Different Clinical Characteristics and Impacts of Carbapenem-Resistance on Outcomes Between *Acinetobacter Baumannii* and *Pseudomonas Aeruginosa* Bacteraemia: A Multicentre Prospective Observational Study

Chan Mi Lee

Seoul National University Bundang Hospital

Young-Jun Kim

Wonkwang University Hospital: Wonkwang University School of Medicine Hospital

Sook-In Jung

Chonnam National University Medical School

Seong Eun Kim

Chonnam National University Medical School

Wan Beom Park

Seoul National University Hospital

Pyoeng Gyun Choe

Seoul National University Hospital

Eu Suk Kim

Seoul National University Bundang Hospital

Chung-Jong Kim

Ewha Womans University Dongdaemun Hospital: Ewha Women's University Mokdong Hospital

Hee Jung Choi

Ewha Womans University Dongdaemun Hospital: Ewha Women's University Mokdong Hospital

Shinwon Lee

Pusan National University Hospital

Sun Hee Lee

Pusan National University Hospital

Younghee Jung

Hallym University Sacred Heart Hospital

Ji Hwan Bang

Seoul Metropolitan Boramae Hospital: Seoul National University Seoul Metropolitan Government Boramae Medical Center

Shinhye Cheon

Chungnam National University Hospital

Yee Gyung Kwak

Inje University Ilsan Paik Hospital

Yu Min Kang

Kangwon National University Hospital

Kyung-Hwa Park

Chonnam National University Medical School

Kyoung-Ho Song (✉ khsongmd@gmail.com)

Seoul National University Bundang Hospital <https://orcid.org/0000-0002-4517-3840>

Hong Bin Kim

Seoul National University Bundang Hospital

Research

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Abstract

Background: Carbapenem-resistance (CR) causes poor clinical outcomes and has limited treatment options. We aim to evaluate the differences in clinical characteristics and impact of carbapenem-resistance on outcomes between *Acinetobacter baumannii* (ABA) and *Pseudomonas aeruginosa* (PAE) bacteraemia.

Methods: We prospectively identified all patients with ABA and PAE bacteraemia in 10 hospitals over a 1-year period and collected their detailed clinical information. Treatment failure was defined as all-cause 30-day mortality, persistent bacteraemia, or recurrence within 30 days.

Results: We included 304 ABA and 241 PAE bacteraemia cases. CR was detected in 216 ABA (71%) and 55 PAE (23%). Treatment failure was significantly higher in CR-ABA than in CR-PAE (60.6% vs. 34.5%, $P = 0.001$). Multivariate analyses were stratified by patient data according to CR and the appropriateness of empirical therapy. For ABA patients, severe sepsis or septic shock and high Pitt bacteraemia score were independent risk factors for treatment failure in the inappropriate empirical antibiotics group. Pneumonia was a significant risk factor in the appropriate group. For PAE patients, hospital-acquired infection and high Pitt bacteraemia score were independent risk factors for treatment failure in both groups. CR was an independent risk factor in ABA for treatment failure in both the inappropriate (adjusted odds ratio [aOR]: 6.17, 95% confidence interval [CI]: 1.13-33.75, $P = 0.036$) and appropriate empirical treatment groups (aOR: 4.15, 95% CI: 1.16-14.84, $P = 0.029$), but not for patients with PAE bacteraemia.

Conclusions: We demonstrated significant differences in the clinical characteristics and impact of CR on the clinical outcomes between ABA and PAE bacteraemia. Our findings suggest that different approaches may be needed to treat ABA and PAE bacteraemia.

Background

Antimicrobial resistance is a major threat to public health. Recent reports from the Centers for Disease Control and Prevention concluded that the threat of antibiotic-resistance was greater than previously understood, and listed carbapenem resistance in non-fermenting gram negative bacteria, such as *Acinetobacter baumannii* (ABA) and *Pseudomonas aeruginosa* (PAE), as urgent threats (1). There are limited treatment options for carbapenem resistance; due to its severity and poor clinical outcomes, it is an emerging public health concern (2–4). Therefore, to further improve treatment for infectious diseases that show resistance to antibiotics, identifying their clinical features is critical.

