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Natural prognosis of carbapenem-resistant *Acinetobacter baumannii* bacteremia in patients who did not receive appropriate antibiotic treatment

A retrospective multicenter study in Korea

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Abstract

Carbapenem-resistant *Acinetobacter baumannii* (CRAB) infection is a major issues in current era. The aim of study was to investigate the natural prognosis and prognostic factors associated with 28-day mortality in patients with CRAB bacteremia who were not receiving appropriate antibiotic treatment.

Adult patients with CRAB bacteremia were retrospectively identified between April 2012 and March 2015 at 5 tertiary hospitals in Republic of Korea. Patients who were transferred to another hospital within 28 days of onset of bacteremia and who receive appropriate antibiotics more than 48 hours were excluded. We investigated prognostic factors associated with 28-day mortality in patients with CRAB bacteremia without appropriate antibiotic treatment.

Of enrolled 205 patients, 143 (69.8%) patients died within 28 days after blood culture. Of patients with 28-day mortality, 88.9% (127/143) of patients died within 5 days. Of 78 patients who survived more than 5 days, the 28-day mortality was 20.5% (16/78). Diabetes mellitus (adjusted odds ratio [aOR] 3.81, 95% confidence interval [95% CI] 1.19–12.20), immunocompromised (aOR 8.72, 95% CI 2.62–29.70), sequential organ failure assessment (SOFA) ≥ 10 (aOR 13.87, 95% CI 3.70–51.96), vasopressor use (aOR 7.03, 95% CI 1.79–27.60), and pneumonia (aOR 4.44, 95% CI 1.67–11.78) were found to be the factors independently associated with the 28-day mortality.

The 28-day mortality in patients with CRAB bacteremia without appropriate treatment was high, although some patients could survive. Severity and underlying conditions were important prognostic factors in patients with CRAB bacteremia.

Abbreviations: AIDS = acquired immunodeficiency syndrome, aOR = adjusted odds ratio, APACHE = acute physiology assessment and chronic health evaluation, CKD = chronic kidney disease, CRAB = carbapenem-resistant Acinetobacter baumannii, DM = diabetes mellitus, HIV = human immunodeficiency virus, IQR = interquartile range, SOFA = sequential organ failure assessment.

Keywords: *Acinetobacter baumannii*, bacteremia, carbapenem-resistant, prognosis

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

The local institutional review board approved this study (2016-02-011).

Informed consent was waived because of the retrospective nature of the study and the analysis used anonymous clinical data.

The corresponding author had full access to all data and had the final responsibility for the decision making to submit the manuscript for publication.

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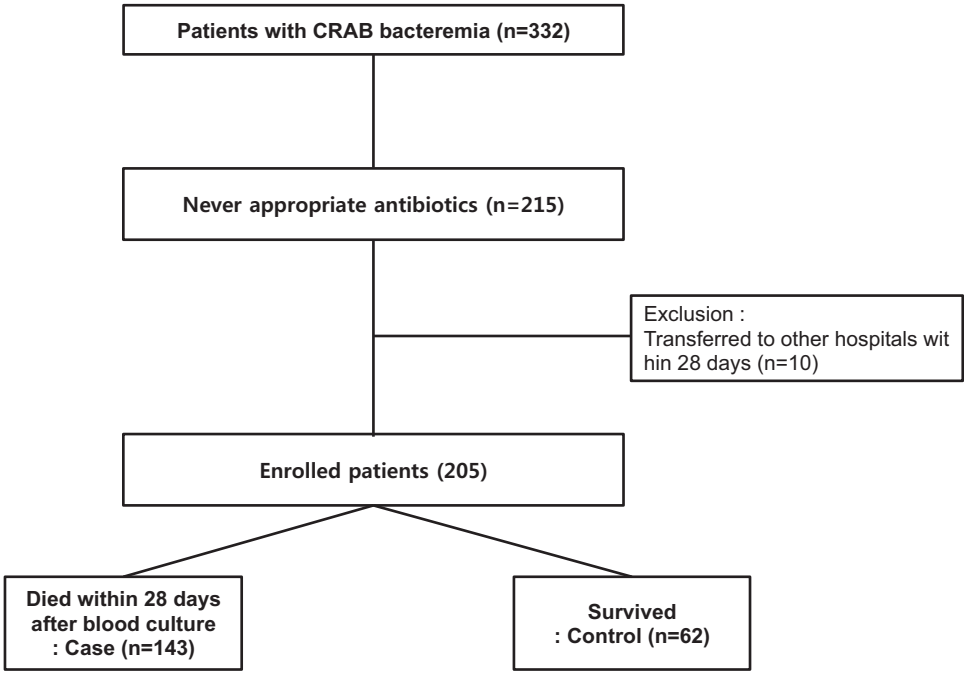

