

Predictors of mortality in *Acinetobacter baumannii* bacteremia

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Received: May 13, 2004 Revised: June 21, 2004 Accepted: July 30, 2004

This study retrospectively investigated 149 episodes of *Acinetobacter baumannii* bacteremia which occurred during a 41-month period from September 1997 to January 2001. Bacteremia was nosocomial in 139 (93%) of the episodes and community-acquired in 10 (7%). Thirty three deaths (22.1%) were attributed to these episodes of *A. baumannii* bacteremia. The mean age of survivors was younger than that of patients who died of bacteremia (60.4 ± 19.9 vs 67.1 ± 17.4) but this result was not significant on univariate analysis ($p=0.084$). Previous intensive care unit stay was longer among survivors than among patients who died of bacteremia (9.5 vs 18 days, $p=0.048$). Factors associated with mortality included immunosuppression ($p=0.019$), shock ($p=0.002$), recent surgery ($p=0.008$), invasive procedures such as central venous catheterization ($p=0.002$), urinary catheterization ($p=0.012$), placement of a nasogastric tube ($p<0.001$), pulmonary catheterization ($p=0.015$), and mechanical ventilation ($p=0.035$). The number of underlying conditions ($p=0.015$) and invasive procedures ($p<0.001$) were positively correlated with mortality. Mortality was significantly associated with lower platelet count ($p=0.001$) and lower serum albumin concentration ($p=0.005$). Patients with catheter-related bacteremia had a high survival rate (96.2%), while survival rate was low in patients with infection originating from the respiratory tract (60.8%). Susceptibility testing by agar dilution test indicated that imipenem was the most effective antibiotic, followed by cefepime and ciprofloxacin. The mortality rate was lower in patients who received 1 or more antibiotics to which the isolates were susceptible, but this difference was not significant ($p=0.197$). On multivariate analysis, factors that independently correlated with mortality were increased age ($p=0.003$), immunosuppressive status ($p=0.001$), recent surgery ($p=0.002$), acute respiratory failure ($p=0.004$), acute renal failure ($p=0.009$) and septic shock ($p<0.001$). These findings highlight the importance of a treatment strategy based on risk stratification among patients with *A. baumannii* bacteremia.

Key words: *Acinetobacter baumannii*, bacteremia, mortality, retrospective studies, risk factors

Acinetobacter baumannii, an aerobic, non-fermentative Gram-negative coccobacillus, has become one of the most important nosocomial pathogens in recent years, especially in patients who are critically ill and those with compromised immunity. *A. baumannii* causes a variety of infections, including pneumonia, meningitis, urinary tract infection, soft tissue infection, peritonitis, endocarditis, and bloodstream infections [1-4]. The long survival and ubiquitous nature of *A. baumannii* as well as its rapid evolution of multidrug-resistant strains in clinical isolates has made it among the most difficult nosocomial pathogens to control and treat [5-8]. *A. baumannii* bloodstream infection is associated with a high overall and attributable mortality [9-11]. Data on

the prognostic factors for mortality has been obtained but such studies have often been limited by small numbers of cases and inadequate parameters. In addition, controversies exist on the impact of appropriate antimicrobial therapy. The aim of this study is to identify clinical, laboratory, and microbiologic features that may be predictive of mortality in *A. baumannii* bacteremia and help achieve an early stratification to identify those at high risk of death.

Materials and Methods

Taipei Veterans General Hospital is a 2900-bed tertiary medical center located in northern Taiwan. All patients with blood cultures positive for *A. baumannii* during the period from September 1997 to February 2001 were included in this retrospective study. Data including demographic characteristics, clinical presentations,

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laboratory examinations, microbiologic studies, treatment and outcome were collected from clinical records.

Definitions

A bacteremic episode was defined as isolation of 1 or more organisms from blood in a patient on 1 or more occasions. A new bacteremic episode was considered if more than 7 days had elapsed since resolution of symptoms and signs of infection resulting from the previous bacteremic episode. The bacteremia was regarded as clinically significant if the isolation of *A. baumannii* was accompanied by 2 or more of the following symptoms and signs which lasted at least 8 h: fever, hypothermia, chills, tachypnea, tachycardia, or leukocytosis. The blood isolates were considered as contaminants if there were no symptoms or signs of infection. Community-acquired bacteremia was defined as a bacteremia that occurred within 48 h of admission in patients without hospitalization in the month prior to the bacteremic episode. The infection was considered hospital-acquired if it developed 48 h or later after admission.

