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ORIGINAL ARTICLE

Mortality risk factors in patients with *Acinetobacter baumannii* ventilator-associated pneumonia

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Background/Purpose: Ventilator-associated pneumonia (VAP) caused by *Acinetobacter baumannii* has contributed to high mortality rate, prolonged stays in the intensive care unit, and the rapid development of antimicrobial resistance to commonly used antimicrobials. This study sought to determine predictors of mortality and carbapenem resistance for patients with *A baumannii* VAP.

Methods: We retrospectively reviewed 541 adult patients with *A baumannii* pneumonia, who were admitted to a medical center between 2005 and 2007; of which 180 (33.3%) had been treated with mechanical ventilation. Of the 180 patients, 98 (54.4%) who survived were categorized as the survivor group, and 82 (45.6%) who died as the mortality group. Eighty-seven (48.3%) with imipenem-sensitive *A baumannii* VAP were categorized as the IS-AB group, and the remaining 93 (51.7%) with imipenem-resistant VAP as the IR-AB group.

Results: Compared with the survivor group, the mortality group had significantly higher Charlson comorbidity index scores, and more neoplastic disease, other sites of infection, bloodstream infections, altered mental status, confusion, urea >7 mmol/L, respiratory rate >30/min, low blood pressure (systolic <90 mmHg or diastolic <60 mmHg), age >65 years (CURB-65) ≥ 3, creatinine > 1.6 mg/dL, C-reactive protein ≥ 100 mg/L, and imipenem resistance. The survivor group had more cases of tracheostomy and diabetes mellitus than the mortality group had. Compared with the IS-AB group, the IR-AB group had higher Charlson comorbidity index scores, longer stays before VAP onset, an increase in other sites of infection, white blood cell count $<4/\mu L$ or $>1.1 \times 10^4/\mu L$, and higher hospital mortality rates.

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Conclusion: Inadequate initial empiric antimicrobial therapy and higher disease severity scores, including CURB $\geq$ 3 and C-reactive protein $\geq$ 120 mg/L, were independent risk factors associated with higher mortality rates for *A baumannii* pneumonia. Length of stay before VAP and white blood cell count $<4/\mu L$ or $>1.1 \times 10^4/\mu L$ were independent risk factors for carbapenem resistance.

Introduction

Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) are important causes of nosocomial infections that are associated with high morbidity and mortality rates. The attributive mortality has been estimated as 33—50%, particularly in critically ill patients.[1,2] VAP refers to pneumonia that develops more than 48—72 hours after intubation with mechanical ventilation.[2,3] For most patients with HAP, the pneumonia is diagnosed by clinical manifestations, chest radiographic presentations, and/or sputum culture. Bronchoscopy is not available for all patients with HAP, thus the exact pathogen is difficult to culture from sputum in patients with HAP.[4] The incidence of colonization in hospitalized patients is high;[5] furthermore, a positive culture cannot always distinguish a pathogen from a colonizing organism. However, sterile culture by means of bronchoscopy from the lower respiratory tract in an intubated patient has been suggested.[6]

Acinetobacter baumannii, an aerobic Gram-negative bacillus, is one of the most important nosocomial pathogens. The phenomenon of rapid development of antimicrobial resistance to commonly used antimicrobial agents has been reported worldwide in recent years.[7] Carbapenems are some of the most effective antibiotics used to treat severe *A baumannii* infection. Unfortunately, an increasing prevalence of carbapenem-resistant pathogens has been observed in patients with HAP, especially in critically ill patients;[8] however, the potential predictors of carbapenem-resistant pneumonia have not been clearly investigated. The aim of this study was to investigate the risk factors of mortality in critically ill patients with *A baumannii* pneumonia. We also analyzed the risk factors and clinical differences between carbapenem-resistant and carbapenem-sensitive *A baumannii* pneumonia in critically ill patients.

Materials and methods

Study design

We conducted a retrospective observational study at KCGMH. KCGMH is a 2500-bed medical facility serving as a primary care and tertiary referral center in Kaohsiung, Taiwan. We reviewed all the medical records of the patients with *A baumannii* pneumonia admitted to KCGMH between January 2005 and December 2007. Adult patients ($\geq$18 years old) with a first episode of *A baumannii* VAP were included in our study. The patient's exclusion criteria included: (1) no first episode of *A baumannii* VAP; (2) *A baumannii* isolated in the absence of clinical disease or chest X-ray findings, which suggested colonization; (3) sputum sample collection was not from the tracheostomy or endotracheal tube after immediate intubation; and (4) known tuberculosis or severe immunosuppression, such as human immunodeficiency virus or solid organ or bone marrow transplantation.