Figure 1. The study algorithm for the analysis of prognostic factors associated with 28-day mortality in patients with carbapenem-resistant *Acinetobacter baumannii* (CRAB) bacteremia who did not receive appropriate antibiotic treatment.

1. Introduction

Acinetobacter baumannii is one of the major pathogens of hospital-acquired infection, which causes various diseases such as pneumonia, catheter-related infection, and urinary tract infection.[1] This nonferment gram-negative rod bacteria has been notorious for its strong ability to acquire resistance to various antibiotics.[1] Especially, high rate of carbapenem-resistant clinical isolates has been reported worldwide.[2–4] In Korea, the rate of carbapenem resistance of *A baumannii* identified in hospitals has been reported to reach 90%.[5]

Understanding of natural prognosis of Carbapenem-resistant *A baumannii* (CRAB) bacteremia is important for establishing diagnostic and treatment strategies. If patients have died before the diagnosis of CRAB bacteremia, and they cannot receive appropriate antibiotics, we need to use a method that can be quickly diagnosed CRAB bacteremia. Choosing antibiotics against CRAB as empirical treatment also should be considered in this case. If patients survive without appropriate antibiotics, they may not need to be given immediately empirical antibiotics than can result in antibiotics toxicity and resistance. Information on risk factors associated with mortality can be useful for development of individualized strategies. Also, knowledge on natural prognosis can be used as comparative data for studies on diagnostic and therapeutic intervention.

Therefore, we investigated the natural history of patients with CRAB bacteremia without receiving appropriate antibiotic treatment. In addition, we investigated prognostic factors associated with 28-day mortality.

2. Methods

2.1. Study population and design

This retrospective multicenter study was conducted at 5 tertiary teaching hospitals located in Seoul, Bucheon, Ilsan, and Cheonan, Republic of Korea. By reviewing the daily computerized reports of blood cultures, the patients aged ≥18 years with a CRAB-positive blood culture were identified between April 2012 and March 2015. Bacteremia was defined as ≥ a positive blood culture for *A baumannii* and the presence of the clinical features compatible with infection. If a patient had undergone recurrent episodes of *A baumannii* bacteremia during the study period, only the first episode was considered.

The algorithm for selecting the research subjects and the research plan is shown in Fig. 1. It was defined as an appropriate antibiotic therapy if at least 1 antimicrobial agent to which the causative pathogen was susceptible was administered for more than 48 hours.[6] Patients who were transferred to another hospital within 28 days of onset of bacteremia were excluded from the study. Among patients not receiving appropriate antibiotic treatment, the case group was defined as a patient who died within 28 days after blood culture test was done and survivors were categorized into the control group. To identify factors associated with 28-day mortality in patients with CRAB bacteremia without appropriate antibiotic treatment, clinical characteristics of case group and control group were compared.

