakteremi Hastalarında Risk Faktörleri ve Sonuçları

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ABSTRACT

Introduction: *Acinetobacter baumannii is a multi-drug resistant (MDR), gram-negative, infectious nosocomial pathogen, commonly affecting critically ill patients admitted to intensive care units (ICU). Patients with ventilator-associated pneumonia (VAP) may contract A. baumannii bacteremia, which may significantly impair prognosis. This study evaluates the risk factors and outcomes in patients with bacteremia secondary to VAP.*

Materials and Methods: *Two hundred thirty one VAP and bacteremia attacks secondary to VAP due to A. baumannii, followed in intensive care units over a six-year period, were examined. Risk factors and outcomes were compared from patient records.*

Results: *The median age and gender distribution of the episodes were similar. In the bacteremia group, the ratio of peripheral venous catheterizations and total parenteral nutrition (TPN) use was significantly higher than in the non-bacteremia group (p= 0.001 vs. p< 0.001, respectively). The median APACHE-II score in the bacteremia group was significantly higher than in the non-bacteremia group (28 vs. 24, respectively, p< 0.001). However, median SOFA 1 (SOFA at ICU admission) and SOFA 2 (SOFA at diagnosis) scores did not differ from those in the non-bacteremia group (6 vs. 5, respectively, p= 0.173 and 9 vs. 9, respectively, p= 0.088). There was no significant difference observed in the distribution of the Charlson comorbidity index between the groups. The incidence of mortality was 2.8 times higher in the bacteremia group compared to the non-bacteremia group.*

Conclusion: *Total parenteral nutrition and venous catheterization are identified as risk factors for bacteremia in patients with VAP caused by A. baumannii, with a 2.4 and 2.2 fold increase, respectively. While SOFA 1 and SOFA 2 scores may not hold significance in the presence of bacteremia, the APACHE-II score alone may be significant. Additionally, prolonged and unsupervised use of proton pump inhibitors (PPI) in critically ill ICU patients may elevate the risk of bacteremia and associated mortalities in VAP patients.*

Key Words: *Acinetobacter baumannii; Proton pump inhibitor; Risk factors; Secondary bacteremia; Ventilator-associated pneumonia*

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ÖZ

Acinetobacter baumannii Etkeniyle Gelişen Ventilatör İlişkili Pnömoniye Sekonder Bakteremi Hastalarında Risk Faktörleri ve Sonuçları

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Giriş: *Acinetobacter baumannii, yoğun bakım ünitelerinde (YBÜ) yatan kritik hastalarda yaygın sorun oluşturan gram-negatif, çok ilaca dirençli (MDR) bir infektif nozokomiyal patojendir. Ventilatörle ilişkili pnömoni (VİP) hastalarında prognozu önemli ölçüde kötüleştirebilecek A. baumannii bakteremisi gelişebilir. Bu çalışmada VİP'e sekonder bakteremi hastalarında risk faktörleri ve sonuçlarını değerlendirmek amaçlanmıştır.*

Materyal ve Metod: *Yoğun bakım ünitelerinde altı yıllık bir sürede takip edilen A. baumannii etkenine bağlı 231 VİP ve VİP'e sekonder bakteremi atağı irdelendi. Hasta kayıtlarından risk faktörleri ve sonuçları karşılaştırıldı.*

Bulgular: *Atakların yaş ortanca düzeyi ve cinsiyet dağılımı benzerdi. Bakteremi grubunda periferik venöz kateter kullanım oranı ve total parenteral nütrisyon (TPN) kullanım oranı bakteremi olmayan gruptan anlamlı düzeyde yüksek bulundu (sırasıyla p= 0.001, p< 0.001). Bakteremi grubundaki APACHE-II skor ortanca değeri, bakteremi olmayan gruptan anlamlı düzeyde yüksek bulundu (sırasıyla 28 ve 24, p< 0.001). Ancak SOFA 1 (YBÜ kabul günündeki SOFA değeri) ve SOFA 2 (tanı tarihinde) ortanca değeri bakteremi olmayan gruptan farklı bulunmadı (sırasıyla 6 ve 5, p= 0.173) ve (sırasıyla 9 ve 9, p= 0.088). Charlson komorbidite indeksi dağılımına bakıldığında gruplar arasında anlamlı fark saptanmadı. Bakteremi grubunda ölüm gerçekleşme sıklığı ise bakteremi olmayan gruba göre 2.8 kat fazla bulundu.*

