Analysis of Prognostic Factors in 95 Patients with *Acinetobacter baumannii* Bacteremia

C.-H. Chen, L.-C. Lin, Y.-J. Chang, C.-C. Huang, C.-E. Liu, T.-G. Young

Abstract

Background: Because *Acinetobacter baumannii* bacteremia is a global problem, we were motivated to characterize this disease in Taiwan.

Patients and Methods: We analyzed findings in 95 patients with documented *A. baumannii* bacteremia between January 1, 1998 and December 31, 2000 (47 men, 48 women; mean age 58.8 years).

Results: The mean length of stay in the hospital was 44.0 days. Clinically, 76 patients had fever and 35 patients developed shock. Fifty patients had respiratory tract infections; 24, urinary tract infections; 11, intra-abdominal infections; three, CNS infections; and two, catheter-related infections. Five patients had primary bacteremia. Empirical antibiotic therapy was initiated at the onset of the clinical signs of infection. Antimicrobial susceptibility test results were variable. 47 patients died and 48 survived; the mortality rate for *A. baumannii* bacteremia was 45.3% (43/95).

Conclusion: Physicians should pay attention to this infection because the early identification of high-risk patients could facilitate prophylaxis and potentially reduce associated problems.

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Introduction

Acinetobacter baumannii infection is difficult to treat and, as a result, it has high mortality and morbidity rates [1–3]. Recently, *A. baumannii* bacteremia has been a serious problem, being associated with increased mortality and prolonged hospital stays [4]. Many authors have pointed out that *A. baumannii* bacteremia is hard to cure because the responsible strains are often resistant to multiple antibiotics [5, 6]. Because *A. baumannii* bacteremia occurred recently in our hospital and because few reports for the risk factors for the disease are available in the literature [7], we sought to characterize the risk factors of *A. baumannii* bacteremia in Taiwan.

Patients and Methods

A cross-sectional , retrospective study of patients with *A. baumannii* bacteremia was conducted by searching the computerized medical records of Changhua Christian Hospital, Taiwan, from January 1, 1998, through December 31, 2000. Infectious disease specialists reviewed the records for the patients during this study.

The clinical status of the patients at admission and during the subsequent hospital stay was obtained from the patients' charts and any mention of risk factors was recorded. The severity of the underlying disease was categorized by using *McCabe* and *Jackson's* criteria [8]. We noted the risk factors associated with bacteremia; these included the use of parenteral nutrition (TPN), antibiotics, mechanical ventilation, any surgery, chemotherapy and catheters, including central venous catheters, Hickman catheters, peripheral venous catheters, arterial catheters and Swan-Ganz catheters. We defined the nosocomial infection using the Centers for Disease Control and Prevention (CDC) criteria [9]. We included only those risk factors that had been recorded within 7 days of the date of nosocomial infection. We excluded those patients whose data were incomplete. The patients were categorized as either those who survived (S group) or those who died (D group).

Microbiological Investigations

Blood cultures were performed for every patient with suspected sepsis. We used the BACTEC NR-860 system (Becton Dickinson Diagnostic Instrument Systems, Franklin Lake, NJ) for detecting pathogens. *A. baumannii* was presumptively identified by using colony morphology, Gram staining, oxidase testing (Dry Slide; Difco Laboratories, Detroit, Michigan) and catalase testing. The presumptive diagnosis of *A. baumannii* was confirmed by using an API-20NE kit (Bio Mérieux Vitek; Hazelwood, MO). All *A. baumannii* strains were retested with the 10% lactose reaction. Routine antibiotic sensitivity testing was performed with the disk diffusion method (BBL, Sensi-Disc; Becton Dickinson, Cockeysville,

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Table 1
Demographic data in 95 patients with *A. baumannii* bacteremia.