2.2. Data collection

Patient's demographic data and information on comorbidity (malignancy, neurologic diseases, chronic lung diseases, diabetes mellitus [DM], liver cirrhosis on Child B or C classification, heart failure, and chronic kidney diseases [CKD]) were collected. Patients were defined as immunocompromised if they had human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS), were on solid organ transplantation, hematopoietic stem cell transplantation, had received chemotherapy within 6 weeks, had received systemic steroid equivalent to or higher than 20 mg of prednisone for 2 weeks or other immunosuppressive agents within 2 weeks before hospitaliza-

tion. The severity of comorbidities was classified according to the McCabe and Jackson Classification system.[7] Source of infection was determined according to the guidelines issued by the Centres for Disease Control and Prevention.[8] Mechanical ventilation, vasopressor use, dialysis, APACHE II score,[9] and the Sequential Organ Failure Assessment (SOFA) score [10] were chosen as the index of severity. Previous CRAB colonization was defined as the isolation of CRAB from any clinical specimens within 30 days of the CRAB blood culture without symptoms or signs. Polymicrobial bacteremia was defined as isolation of any organism from blood within 2 days of the CRAB blood culture. The practice of 3rd generation antibiotics such as cephalosporins, cefepime, piperacillin/tazobactam, fluoroquinolones, carbapenems, tigecycline, and colistin just before CRAB blood culture was investigated.

2.3. Microbiologic methods

A baumannii identification was performed using standard methods. At least 4 species, *A calcoaceticus, A baumannii, A nosocomialis,* and *A pitti*, are invariably reported as *A baumannii* by clinical microbiology laboratories because biochemical methods cannot further differentiate them to the species level. Susceptibility testing was done using the microdilution method (MicroScan system; Baxter Health Care, West Sacramento, CA), and results were interpreted according to the National Committee for Clinical Laboratory Standards guidelines.[11] Imipenem resistance was defined as a minimal inhibitory concentration of 16 μg/mL or above. *A baumannii* isolates with imipenem resistance were considered CRAB.

2.4. Statistical analysis

Statistical analyses were performed with SPSS for Windows (version 14.0); SPSS Inc, Chicago, IL). Continuous variables were compared using the Mann–Whitney *U* test or Student *t* test, as appropriate. Categorical variables were compared using Pearson χ^2 test or Fisher exact test. A binary logistic regression was used to identify variables significantly associated with 28-day mortality in patients with CRAB bacteremia who did not receive appropriate antibiotic treatment. The variables found to be statistically significant at a 5% level in the univariate analysis were included in the multivariate analysis. Among indices of severity, SOFA score ≥ 10 was chosen as a binary variable according to the calculation of receiver operating curve. All significance testing was 2-tailed, and $P < .05$ was considered statistically significant.

3. Results

A total of 332 patients with CRAB bacteremia were identified. One hundred eleven patients who received appropriate antibiotics and 10 patients who were transferred to other hospitals within 28 days after the blood culture test was done were excluded. Finally, 205 patients who did not appropriate antibiotics were enrolled in the study. It usually took 4 days (range, 2–8 days) to receive results after blood culture was done. Among patients who did not receive appropriate antibiotics, carbapenems (114, 55.6%) were most commonly prescribed as antibiotics for gram-negative bacteremia, followed by piperacillin/tazobactam (40, 19.5%) and cefepime (1.4%). Thirteen patients were categorized into the group who did not receive appropriate antibiotics despite of colistin usage, because they died before administration of colistin for more than 48 hours. The 28-day mortality in patients with CRAB bacteremia without appropriate antibiotic treatment was 69.8% (143/205). Of patients with 28-day mortality, 88.9% (127/143) of patients died within 5 days. Patients who died within 28 days were included in the case group and survivors were classified as the control group.