Sonuç: *A. baumannii ile VİP gelişen hastalarda, TPN ve venöz kateterizasyon bakteremi gelişmesi için risk faktörüdür (sırasıyla 2.4 ve 2.2 kat artış). Bakteremi varlığında SOFA 1 ve SOFA 2 anlamlı olmasa da sadece APACHE-II skoru anlamlı olabilir. Yoğun bakım ünitesinde kritik hastalarda uzun süre kontrolsüz PPİ kullanımı VİP hastalarında bakteremi riskini arttırabilmekte ve buna bağlı mortalite artabilmektedir.*

Anahtar Kelimeler: *Acinetobacter baumannii; Proton pompa inhibitörü; Risk faktörleri; Sekonder bakteremi, Ventilatör ilişkili pnömoni*

INTRODUCTION

Among other genomic types, *Acinetobacter baumannii* is the most common and most resistant, non-fermenting gram-negative microorganism that frequently affects critically-ill patients with ventilator-associated pneumonia (VAP), receiving treatment in intensive care units (ICUs). As an opportunistic pathogen, *A. baumannii* typically spreads rapidly, often leading to outbreaks. It exhibits resilience against harsh environmental conditions, enabling it to develop resistance to all conventional antimicrobials[1,2]. Despite significant advances in the diagnosis, treatment, and prevention of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) in ICU settings, *A. baumannii* remains the most common and fatal nosocomial infection. Previous studies have recommended cluster-based approaches to address this persistent challenge. Intensive care unit VAP rates vary across countries, hospitals, and ICUs, ranging between 2.5 and 40.0% in Türkiye and around the world[3-5].

Ventilator-associated pneumonia patients frequently acquire *Acinetobacter* bacteremia in ICUs, significantly impairing prognosis. The incidence of multi-drug resistant (MDR) *A. baumannii* bacteremia in intensive care patients is rising due to VAP caused by carbapenem-resistant *A. baumannii* strains[6].

This study aims to identify the prognostic outcomes and risk factors of bacteremia in *A. baumannii* VAP patients. This may not only help improve prognosis through early detection and appropriate empirical treatment but also aid in the development of measures for controlling infection.

MATERIALS and METHODS

Patient Population

This retrospective cohort study assessed patients treated in the adult, 29-bed, third-line intensive care units at our hospital over five years. Patients who did not meet the inclusion criteria were excluded, and the remainder were split into two groups: Group 1 included patients who recently acquired VAP, but not bacteremia, based on positive sputum-culture results for *A. baumannii* 48 hours after initiation of mechanical ventilation, and group 2 included patients who recently acquired VAP, and subsequently *A. baumannii* bacteremia within that timeframe, based on positive sputum-culture results for *A. baumannii* 48 hours after initiation of mechanical ventilation. The VAP secondary bacteremia group included patients who experienced an episode of *Acinetobacter* spp. bacteremia at any time after the initial 48 hours following diagnosis of VAP.

Microbiological Evaluation

Blood cultures were transferred to vials containing BD BACTEC TM Standard Aerobic Medium (Becton Dickinson, Sparks, MD, USA). BD PHOENIX M50 Medium (Becton Dickinson, Sparks, MD, USA) was used to identify and determine antibiotic susceptibility of microorganisms growing in vials that showed growth signs after incubating for an appropriate duration.

Definitions

Ventilator-associated pneumonia is defined as pneumonia that occurs within 48 hours after intubation in a patient undergoing invasive mechanical ventilation, provided that pneumonia was not present at the time of intubation[7,8]. Patients who received a diagnosis of VAP within four days after initiation of mechanical ventilation were defined as early-onset, and the others as late-onset. The CDC criteria were used for diagnosing VAP[9]. The severity of disease and multi-organ failure were evaluated using APACHE-II scores, calculated 24 hours after admission to intensive care, and SOFA scores calculated at diagnosis (date of pathogen growth in respiratory samples for group 1, and date of pathogen growth in blood samples for group 2)[9-11]. Mortality assessment was made during the hospital stay of the patients.

