Subsequent Multidrug-Resistant Bacteremia Is a Risk Factor for Short-Term Mortality of Patients with Ventilator-Associated Pneumonia Caused by *Acinetobacter baumannii* in Intensive Care Unit: A Multicenter Experience

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Acinetobacter baumannii has been considered the prevailing pathogen responsible for ventilator-associated pneumonia (VAP), a condition associated with high morbidity and mortality, among patients in Intensive Care Units (ICUs).[1-3] However, data regarding VAP caused by *A. baumannii* (AbVAP) in China are limited. In this retrospective study, we aimed to assess the clinical features and outcomes of Chinese patients with AbVAP and thus identify risk factors for 30-day ICU mortality. The medical and surgical ICUs of four tertiary hospitals in Shanghai (Zhongshan Hospital of Fudan University, Shanghai Seventh People's Hospital, Qingpu Branch of Zhongshan Hospital of Fudan University, and Huashan Hospital of Fudan University) participated in this study, and the collection of data was started in March 2017. The study was reviewed and approved by the Clinical Research Ethics Committees of Zhongshan Hospital (No. 2011212), Huashan Hospital (No. 2013302), and Shanghai Seventh People's Hospital (No. 2017IRBQY14). The requirement for informed patient consent was waived for this study, and patients' identities were coded to ensure the confidentiality of data.

The following patient inclusion criteria were set: (i) ICU patients from the four participating hospitals who were newly diagnosed with AbVAP between January 2014 and October 2015, as confirmed by the hospital database and (ii) an age older than 18 years. *A. baumannii* was identified using a Phoenix™-100 automated microbiology system (Becton Dickinson and Company, Franklin Lakes, NJ, USA). The following patient data were recorded: age, gender, length of ICU stay, disease severity at the time of diagnosis, surgery within 1 month before diagnosis, underlying systemic diseases, invasive procedures, antimicrobial susceptibility of *A. baumannii* to tigecycline, blood culture findings, medical imaging features, and antimicrobial treatment after obtaining culture results. Subsequent bacteremia was defined as at least one *A. baumannii*-positive blood culture in the absence of a different infection source and at least one *A. baumannii*-positive tracheal aspirate culture after the development of newly diagnosed AbVAP. Other bacterial co-pathogens were also investigated. The study outcome was overall 30-day mortality in the ICU. All patients were included in a survival follow-up until death or 30 days after the onset of VAP.

All study data were processed using SPSS software version 22.0 (SPSS, Inc., Chicago, IL, USA). Student's *t*-test or the Mann–Whitney *U*-test was used to analyze continuous variables, whereas the Chi-square test or Fisher's exact test was used for categorical variables. The risk factors for 30-day mortality were identified through a logistic regression analysis. $P < 0.05$ was considered to indicate statistical significance.

This study included 158 patients with a 30-day mortality rate of 31.0% (49/158). The mean age was 59.8 years among

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Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.223859

Received: 11-10-2017 **Edited by:** Li-Shao Guo
How to cite this article: Ju MH, Yao YL, Du CL, Chen S, Song YL. Subsequent Multidrug-Resistant Bacteremia Is a Risk Factor for Short-Term Mortality of Patients with Ventilator-Associated Pneumonia Caused by *Acinetobacter baumannii* in Intensive Care Unit: A Multicenter Experience. Chin Med J 2018;131:361-3.

Table 1: Demographic and clinical characteristics of patients with VAP caused by *A. baumannii*