The differences in the clinical characteristics of case group and control groups are shown in Table 1. Patients with 28-day mortality were less likely to be included in the nonfatal McCabe classification (case group 53, 37.1% vs control group 43, 69.4%; $P < .01$). Malignancy (case group 51, 35.7% vs control group 13, 21.0%; $P = .048$), DM (case group 50, 35.0% vs control group 13, 21.0%; $P = .049$), CKD (case group 23, 16.0% vs control group 3, 4.8%; $P = .04$) and immunocompromised status (case group 41, 28.7% vs control group 8, 12.9%; $P = .02$) were underlying medical conditions that were more frequently found in patients who died within 28 days. CRAB bacteremia was more frequently developed during intensive care unit hospitalization in patients with 28-day mortality (case group 117, 81.8% vs control group 31, 50.0%; $P < .01$). Of severity indices, the SOFA score (median 13, interquartile range [IQR] 9–16 vs 5, 4–7; $P < .001$) and APACHE II score (median 22, IQR 14–31 vs 15, 4–21; $P < .001$) of patients who died within 28 days were higher than those who survived. Also, patients with 28-day mortality were more likely to receive mechanical ventilation (case group 95, 66.4% vs control group 17, 27.4%; $P < .001$), vasopressor use (case group 92, 64.3% vs 4, control group 6.5%; $P < .01$), or dialysis (case 46, 32.2% vs control group 3, 4.8%; $P < .01$). As shown in Table 2, variables of McCabe classification, malignancy, DM, CKD, immunocompromised status, ICU admission, SOFA ≥ 10, mechanical ventilation, vasopressor use, dialysis, and pneumonia as a source of bacteremia were included in the multivariate analysis. Finally, DM (adjusted odds ratio [aOR] 3.81, 95% confidence interval [95% CI] 1.19–12.20), immunocompromised (aOR 8.72, 95% CI 2.62–29.70), SOFA ≥ 10 (aOR 13.87, 95% CI 3.70–51.96), vasopressor use (aOR 7.03, 95% CI 1.79–27.60), and pneumonia (aOR 4.44, 95% CI 1.67–11.78) were found to be the factors independently associated with the 28-day mortality in patients with CRAB bacteremia who did not receive appropriate antibiotic treatment.

The survival distribution of patients with CRAB bacteremia without adequate antibiotic treatment is shown in Fig. 2. Of patients who survived more than 5 days, the 28-day mortality was 20.5% (16/78). All of 23 patients who survived more than 5 days and did not have any of bad prognostic factors survived more than 28 days despite not receiving appropriate antibiotic treatment.

4. Discussion

This study reports that patients with CRAB bacteremia who did not receive appropriate antibiotic treatment died early. Despite high mortality in patients with CRAB bacteremia, it is interesting to note that some patients survived from CRAB bacteremia even after not receiving appropriate antibiotic treatment. This is the first clinical study that shows natural prognosis of patients with CRAB bacteremia without appropriate antibiotics. The present study was expected to be used for anticipating prognosis of patients with CRAB bacteremia and establishing treatment strategies for CRAB bacteremia.

Major cases of mortality occurred within 5 days and this was also the case in patients without any risk factor associated with

Table 1

Comparison of clinical characteristics between case and control groups with carbapenem-resistant *Acinetobacter baumannii* (CRAB) bacteremia in patients who did not receive appropriate antibiotic treatment.