Both carbapenem-resistant ABA (CR-ABA) and carbapenem-resistant PAE (CR-PAE) are important causes of healthcare-associated infections (5). Further, it is known that antibiotic susceptibility and clinical features vary between them. However, there are no integrated observational clinical studies assessing the clinical impacts of carbapenem resistance in ABA and PAE. Due to the limited treatment options for CR-ABA and CR-PAE, it is important to elucidate the impact of carbapenem resistance on the clinical outcomes and risk factors for treatment failure. Therefore, we aimed to evaluate the differences in the

clinical characteristics and impacts of carbapenem resistance on clinical outcomes between ABA and PAE bacteraemia.

Methods

Patient population and clinical data

All patients with ABA or PAE bacteraemia were identified prospectively from clinical microbiology laboratories in 10 hospitals over a 1-year period from 1 September 2017 to 31 August 2018. We prospectively collected patients' demographic and microbiological data, underlying medical conditions, source of bacteraemia, clinical severity, antibiotic therapy, and clinical outcomes. This study was approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (IRB no. B-1804-463-105) and the IRBs of each participating hospital. The study was conducted in accordance with the principles outlined in the 1964 Declaration of Helsinki and its later amendments. The need for informed consent was waived by the IRBs.

Definitions

Mixed bacteraemia was defined as the isolation of other organisms except common skin flora, such as coagulase-negative staphylococci (6), from the first blood culture that yielded PAE or ABA. Bacteraemia detected in patients who were hospitalised for over 48 hours was classified as a hospital-acquired infection (HAI). Healthcare-associated infection was defined as fulfilling at least one of the following criteria: (1) hospitalisation for 2 or more days in the previous 12 months; (2) residence in a nursing home in the previous 12 months; (3) treatment with parenteral antibiotics within 30 days; and (4) renal replacement therapy within 30 days. Use of immunosuppressant was defined as the use of any anticancer chemotherapy, corticosteroids more than 20 mg of prednisolone equivalent over 1 week, or any other immunosuppressive agent within the past 30 days.

The severity of illness was assessed using the Pitt bacteraemia score (7), and the severity of underlying disease was assessed using Charlson's weighted index of comorbidity (WIC) (8). Empirical antimicrobial therapy was defined as initial treatment used more than 24 hours after the sampling of the first positive blood culture. Antibiotic therapy was considered inappropriate if the isolate was not susceptible to the treatment regimen *in vitro*.

Treatment failure was defined as fulfilling any of the following events: (1) all-cause 30-day mortality; (2) persistent bacteraemia defined as positive blood cultures after ≥ 7 days of appropriate antimicrobial therapy; (3) recurrent bacteraemia within 30 days after discontinuation of appropriate antimicrobial therapy (9).

Data management and statistical analysis

The chi-squared test or Fisher’s exact test were used to compare categorical variables, and the Student t-test or Mann Whitney U test were used to compare continuous variables. A stepwise multiple logistic regression was used to identify independent risk factors for treatment failure. Risk factors with a *P* value of <0.10 in univariate analysis and other variables of clinical significance were included in multivariate analysis. To avoid multicollinearity, severe sepsis or septic shock and Pitt bacteraemia score were analysed in a separate multivariate model. All underlying diseases and Charlson’s WIC were analysed in a separate multivariate model for the same reason. *P* values <0.05 were considered statistically significant. The Hosmer-Lemeshow test was used to assess the goodness of fit for logistic regression models. All statistical analyses were performed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Clinical characteristics of ABA and PAE bacteraemia

Of the 545 cases identified during the 1-year study period, 304 were ABA bacteraemia and 241 were PAE bacteraemia. Of the 304 ABA bacteraemia cases, 216 (71%) were CR-ABA and 88 (29%) were carbapenem-susceptible ABA (CS-ABA). Of the 241 PAE bacteraemia cases, 55 (23%) were CR-PAE and 186 (77%) were carbapenem-susceptible PAE (CS-PAE).