Definitions

HAP was defined as pneumonia that occurred within 48 hours after admission or if the patient was readmitted within a week after the last discharge. VAP was defined as pneumonia that occurred within 48 hours after commencing mechanical ventilation.[2,3] Pneumonia was defined according to the criteria of the US Centers for Disease Control and Prevention. Pneumonia required two or more of the following criteria to be satisfied: (1) fever (increase of $\geq$1°C or body temperature $>$38.3°C); (2) leukocytosis (25% increase and $\geq$10,000/mm^3) or leukopenia (25% decrease and $\leq$5000/mm^3); and (3) purulent tracheal secretion ($>$25 neutrophils per high power field). It also required one of following criteria: (1) new or persistent infiltration on chest radiography; (2) some microorganisms isolated from pleural effusion and tracheal secretion; (3) radiographic cavitation or histological evidence of pneumonia pathogens; or (4) positive sputum culture from a quantitative bacterial bronchoalveolar lavage culture of 10^5 colony-forming units/mL. Intensive care unit (ICU) stay was defined as the number of days the patient stayed in the ICU after *A baumannii* had been isolated from sputum. The susceptibility of *A baumannii* isolates to antimicrobial agents was determined by using the disk-diffusion test as recommended by the National Committee for Clinical Standards.[9] Indeterminate susceptibility to antimicrobials was considered as resistance, excluding cases in which the specimens and/or cultures had been contaminated.

Previous antimicrobial therapy was defined as receiving a systemic antimicrobial agent for at least 48 hours in the 2 weeks preceding sputum culture collection. Antimicrobial therapy was considered to be appropriate if all pathogens isolated from culture were sensitive to it and inadequate if any pathogen was resistant to it. After 7 days of antimicrobial treatment, the pneumonia condition was re-evaluated and classified as improved if the fever had subsided, tracheal purulent secretion decreased, pneumonia consolidation or infiltration regressed on chest radiography, and there was an improvement in laboratory data [including white blood cells (WBCs) and C-reactive protein (CRP)]. Otherwise, the clinical status after 7 days of antibiotic treatment was identified as improved or not

improved. When the status was indeterminate, it was classified as not improved.

Data collection

The demographic characteristics including age, sex, underlying disease or condition, length of hospital stay, initial empirical antimicrobial therapy, susceptibility to antimicrobial agents, and discharge status were reviewed and obtained from medical charts. Information regarding initial clinical and laboratory condition was also collected. The Charlson comorbidity index, confusion, urea >7 mmol/L, respiratory rate >30/min, low blood pressure (systolic <90 mmHg or diastolic <60 mmHg), age >65 years (CURB-65) score,[10,11] other sites of infection, ICU stay, invasive procedures (including those required for tracheostomy or mechanical ventilation), and previous antimicrobial treatment were considered as possible risk factors.

Statistical analysis

All statistical analyses were performed using SPSS version 14.0 software (Chicago, IL, USA). Categorical variables were analyzed using the χ^2 test or Fisher's exact test. Continuous variables were compared using Student *t* test or the Mann–Whitney *U* test. Multivariate logistic regression analyses were performed to identify the risk factors for mortality and imipenem resistance. Each variable considered a risk factor, and with a *p* value <0.05 in the univariate analysis, it was entered into the multivariate model. The enter method was used to define the final independent risk factors, and the Hosmer-Lemeshow test was used to assess goodness-of-fit. A *p* value <0.05 was considered statistically significant.

Results

A total of 541 adult patients with *A baumannii* pneumonia were admitted to KCGMH between January 2005 and December 2007. This included 180 (33.3%) patients with intubation and mechanical ventilation. Among these 180 patients, 98 (54.4%) survived and were classified as the survivor group, and 82 (45.6%) who died were classified as the mortality group. Furthermore, 87 (48.3%) patients with imipenem-sensitive *A baumannii* VAP were classified as the IS-AB group, and the remaining 93 (51.7%) with imipenem-resistant VAP were classified as the IR-AB group.

