Infection and Drug Resistance Dovepress

Open Access Full Text Article ORIGINAL RESEARCH

Risk Factors for Development and Mortality of Bloodstream Infections Caused by Carbapenem-Resistant *Acinetobacter baumannii*

Liubing Li[1,*], Dubo Chen[1,*], Pingjuan Liu[1,*], Luqi Dai[2], Zhaoxia Tang[3], Siting Yi[1], Mengmin Ye[1]

[1]Department of Laboratory Medicine, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, People's Republic of China; [2]Division of Pulmonary and Critical Care Medicine, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, People's Republic of China; [3]Department of Critical Care Medicine, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Mengmin Ye; Siting Yi, Department of Laboratory Medicine, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, People's Republic of China, Email yemm7@mail.sysu.edu.cn; yist@mail.sysu.edu.cn

Background: Bloodstream infections (BSIs) caused by *Acinetobacter baumannii* (AB), especially carbapenem-resistant *Acinetobacter baumannii* (CRAB), can lead to a high patient mortality rate.

Methods: This study aimed to analyze the clinical data and prognosis of 191 patients with AB-BSI hospitalized in Southern China from January 2017 to December 2023.

Results: CRAB was diagnosed in 128 (67.0%) of the 191 patients with AB-BSI. Endotracheal intubation (OR = 23.957, 95% CI: 5.123–112.022, P < 0.001), carbapenem treatment (OR = 6.422, 95% CI: 1.554–26.542, P = 0.010) and ≥2 antimicrobial drugs therapy (OR = 6.131, 95% CI: 1.763–21.324, P = 0.004) prior to the onset of BSI were independent risk factors for the development of CRAB-BSI, as revealed by the binary logistic regression analysis. The overall mortality rate of patients with AB-BSI was 27.7%, while that of patients with CRAB was significantly higher than that of patients with carbapenem-sensitive *Acinetobacter baumannii* (CSAB) (39.1% vs 4.8%, P < 0.001). Multivariate Cox regression analysis revealed septic shock (HR = 3.664, 95% CI: 1.537–8.736, P = 0.003) as an independent risk factor for mortality in CRAB-BSI patients. Kaplan–Meier survival analysis showed a significantly lower 28-day survival rate for CRAB-BSI patients who developed septic shock compared to those who did not (58.4% vs 87.1%, P = 0.001).

Conclusion: Clinicians should closely monitor patients at high risk for CRAB-BSI, focusing on invasive procedure management and antimicrobial stewardship. Timely supportive care is crucial for CRAB-BSI patients at risk of septic shock to improve survival outcomes.

Keywords: risk factors, bloodstream infections, carbapenem-resistant *Acinetobacter baumannii*

Introduction

Acinetobacter baumannii (AB) is a gram-negative coccobacillus of the genus Acinetobacter and one of the ESKAPE pathogens, which are the leading cause of nosocomial infections worldwide. This bacterium is able to survive in both dry and humid environments, is resistant to a wide range of disinfectants and antibiotics and is prone to form biofilms on the surface of medical devices. These characteristics make it capable of transmission and infections in healthcare settings.[1,2] For example, ventilator-associated pneumonia caused by AB, which forms a biofilm in the endotracheal tube of a ventilator, causes mortality in patients ranging from 40% to 70%.[3] In addition, AB is generally very resistant to commonly used antibiotics such as meropenem and ciprofloxacin, with significant regional variations globally, ranging from 30% to 80%. A rapid rise in the presence of carbapenem-resistant *Acinetobacter baumannii* (CRAB) in Southeast and South Asia has been reported, with rates exceeding 50% in most AB isolates, especially in the Intensive Care Unit (ICU).[4] The 58% of AB isolates in North America are resistant to carbapenems, and more than 70% in eastern and southern Europe are insensitive.[5,6] The latest report from the European Centre for Disease Prevention and Control