Variables	Nonsurvivors (n = 49)	Survivors (n = 109)	Statistics	P
Age (years), mean ± SD	59.8 ± 11.5	56.7 ± 13.5	1.394†	0.165
Male, *n* (%)	38 (77.6)	80 (73.4)	0.309*	0.578
Early onset, *n* (%)	20 (40.8)	26 (23.9)	4.713*	0.030
Prior surgery, *n* (%)	30 (61.2)	95 (87.2)	13.757*	<0.001
Onset APACHE II score (points), mean ± SD	16.4 ± 5.9	13.0 ± 3.9	4.344†	<0.001
Length of ICU stay (days), median (interquartile range)	23 (11.5–27.75)	20 (16–31)	1.838‡	0.066
Comorbid condition, *n* (%)				
Diabetes mellitus	8 (16.3)	12 (11.0)	0.864*	0.352
Cardiac diseases	31 (63.3)	78 (71.6)	1.087*	0.297
Malignancy	14 (28.6)	23 (21.1)	1.052*	0.305
COPD	6 (12.2)	5 (4.6)	1.992*	0.158
Liver cirrhosis	2 (4.1)	2 (1.8)	0.081*	0.776
Chronic kidney disease	4 (8.2)	2 (1.8)	2.176*	0.140
Cerebrovascular accident	5 (10.2)	12 (11.0)	0.023*	0.880
Transplant	5 (10.2)	5 (4.6)	0.976*	0.323
Invasive procedures, *n* (%)				
Tracheostomy	30 (61.2)	81 (74.3)	2.771*	0.096
Central venous catheter	33 (67.3)	46 (42.2)	8.549*	0.003
Image features, *n* (%)				
Pleural effusion	29 (59.2)	75 (68.8)	1.392*	0.238
Tigecycline resistant	10 (20.4)	16 (14.7)	0.807*	0.369
Polymicrobial, *n* (%)	15 (30.6)	33 (30.3)		
P. aeruginosa	12 (24.5)	24 (22.0)	0.117*	0.732
K. pneumonia	4 (8.2)	11 (10.1)	0.008*	0.929
Other pathogen	2 (4.1)	5 (4.6)	0.000*	1.000
Subsequent *A. baumannii* bacteremia, *n* (%)	7 (14.3)	6 (5.5)	2.387*	0.122
Inappropriate antibiotics treatment, *n* (%)	32 (65.3)	40 (36.7)	11.155*	0.001

*Chi-square test, †Fisher's exact test, ‡Mann–Whitney rank sum test. VAP was classified as either early onset (<5 days within mechanical ventilation) or late onset (≥5 days). Prior surgery is defined as surgery within 30 days before diagnosis; APACHE II: Acute Physiology and Chronic Health Evaluation II; Cardiovascular disease includes coronary artery disease, cardiomyopathy, and valvular heart disease; Malignancy includes hematologic malignancies and solid tumor; COPD: Chronic obstructive pulmonary disease; cerebrovascular accident includes cerebral infarction or cerebral hemorrhage. Other pathogens including *E. coli*, *S. maltophilia*, *H. influenzae*, and *Enterococcus* spp. Appropriate antibiotic therapy was defined as the receipt of one or more antimicrobial agents to which *A. baumannii* was susceptible at a therapeutic dosage within 72 h of diagnosis, if not, the treatment was thought to be inappropriate. VAP: Ventilator-associated pneumonia; *A. baumannii*: *Acinetobacter baumannii*; SD: Standard deviation; *P. aeruginosa*: *Pseudomonas aeruginosa*; *K. pneumonia*: *Klebsiella pneumoniae*; *E. coli*: *Escherichia coli*; *S. maltophilia*: *Stenotrophomonas maltophilia*; *H. influenza*: *Haemophilus influenza*.

nonsurvivors and 56.7 years among survivors. Moreover, 125 (79.1%) patients had recently undergone surgery, and 46 (29.1%) had developed early-onset VAP. The mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score at the time of VAP diagnosis was significantly higher among nonsurvivors (16.4 vs. 13.0 for survivors and nonsurvivors respectively, $P < 0.001$). Cardiovascular disease was the most common underlying systemic disease, occurring in 69.0% of the patients. Tracheostomy was the most common invasive procedure performed during the hospital stay (111, 70.3%).

Forty-eight patients (30.4%) in our study were infected with co-pathogens, of which the most common were *Pseudomonas aeruginosa* (36, 22.8%) and *Klebsiella pneumoniae* (15, 9.5%). Notably, the frequency of tigecycline-resistant *A. baumannii* increased to 16.5% in our study population. Thirteen patients were found to develop subsequent *A. baumannii* bacteremia, and all cases involved multidrug resistance. However, only 54.4% of the patients received appropriate antibiotic therapy, as shown in Table 1.