Clinical characteristics	Case (n = 143)	Control (n = 62)	*P* value
Demographics			
Age, median (IQR)	69 (58–77)	73 (55–78)	.65
Gender, male	87 (60.8)	56 (39.2)	.53
Underlying medical conditions			
McCabe classification			
Nonfatal	53 (37.1)	43 (69.4)	<.01
Fatal	60 (42.0)	18 (29.0)	
Rapid fatal	30 (21.0)	1 (1.6)	
Malignancy	51 (35.7)	13 (21.0)	.048
Neurologic disease	39 (27.3)	25 (40.3)	.07
Chronic lung disease	36 (25.2)	9 (14.5)	.10
Diabetes mellitus	50 (35.0)	13 (21.0)	.049
Liver cirrhosis	17 (11.9)	4 (6.5)	.32
Heart failure	15 (10.5)	4 (6.5)	.44
Chronic kidney disease	23 (16.0)	3 (4.8)	.04
ESRD	12 (8.4)	1 (1.6)	.11
Immunocompromised	41 (28.7)	8 (12.9)	.02
Previous surgery	33 (23.1)	11 (17.7)	.46
Previous HD (IQR)	14 (8–31)	14 (7–32)	.74
In ICU admission	117 (81.8)	31 (50.0)	<.01
Previous ICU days (IQR)	8 (5–14)	11 (7–26)	.07
Severity			
SOFA score, median (IQR)	13 (9–16)	5 (4–7)	<.01
APACHE II (IQR)	22 (14–31)	15 (4–21)	<.01
Mechanical ventilation	95 (66.4)	17 (27.4)	<.01
Vasopressor	92 (64.3)	4 (6.5)	<.01
Dialysis	46 (32.2)	3 (4.8)	<.01
Central venous catheter	98 (68.5)	36 (58.1)	.15
Previous CRAB colonization	40 (28.0)	11 (17.7)	.12
Candida colonization	22 (15.4)	10 (16.1)	>.99
Polymicrobial bacteremia	21 (14.7)	15 (24.2)	.11
Source of bacteremia			
Pneumonia	79 (55.2)	16 (25.8)	<.01
Catheter-related infection	6 (4.2)	8 (12.9)	.03
Intraabdominal infection	7 (4.9)	4 (6.5)	.74
Unknown	45 (31.5)	28 (45.2)	.08
Previous antibiotics			
Fluoroquinolones	46 (32.2)	21 (33.9)	.87
Broad-spectrum cephalosporin	49 (34.3)	20 (32.3)	.87
Antipseudomonal penicillin/beta-lactamase inhibitor	66 (46.2)	23 (37.7)	.28
Carbapenems	71 (49.7)	27 (43.5)	.45

Data are numbers (%) of patients.

Case group, patients who died within 28 days without receiving appropriate antibiotic treatment; Control group, patients who survived for more than 28 days without receiving appropriate antibiotic treatment. APACHE II = acute physiology and chronic health evaluation II, ESRD = end-stage renal disease, HD = hospital days, ICU = intensive care unit, IQR = interquartile range, SOFA = sequential organ failure assessment.

Table 2

Prognostic factors associated with 28-day mortality in patients with carbapenem-resistant *Acinetobacter baumannii* (CRAB) bacteremia who did not receive appropriate antibiotic treatment.

Clinical characteristics	Univariate analysis, odds ratio (95% CI)	Multivariate analysis Adjusted odds ratio (95% CI)
Underlying conditions		
Fatal or rapidly fatal vs nonfatal McCabe classification	3.84 (2.03–7.27)	
Malignancy	2.09 (1.04–4.21)	
Diabetes mellitus	2.03 (1.01–4.09)	3.81 (1.19–12.20)
Chronic kidney disease	3.77 (1.09–13.06)	
Immunocompromised vs immunocompetent	2.71 (1.19–6.20)	8.72 (2.62–29.07)
In ICU vs in general ward	4.50 (2.34–8.66)	
Severity		
SOFA ≥10 vs SOFA < 10	30.79 (10.45–90.73)	13.87 (3.70–51.96)
Mechanical ventilation	5.35 (2.77–10.34)	
Vasopressor usage	26.16 (8.98–76.21)	7.03 (1.79–27.60)
Dialysis	9.33 (2.78–31.34)	
Source of bacteremia		
Pneumonia vs others	3.55 (1.84–6.85)	4.44 (1.67–11.78)

ICU = intensive care unit, SOFA = sequential organ failure assessment.