Received: 27 June 2024
Accepted: 12 December 2024
Published: 20 December 2024

(ECDC) indicates that 39.9% of AB are resistant to carbapenems.[7] The 2022 China Antimicrobial Surveillance Report shows that AB is highly resistant to carbapenems, especially in ICU, with a CRAB detection rate of 77.8%. The US Centers for Disease Control and Prevention listed AB as one of the most urgent threats.[8]

AB causes a variety of infections, including those to the skin and soft tissues, endocarditis, meningitis, pneumonia, and bloodstream infections (BSIs). The prognosis of patients suffering from AB-BSI is generally poor[9,10] because of the difficulty of treating the infections, leading to serious morbidity and high mortality. A study in northwestern Ethiopia revealed that AB accounts for 9% of hospital BSI.[11] AB-BSI is developed in 13% of patients who underwent neurosurgery, and 90% of AB were carbapenem-resistant.[12] The mortality rate due to CRAB-BSI is as high as 60%.[13] Polymyxin and tetracyclines (tigecycline and minocycline) are commonly used in the treatment of CRAB-BSI,[14] which are effective to a certain extent, but with a cure rate challenging as the bacterial resistance to these drugs increases. This increases the mortality risk of patients, as well as causing a significant increase in healthcare costs, placing a heavy burden on patients and the healthcare system. There is an urgent necessity for the development of novel and more effective antibiotics to combat infections caused by CRAB. Currently, cefiderocol is a promising agent against CRAB;[15] however, further clinical evidence is required to confirm its effectiveness.

AB is currently of great concern due to its widespread presence in hospitals, the multiple infections it causes, and its multidrug resistance and virulence, being a major challenge to global public health.[16] This study aims to investigate the risk factors and mortality factors in patients with CRAB-BSI in Southern China, in order to improve medical professionals' understanding of the prevention and treatment of CRAB-BSI.

Materials and Methods

Study Design and Patients

AB-BSI patients hospitalized in the First Affiliated Hospital of Sun Yat-sen University from January 2017 to December 2023 were retrospectively analyzed, and the strains repeatedly isolated from the same patients were discarded. A total of 191 patients with AB-BSI were enrolled, including 128 (67.0%) with CRAB and 63 (33.0%) with CSAB. The inclusion criteria were the following: (1) age >18 years old; (2) isolation of only one pathogenic bacterium in one blood culture, which should be AB, and more than one blood culture specimens positive for AB, with a clinical evidence of corresponding BSI, which included one or more of the following symptoms: body temperature < 36°C or ≥ 38°C, shaking chills, hypotension, heart rate >90 beats/minute, respiratory rate >20 breaths/minute, and disorders of consciousness;[17] (3) only the first culture strain of AB from the same patient was included in this study; (4) complete patient's clinical data. Patients with polymicrobial bloodstream infection were excluded.

Definitions

According to the Clinical and Laboratory Standards Institute (CLSI) standards, carbapenem resistance was defined as a minimum inhibitory concentration (MIC) of ≥4 mg/L for meropenem or imipenem, or ≥2 mg/L for ertapenem. Based on the clinical pharmacotherapy practices in our hospital, carbapenem, a class of antimicrobial drugs, included meropenem, imipenem, and ertapenem. The beta-lactam combinations included cefoperazone/sulbactam, piperacillin/tazobactam, and ceftazidime/avibactam. ≥2 antimicrobial drugs referred to the exposure to at least two different classes of antimicrobial drugs; these classes included cephalosporins, carbapenems, penicillins, beta-lactam combinations, aminoglycosides, glycopeptides, quinolones, tetracycline derivatives, polymyxins, and oxazolidinones. The term, antimicrobial use prior to BSI, referred to the administration of one or more antimicrobial drugs to the patient at any time point from the time of hospital admission until the onset of AB-BSI.

Microbiological Methods

Blood culture samples were analyzed and those positive to AB were identified using VITEK 2 automatic microbial identification and antimicrobial susceptibility analysis system (Biomerieux, France). The results of strain identification and antimicrobial susceptibility tests were evaluated and interpreted according to the standards recommended by the

Clinical and Laboratory Standards Institute (CLSI, 2023). Pseudomonas aeruginosa ATCC27853 was used as the quality control strain.