Data

The data evaluated included demographics, clinical characteristics, invasive procedures performed at ICU, number of days in hospital and ICU, and GCS and SOFA scores at ICU admission and APACHE-II at diagnosis, Charlson Comorbidity Index, and laboratory data. The data were retrieved from patients' files, records of infection control committee, and hospital data management system, and recorded on case assessment forms.

Statistics

The SPSS 17.0 package (Statistical Package for Social Sciences, Chicago, IL, 2008) was used for the analyses. All patient results were appropriately expressed as mean ± standard deviation (SD) or number (n) and percentage (%). The distribution of patients' data was evaluated using the Kolmogorov-Smirnov test. Data meeting the $p > 0.05$ threshold were classified as data with a parametric distribution, and those below it as data with a non-parametric distribution. The Student t-test was employed for continuous variables that followed a normal distribution, while the Mann-Whitney U test was utilized for outliers, in the comparisons between the two groups. Kruskal-Wallis was used for comparisons of continuous variables in more than two groups. The Bonferroni correction was applied to determine the differentiating group among multiple groups. Categorical variables were expressed as frequency (n) and percentage (%) and analyzed using Pearson Chi-square and Fisher's exact. The Wilcoxon signed-rank test was used for comparing repeated readings of hemogram, lactate dehydrogenase (LDH), albumin, C-reactive protein (CRP), and blood gas analysis results, taken at two different time points (at presentation and diagnosis). To examine the correlation of these values, Spearman's correlation test was applied since the values did not show a regular distribution.

Logistic regression analysis was performed to determine independent risk factors for bacteremia and mortality and variables with a significance

level below 0.10 in one-way analysis, and the results were shown with estimated relative risk (OR) and 95% confidence interval (95% CI). The statistical significance threshold was set to $p< 0.05$. Receiver operating characteristic (ROC) analysis was performed to calculate the area under the curve (AUC), cut-off values, sensitivity, specificity, and negative predictive value (NPV) and positive predictive value (PPD). ROC analysis was utilized to plot the graphics, and it was also employed to determine the SOFA score associated with mortality, APACHE-II score, Charlson comorbidity score, and the values for specific laboratory parameters for both mortality and bacteremia.

RESULTS

Finding

Clinical and laboratory data from 231 VAP episodes in 214 patients were analyzed. According to the 6-year data of our hospital, our VAP rates are between 10 and 25%. One hundred twenty-five episodes were evaluated in the VAP group (controls) and 106 episodes in the bacteremia group. All episodes represented late-onset (starting at least four days after intubation) VAP. The median age of a total of 231 episodes was 74 years (IQR= 19, 23-95 years); 63.2% (n= 146) of the subjects were male, and 36.8% (n= 85) were female. Forty point three percent (n= 146) of patients were followed up in intensive care, 28.6% (n= 66) in anesthesia intensive care, and 27.8% (n= 62) in surgical intensive care. Respiratory failure was the most common cause of admission to intensive care (50.7%, n= 117) (Table 1).

Although having a history of hospitalizations and admissions to intensive care in the presence of VAP without bacteremia was significantly common [n (%) 19 (15.2), 7 (6.6) p= 0.039 vs. 61 (48.8) 33 (31.1) p= 0.006, respectively], the number of days patients were hospitalized and remained in intensive care did not vary by bacteremia status (p= 0.152 vs. p= 0.078, respectively). The ratio of proton pump inhibitor use in non-bacteremia patients was significantly lower than in the bacteremia group (72.8% vs. 87.7%, respectively, p= 0.005). The ratio of

Table 1. Patient demographics and comparisons

	Bacteremia (n= 125)	Non-Bacteremia (n= 106)	p
Age (years)[a]	72 (20)	76 (16)	0.184
Gender, n (%)			0.101
Male	85 (68.0)	61 (57.5)	
Female	40 (32.0)	45 (42.5)	
ICU, n (%)			**0.044**
IICU	54 (43.2)	39 (36.8)	
AICU	39 (31.2)	27 (25.5)	
SICU	27 (21.6)	35 (33.0)	
CVS-ICU	4 (3.2)	5 (4.7)	
COR-ICU	1 (0.8)	0	
Diagnosis at Admission			**0.002**
Respiratory failure	68 (54.4)	49 (46.2)	
Cerebrovascular disease	9 (7.2)	23 (21.7)	
Trauma/surgery	15 (12)	13 (12.3)	
Kidney disease	16 (12.8)	3 (2.8)	
Other internal disorders	17 (13.6)	18 (17)	

[a]: Median (interquartile range).
IICU: Internal disease intensive care unit, AICU: Anesthesia intensive care unit, SICU: Surgical intensive care unit, CVS-ICU: Cardio-vascular surgery intensive care unit, COR-ICU: Coronary intensive care unit.

