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). 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...
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% \([58/145]\), \( P = 0.010 \)). 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.

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**Conflicts of interest**

There are no conflicts of interest.

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