Statistical Analysis

SPSS 26.0 software was used to perform Kaplan–Meier survival analysis and the Log rank test. R 4.1.2 software was used for binary logistic regression analysis and Cox regression analysis. Binary logistic regression model was used to determine the factors associated with the development of CRAB-BSI, and Cox regression analysis was used to identify factors associated with mortality in patients with CRAB-BSI. Potential predictors were identified using a univariate logistic regression model, then significant univariate predictors ($P < 0.1$) were entered into multivariable logistic regression to identify the independent factors. A value of $P < 0.05$ was considered statistically significant.

Results

Patients

Among the 191 patients with AB-BSI, 69.1% were male, 34.6% were 65 years or older, and 77.0% had hospital-acquired infections, as shown in Table 1. The most common underlying diseases among these patients were respiratory diseases (41.9%), hypertension (35.1%), and hepatobiliary diseases (26.7%). More than half of the patients were subjected to invasive procedures, 61.3% were treated with carbapenems, 42.4% with β-lactam combinations, and 62.3% with antimicrobial combinations prior to the onset of BSI. AB was isolated from respiratory tract samples in 38.7% of the patients before the development of AB-BSI.

Independent Factors in the Development of CRAB-BSI

CRAB-BSI was diagnosed in 67.0% of the 191 patients with AB-BSI. A total of 128 cases of CRAB-BSI were compared with 63 cases of CSAB-BSI to determine the independent factors in the development of CRAB-BSI. Univariate binary

Table 1 Binary Logistic Regression Analysis of Independent Factors for the Occurrence of CRAB-BSI

Variable, n (%)	CRAB-BSI	CSAB-BSI	*P*	Multivariate Analysis		
				OR	95% CI	*P*
Male	87 (68.0)	45 (71.4)	0.627			
Age ≥65 years	46 (35.9)	20 (31.7)	0.567			
Hospital-acquired infection	104 (81.3)	43 (68.3)	0.047	1.683	0.448–6.325	0.441
Source of infection of the respiratory tract	68 (53.1)	6 (9.5)	<0.001	1.645	0.345–7.855	0.532
Comorbidities						
Hypertension	50 (39.1)	17 (27.0)	0.102			
Diabetes	31 (24.2)	8 (12.7)	0.068	3.095	0.621–15.433	0.168
Cardiovascular disease	36 (28.1)	14 (22.2)	0.384			
Respiratory disease	72 (56.3)	8 (12.7)	<0.001	0.767	0.180–3.272	0.721
Hepatobiliary disease	35 (27.3)	16 (25.4)	0.775			
Kidney Disease	43 (33.6)	7 (11.1)	0.002	4.052	0.733–22.401	0.109
Invasive operation						
Arteriovenous catheterization	115 (89.8)	32 (50.8)	<0.001	3.276	0.810–13.259	0.096
Endotracheal intubation	113 (88.3)	7 (11.1)	<0.001	23.957	5.123–112.022	<0.001
Urinary catheter	81 (63.3)	29 (46.0)	0.024	0.307	0.073–1.296	0.108
Antimicrobial use prior to BSI						
Beta-lactam combinations	59 (46.1)	22 (34.9)	0.143			
Carbapenem	106 (82.8)	11 (17.5)	<0.001	6.422	1.554–26.542	0.010
≥2 antimicrobial drugs	109 (85.2)	10 (15.9)	<0.001	6.131	1.763–21.324	0.004

Abbreviations: CRAB, carbapenem-resistant *Acinetobacter baumannii*; CSAB, carbapenem-sensitive *Acinetobacter baumannii*; BSI, bloodstream infection; OR, odd ratio; CI, confidence interval.

logistic regression analysis suggested that hospital-acquired infection, source of infection of the respiratory tract, diabetes, respiratory disease, kidney disease, arteriovenous catheterization, endotracheal intubation, urinary catheter, antimicrobial drugs such as carbapenem, and ≥2 antimicrobial drugs prior to the onset of BSI, were the potential predictors of the development of CRAB-BSI ($P < 0.1$, Table 1). The results of multivariate binary logistic regression analysis (Table 1) showed that endotracheal intubation (OR = 23.957, 95% CI: 5.123–112.022, $P < 0.001$), carbapenem treatment (OR = 6.422, 95% CI: 1.554–26.542, $P = 0.010$) and ≥2 antimicrobial drugs therapy (OR = 6.131, 95% CI: 1.763–21.324, $P = 0.004$) prior to the onset of BSI were independent risk factors for the development of CRAB-BSI.