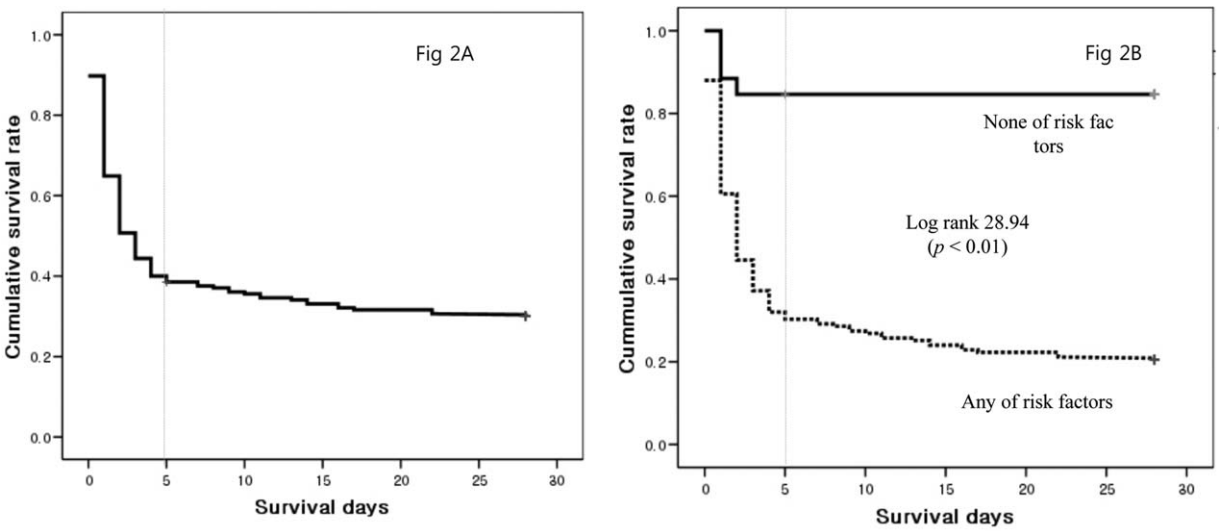

Figure 2. Kaplan–Meier survival curve of patients with carbapenem-resistant *Acinetobacter baumannii* (CRAB) bacteremia without appropriate antibiotic treatment. Figure B shows the comparison of survival between patients with any of risk factor and with none of risk factor.

28 day mortality (Fig. 2). However, none of patients who did not have any poor prognostic factors died if they survived from CRAB bacteremia for more than 5 days. This result suggests that diagnostics and therapeutic strategies for CRAB bacteremia should focus on reducing mortality of those who died within 5 days. As delayed treatment increases the mortality,[12] empirical treatment including antibiotics against CRAB which can reach the therapeutic level quickly could be a possible option in endemic areas. To make use of early diagnostic tools such as matrix-assisted laser desorption ionization time-of-flight mass spectrometry,[13] an effective therapeutic regimen is mandatory. However, colistin, the current drug of choice for CRAB, may not be suitable weapon owing to its pharmacokinetic/ pharmacodynamic characteristics.[14] Hopefully, ongoing research will lead to the development of a monoclonal antibody that binds to the surface of *A baumannii*.[15]

Three aspects to determine the prognosis of patients with CRAB bacteremia include host factor, therapeutic factor and microbiologic factor. First, comorbidity of host is a well-known prognostic factor associated with mortality in patients with CRAB bacteremia. In a previous observation-based study, Charlson index (hazard ratio 1.16, 95% CI 1.02–1.32; *P* .028) was associated with 30-day crude mortality of patients with CRAB bacteremia.[16] A prospective cohort study involving adult patients with CRAB infection also reported McCabe classification as a prognostic factor associated with overall mortality.[17] The association of DM and immunocompromised status with higher 28-day mortality in our study is consistent with the previous studies. Second, it is evident that severity was associated with prognosis in CRAB bacteremia as SOFA $\geq$ 10 was associated with higher 28-day mortality in our study. In addition to the SOFA score,[18] Pitt Bacteremia Score,[19] septic shock,[12] and APACHE II score [20] have been reported as severity index associated with mortality in CRAB infection. The severity of bacteremia is not only affected by the host factor but also by the virulence of microorganisms. Biofilm formation, phospholipase C production, hemolytic activity, acinetobactin production, and rpoB gene encoding the β-subunit of the RNA polymerase have been known as virulence factors of *A baumannii*.[21,22] Interestingly, there are reports stating that mortality varies depending on the clone.[18,23,24] This phenomenon can be explained by the fact that only certain clone has a virulence factor.[25] Unfortunately, in our retrospective study, microbiologic factors associated with severity of CRAB bacteremia could not be evaluated, because isolates of CRAB were not collected during the study period. This result emphasizes the necessity of microbiologic analysis in the future.