The clinical characteristics of ABA bacteraemia according to carbapenem susceptibility are described in Table S1. Catheter related bloodstream infection and pneumonia were more frequent in the CR-ABA group than in the CS-ABA group (42.1% vs. 28.4%, *P* = 0.026; 36.1% vs. 9.1%, *P* < 0.001). The CR-ABA group showed significantly higher percentages of severe sepsis or septic shock (53.2% vs. 21.6%, *P* < 0.001) and inappropriate empirical therapy (75.0% vs. 19.3%, *P* < 0.001) than the CS-ABA group. All-cause 30-day mortality and treatment failure rates were significantly higher in the CR-ABA group than the CS-ABA group (57.5% vs. 15.5%, *P* < 0.001; 60.6% vs. 15.9%, *P* < 0.001).

The clinical characteristics of PAE bacteraemia according to carbapenem susceptibility are described in Table S2. The CR-PAE group showed significantly higher percentages of HAI (61.8% vs. 45.2%, *P* = 0.030) and underlying liver disease (25.5% vs. 14.0%, *P* = 0.044) than the CS-PAE group. The CR-PAE group showed significantly higher percentages of inappropriate empirical therapy than the CS-PAE group (52.7% vs. 26.3%, *P* < 0.001). There was no significant difference in treatment failure between the CR-PAE and CS-PAE groups (34.5% vs. 24.7%, *P* = 0.150).

Comparisons of clinical characteristics of the CR-ABA and CR-PAE groups are shown in Table 1. The CR-ABA group showed significantly higher percentages of severe sepsis or septic shock than the CR-PAE group. Inappropriate empirical therapy was more frequent in the CR-ABA group than the CR-PAE group. All-cause 30-day mortality and treatment failure were significantly higher in the CR-ABA group than the CR-PAE group.

Clinical characteristics of patients with carbapenem-resistant *Acinetobacter baumannii* (CR-ABA) and carbapenem-resistant *Pseudomonas aeruginosa* (CR-PAE) bacteraemia

Variables	Total (n=271)	CR-ABA (n=216)	CR-PAE (n=55)	<i>P</i>
Age, mean ($\pm$ SD)	65.6 ($\pm$ 16.9)	66.0 ($\pm$ 17.2)	64.1 ($\pm$ 15.4)	0.469
Male	177 (65.3)	143 (66.2)	34 (61.8)	0.542
ICU stay at bacteraemia onset	139 (51.3)	127 (58.8)	12 (21.8)	<0.001
Hospital-acquired infection	218 (80.4)	184 (85.2)	34 (61.8)	<0.001
Healthcare-associated infection	260 (95.9)	211 (97.7)	49 (89.1)	0.004
Mixed bacteraemia	29 (10.7)	18 (8.3)	11 (20.0)	0.012
Site of infection				
Primary bacteraemia	76 (28.0)	58 (26.9)	18 (32.7)	0.387
CRBSI	103 (38.0)	91 (42.1)	12 (21.8)	0.006
Pneumonia	82 (30.3)	78 (36.1)	4 (7.3)	<0.001
Urinary tract infection	55 (20.3)	45 (20.8)	10 (18.2)	0.662
Intra-abdominal infection	26 (9.6)	16 (7.4)	10 (18.2)	0.015
Underlying medical condition				
Charlson's WIC $\geq$ 3	216 (79.7)	172 (79.6)	44 (80.0)	0.951
Heart disease	28 (10.3)	24 (11.1)	4 (7.3)	0.404
Lung disease	27 (10.0)	26 (12.0)	1 (1.8)	0.024
Chronic kidney disease	51 (18.8)	43 (19.9)	8 (14.5)	0.364
Liver disease	56 (20.7)	42 (19.4)	14 (25.5)	0.326
Diabetes mellitus	79 (29.2)	69 (31.9)	10 (18.2)	0.045
Malignancy	78 (28.8)	55 (25.5)	23 (41.8)	0.017
Cerebrovascular disease	59 (21.8)	48 (22.2)	11 (20.0)	0.721
Transplantation	16 (5.9)	11 (5.1)	5 (9.1)	0.332
Immunosuppressant use	37 (13.7)	28 (13.0)	9 (16.4)	0.512
Clinical severity				
Severe sepsis or septic shock	136 (50.2)	115 (53.2)	21 (38.2)	0.046
Pitt score, median (IQR)	4.00 (2.00-6.00)	5.00 (2.00-7.00)	2.00 (1.00-4.00)	<0.001