Independent Prognostic Factors for CRAB-BSI

The overall mortality rate of patients with CRAB was significantly higher than that of patients with CSAB (39.1% vs 4.8%, $P < 0.001$). Data from 50 patients who died and those of 78 patients who survived were compared to identify the independent factors for mortality in patients with CRAB-BSI. Univariate Cox regression analysis suggested that male, source of infection of the respiratory tract, septic shock, cardiovascular disease, and tigecycline treatment, were the potential predictors of mortality in patients with CRAB-BSI ($P < 0.1$, Table 2). The results of multivariate Cox regression analysis (Table 2) showed that septic shock (HR = 3.664, 95% CI: 1.537–8.736, $P = 0.003$) was an independent risk factor for mortality in patients with CRAB-BSI.

Table 2 Cox Regression Analysis of Risk Factors for Mortality in CRAB-BSI

Variable, n (%)	Death	Survivors	*P*	Multivariate Analysis		
				HR	95% CI	*P*
Male	37 (74.0)	50 (64.1)	0.093	1.591	0.807–3.137	0.180
Age ≥65 years	18 (36.0)	28 (35.9)	0.689			
Hospital-acquired infection	41 (82.0)	63 (80.8)	0.904			
Source of infection of the respiratory tract	26 (52.0)	42 (53.8)	0.090	1.318	0.716–2.429	0.375
ICU admission	48 (96.0)	72 (92.3)	0.230			
Septic shock	44 (88.0)	45 (57.7)	0.001	3.664	1.537–8.736	0.003
Comorbidities						
Hypertension	17 (34.0)	33 (42.3)	0.377			
Diabetes	10 (20.0)	21 (26.9)	0.848			
Cardiovascular disease	19 (38.0)	17 (21.8)	0.033	1.397	0.752–2.594	0.291
Respiratory disease	31 (62.0)	41 (52.6)	0.209			
Hepatobiliary disease	12 (24.0)	23 (29.5)	0.138			
Kidney Disease	15 (30.0)	28 (35.9)	0.534			
Invasive operation						
Arteriovenous cannulation	44 (88.0)	71 (91.0)	0.164			
Endotracheal intubation	47 (94.0)	66 (84.6)	0.207			
Urinary catheter	31 (62.0)	50 (64.1)	0.633			
Antimicrobial use prior to BSI						
Beta-lactam combinations	27 (54.0)	32 (41.0)	0.242			
Carbapenem	42 (84.0)	64 (82.1)	0.716			
≥2 antimicrobial drugs	41 (82.0)	68 (87.2)	0.319			
Targeted antimicrobial treatment						
Tigecycline	8 (16.0)	23 (29.5)	0.097	0.549	0.255–1.183	0.126
Polymyxin	8 (16.0)	13 (16.7)	0.810			
Tigecycline and polymyxin combination	17 (34.0)	20 (25.6)	0.376			

Abbreviations: CRAB-BSI, carbapenem-resistant *Acinetobacter baumannii* bloodstream infection; HR, hazard ratio; CI, confidence interval.