Comparisons between survivor and mortality groups

Table 1 shows the comparisons of demographic and clinical characteristics of patients with *A baumannii* VAP between the survivor and mortality groups. There were no significant differences in sex, age, previous antimicrobial therapy, late-onset VAP, ICU stay, congestive heart failure, chronic obstructive pulmonary disease, chronic liver or renal disease, and presence of polymicrobial pneumonia between both groups. Furthermore, there were significant differences in Charlson comorbidity index score, neoplastic disease, other sites of infection, bloodstream infection, altered mental status, CURB-65 $\geq$ 3, blood urea nitrogen >20 mg/dL, otherwise, creatinine >1.6 mg/dL, CRP $\geq$ 100 mg/L, and imipenem resistance between both groups. The incidences of patients with tracheostomy and diabetes mellitus (DM) were significantly higher in the survivor group. Patients in the survivor group received more adequate empiric antibiotic treatment ($p = 0.017$) and had a more improved response ($p < 0.001$) than those in the mortality group.

Comparisons between IS-AB and IR-AB groups

Table 2 shows the comparisons of demographic and clinical characteristics of patients with *A baumannii* VAP between the IS-AB and IR-AB groups. There were significant differences in Charlson comorbidity index score, length of stay before VAP onset, other sites of infection, WBC count <4 μL or >1.1 × 10^4/μL and hospital mortality rate between both groups.

Copathogens and antimicrobial treatment

Fifty *A baumannii* VAP patients had copathogens. *Pseudomonas aeruginosa* ($n = 14$, 28%), *Staphylococcus aureus* ($n = 13$, 26%) and *Corynebacterium* spp. ($n = 11$, 22%) were the three most frequent copathogens combined with *A baumannii* infection (Table 3). The most frequently used initially adequate antibiotics were carbapenems (41.46%) and sulbactam (48.78%). Inadequate antibiotic therapy included cephalosporins (35.25%), carbapenems (29.9%) and quinolones (18.71%) in the distribution of clinical differences in antimicrobial management. Decreasing trends in the susceptibility rates of carbapenems (from 72.5% to 36%) and sulbactam (from 70% to 50.7%) were observed (Table 4).

Risk factors for mortality associated with *A baumannii* VAP

Multivariate analysis (Table 5) revealed that 30 days in-hospital mortality, creatinine >1.6 mg/dL, inadequacy of initial empirical antibiotics, CURB $\geq$ 3, and CRP $\geq$ 120 mg/L were independent risk factors for the mortality group ($p < 0.05$). Otherwise, tracheostomy and DM seemed to provide some survival benefits. Multivariate analysis (Table 5) also revealed that the length of stay before VAP onset and WBC count <4 μL or >1.1 × 10^4/μL were independent risk factors for the IR-AB group.

Discussion

HAP is difficult to diagnosis; therefore, most patients with pneumonia are diagnosed by clinical manifestations, chest radiographic presentations, and/or sputum culture reports. The sputum culture with a high incidence rate of colonization was observed in hospitalization patients. Instead, a sterile sputum culture from the lower respiratory tract was usually requested. One previous study reported that sputum cultures by means of endotracheal tube aspiration

Table 1 Comparisons of demographic and clinical characteristics of patients with *Acinetobacter baumannii* ventilator-associated pneumonia between the survivor and mortality groups