Inappropriate empirical antibiotics	191 (70.5)	162 (75.0)	29 (52.7)	0.001
All-cause 30-day mortality	135 (51.1)	122 (57.5)	13 (25.0)	<0.001
Treatment failure	150 (55.4)	131 (60.6)	19 (34.5)	0.001
SD, standard deviation; ICU, intensive care unit; CRBSI, catheter-related bloodstream infection; WIC, weighted index of comorbidity; IQR, interquartile range				

Antibiotic susceptibility of carbapenem-resistant isolates

Antibiotic susceptibility of carbapenem-resistant isolates is described in Table 2. Not all results of susceptibility tests were available for carbapenem-resistant isolates. For all antibiotics except colistin and trimethoprim/sulfamethoxazole, the percentages of non-susceptible isolates were significantly different between the CR-ABA and CR-PAE groups. The percentages of non-susceptible isolates, except for tigecycline and minocycline, were significantly higher in the CR-ABA group than the CR-PAE group.

Table 2

Antibiotic susceptibility of carbapenem-resistant *Acinetobacter baumannii* (CR-ABA) and carbapenem-resistant *Pseudomonas aeruginosa* (CR-PAE) isolates

Non-susceptible (I+R) isolate No. (%)	Total* (n=271)	CR-ABA (n=216)	CR-PAE (n=55)	<i>P</i>
Ceftazidime	240/268 (89.6)	209 (97.2)	31 (58.5)	<0.001
Cefepime	242/265 (91.3)	211 (98.6)	31 (60.8)	<0.001
Ciprofloxacin	239/269 (88.8)	210 (97.2)	29 (54.7)	<0.001
Amikacin	66/130 (50.8)	58 (70.7)	8 (16.7)	<0.001
Gentamicin	175/245 (71.4)	161 (77.8)	14 (36.8)	<0.001
Tobramycin	45/88 (51.1)	40 (74.1)	5 (14.7)	<0.001
Piperacillin/tazobactam	225/243 (92.6)	191 (99.0)	34 (68.0)	<0.001
Trimethoprim/sulfamethoxazole	145/174 (83.3)	134 (82.2)	11 (100.0)	0.215
Imipenem	252/260 (96.9)	211 (99.1)	41 (87.2)	0.001
Meropenem	254/261 (97.3)	213 (99.5)	41 (87.2)	<0.001
Tigecycline	24/118 (20.3)	16 (14.5)	8 (100.0)	<0.001
Colistin	4/217 (1.8)	3 (1.7)	1 (2.7)	0.529
Minocycline	47/174 (27.0)	38 (23.2)	9 (90.0)	<0.001
I, intermediate; R, resistant; *Not all isolate susceptibility test results were available, and results were presented as non-susceptible isolate number/available total (%).				

Risk factors for treatment failure

The results of univariate analysis between risk factors and treatment failure in ABA are listed in Table S3. We stratified the patients' data according to carbapenem resistance and the appropriateness of empirical therapy in the multivariate analyses of risk factors for treatment failure, because of the significant interaction between those factors.

Table 3 shows the risk factors for treatment failure in ABA identified using multivariate analysis according to the appropriateness of empirical therapy. While severe sepsis or septic shock and high Pitt bacteriaemia score were independent risk factors for treatment failure in the inappropriate empirical antibiotics group, pneumonia, and Charlson's WIC ≥ 3 were independent risk factors for treatment failure in the appropriate empirical antibiotics group.