Information on risk factors and underlying conditions were retrieved from medical records. Patients were classified as having immunosuppression if any of the following criteria were met: having received solid organ or stem cell transplantation; presentation of leukopenia (white blood cell count, $<4 \times 10^9/L$); infection with human immunodeficiency virus; and treatment with cytotoxic chemotherapy within the previous 6 weeks or more than 2 doses of steroids or other immunosuppressive agents within 2 weeks prior to the first episode of *A. baumannii* bacteremia. Recent surgeries, major trauma, or shock due to various causes were also recorded if they occurred within 2 weeks of the episode. Underlying diseases were recorded. Data was collected about recent stay in an intensive care unit (ICU) and use of antimicrobial agents within the previous month of the first *A. baumannii* bacteremic episode. Invasive procedures, including abdominal catheterization, central venous catheterization, arterial catheterization, urinary catheterization, placement of a pulmonary arterial catheter or a nasogastric tube, tube thoracostomy or thoracocentesis, administration of total parenteral nutrition and use of mechanical ventilation were considered risk factors if performed or existing within 48 h prior to the first *A. baumannii* bacteremic episode.

The source of bacteremia was determined if there was concomitant or previous (in the past 7 days) isolation

of the same organism from stool, urine, wounds, aspirates from abscess, or cerebrospinal fluid. The source was considered to be an intravascular catheter when the same organism was isolated from blood and the catheter tip and not from any other body sites and there were more than 15 colony forming units in the semiquantitative culture of the tip [12], or when local clinical findings of infection over the insertion site of the catheter were evident without any other possible sources of bacteremia. The bacteremia was considered to have originated from the respiratory tract when clinical or radiologic evidence of a new-onset or progressing pneumonia was found with concomitant isolation of *A. baumannii* isolated from blood, or when strains with an antibiotic susceptibility pattern identical to those isolated from blood were recovered from sputum, bronchial secretion, or other respiratory specimens. Other data recorded included previous bacteremia with microorganisms other than *A. baumannii* in the past month, polymicrobial bacteremia with other microorganisms isolated from blood during the same bacteremic episode, and superinfection that occurred after the first *A. baumannii* bacteremic episode.

Antibiotic therapy was considered empiric when antimicrobial agents were administered for treating *A. baumannii* bacteremia before the results of in vitro susceptibility tests were available. Antibiotic therapy was considered as appropriate if *A. baumannii* isolated from blood was susceptible in vitro to at least 1 of the antibiotics used. Appropriate antibiotic therapy administered more than 48 h after onset of bacteremic symptoms was considered as delayed. Antimicrobial therapy was considered inappropriate if none of the antibiotics to which *A. baumannii* was susceptible were included in the treatment. Pandrug-resistant *A. baumannii* was defined as an isolate that was resistant to all available antibiotics, which in this study included: third- and fourth-generation cephalosporins, broad-spectrum penicillins including ampicillin-sulbactam, trimethoprim-sulfamethoxazole, aminoglycosides, monobactam, ciprofloxacin, and imipenem.

The following clinical and laboratory data were recorded. Fever was defined as a temperature of more than 38.0°C and hypothermia as less than 35.0°C. Defervescence was defined as a body temperature of less than 37.5°C for 3 consecutive days. Results of laboratory studies during the bacteremic episode, including complete blood counts and biochemical profile, were retrieved from medical records.

The following complications were recorded if they occurred within 7 days of the bacteremic episode: septic shock, defined according to the definition of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference [13]; acute renal failure, defined as an increase in serum creatinine of >2 mg/dL after a bacteremic episode; acute respiratory failure, defined as a new-onset respiratory failure after the bacteremic episode requiring mechanical ventilatory support.