	Survivor group $n = 98$ (54.4%)	Mortality group $n = 82$ (45.6%)	p
Demographics			
M/F	56/42	52/30	0.392
Age (y)	70.4 ± 13.5	68.8 ± 16.0	0.463
Antibiotic in past 14 d	95 (97.9)	82 (100.0)	0.191
Late-onset VAP (≥5 d)	63 (64.3)	58 (70.7)	0.359
ICU stay	82 (83.7)	75 (91.5)	0.119
LOS	67.4 ± 34.4	38.9 ± 26.5	<0.001
Before VAP onset	28.6 ± 24.2	30.8 ± 25.5	0.538
After VAP onset[b]	38.8 ± 24.7	8.1 ± 7.7	<0.001
Comorbidity			
Charlson comorbidity index[b]	2.86 ± 1.98	3.53 ± 2.19	0.033
Neoplastic disease[b]	17 (17.3)	31 (37.8)	0.002
CHF	22 (22.4)	13 (15.9)	0.266
Diabetes mellitus[b]	39 (39.8)	19 (23.2)	0.017
Chronic respiratory disease[a]	22 (22.4	19 (23.2)	0.908
Liver disease[a]	12 (12.2)	14 (17.1)	0.359
Renal disease[a]	23 (23.5)	24 (29.3)	0.378
Clinical features			
Polymicrobial infection	33 (33.7)	17 (20.7)	0.054
Other site of infection[b]	25 (25.5)	44 (53.7	<0.001
Bloodstream[b]	18 (18.4	39 (47.6	<0.001
Catheter	6 (6.1)	4 (4.9)	0.717
Urinary	8 (8.2)	6 (7.3	0.833
Other	0 (0.0)	3 (3.7)	0.093
Tracheostomy[b]	33 (33.7)	9 (11.0)	<0.001
Altered mental status[b]	22 (22.4)	37 (45.1)	0.001
CURB-65 ≥ 3[b]	33 (33.7)	48 (48.8)	0.040
BUN ≥ 30 mg/dL[b]	42 (42.9)	60 (73.2)	<0.001
Cr > 1.6 mg/dL[b]	26 (26.5)	45 (54.9)	<0.001
WBC <4 or >1.1 × $10^4/\mu L$	51 (52.0)	51 (62.2)	0.171
CRP ≥ 100 mg/L[b]	29 (29.6)	40 (48.8)	0.008
Imipenem resistance[b]	44 (44.9)	49 (59.8)	0.047
Ampicillin/sulbactam resistance	38 (38.8)	38 (46.3)	0.306
Initial antibiotic therapy[b]			0.017
Inadequate	69 (70.4)	70 (85.4)	
Adequate	29 (29.6)	3 (3.7)	
Pneumonia status within 7 d			<0.001
Improved	61 (62.2)	8 (9.8)	
Not improved	37 (37.8)	74 (80.2)	

Data are represented as mean ± standard deviation or *n* (%).
[a] Disease was defined as in the Charlson comorbidity index.
[b] Variable was entered into the multivariate logistic regression analysis.
BUN = blood urea nitrogen; CHF = congestive heart failure; Cr = creatinine; CRP = C-reactive protein; CURB-65 = confusion, urea >7 mmol/L, respiratory rate >30/min, low blood pressure (systolic <90 mmHg or diastolic <60 mmHg), age >65 years; ICU = intensive care unit; LOS = length of stay; Other sites of infection=*Acinetobacter baumannii* cultured from other than sputum; VAP = ventilator-associated pneumonia; WBC = white blood cell.

had identified the same microorganisms as that by means of bronchoalveolar lavage in 83% of the patients with suspicion of VAP, and provided adequate information for therapy in 95% of the patients.[12] Therefore, we only enrolled patients with *A baumannii*-positive sputum cultures obtained via endotracheal tube aspiration, to avoid contamination. Patients with tuberculosis were not enrolled in the study. We excluded patients that were positive for acid-fast bacilli and *A baumannii*, because this could have led to confusion between pathogenic and colonizing organisms.

The mean total duration of hospitalization in this study was 47 days, which is slightly longer than that reported in western countries (range: 29—40 days).[13,14] *A baumannii* is the pathogen that contributes to a significantly higher mortality rate was compared to other nosocomial pathogen.[15] The mortality rates associated with *A baumannii*

Table 2 Comparisons of demographic and clinical characteristics of patients with *Acinetobacter baumannii* ventilator-associated pneumonia between imipenem-sensitive and imipenem-resistant groups