Table 3

Risk factors for treatment failure in patients with *Acinetobacter baumannii* bacteraemia, according to the appropriateness of empirical therapy

Risk factors	Inappropriate empirical antibiotics (n=179)		Appropriate empirical antibiotics (n=125)	
	aOR (95% CI)	P	aOR (95% CI)	P
Male	-	-	2.36 (0.89-6.23)	0.084
ICU stay at bacteraemia onset	-	-	1.23 (0.36-4.25)	0.746
Healthcare-associated infection	5.14 (0.43-61.37)	0.196	-	-
Site of infection				
Primary bacteraemia	-	-	1.50 (0.47-4.78)	0.489
CRBSI	2.35 (0.98-5.64)	0.055	-	-
Pneumonia	-	-	10.56 (2.68-41.57)	0.001
Underlying medical condition				
Charlson's WIC ≥ 3	-	-	4.66 (1.07-20.36)	0.041
Heart disease	2.72 (0.66-11.31)	0.168	-	-
Lung disease	-	-	4.32 (0.65-28.67)	0.130
Clinical severity				
Severe sepsis or septic shock	22.70 (9.48-54.39)	<0.001	1.67 (0.60-4.66)	0.330
Pitt score	1.58 (1.36-1.83)	<0.001	1.15 (0.94-1.41)	0.169
Carbapenem resistance	6.17 (1.13-33.75)	0.036	4.15 (1.16-14.84)	0.029
aOR, adjusted odds ratio; CI, confidence interval; ICU, intensive care unit; CRBSI, catheter related bloodstream infection; WIC, weighted index of comorbidity; -, the variable was not included in the multivariate analysis model, because it was not significant in univariate analysis ($P > 0.10$).				

The results of multivariate analysis between risk factors and treatment failure in ABA according to carbapenem susceptibility are listed in Table S4. In the CR-ABA group, severe sepsis or septic shock (adjusted odds ratio [aOR]: 9.70, 95% confidence interval [CI]: 5.02-18.76, $P < 0.001$) and high Pitt bacteraemia score (aOR: 1.44, 95% CI: 1.27-1.63, $P < 0.001$) were significantly associated with treatment failure.

The results of univariate analysis between risk factors and treatment failure in PAE bacteraemia are listed in Table S5. Significant risk factors for treatment failure in PAE identified by multivariate analysis are

listed by the appropriateness of empirical therapy in Table 4. HAI, severe sepsis or septic shock, and high Pitt score were independent risk factors for treatment failure in both the inappropriate and appropriate empirical antibiotics groups. Urinary tract infection was associated with decreased treatment failure in the appropriate antibiotics group. Table S6 shows the significant risk factors for treatment failure in PAE by multivariate analysis according to carbapenem susceptibility. In the CR-PAE group, HAI (aOR: 25.03, 95% CI: 2.15-291.99, $P = 0.010$), use of immunosuppressant (aOR: 32.08, 95% CI: 1.58-652.62, $P = 0.024$), and high Pitt bacteraemia score (aOR: 1.47, 95% CI: 1.05-2.07, $P = 0.025$) were significantly associated with treatment failure.

Carbapenem resistance and treatment failure

In ABA, carbapenem resistance was independently associated with treatment failure in both the inappropriate (aOR: 6.17; 95% CI: 1.13-33.75; $P = 0.036$) and appropriate empirical treatment groups (aOR: 4.15; 95% CI: 1.16-14.84; $P = 0.029$; Table 3). In PAE, carbapenem resistance was not significantly associated with treatment failure in both the inappropriate (aOR: 0.91, 95% CI: 0.27-3.03, $P = 0.879$) and appropriate empirical antibiotics groups (aOR: 1.76, 95% CI: 0.45-6.87, $P = 0.418$; Table 4).