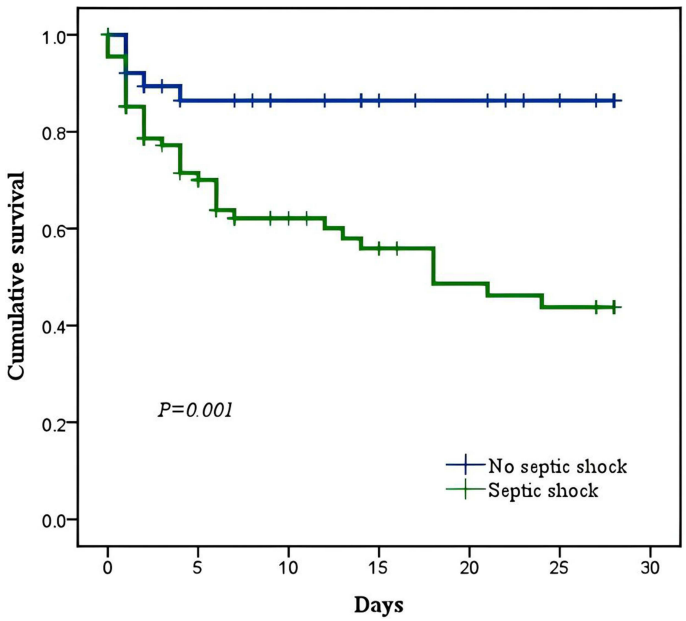

Figure 1 Kaplan-Meier survival analysis of patients with CRAB-BSI who developed septic shock. CRAB-BSI: carbapenem-resistant *Acinetobacter baumannii* bloodstream infection.

Kaplan–Meier Survival Analysis of CRAB-BSI Patients with Septic Shock

The overall mortality rate of patients with AB-BSI was 27.7% (53/191). Septic shock occurred in 69.5% (89/128) of patients with CRAB-BSI. The proportion of septic shock among patients who died of CRAB-BSI was significantly higher than that among patients who survived (88.0% vs 57.7%, P < 0.001, Table 2). The 28-day survival rate of patients with CRAB-BSI who developed septic shock was significantly lower than that of patients without septic shock (58.4% vs 87.1%, P = 0.001, Figure 1).

Discussion

AB survives in harsh environments, including the surface of hospital facilities. It forms a biofilm that allows the survival in medical devices and medical settings, increasing the risk of transmission, its resistance and virulence. Thereby, it is prone to form drug-resistant strains.[18] In addition, AB can evade the host's immune system and acquire new mechanisms of resistance to antibiotics. These abilities make treatment complex and difficult.[19,20] This study analyzed the epidemiological data of CRAB-BSI in Southern China and the independent factors of its development and mortality to help in the identification of the risk of development of CRAB-BSI and mortality.

CRAB was isolated from the respiratory tract samples of 53.1% of the patients before they developed CRAB-BSI in this study. To eliminate the potential confounding effect, multivariate binary logistic regression analysis was used to identify independent factors for the occurrence of CRAB-BSI. Endotracheal intubation was an independent risk factor in the development of CRAB-BSI. It destroyed the skin barriers of these patients, providing a direct entrance for CRAB into the lower respiratory tract, thus increasing the chance of CRAB infection. This finding suggests that enhancing hand hygiene management, disinfecting the environment and medical equipment, regular screening, and monitoring the patients with CRAB may be measures controlling infections to reduce the risk of developing CRAB-BSI. Carbapenem use and antimicrobial combinations are also independent risk factors in the development of CRAB-BSI. A potential reason might be the selection of resistant AB due to antimicrobial drug and the consequent growth of bacteria carrying resistance genes,[21] being an important factor in the spread of CRAB strains. This suggests that clinicians need to pay attention to the initial antimicrobial therapy of patients with CRAB-BSI, they should perform regular antimicrobial monitoring and avoid unnecessary antimicrobial exposure to reduce the development and spread of drug resistance.