	IS-AB group $n = 87$ (48.3%)	IR-AB group $n = 93$ (51.7%)	p
Demographics			
M/F	55/32	53/40	0.394
Age (y)	70.9 ± 13.6	68.5 ± 15.6	0.279
Antibiotic in past 14 d	85 (97.7)	92 (98.9)	0.611
Late-onset VAP (≥5 d)	59 (67.8)	62 (66.7)	0.870
ICU stay	76 (87.4)	81 (87.1)	0.958
LOS	50.8 ± 31.5	57.8 ± 36.2	0.165
Before VAP onset[b]	24.1 ± 20.4	34.7 ± 27.4	0.004
After VAP onset	26.7 ± 24.3	23.1 ± 24.3	0.331
Comorbidity			
Charlson comorbidity index[b]	2.76 ± 1.97	3.56 ± 2.16	0.010
Neoplastic disease	20 (23.0)	28 (30.1)	0.280
CHF	19 (21.8)	16 (17.2)	0.432
Diabetes mellitus	27 (31.0)	31 (33.3)	0.742
Chronic respiratory disease[a]	20 (23.0)	21 (22.6)	0.948
Liver disease[a]	10 (11.5)	16 (17.2)	0.276
Renal disease[a]	21 (24.1)	26 (28.0)	0.560
Clinical features			
Polymicrobial infection	30 (34.5)	20 (21.5)	0.052
Other site of infection[b]	26 (29.9)	43 (46.2)	0.024
Bloodstream	22 (25.3)	35 (37.6)	0.075
Catheter	4 (4.6)	6 (6.5)	0.587
Urinary	4 (4.6)	10 (10.8)	0.123
Other	0 (0.0)	3 (3.2)	0.247
Tracheostomy	24 (27.6)	18 (19.4)	0.192
Altered mental status	25 (28.7)	34 (36.6)	0.264
CURB-65 ≥ 3	31 (35.6)	42 (45.2)	0.193
BUN ≥ 30 mg/dL	47 (54.0)	55 (59.1)	0.489
Cr > 1.6 mg/dL	33 (37.9)	38 (40.9)	0.688
WBC <4 or >1.1 × $10^4/\mu L$[b]	39 (44.8)	63 (67.7)	0.002
CRP ≥ 100 mg/L	27 (31.0)	42 (45.2)	0.051
Imipenem resistance	—	—	—
Ampicillin/sulbactam resistance	31 (35.6)	45 (48.4)	0.083
Initial antibiotic therapy			0.674
Inadequate	66 (75.9)	73 (78.5)	
Adequate	21 (24.1)	20 (21.5)	
Pneumonia status within 7 d			0.124
Improved	40 (46.0)	29 (31.2)	
Not improved	47 (54.0)	64 (68.8)	
In-hospital mortality[b]	40 (46.0)	57(61.3)	0.039

Data are represented as mean ± standard deviation or *n* (%).

[a] Disease was defined as in the Charlson comorbidity index.

[b] Variable was entered into the multivariate logistic regression analysis.

AB = imipenem-sensitive *A baumannii*; BUN = blood urea nitrogen; CHF = congestive heart failure; Cr = creatinine; CRP = C-reactive protein; CURB-65 = confusion, urea >7 mmol/L, respiratory rate >30/min, low blood pressure (systolic <90 mmHg or diastolic <60 mmHg), age >65 years; ICU = intensive care unit; IS-IR-AB = imipenem-resistant *A baumannii*; LOS = length of stay; Other sites of infection=*Acinetobacter baumannii* cultured from other than sputum; VAP = ventilator-associated pneumonia; WBC = white blood cell.

infection have ranged from 19% to 54% in recent studies,[16,17] and it was 53.9% in our study. Whereas, the IR-AB group had a significantly higher mortality rate than the IS-AB group ($p = 0.039$). This is different from other studies that have shown that IR-AB is not associated with hospital mortality.[18]

In our study, polymicrobial infection was common in nosocomial pneumonia caused by *P aeruginosa*, *S aureus*, and *Corynebacterium* spp. These were the three most frequently found copathogens combined with *A baumannii* infection. The results showed that polymicrobial infection was not associated with hospital mortality and carbapenem

Table 3 Distribution of copathogens with *Acinetobacter baumannii* pneumonia

	Survivor group $n = 33$ (66%)	Mortality group $n = 17$ (34%)	p
Pseudomonas aeruginosa	8 (16)	6 (12)	0.833
Staphylococcus aureus	7 (14)	6 (12)	0.964
Corynebacterium spp.	11 (22)	0 (0)	0.001
Stenotrophomonas maltophilia	3 (6)	3 (6)	1.000
Klebsiella pneumoniae	1 (2)	1 (2)	1.000
Escherichia coli	0 (0)	1 (2)	0.456
Enterobacter spp.	1 (2)	0 (0)	1.000
Other	3 (6)	0 (0)	0.252

There were a total of 51 pathogens from 50 patients.
Data are represented as *n* (%).