Table 4

Risk factors for treatment failure in patients with *Pseudomonas aeruginosa* bacteraemia, according to the appropriateness of empirical therapy

Risk factors	Inappropriate empirical antibiotics (n=78)		Appropriate empirical antibiotics (n=163)	
	aOR (95% CI)	<i>P</i>	aOR (95% CI)	<i>P</i>
Male	-	-	3.61 (1.23-10.65)	0.020
ICU stay at bacteraemia onset	-	-	1.32 (0.41-4.29)	0.645
Hospital-acquired infection	4.57 (1.34-15.54)	0.015	2.88 (1.09-7.65)	0.033
Site of infection				
Primary bacteraemia	-	-	2.79 (0.94-8.25)	0.064
Pneumonia	4.61 (0.68-31.20)	0.117	3.82 (1.09-13.32)	0.036
Urinary tract infection	-	-	0.13 (0.02-0.79)	0.027
Underlying medical condition				
Malignancy	2.09 (0.55-7.91)	0.276	1.81 (0.66-4.96)	0.251
Immunosuppressant use	3.31 (0.78-14.11)	0.105	1.58 (0.54-4.63)	0.406
Clinical severity				
Severe sepsis or septic shock	5.43 (1.42-20.76)	0.013	10.33 (3.56-29.94)	<0.001
Pitt score	1.59 (1.21-2.10)	0.001	1.59 (1.27-1.99)	<0.001
Carbapenem resistance	0.91 (0.27-3.03)	0.879	1.76 (0.45-6.87)	0.418

aOR, adjusted odds ratio; CI, confidence interval; ICU, intensive care unit

Discussion

Resistance to carbapenem is an important concern in both ABA and PAE bacteraemia. Here, we found different clinical characteristics and impacts of carbapenem-resistance on outcomes in ABA and PAE bacteraemia.

Carbapenem resistance was an independent risk factor for treatment failure in ABA bacteraemia regardless of the appropriateness of empirical antibiotics. This finding agrees with previous studies, which report that carbapenem resistance is significantly associated with mortality in ABA bacteraemia (10, 11). A systematic review showed that carbapenem resistance may increase the risk of mortality of ABA infection (12). In contrast, we found that carbapenem resistance was not an independent risk factor for treatment failure in PAE bacteraemia regardless of the appropriateness of empirical antibiotics. This

is in agreement with a previous study showing that carbapenem resistance was not an independent risk factor for mortality in PAE bacteraemia (13). This difference in the impact of carbapenem-resistance on ABA and PAE may be due to available treatment options, different sites of infection, and differences of clinical severity.

We found different susceptibilities and clinical characteristics in ABA and PAE bacteraemia. In ABA bacteraemia, 71.1% (216/304) of the cases were carbapenem resistant, while only 22.8% (55/241) of the cases in PAE bacteraemia were carbapenem resistant. The higher percentage of carbapenem resistance in ABA compared with PAE bacteraemia is consistent with previous results, which showed that the proportion of carbapenem resistance was 92.1% in ABA strains and the proportions of resistance were 19.5% to imipenem and 18.1% to meropenem in PAE strains (14). We found that CR-ABA have resistance to almost all antibiotics; however, CR-PAE is susceptible to some antibiotics such as ciprofloxacin and amikacin. The difference in antibiotic susceptibility might explain the difference in the proportion of inappropriate empirical therapies between the groups. However, the results of multivariate analysis using stratification to the appropriateness of empirical therapy showed that carbapenem resistance is an independent risk factor for treatment failure in ABA, even if the empirical therapy was appropriate. This might be related to the virulence of ABA. A previous study suggested that high bacterial cytotoxicity significantly affected the mortality in ABA ventilator-associated pneumonia (15).

Treatment failure was not significantly different between CR-PAE and CS-PAE, whereas it was significantly different between CR-ABA and CS-ABA. Moreover, a previous study found a significant difference in hospital mortality between CR-ABA and CS-ABA, but not between CR-PAE and CS-PAE (16). Compared to the CR-PAE group, the CR-ABA group showed a significantly higher percentage of treatment failure (60.6% vs. 34.5%). The different clinical severity and antibiotics susceptibility between CR-ABA and CR-PAE might contribute to the differences in treatment failure. Clinicians should consider the higher rates of treatment failure when carbapenem resistance is detected in ABA.