Table 2. Comparison of episode risk factors by bacteremia

	Non-Bacteremia (n= 125)	Bacteremia (n= 106)	p
Duration of hospital stay (day)[a]	52 (48)	43.5 (40)	0.152
Duration of ICU stay (day)[a]	39 (30)	31 (33)	0.078
Intensive care history, n (%)	19 (15.2)	7 (6.6)	**0.039**
Hospitalization history, n (%)	61 (48.8)	33 (31.1)	**0.006**
Patients' risk factors, n (%)			
Surgical drain, n (%)	6 (4.8)	3 (2.8)	0.513
Presence of decubiti, n (%)	17 (13.6)	22 (20.8)	0.148
Extra biliary drainage, n (%)	2 (1.6)	0	0.501
Enteral nutrition, n (%)	93 (74.4)	68 (64.2)	0.091
Presence of tracheal tube, n (%)	7 (5.6)	3 (2.8)	0.350
Proton pump inhibitor use, n (%)	91 (72.8)	93 (87.7)	**0.005**
Cardiopulmonary resuscitation, n (%)	5 (4.0)	4 (3.8)	1.000
Presence of hemodialysis, n (%)	17 (13.6)	16 (15.1)	0.746
Urinary catheterization, n (%)	119 (95.2)	105 (99.1)	0.128
Immunosuppression, n (%)	12 (9.6)	5 (4.7)	0.157
Nasogastric, n (%)	106 (84.8)	88 (83.0)	0.713
Peripheral arterial catheterization, n (%)	112 (89.6)	93 (87.7)	0.655
Percutaneous enterogastrostomy, n (%)	8 (6.4)	6 (5.7)	0.814
Peripheral venous catheterization, n (%)	82 (65.6)	90 (84.9)	**0.001**
AV fistula, n (%)	3 (2.4)	0	0.252
Central venous catheterization, n (%)	106 (84.8)	92 (86.8)	0.709
Steroid use, n (%)	10 (8.1)	0	**0.002**
Total parenteral nutrition, (TPN) n (%)	31 (24.8)	51 (48.1)	**0.000**
Tracheotomy, n (%)	47 (37.6)	45 (42.5)	0.453
Transfusion, n (%)	20 (16.0)	16 (15.1)	0.850

[a]: Median (interquartile range).

peripheral venous catheterizations in the non-bacteremia group was significantly lower than in the bacteremia group (65.6% vs. 84.9%, respectively, p= 0.001). The TPN ratio in the non-bacteremia group was significantly lower than in the bacteremia group (Table 2). When independent variables were compared with the frequency of death, proton pump inhibitor use (p= 0.088), immunosuppression (p= 0.016), presence of peripheral arterial catheter (p= 0.008), presence of percutaneous enterogastrostomy (p= 0.008), trauma (p= 0.067), bacteremia (p= 0.001) was determined.

There was no significant difference observed in the distribution of the Charlson comorbidity index between the groups. The median APACHE-II scores in the non-bacteremia group were significantly lower than in the bacteremia group (24 vs. 28, respectively, p< 0.001). The median SOFA 1 score in the non-bacteremia group did not differ from the bacteremia group (6 vs. 5, respectively, p= 0.17). Similarly, the median SOFA 2 score in the non-bacteremia group did not differ from the bacteremia group (9 vs. 9, respectively p= 0.08) (Table 3).

Regression Analysis

Logistic regression analysis was applied to independent variables below a p-value of 0.10 in one-way comparisons to determine independent variables of relevance.