resistance, but coinfection may be synergistic in clinical manifestation. However, polymicrobial infection is frequently encountered in clinical practice. Thus, we could not disregard the importance of polymicrobial infection as a coinfection. Therefore, it is necessary to pay attention to the presence of *A baumannii* in polymicrobial infection, and careful selection of appropriate antibiotics for empirical therapy of *A baumannii* pneumonia should also consider copathogens. Carbapenem and sulbactam are effectively therapeutic and frequently prescribed for the treatment *A baumannii* pneumonia.[19] However, in recent decades, *A baumannii* has developed a remarkably rapid antibiotic resistance, leading to multidrug-resistant pathogens with limited therapeutic options.[20,21] Carbapenems and third-generation cephalosporins were not initially appropriate antibiotics for nearly half of the patients with *A baumannii* pneumonia in our study. This might have been because the number of pathogens with antibiotic resistance has increased, and that carbapenem and sulbactam susceptibility rates have gradually decreased in recent years. Carbapenems and third-generation cephalosporins are recognized as the most important risk factors for multidrug resistance.[22] Early and adequate antibiotic therapy are important to optimize the management of HAP.[7,9,23,24] Initially appropriate antibiotics are very important for patients with HAP, especially for those with antibiotic-resistant pathogens. Initially inappropriate antibiotic therapy for VAP is associated with a significantly greater incidence of 30 days in-hospital mortality.[23] In our study, the adequacy of initial empiric antibiotic therapy for patients with *A baumannii* pneumonia was correlated with hospital survival, and the inadequacy of initial antibiotic therapy was an independent predictive factor for hospital mortality by multivariate analysis. Lee et al[15] have reported that the mortality rate is significantly higher in patients with inappropriate initial empiric antibiotic therapy, even when subsequent antibiotic therapy is appropriate. As long as a good quality sputum culture is done as early as possible, appropriate antimicrobial therapy has an impact on the clinical outcome in patients with *A baumannii* pneumonia. Sulbactam, tigecycline, and colistin represent the present therapy associated with satisfactory efficacy.[22] In our study, the tigecycline susceptibility rate of *A baumannii* was only 68% *in vitro* in the first year.

Table 4 *In vitro* susceptibility analysis of *Acinetobacter baumannii*

	Overall	2005	2006	2007
Amikacin	11.1	15.0 (6/40)	7.7 (5/65)	12.0 (9/75)
Amoxicillin/clavulanic acid	0.0	0.0 (0/40)	0.0 (0/12)	—
Ampicillin/sulbactam	57.8	70.0 (28/40)	58.5 (38/65)	50.7 (38/75)
Aztreonam	0.0	0.0 (0/40)	0.0 (0/65)	0.0 (0/75)
Cefepime	6.7	15.0 (6/40)	7.7 (5/65)	1.3 (1/75)
Ceftazidime	5.6	15.0 (6/40)	6.2 (4/65)	0.0 (0/75)
Ceftriaxone	0.6	2.5 (1/40)	0.0 (0/65)	0.0 (0/75)
Cefuroxime	2.0	2.5 (1/40)	0.0 (0/11)	—
Cephalothin	0.0	0.0 (0/40)	0.0 (0/11)	—
Ciprofloxacin	3.3	7.5 (3/40)	4.6 (3/65)	0.0 (0/75)
Gentamicin	5.6	12.5 (5/40)	6.2 (4/65)	1.3 (1/75)
Imipenem	48.3	72.5 (29/40)	47.7 (31/65)	36.0 (27/75)
Piperacillin	1.8	5.0 (2/40)	1.5 (1/65)	0.0 (0/58)
Piperacillin/tazobactam	1.6	—	3.8 (2/53)	0.0 (0/75)
Sufamethoxazole/trimethoprim	3.9	10.0 (4/40)	4.6 (3/65)	0.0 (0/75)
Tigecycline	68.0	—	—	68.0 (17/25)

Table 5 Independent risk factors in multivariate analyses

Variables	AOR (95% CI)	*p*
Imipenem resistance		
LOS prior to VAP onset (d)	1.02 (1.00–1.04)	0.012
WBC <4 or >1.1 × 10^4/μL	2.48 (1.31–4.72)	0.005
30-d mortality		
Diabetes mellitus	0.34 (0.13–0.85)	0.022
Tracheostomy	0.20 (0.07–0.58)	0.003
Cr > 1.6 mg/dL	3.90 (1.26–12.08)	0.018
Inadequacy of initial empiric antibiotic	4.06 (1.39–11.87)	0.010
CURB ≥ 3	13.22 (2.40–72.71)	0.003
CRP ≥ 120	2.63 (1.11–6.28)	0.029

AOR = adjusted odd ratio; CI = confidence interval; Cr = creatinine; CRP = C-reactive protein; CURB = confusion, urea >7 mmol/L, respiratory rate >30/min, low blood pressure (systolic <90 mmHg or diastolic <60 mmHg); LOS = length of stay; VAP = ventilator-associated pneumonia; WBC = white blood cell.