Characteristic	Total no.	S Group		D Group		P-value[a]
		No.	%	No.	%	
Age (years)	95	48	50.5	47	49.5	0.029
Sex						0.759
Male	47	23	48.9	24	51.1	
Female	48	25	52.1	23	47.9	
Severity of underlying diseases[b]						0.000
A	37	34	91.9	3	8.1	
B	14	11	78.6	3	21.4	
C	44	3	4.7	41	95.3	
Surgery						0.010
No	48	18	37.5	30	62.5	
Yes	47	30	63.8	17	36.2	
Use the effective antibiotics						
No	4	2	50.0	2	50.0	> 0.999
Yes	91	46	51.1	45	48.9	
Type of infection						0.083
Nosocomial	76	35	44.8	41	55.2	
Community-acquired	19	13	64.3	6	35.7	
Source of infection[c]						0.495
Primary	5	3	100.0	2	0.0	
Secondary	90	45	50.0	45	50.0	
Respiratory tract infection	50	20	40.0	30	60.0	
Urinary tract infection	24	14	58.3	10	31.7	
Catheter-related infection	2	0	0.0	2	100	
Intra-abdominal infection	11	3	27.3	8	72.7	
CNS infection	3	3	100	0	0	

[a] p-values were determined by the Pearson χ^2-test, Fisher's exact test or the Mantel-Haenszel χ^2-test, as appropriate; [b] the severity of the disease was categorized using *McCabe* and *Jackson* criteria [8]; [c] the source of infection was determined according to clinical and microbiological evidence. The source of infection was categorized according to its original site; examples included respiratory tract infection, urinary tract infection and intra-abdominal infection. Primary bacteremia was defined as bacteremia with no apparent original source

MD), according to the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) [10].

Statistics

The Pearson χ^2-test, Fisher's exact test or the Mantel-Haenszel χ^2-tests were used to compare the categorical outcomes of the S group and the D group. Results were considered significant if the p-value was < 0.05. All data were analyzed by using a personal computer with SAS software v6.12 (SAS, Cary, NC).

Results

We analyzed findings in 103 patients with documented *A. baumannii* bacteremia between 1 July 1, 1998 and June 30, 2001. Only 95 patients were enrolled in our study because the records for eight patients lacked complete data. The male-to-female ratio of our patients was 0.98 (47 male, 48 female) and the mean age was 58.8 years (range 0–87 years). McCabe and Jackson's criteria were used to evaluate the severity of disease at the onset of *A. baumannii* bacteremia. A total of 44 patients had fatal outcomes, another 14 patients ultimately had fatal outcomes and 37 patients had nonfatal outcomes. The mean length of stay in hospital was 44.0 days (range 1–375 days). The demographic data of the patients is shown in table 1, the distribution of the hospitalized days

Table 2
Distribution of the hospitalized days and catheter usage days in 95 patients with *A. baumannii* bacteremia.

Risk Factor	S Group					D group					P-value
	No.	Mean	SD	Median	Range	No.	Mean	SD	Median	Range	
Hospitalized ICU days	22	22.3	16.3	19.0	0–65	30	37.5	71.7	21.5	1–391	0.802
Total hospitalized days	48	42.8	58.1	31.0	5–375	47	45.2	60.1	30.0	1–293	0.845
Duration of use (days)											
Central venous catheter	21	34.4	28.4	22.0	5–111	33	39.1	64.1	17.0	0–290	0.189
Peripheral venous catheter	48	43.3	62.4	21.0	2–369	47	42.1	49.2	29.0	1–293	0.925
Arterial catheter	14	21.0	25.1	9.0	0–71	11	19.3	20.4	16.0	0–56	0.869
Swan-Ganz catheter	1	5.0	–	–	–	3	10.0	8.9	7.0	3–20	0.655
TPN	9	40.7	40.3	23.0	10–136	8	25.1	44.0	12.0	0–132	0.075
Antibiotics	48	24.5	30.6	14.5	0–164	47	41.2	60.6	23.0	1–290	0.099
Ventilators	26	31.8	35.4	19.5	0–144	34	37.7	67.9	13.0	0–292	0.416
Foley catheter	27	26.4	21.2	22.0	2–89	32	39.9	68.6	24.5	0–293	0.976

ICU: intensive care unit; TPN: parenteral nutrition

and catheter usage days are shown in table 2. The clinical manifestations of *A. baumannii* bacteremia varied. Concerning the initial systolic blood pressure, there was a slight difference among those two groups (S group, mean 127 mmHg vs D group119 mmHg), but no significant statistical difference ($p = 0.161$). There was little difference between the two groups regarding the initial diastolic blood pressure (S group, mean 72 mmHg vs D group 66 mmHg; $p = 0.107$, not significant). The initial white cell counts were not statistically significant (S group, mean 12,500 vs D group 16,100; $p = 0.103$), nor were the 1st week white cell counts (S group, 11,600 vs D group 14,800; $p = 0.028$, not significant).