Table 3. Comparison of disease severity scores by bacteremia

	Non-Bacteremia (n= 125)	Bacteremia (n= 106)	p
Charlson index, n (%)			
0	8 (6.4)	8 (7.5)	
1	8 (6.4)	6 (5.7)	
2	12 (9.6)	9 (8.5)	
3	22 (17.6)	18 (17.0)	
4	32 (25.6)	26 (24.5)	
5	19 (15.2)	21 (19.8)	
6	13 (10.4)	11 (10.4)	
7	7 (5.6)	5 (4.7)	
8	4 (3.2)	1 (0.9)	
9	0	1 (0.9)	
Scores (unit)[b]			
APACHE-II	24 (9)	28 (7)	**0.000**
SOFA 1	6 (1)	5 (2)	0.173
SOFA 2	9 (3)	9 (2)	0.088

[a]: Median (interquartile range), [b]: Mean (standard deviation).

Table 4. Primary independent variables affecting bacteremia

	B	SE	p	OR	95% CI
ICU history	-0.73	0.51	0.151	0.47	0.17-1.30
History of antibiotic use	-0.65	0.31	0.038	0.51	0.28-0.96
Enteral nutrition	-0.78	0.32	0.016	0.45	0.24-0.86
Peripheral venous catheterization	0.83	0.37	0.028	2.29	1.09-4.81
Steroid use	-20.2	12502.5	0.999	0.00	0.000
TPN	0.89	0.32	0.006	2.44	1.29-4.60

Gender (p= 0.101), diagnosis at admission (p= 0.002), ICU history (p= 0.039), hospitalization history (p= 0.006), history of antibiotic use (p= 0.001), diabetes mellitus (p= 0.025), steroid use (p= 0.002), TPN (p= 0.0001), enteral nutrition use (p= 0.091), proton pump inhibitor use (p= 0.005) and peripheral venous catheterization (p= 0.001) were included in the model (Table 4).

The mortality rate was 2.8 times higher in the bacteremia group than in the non-bacteremia group.

In the presence of bacteremia, the APACHE-II score was significant (Figure 1).

At an APACHE-II score of higher than 22, sensitivity for presence of bacteremia was 99.1%, specificity was 40.8%, PPD was 58.7%, and NPD was 98.1%.

DISCUSSION

This study evaluated the risk factors for bacteremia secondary to VAP caused by *A. baumannii* at intensive care units.

Based on the general weight average of pathogens (sum) for antimicrobial resistance rates and distributions from a summary report of the Turkish National Hospital Infections Surveillance Network (UHESA), corresponding to the date range covered by this study, the most common infections were with carbapenem-resistant (>90 percentile) *Acinetobacter* species[5]. Considering that the resistance ratio of *Acinetobacter* has

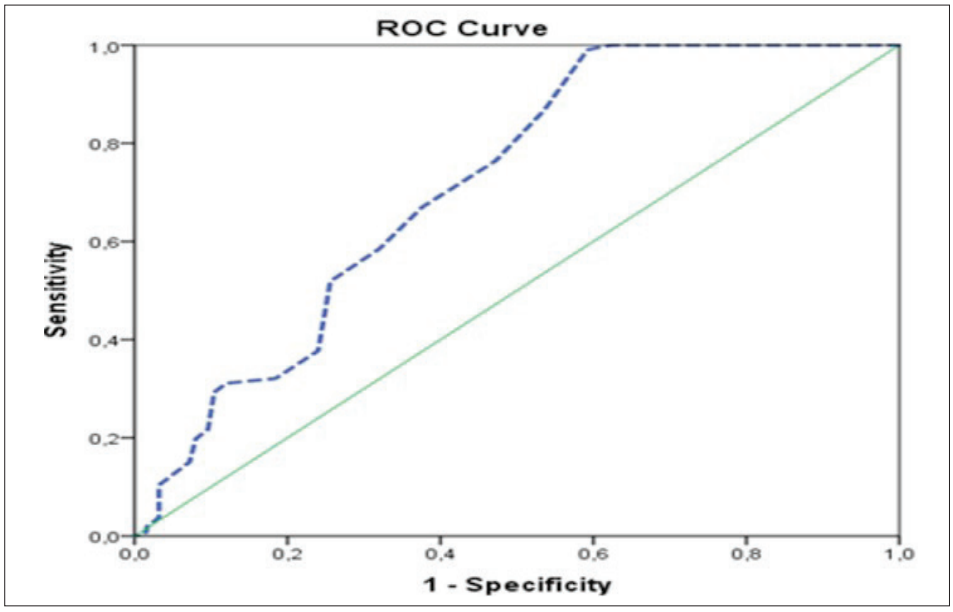

Figure 1. ROC curve of APACHE-II score bacteremia prediction.

grown to over 100% from 90%, as confirmed by previous studies, the prognostic risk for critically ill patients remains relevant[1,2,12]. This pathogen ranks first for VAP, and second for bloodstream infections, and is considered to be an independent risk factor for bacteremia in patients with VAP[13].