CRAB infections have a significantly higher mortality rate compared to those caused by non-resistant strains, ranging from 35% to 60%.[22] In this study, the mortality rate for CRAB-BSI was 39.1%, which is significantly higher than that for CSAB-BSI. Septic shock was an independent risk factor for mortality in patients with CRAB-BSI, which was in accordance with other studies.[13,23] Septic shock is one of the common causes of BSI, which is associated with uncontrolled inflammatory response that leads to microcirculatory disorders, cellular damage, and metabolic disturbances, ultimately increasing the risk of mortality.[24] Thus, an early and effective anti-infective therapy is essential to reduce the probability that CRAB-BSI develops into septic shock. However, the current antimicrobial options for CRAB-BSI are notably limited, including ampicillin-sulbactam, tetracycline derivatives, polymyxin, and extended infusions of meropenem, as recommended by the Infectious Diseases Society of America (IDSA).[25] It is important to note that the use of polymyxin loading doses is associated with renal impairment.[26] Furthermore, tigecycline is not recommended for the treatment of patients with BSI due to its low plasma concentrations and the absence of an established susceptibility threshold.[27] Currently, the polymyxin-based combination regimen is the first choice in the treatment of CRAB infection,[28] but the data are insufficient to support the use of this regimen in this context. In the targeted antibiotic treatment of patients with CRAB-BSI, the administration of tigecycline alone, polymyxin alone, or the combination of these two drugs did not demonstrate a significant association with mortality risk. This suggested that the mortality associated with CRAB-BSI infection might involve a variety of factors, including the host's immune status, bacterial virulence, antimicrobial efficacy, hospital environment, and medical means.[19,29] The successful treatment of patients with CRAB-BSI through the combined administration of fosfomycin and cefiderocol is demonstrated, suggesting that this intravenous dosing regimen may serve as an effective therapeutic strategy.[30] In cases where alternative treatment options have proven ineffective or are not well tolerated, clinical guidelines advocate for the incorporation of cefiderocol into combination therapy regimens. This strategy aims to enhance its therapeutic efficacy and mitigate the risk of resistance, particularly in critically ill patients suffering from infections caused by CRAB.[22] Further evaluation of treatment outcomes is needed to confirm these findings. It is necessary to consider the patient's overall condition and the severity of infection during clinical practice apart from antimicrobial therapy, as well as other supportive treatments that might be necessary, such as source control, appropriate fluid management, and hemodynamic support. These factors might help the achievement of the best treatment effect.

The limitation of this study was mainly the inclusion of patients from a single medical center, so the drawn conclusion might be valid for the specific patient population and treatment practices of the selected medical center, although it might help to raise awareness among doctors around the world regarding this widespread problem. Future research should involve a multicenter prospective cohort study to gather comprehensive and detailed clinical and microbiological data, with the aim of analyzing the impact of various treatment protocols on the progression of CRAB-BSI. Furthermore, the utilization of deep learning and artificial intelligence methodologies could be explored for the identification and progression of CRAB-BSI.

Conclusion

The incidence of CRAB-BSI in patients with AB-BSI in Southern China is 67.0%. Endotracheal intubation, as well as carbapenem treatment and ≥2 antimicrobial drugs therapy prior to the onset of BSI are independent risk factors in the development of CRAB-BSI. Septic shock is an independent risk factor for mortality of CRAB-BSI patients. This study highlighted the critical need to identify patients at elevated risk for CRAB-BSI who necessitated the optimization of invasive procedure management and antimicrobial therapies, and delivering timely supportive care to CRAB-BSI patients vulnerable to septic shock, thereby improving their likelihood of attaining a favorable outcome.

Data Sharing Statement

The datasets used or analyzed during the current study available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study complies with the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University. The requirement for written informed consent was waived because of the retrospective analysis of the anonymized data.