The sources of infection were analyzed and the results were as follows: Fifty cases were due to respiratory tract infection; 24 cases, urinary infection; 11 cases, intra-abdominal infection; three cases, CNS infection; and two cases, catheter-related infection. Five cases involved primary bacteremia. Empirical antibiotics were commenced at the onset of the clinical signs of infection. The antibiotics were changed to those indicated by the results of susceptibility tests, as required. The results of antimicrobial susceptibility testing were as follows. Of the 80 strains that were resistant to ampicillin, 32 strains were in S group and 48 in D group. Of the 78 cefazoline-resistant strains, 37 were in S group and 41 in D group. Of 56 strains resistant to cefuroxime, 25 were in S group and 31 in D group. Of 41 strains resistant to amikacin, 17 were in S group and 24 in D group. Of 28 strains resistant to unasyn (amoxicillin-clavulanate), 15 were in S group and 13 in D group. Of 46 strains resistant to cefazidime, 17 were in S group and 29 in D group.

Of the 95 patients, 47 patients died and 48 survived; 20 deaths were directed related to *A. baumannii* bacteremia, 23 were indirectly related to *A. baumannii* bacteremia and the other four were unrelated. Therefore, the mortality rate for *A. baumannii* bacteremia was 45.3% (43/95). The relationship between the mortality rate and *A. baumannii* bacteremia risk factors are listed in table 3. During the study period, no outbreak of *A baumannii* infection occurred.

Discussion

The risk factors for *A. baumannii* bacteremia are variable. *Koprnova* et al. [11] pointed out that wound infection ($p < 0.01$) and ventilator support ($p < 0.001$) were significantly related to *A. baumannii* bacteremia in surgical patients. *Garcia-Garmendia* et al. [12] found that independent risk factors associated with *A. baumannii* bacteremia are immunosuppression, unscheduled admission to the hospital, respiratory failure during admission to the intensive

Table 3
Relationship between mortality and risk factors in patients with *A. baumannii* bacteremia.

Risk factor and relationship	No.	Mean	SD	Median	Range	P-value[a]
Central venous catheter						0.004
Unrelated[b]	4	48.5	56.3	26.5	9–132	
Indirectly related[b]	19	53.9	76.8	26.0	5–290	
Directly related[b]	10	7.0	9.5	1.5	0–27	
Peripheral venous catheter use						0.000
Unrelated	6	69.0	43.5	54.0	36–132	
Indirectly related	22	55.3	60.4	36.0	15–293	
Directly related	17	17.3	9.7	16.0	1–36	
Arterial catheter use						0.197
Indirectly related	5	29.6	24.6	22.0	0–56	
Directly related	6	10.7	12.5	7.0	0–32	
Swan-Ganz catheter use						0.221
Indirectly related	2	5.0	2.8	5.0	3–7	
Directly related	1	20.0	–	–	–	
TPN use						0.130
Unrelated	1	132.0				
Indirectly related	6	11.5	9.0	12.0	1–24	
Directly related	1	0.0				
Antibiotic use						0.000
Unrelated	5	67.0	46.6	50.5	33–134	
Indirectly related	23	60.4	76.7	31.5	15–290	
Directly related	19	12.1	9.8	11.0	1–37	
Ventilator use						0.008
Unrelated	2	31.0	5.7	31.0	27–35	
Indirectly related	17	62.2	89.9	29.0	1–292	
Directly related	15	10.8	10.2	11.0	0–34	
Foley catheter use						0.030
Unrelated	3	40.0	20.0	45.0	18–57	
Indirectly related	17	58.9	89.6	29.0	1–293	
Directly related	12	13.0	12.8	10.0	0–36	