The number of subjects included in this study was adequate, considering other literature studies conducted on the same topic. In the examined studies, the number of VAP patients was n= 25, n= 115, and in studies related to bacteremia where the causative agent was *A. baumannii*, the number of patients was n= 79, n= 245, n= 83, n= 125, n= 241, n= 122[12,14,15]. In a recent study conducted in pediatric ICU patients, the number of patients was n= 102[16].

In international, multi-center studies in ICU patients, the VAP rates vary between countries, hospitals, and intensive care units, and have been reported between 2.5 and 40.0%[3,17-19]. Based on data spanning six years from the hospital used in this study, the VAP rates vary between 10 and 25%. Compared to data from across Türkiye over the years, the VAP rates in the hospital fall within the 50th and 90th percentiles, as reported in the UHESA reports. which are comparable to global averages[5].

In this study, the rate of developing bacteremia in VAP episodes was 45.8% (106/231). In a retrospective study of clinical and laboratory records of 129 ICU patients at a single site over a period of six years, Brotfain et al. reported that 46 patients (35%) had *A. baumannii* bacteremia with VAP[6]. Magret et al. reported a general bacteremia rate of 14.6% in VAP patients in a prospective, multi-center (27 ICUs in nine European countries), observational study, and suggested that bacteremia was an independent risk factor for mortality[13]. In a study associating bacteremia development in VAP patients with increased mortality, Agbaht et al. reported that bacteremia developed in 35 of 199 microbiologically-confirmed VAP episodes (17.6%) in 313 VAP patients from an ICU population, and that bacteremia was late-onset (p= 0.03), and more frequent in patients who had a history of hospitalization (p= 0.03) and patients who were geriatric (p< 0.001)[20].

Based on an evaluation of risk factors of bacteremia patients included in this study, there was not a significant difference in age or gender of VAP patients who developed bacteremia (p= 0.184 and p= 0.101, respectively), and some other studies that used a larger or smaller number of subjects found similar results[6,19]. In another study by Gu et al. and Ballouz et al., the ratio

of males was higher in the groups with *A. baumannii* bacteremia[12,21]. A prospective, multi-center study by Liu et al. compared bacteremia patients with carbapenem-resistant *A. baumannii* complex (CRAB) with patients with carbapenem-susceptible *A. baumannii* complex (CSAB), and reported that based on a single-variable analysis, the ratio of males was higher in the CRAB group and that the male sex was an independent risk factor for CRAB bacteremia[22].

Other studies on risk factors for bacteremia have identified a history of hospitalization and admission to the ICU as significant risk factors[21,23]. A Turkish study found that history of hospitalizations was significant, but a history of admission to ICU was not significant[24]. In this study, the ratios of subjects in the VAP group who had a history of ICU admission or hospitalization was significantly higher than in the group with bacteremia secondary to VAP (p= 0.039 vs. p= 0.006, respectively). A history of hospitalizations is not considered to be a risk factor for acquiring bacteremia.

In our subjects, the ratio of proton pump inhibitor (PPI) use in the bacteremia group was significantly higher than in the non-bacteremia group (p= 0.005). Proton pump inhibitor has long been indicated for preventing stress ulceration in mechanical ventilation patients as part of the critical care regimen[25]. However, such increased use of PPIs over the past two decades warrant questioning their long-term implications. Proton pump inhibitors have been associated with an increased infection risk. It has been suggested that alteration of the microflora is conducive to the development of infection, and the relationship between *Clostridium difficile*, in particular, and pneumonia has been the subject matter of several studies[26,27]. Nevertheless, some studies did not associate the prophylactic use of PPIs for stress ulcers with an increased risk of bloodstream infections in the ICU and maintained that concerns for ICU-acquired bacteremia must not affect decisions on PPI use[28].