Funding

There is no funding to report.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Greene C, Vadlamudi G, Newton D, Foxman B, Xi C. The influence of biofilm formation and multidrug resistance on environmental survival of clinical and environmental isolates of Acinetobacter baumannii. *Am J Infect Control*. 2016;44(5):e65–71. doi:10.1016/j.ajic.2015.12.012
2. McConnell MJ, Actis L, Pachón J. Acinetobacter baumannii: human infections, factors contributing to pathogenesis and animal models. *FEMS Microbiol Rev*. 2013;37(2):130–155. doi:10.1111/j.1574-6976.2012.00344.x
3. Garnacho-Montero J, Ortiz-Leyba C, Fernández-Hinojosa E, et al. Acinetobacter baumannii ventilator-associated pneumonia: epidemiological and clinical findings. *Intensive Care Med*. 2005;31(5):649–655. doi:10.1007/s00134-005-2598-0
4. Hsu LY, Apisarnthanarak A, Khan E, Suwantarat N, Ghafur A, Tambyah PA. Carbapenem-resistant Acinetobacter baumannii and Enterobacteriaceae in South and Southeast Asia. *Clin Microbiol Rev*. 2017;30(1):1–22. doi:10.1128/CMR.masthead.30-1
5. Ayobami O, Willrich N, Suwono B, Eckmanns T, Markwart R. The epidemiology of carbapenem-non-susceptible Acinetobacter species in Europe: analysis of EARS-Net data from 2013 to 2017. *Antimicrob Resist Infect Control*. 2020;9(1):89. doi:10.1186/s13756-020-00750-5
6. Lima WG, Silva Alves GC, Sanches C, Antunes Fernandes SO, de Paiva MC. Carbapenem-resistant Acinetobacter baumannii in patients with burn injury: a systematic review and meta-analysis. *Burns*. 2019;45(7):1495–1508. doi:10.1016/j.burns.2019.07.006
7. World Health Organization. *Antimicrobial Resistance Surveillance in Europe 2023—2021 Data*. Geneva, Switzerland: World Health Organization; 2023.
8. Rello J, Kalwaje Eshwara V, Lagunes L, et al. A global priority list of the TOp TEn resistant Microorganisms (TOTEM) study at intensive care: a prioritization exercise based on multi-criteria decision analysis. *Eur J Clin Microbiol Infect Dis*. 2019;38(2):319–323. doi:10.1007/s10096-018-3428-y
9. Galani I, Papoutsaki V, Karaiskos I, et al. In vitro activities of omadacycline, eravacycline, cefiderocol, apramycin, and comparator antibiotics against Acinetobacter baumannii causing bloodstream infections in Greece, 2020–2021: a multicenter study. *Eur J Clin Microbiol Infect Dis*. 2023;42(7):843–852. doi:10.1007/s10096-023-04616-7
10. Mea HJ, Yong PVC, Wong EH. An overview of Acinetobacter baumannii pathogenesis: motility, adherence and biofilm formation. *Microbiol Res*. 2021;247:126722. doi:10.1016/j.micres.2021.126722
11. Motbainor H, Bereded F, Mulu W. Multi-drug resistance of blood stream, urinary tract and surgical site nosocomial infections of Acinetobacter baumannii and Pseudomonas aeruginosa among patients hospitalized at Felegehiwot referral hospital, Northwest Ethiopia: a cross-sectional study. *BMC Infect Dis*. 2020;20(1):92. doi:10.1186/s12879-020-4811-8
12. Tsitsopoulos PP, Iosifidis E, Antachopoulos C, et al. Nosocomial bloodstream infections in neurosurgery: a 10-year analysis in a center with high antimicrobial drug-resistance prevalence. *Acta Neurochir*. 2016;158(9):1647–1654. doi:10.1007/s00701-016-2890-5
13. Cogliati Dezza F, Covino S, Petrucci F, et al. Risk factors for carbapenem-resistant Acinetobacter baumannii (CRAB) bloodstream infections and related mortality in critically ill patients with CRAB colonization. *JAC Antimicrob Resist*. 2023;5(4):dlad096. doi:10.1093/jacamr/dlad096
14. Kanj SS, Bassetti M, Kiratisin P, et al. Clinical data from studies involving novel antibiotics to treat multidrug-resistant Gram-negative bacterial infections. *Int J Antimicrob Agents*. 2022;60(3):106633. doi:10.1016/j.ijantimicag.2022.106633
15. Stracquadanio S, Nicolosi A, Privitera GF, et al. Role of transcriptomic and genomic analyses in improving the comprehension of cefiderocol activity in Acinetobacter baumannii. *mSphere*. 2024;9(1):e0061723. doi:10.1128/msphere.00617-23
16. Ibrahim S, Al-Saryi N, Al-Kadmy IMS, Aziz SN. Multidrug-resistant Acinetobacter baumannii as an emerging concern in hospitals. *Mol Biol Rep*. 2021;48(10):6987–6998. doi:10.1007/s11033-021-06690-6
17. Wang J, Wang M, Zhao A, et al. Microbiology and prognostic prediction model of bloodstream infection in patients with hematological malignancies. *Front Cell Infect Microbiol*. 2023;13:1167638. doi:10.3389/fcimb.2023.1167638
18. Roy S, Chowdhury G, Mukhopadhyay AK, Dutta S, Basu S. Convergence of biofilm formation and antibiotic resistance in Acinetobacter baumannii infection. *Front Med Lausanne*. 2022;9:793615. doi:10.3389/fmed.2022.793615
19. Shields RK, Paterson DL, Tamma PD. Navigating available treatment options for carbapenem-resistant Acinetobacter baumannii-calcoaceticus complex infections. *Clin Infect Dis*. 2023;76(Suppl 2):S179–s193. doi:10.1093/cid/ciad094
20. Wong D, Nielsen TB, Bonomo RA, Pantapalangkoor P, Luna B, Spellberg B. Clinical and pathophysiological overview of Acinetobacter infections: a century of challenges. *Clin Microbiol Rev*. 2017;30(1):409–447. doi:10.1128/cmr.00058-16
21. Chusri S, Silpapojakul K, McNeil E, Singkhamanan K, Chongsuvivatwong V. Impact of antibiotic exposure on occurrence of nosocomial carbapenem-resistant Acinetobacter baumannii infection: a case control study. *J Infect Chemother*. 2015;21(2):90–95. doi:10.1016/j.jiac.2014.10.002
22. Marino A, Augello E, Stracquadanio S, et al. Unveiling the secrets of Acinetobacter baumannii: resistance, current treatments, and future innovations. *Int J Mol Sci*. 2024;25(13):6814. doi:10.3390/ijms25136814