This study had several limitations. First, some variables that affected the outcomes in patients with CRAB bacteremia may have been omitted from the analysis due to the retrospective nature of the study. Second, death in some patients might not have been caused by CRAB bacteremia, but rather by alternative causes such as terminal cancer or impediments to care such as refusal of intensive care treatment. Third, the definition of appropriate empirical antibiotics can be controversial. In our previous analysis, appropriate empirical antimicrobial therapy for more than 48 hours, within 5 days of the onset of bacteremia, was observed as an associated factor with survival in patients with CRAB bacteremic pneumonia.[6] Based on this analysis, we defined appropriate antibiotics as described in the method. Lastly, we studied *A baumannii complex* rather than *A baumannii*. A variable of species that could affect mortality was not evaluated,[26] although previous studies reported that about 90% of *A baumannii complex* with multidrug or carbapenem resistance belonged to the genomic species of *A baumannii*. We are in the process of carrying out prospective studies on carbapenem-resistant gram-negative bacteremia including microbiological analysis.

In conclusion, most of the patients with CRAB bacteremia died early, although some patients with CRAB bacteremia can survive without appropriate antibiotic treatment. Severity and underlying conditions were important prognostic factors in patients with CRAB bacteremia. This study suggests that efforts should be made to find ways to reduce the early mortality in patients CRAB bacteremia.

Author contributions

Conceptualization: Tark Kim, Eun Jung Lee, Seong Yeon Park, Ki-Ho Park.

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Validation: Tark Kim, Eun Jung Lee.
Writing – original draft: Tark Kim.
Writing – review & editing: Tark Kim, Eun Jung Lee.

References

[1] Phillips M. *Acinetobacter* species. In: Jonh E. Bennett RD, Martin J. Blaser, ed. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. Vol 2. Elsevier Saunders; 2015:2552–2558.

[2] Hsu LY, Apisarnthanarak A, Khan E, et al. Carbapenem-Resistant *Acinetobacter baumannii* and Enterobacteriaceae in South and Southeast Asia. Clin Microbiol Rev 2017;30:1–22.

[3] Labarca JA, Salles MJ, Seas C, et al. Carbapenem resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in the nosocomial setting in Latin America. Crit Rev Microbiol 2016;42:276–92.

[4] Lob SH, Hoban DJ, Sahm DF, et al. Regional differences and trends in antimicrobial susceptibility of *Acinetobacter baumannii*. Int J Antimicrob Agents 2016;47:317–23.

[5] Kim D, Ahn JY, Lee CH, et al. Increasing resistance to extended-spectrum cephalosporins, fluoroquinolone, and carbapenem in gram-negative bacilli and the emergence of carbapenem non-susceptibility in klebsiella pneumoniae: analysis of korean antimicrobial resistance monitoring system (KARMS) data from 2013 to 2015. Ann Lab Med 2017;37:231–9.

[6] Park SY, Lee EJ, Kim T, et al. Early administration of appropriate antimicrobial agent to improve the outcome of carbapenem resistant *acinetobacter baumannii* complex bacteremic pneumonia. Int J Antimicrob Agents 2018;51:407–12.

[7] McCabe WR, Jackson GG. Gram-negative bacteremia. l. Etiology and ecology. Arch Intern Med 1962;110:847–55.