Previous studies have reported that 10–30% of *A baumannii* pneumonia is accompanied by bacteremia,[7] and that bacteremic pneumonia may clinically manifest from benign transient to fulminant septic shock, which consequently has a high mortality rate.[25] Among our patients, the incidence and mortality rates of bacteremia were 31.7% and 47.6%, respectively.

Charlson comorbidity index, CURB-65, and CRP as independent markers of severity scores have been used to predict mortality in HAP.[26,27] The identification of these severity scores is useful in the recognition of the individual clinical course and outcome. In our study, severity scores of CURB ≥ 3, CURB-65 ≥ 3, and CRP ≥ 100 mg/L had similar area under the curve values. CURB-65 ≥ 3 and CRP ≥ 120 mg/L had higher specificity, positive predictive value, and negative predictive value, and they were used for multivariate analysis. In recent studies, malignancy, septic shock, and organ failure have been shown to be independent factors associated with mortality in *A baumannii* infection.[15] In our study, we found that creatinine >1.6 mg/dL, CURB ≥ 3, and CRP ≥ 120 mg/L were independent risk factors for mortality in patients with *A baumannii* pneumonia. Moreover, it was not surprising that the length of stay before VAP onset and WBC count <4 μL or >1.1 × 10^4/μL were independent risk factors for imipenem resistance. In a recent study, neutropenia and prolonged use of carbapenem induced production of metallo-β-lactamase, which then developed imipenem-resistant *A baumannii* pathogens.[28] However, an interesting finding in our study was that DM was associated with a lower mortality risk, which is in discordance with other reports.[29] DM is a common disease in the developed world and a cause of disability. Impaired glucose metabolism has been associated with several complications, including induced leukocyte adherence, chemotaxis, and phagocytosis dysfunction of WBCs, which increases the development and mortality of community-acquired pneumonia. In contrast, one review has reported that DM is not a risk factor for the development of HAP, nor increased mortality associated with nosocomial complications.[30] However, further research is needed to help determining the impact of DM on the incidence and/or severity of HAP.

Sputum cultures of the lower respiratory tract by means of a tracheostomy tube are not contaminated by the normal flora of the oral cavity, because liberation of the vocal cords results in normal closure and reduces the risk of aspiration of secretions from the oropharyngeal cavity. However, based on the pathophysiology of VAP, tracheostomy could be protective against VAP.[31] Many researchers have shown that tracheostomy decreases the risk of VAP.[32,33] Patients with early tracheostomy are associated with lower rates of VAP and mortality as compared with those with late tracheostomy.[32] In our study, tracheostomy was demonstrated to have a potentially significant protective effect in both univariate and multivariate analysis. A possible explanation for this finding is that the patients who received tracheostomy had a decreased risk of aspiration of secretion and reduced mortality. The relationship between VAP, disease severity and timing of tracheostomy and intubation are still unclear, further investigations are needed.

This retrospective study had several limitations. First, this study was conducted at a single medical center, and there may have been patient selection bias and referral patterns. Second, this study was a retrospective survey, which not only resulted in incomplete data for some patients, but also did not control for laboratory examinations and the clinical courses of all VAP patients. Therefore, some important risk factors for VAP, such as re-intubation and nutritional status, were not investigated. Further prospective investigations should be conducted. Despite these limitations, this study provides relatively rare data regarding a series of VAP patients with *A baumannii*.

In conclusion, this study conducted a series-based study of VAP patients with *A baumannii* cultured by means of endotracheal tube aspiration. Inadequate initial empiric antimicrobial therapy and higher severity scores, including CURB ≥ 3 and CRP ≥ 120 mg/L, were independent risk factors associated with a higher mortality rate for *A baumannii* pneumonia. Length of stay and WBC <4/μL or >1.1 × 10^4/μL were independent risk factors for carbapenem resistance. Further studies are needed to determine the risk factors for antibiotic resistance in these patients.

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