23. Russo A, Bassetti M, Ceccarelli G, et al. Bloodstream infections caused by carbapenem-resistant Acinetobacter baumannii: clinical features, therapy and outcome from a multicenter study. *J Infect*. 2019;79(2):130–138. doi:10.1016/j.jinf.2019.05.017
24. Liang P, Yu F. Predictive value of procalcitonin and neutrophil-to-lymphocyte ratio variations for bloodstream infection with septic shock. *Med Sci Monit*. 2022;28:e935966. doi:10.12659/msm.935966
25. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious diseases society of America guidance on the treatment of AmpC β-Lactamase-producing enterobacterales, carbapenem-resistant Acinetobacter baumannii, and stenotrophomonas maltophilia infections. *Clin Infect Dis*. 2022;74(12):2089–2114. doi:10.1093/cid/ciab1013
26. Kaye KS, Marchaim D, Thamlikitkul V, et al. Colistin monotherapy versus combination therapy for carbapenem-resistant organisms. *NEJM Evid*. 2023;2(1). doi:10.1056/evidoa2200131
27. Abdul-Mutakabbir JC, Griffith NC, Shields RK, Tverdek FP, Escobar ZK. Contemporary perspective on the treatment of Acinetobacter baumannii infections: insights from the society of infectious diseases pharmacists. *Infect Dis Ther*. 2021;10(4):2177–2202. doi:10.1007/s40121-021-00541-4
28. O'Donnell JN, Putra V, Lodise TP. Treatment of patients with serious infections due to carbapenem-resistant Acinetobacter baumannii: how viable are the current options? *Pharmacotherapy*. 2021;41(9):762–780. doi:10.1002/phar.2607
29. Zheng X, Wang JF, Xu WL, Xu J, Hu J. Clinical and molecular characteristics, risk factors and outcomes of Carbapenem-resistant Klebsiella pneumoniae bloodstream infections in the intensive care unit. *Antimicrob Resist Infect Control*. 2017;6:102. doi:10.1186/s13756-017-0256-2
30. Marino A, Stracquadanio S, Campanella E, et al. Intravenous Fosfomycin: a potential good partner for cefiderocol. Clinical experience and considerations. *Antibiotics*. 2022;12(1). doi:10.3390/antibiotics12010049