The logistic regression analysis included all factors that received $P < 0.20$, as shown in Table 1. Our multivariate analysis identified a higher APACHE II score at onset (odds ratio [*OR*]: 1.12; 95% confidence interval [*CI*]: 1.03–1.23; $P = 0.010$), subsequent *A. baumannii* bacteremia (*OR*: 5.34; 95% *CI*: 1.26–22.68; $P = 0.023$), central venous catheter placement (*OR*: 2.65; 95% *CI*: 1.12–6.18; $P = 0.027$), and inappropriate antibiotic treatment (*OR*: 4.90; 95% *CI*: 1.96–12.28; $P = 0.001$) as risk factors for 30-day ICU mortality in patients with AbVAP. By contrast, a history of surgery was identified as a protective factor against 30-day ICU mortality (*OR*: 0.18; 95% *CI*: 0.06–0.49; $P < 0.001$).

Our research demonstrated that subsequent multidrug-resistant bacteremia is a risk factor for short-term mortality among patients with AbVAP in the ICU. This finding may be attributed to the increased usage of a central venous catheter before bacteremia onset (76.9% [10/13] vs. 40.0% [58/145], $P = 0.010$).[4] Therefore, physicians should emphasize the importance of barrier precautions, as well as appropriate antibiotic treatment. However, our

study failed to find a higher ICU mortality rate among patients with multidrug-resistant *A. baumannii* bacteremia, compared to the nonbacteremic patients (53.8% [7/13] vs. 31.7% [46/145], $P = 0.190$). In addition, the two groups did not differ significantly in terms of the APACHE II score (14.8 ± 4.3 vs. 14.0 ± 4.9, $P = 0.552$) or frequency of tigecycline resistance (16.6% [2/13] vs. 15.4% [24/145], $P = 0.913$).

This study had some inherent limitations of note. Particularly, all clinical information related to the risk factors was collected retrospectively, which restricts the generalization of our findings to additional patients. Further prospective studies should be conducted.

In conclusion, AbVAP often develops as a nosocomial infection and is associated with a high mortality rate. Limitations on central venous catheter use, the avoidance of subsequent *A. baumannii* bacteremia, and the judicious use of antibiotics may reduce the mortality associated with AbVAP in the ICU.

Financial support and sponsorship

This study was supported by grants from the National Natural Science Foundation of China (No. 81770055, No. 81630001, No. 81490533), and Shanghai Science and Technology Committee Grant (No. 15DZ1930600, No. 15DZ1930602).

Conflicts of interest

There are no conflicts of interest.

References

1. Garnacho-Montero J, Ortiz-Leyba C, Fernández-Hinojosa E, Aldabó-Pallás T, Cayuela A, Marquez-Vácaro JA, *et al*. *Acinetobacter baumannii* ventilator-associated pneumonia: Epidemiological and clinical findings. Intensive Care Med 2005;31:649-55. doi: 10.1007/s00134-005-2598-0.
2. Chaari A, Mnif B, Bahloul M, Mahjoubi F, Chtara K, Turki O, *et al*. *Acinetobacter baumannii* ventilator-associated pneumonia: Epidemiology, clinical characteristics, and prognosis factors. Int J Infect Dis 2013;17:e1225-8. doi: 10.1016/j.ijid.2013.07.014.
3. Nhu NT, Lan NP, Campbell JI, Parry CM, Thompson C, Tuyen HT, *et al*. Emergence of carbapenem-resistant *Acinetobacter baumannii* as the major cause of ventilator-associated pneumonia in Intensive Care Unit patients at an infectious disease hospital in Southern Vietnam. J Med Microbiol 2014;63:1386-94. doi: 10.1099/jmm.0.076646-0.
4. Guo N, Xue W, Tang D, Ding J, Zhao B. Risk factors and outcomes of hospitalized patients with blood infections caused by multidrug-resistant *Acinetobacter baumannii* complex in a hospital of Northern China. Am J Infect Control 2016;44:e37-9. doi: 10.1016/j.ajic.2015.11.019.