[a] p-values were determined by the Kruskal-Wallis test; [b] the relationship between the death and *A. baumannii* was analyzed by the infectious specialists according to the clinical presentations. Patients who died within 3 days of becoming infected with *A. baumannii* and those without evidence of deterioration in the underlying diseases were categorized as having died directly due to *A. baumannii* infection. Patients who died within 7 days of becoming infected and those without clues indicating the deterioration of underlying diseases were categorized as having died indirectly due to *A. baumannii*. Those patients who died more than 7 days after becoming infected with *A. baumannii* and those whose underlying diseases worsened were categorized as having died of causes unrelated to *A. baumannii*; TPN: parenteral nutrition

care unit (ICU), previous antimicrobial therapy, previous sepsis in the ICU and the invasive procedures index. Reviewing the literature, we found that the risk of *A. baumannii* infection is related to many factors: the APACHE II score, previous antibiotic therapy, the use of a mechanical ventilator and gastrointestinal surgery [13, 14]. Additionally, previous studies of postoperative infection revealed the following risk factors: high American Society of Anesthesiology score, prolonged preoperative hospitalization, arterial catheter use and the presence of an infection[15]. In our study, the risk factors of the 95 patients with *A. baumannii* bacteremia were variable. When comparing the S group and the D group, the most important risk factor was surgery ($p = 0.010$). Apparently, the risk factors predisposing an individual to *A. baumannii* infection is multifactorial.

The clinical manifestations of *A. baumannii* bacteremia varied as well. In our study, 50 patients had respiratory tract infections, 24 had urinary tract infections, 11 had intra-abdominal infections, three had CNS infections, two had catheter-related infections and five had primary infections. Most previously reported episodes of *A. baumannii* infection were caused by pneumonia [16]. Our findings were similar. In our study, 89 patients had fever and 35 patients developed shock (data not shown). However, the clinical presentations and courses were not significantly different between the S group and the D group. In fact, predicting the clinical outcome on the basis of the clinical conditions alone was difficult.

A. baumannii had been documented as an important nosocomial pathogen [3]. In our study, five patients had undergone invasive procedures, including one who underwent endoscopic papillotomy; one, percutaneous transhepatic cholangial drainage; and one, endoscopic retrograde biliary drainage. Although we suspected the relationship between the procedures and the infections, we were not sure of the association. *Baumann* [17] isolated the *Acinetobacter* organism from soil and water and *Wagenvoort* et al. [18] hypothesized that *A. baumannii*, carried by health-care staff had behavior similar to that of methicillin-resistant *Staphylococcus aureus*. The possible source of *A. baumannii* infection may be the environment, including contaminated soil and water or the health-care staff, who become involved in a vicious cycle of infection and transmission. Further investigations are necessary to prove this hypothesis.

In a multiple logistic regression model, decubitus ulcers and/burns (as underlying disease) and nosocomial pneumonia were independent predictors of mortality in the study by *Koprnova* et al. [11] . In our study, the crude mortality rate of *A. baumannii* was 45%. In the study by *Wang* et al. [7], the mortality rate was 58%. The difference may been due to the severity of the disease. In the study by *Wang* et al., 11 patients (58%) developed shock and only patients with community-acquired infection were enrolled. However, 35 patients (36.8%) had shock in our study. *Beck-Sague* et al. [14] found no difference in mortality between patients with *A. baumannii* bacteremia and selected control subjects. In our study, we directly compared overall mortality rates. We found that the duration of peripheral venous catheter use and the duration of antibiotic treatment were significantly, different in terms of unrelated mortality, indirectly related mortality and directly related mortality. These results are similar to previous findings [11, 12].

Regarding limitations in our study, we realize that the total number of patients was small and that the number of deaths directly attributable to the episode of bacteremia is difficult to ascertain in some situations. In conclusion, we assessed the consequences and risk factors of *A. baumannii* bacteremia. To find the risk factors and prevent them can potentially reduce the impact of this infection.

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