[8] Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008;36:309–32.

[9] Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med 1985;13:818–29.

[10] Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 1996;22:707–10.

[11] CLSI (2011) Performance standards for antimicrobial susceptibility testing; twenty-first informational supplement, Wayne, PA.

[12] Freire MP, de Oliveira Garcia D, Garcia CP, et al. Bloodstream infection caused by extensively drug-resistant *Acinetobacter baumannii* in cancer patients: high mortality associated with delayed treatment rather than with the degree of neutropenia. Clin Microbiol Infect 2016;22:352–8.

[13] Wenzler E, Goff DA, Mangino JE, et al. Impact of rapid identification of *Acinetobacter Baumannii* via matrix-assisted laser desorption ionization time-of-flight mass spectrometry combined with antimicrobial stewardship in patients with pneumonia and/or bacteremia. Diagn Microbiol Infect Dis 2016;84:63–8.

[14] Nation RL, Velkov T, Li J. Colistin and polymyxin B: peas in a pod, or chalk and cheese? Clin Infect Dis 2014;59:88–94.

[15] Nielsen TB, Pantapalangkoor P, Luna BM, et al. Monoclonal antibody protects against *Acinetobacter baumannii* infection by enhancing bacterial clearance and evading sepsis. J Infect Dis 2017;216:489–501.

[16] Amat T, Gutierrez-Pizarraya A, Machuca I, et al. The combined use of tigecycline with high-dose colistin might not be associated with higher survival in critically ill patients with bacteraemia due to carbapenem-resistant *Acinetobacter baumannii*. Clin Microbiol Infect 2018;24:630–4.

[17] Hernandez-Torres A, Garcia-Vazquez E, Gomez J, et al. Multidrug and carbapenem-resistant *Acinetobacter baumannii* infections: factors associated with mortality. Med Clin (Barc) 2012;138:650–5.

[18] Nutman A, Glick R, Temkin E, et al. A case-control study to identify predictors of 14-day mortality following carbapenem-resistant *Acinetobacter baumannii* bacteraemia. Clin Microbiol Infect 2014;20:O1028–34.

[19] Gu Z, Han Y, Meng T, et al. Risk factors and clinical outcomes for patients with *Acinetobacter baumannii* bacteremia. Medicine (Baltimore) 2016;95:e2943.

[20] Liu CP, Shih SC, Wang NY, et al. Risk factors of mortality in patients with carbapenem-resistant *Acinetobacter baumannii* bacteremia. J Microbiol Immunol Infect 2016;49:934–40.

[21] Ali HM, Salem MZM, El-Shikh MS, et al. Investigation of the virulence factors and molecular characterization of the clonal relations of multidrug-resistant *Acinetobacter baumannii* isolates. J AOAC Int 2017;100:152–8.

[22] Perez-Varela M, Corral J, Vallejo JA, et al. Mutations in the beta-subunit of the RNA polymerase impair the surface-associated motility and virulence of *Acinetobacter baumannii*. Infect Immun 2017;85:e00327-17.

[23] de Breij A, Eveillard M, Dijkshoorn L, et al. Differences in *Acinetobacter baumannii* strains and host innate immune response determine morbidity and mortality in experimental pneumonia. PLoS One 2012;7:e30673.

[24] Jones CL, Clancy M, Honnold C, et al. Fatal outbreak of an emerging clone of extensively drug-resistant *Acinetobacter baumannii* with enhanced virulence. Clin Infect Dis 2015;61:145–54.

[25] Eijkelkamp BA, Stroeher UH, Hassan KA, et al. Comparative analysis of surface-exposed virulence factors of Acinetobacter baumannii. BMC Genomics 2014;15:1020.

[26] Liu YM, Lee YT, Kuo SC, et al. Comparison between bacteremia caused by *Acinetobacter pittii* and *Acinetobacter nosocomialis*. J Microbiol Immunol Infect 2017;50:62–7.