In our subjects, the ratios of peripheral venous catheterization (p= 0.001) and TPN use (p= 0.000) in the bacteremia group were significantly higher than in the non-bacteremia group. Advanced analyses have concluded that enteral nutrition had a protective value; venous catheterization and TPN use were independent risk factors for bacteremia; and the risk of bacteremia was increased 2.2-fold by venous catheterization, and 2.4-fold by TPN. Catheterization-related bloodstream infections (CRBSI) are associated with peripheral intravascular (IV) catheterization and central venous catheterization (CVC). It is estimated that approximately 90% of CRBSI cases occur with CVC. Moreover, CRBSI is a leading cause of morbidity and mortality and a primary source of bacteremia and septicemia in hospitalized patients. The role of peripheral IVs is perhaps overlooked as a cause of bloodstream infections (BSI)[29-31].

In this study, a significant difference in Charlson Comorbidity index distribution was not found between the groups. The median APACHE-II scores were significantly higher (p< 0.001), but SOFA 1 and SOFA 2 medians were comparable to those in the non-bacteremia group (p= 0.173 vs. p= 0.088, respectively). In a study of 129 ICU patients with VAP caused by MDR-*A. baumannii*, Brotfain et al. compared 46 (35%) VAP patients with 83 (75%) patients with bacteremia secondary to VAP, and reported that the SOFA scores at diagnosis in the bacteremia group were higher than those in the VAP group (p< 0.001), but that the APACHE scores were comparable[6]. Similarly, in a retrospective, matched-pair case-control study Chopra et al. investigated the risk factors for bacteremia caused by *A. baumannii* complex *ABC*; the highlights included a Charlson comorbidity score of 3 or higher, direct referral from another healthcare facility, a history of hospitalization, presence of central venous catheterization, total parenteral nutrition use, and history of β-lactam, carbapenem or other chemotherapeutics[23].

In this study, the identified risk factors for bacteremia from one-way analyses were the diagnosis at admission (p= 0.002), history of ICU admissions (p= 0.039), history of hospitalizations (p= 0.006), history of antibiotic use (p= 0.001), diabetes mellitus (p= 0.025),

steroid use (p= 0.002), TPN (p< 0.001), proton pomp inhibitor use (p= 0.005), and peripheral venous catheterization (p= 0.001). Advanced analyses have revealed that enteral nutrition had a prophylactic effect. Specifically, venous catheterization and total parenteral nutrition (TPN) use were identified as independent risk factors for bacteremia. The risk of bacteremia increased by 2.2-fold with venous catheterization and 2.4-fold with TPN use.

Previous studies have suggested that bacteremia was an independent risk factor for mortality and showed that the crude mortality rates varied between 30% and 76% in patients with *A. baumannii* bacteremia[12,13,24,32]. In this study, the mortality rates were 2.8 times higher in the bacteremia group than in the non-bacteremia group; with 60.3% (64/106) mortality rate in the bacteremia group. Regression analysis by one-way comparison identified presence of bacteremia as an independent risk factor (p= 0.002).

CONCLUSION

In conclusion, the poor prognostic outcomes associated with VAP caused by *A. baumannii*, which exhibits rapid resistance development, and secondary bacteremia from VAP, underscore the necessity for clinicians to enhance precautionary measures. Especially in critically ill ICU patients, it is imperative to minimize invasive procedures, mitigate colonization risks, and ensure maximum compliance with established VAP prevention guidelines. Blood culture, in addition to quantitative respiratory tract cultures, must be used in VAP patients to detect concurrent bacteremia. In patients with VAP caused by *A. baumannii*, an APACHE-II score of 22 or higher should suggest predisposition to bacteremia, and starting early empirical treatment against *A. baumannii* should be considered, in cases of TPN use, unsupervised PPI use, or venous catheterization. Early and effective empirical treatment can help mitigate the development of resistance to less potent interventions and improve prognosis. However, further comprehensive investigations are warranted to better elucidate the underlying risk factors.

ETHICS COMMITTEE APPROVAL

This study was approved by the Recep Tayyip Erdoğan University Non-Invasive Clinical Research Ethics Committee (Decision no: 2019/76, Date: 08.05.2019).

CONFLICT of INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: SÖA, AE, UK, İEY

Analysis/Interpretation: SÖA, AE, AO

Data Collection or Processing: SÖA, AO

Writing: SÖA, AE, AO

Review and Correction: AE, UK, İEY

Final Approval: UK, İEY

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