In ABA bacteraemia, we found independent risk factors, including pneumonia, Charlson's WIC ≥ 3 , and carbapenem resistance in the appropriate empirical antibiotics group. We speculate that if pneumonia was the source of bacteraemia, or if carbapenem resistance was detected in ABA bacteraemia, the risk of treatment failure would be high, even if appropriate empirical antibiotics were administered. One study identified independent risk factors for mortality, including carbapenem resistance, neutropenia, and prolonged intensive care unit stay in ABA bacteraemia (10). Another study showed that septic shock, carbapenem resistance, pneumonia, and inappropriate definite antimicrobial therapy are independent risk factors for 14-day mortality (17).

Independent risk factors for treatment failure in PAE bacteraemia included HAI, severe sepsis or septic shock, and high Pitt bacteraemia score, regardless of the appropriateness of empirical antibiotics. One retrospective study reported the presence of septic shock and high Acute Physiologic Assessment and Chronic Health Evaluation II score as independent risk factors for 14-day mortality (13). Another study showed that recent hospitalisation, corticosteroid treatment, Charlson WIC, non-urinary source, and high

Sequential Organ Failure Assessment score are significant risk factors for 30-day mortality in PAE bacteraemia (18).

By additional analysis according to carbapenem resistance, we found that inappropriate empirical antibiotics were independently associated with treatment failure in the CS-PAE group. Appropriate empirical antibiotics, including antipseudomonal coverage, may be important in the management of patients with risk of *Pseudomonas* infection. The independent risk factors for treatment failure in the CR-PAE group were HAI, use of immunosuppressants, and high Pitt bacteraemia score. This is consistent with a previous study reporting that high Pitt bacteraemia score is a predictor of death in CR-PAE bacteraemia (19).

In both the CR-ABA and CS-ABA groups, inappropriate empirical antibiotics was not an independent factor for treatment failure. Furthermore, a previous study found that 28-day mortality was not independently associated with appropriate empirical antimicrobial therapy in invasive *Acinetobacter* infection (20). Although studies found that appropriate antimicrobial therapy decreased 14-day mortality (21, 22), these defined appropriate antimicrobial therapy as antibiotics administration within 48 hours after the onset of bacteraemia and did not address the appropriateness of empirical antibiotics.

This study has several limitations. First, being an observational study, it was prone to bias and unmeasured confounding factors. Second, no microbiologic investigation other than antibiotic susceptibility tests was conducted on the strains. As the effect of carbapenemase on clinical outcomes is not clear, further studies on the effect of the microbiological characteristics on the outcome in ABA and PAE are needed. Lastly, while colistin was the only drug available in Korea for pandrug-resistant ABA and difficult-to-treat PAE at the time of the study, several new drugs, such as ceftolozane-tazobactam, ceftazidime-avibactam, imipenem-relebactam, and cefiderocol were available in other countries (23, 24). This difference in availability of drugs may have contributed to the differences in prognosis.

Conclusions

In conclusion, we identified clinical characteristics and risk factors associated with treatment failure in ABA and PAE bacteraemia. Carbapenem resistance was associated with increased risk of treatment failure in ABA, but not in PAE bacteraemia. Because carbapenem resistance is significantly associated with treatment failure in the appropriate empirical antibiotics group with ABA, this study suggests that appropriate empirical antibiotics cannot improve the clinical outcomes in CR-ABA. Hence, we suggest that it would be important to reduce the occurrence of CR-ABA through infection control in high-risk groups such as patients in intensive care units.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (IRB no. B-1804-463-105) and the IRBs of each participating hospital. The study was conducted in accordance with the principles outlined in the 1964 Declaration of Helsinki and its later amendments. The need for informed consent was waived by the IRBs.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author, KHS, upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

KHS and KHP conceptualized the study. CML and YJK analyzed the data and drafted the initial manuscript. SIJ, SEK, WBP, PGC, ESK, CJK, HJC, SL, SHL, YJ, JHB, SC, YGK, YMK and HBK collected patient data and made contributions to the manuscript. KHS and HBK administrated the project. KHS and KHP revised and edited the final manuscript. All authors approved the final manuscript for publication.

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