Outcome

Death of a patient was considered directly related to the bacteremia if it occurred in the phase of active infection without evidence of any other attributable cause [14]. Under other circumstances, the death was regarded as unrelated to the bacteremia.

Microbiologic investigation and antimicrobial susceptibility testing

Blood specimens were processed with the BACTEC system (NR660, Becton Dickinson Sparks, MD, USA). Species identification was accomplished by biochemical tests using the API 32 GN system (bioMerieux, France) and by the ability to grow at 44°C [15]. Antimicrobial susceptibility testing was performed using the agar dilution method according to the National Committee for Clinical Laboratory Standards (NCCLS) guidelines [16]. Minimal inhibitory concentration was defined as the lowest antimicrobial concentration able to totally inhibit visible bacterial growth. The interpretive standards for susceptibility and resistance breakpoints were based on the recommendations of the Subcommittee on Antimicrobial Susceptibility Testing of the NCCLS [16].

Statistical analysis

Chi-squared test with Yates' correction or Fisher's exact test was used to compare differences in discrete variables, and Student's *t* test or Mann-Whitney

rank sum test was used to analyze continuous variables as appropriate. A multivariate analysis with logistic regression was performed to identify prognostic factors independently associated with mortality from *A. baumannii* bacteremia. A *p* value of 0.1 was the limit for entering or removing variables. All analyses were performed with SPSS version 11 (SPSS Institute, Chicago, IL, USA). A *p* value <0.05 was considered statistically significant.

Results

Bacteremic episodes

During the period between September 1997 and January 2001, 238 specimens from 186 patients grew *A. baumannii*. Adequate medical data for this study were available for 163 (87.6%) of these patients. Bacteremia was considered clinically significant in 149 episodes occurring in 146 patients. Fourteen episodes (8.6%) were excluded from this study because the positive blood isolates were considered contaminants. Three patients experienced 2 episodes of *A. baumannii* bacteremia during the study period.

Demographic data, underlying illness and invasive procedures

Patients survived in 116 of the 149 *A. baumannii* bacteremic episodes. Death was considered directly related to *A. baumannii* bacteremia in the other 33 bacteremic episodes (22.1%). The mean age of survivors was slightly younger than those who died, although this difference was not significant on univariate analysis (60.4 ± 19.9 vs 67.1 ± 17.4 years, $p=0.084$).

The results of univariate analysis of the relationships between clinical characteristics and mortality are listed in Table 1. Of the 149 bacteremic episodes, 131 (87.9%) were categorized as nosocomial, 10 (6.7%) as community-acquired and 8 episodes could not be categorized into either of these categories according to our definitions. Nosocomial bacteremia developed in

Table 1. Univariate analysis of clinical characteristics associated with mortality in 149 episodes of *Acinetobacter baumannii* bacteremia

Characteristic	Percentage of deaths (no. of deaths/no. of cases)		<i>p</i>
	With factor	Without factor	
Male gender	20.9 (23/110)	25.6 (10/39)	0.699
Community-acquired bacteremia ^a	30.0 (3/10)	22.9 (30/131)	0.274
Bacteremic episodes occurred in intensive care unit	30.0 (15/50)	18.2 (18/99)	0.152
Recent intensive care unit stay	27.4 (17/62)	18.4 (16/87)	0.268

^aEight bacteremic episodes could not be categorized to either the nosocomial or community-acquired group according to the definitions.

ICUs in 50 episodes (38.1%), in ordinary wards in 75 (57.3%), and in the observation room of the emergency department in 6 (4.6%). Fatal bacteremia that developed in the ICU was associated with a shorter duration of ICU stay before onset (9.5 vs 18 days, $p=0.048$). Antimicrobial agents had been administered during the month before the first *A. baumannii* bacteremic episode in most patients (62.4%). The most commonly used antibiotics were cephalosporins (used in 42.3% of all patients), followed by aminoglycosides (35.6%) and penicillins (16.1%). Carbapenems had been previously used in 4 patients (2.6%) and a subsequent blood isolate from 1 of these patients was carbapenem-resistant.

Underlying comorbid illnesses and invasive procedures associated with prognosis of the bacteremic episodes are listed in Table 2. The majority (144/149, 96.6%) of patients had 1 or more underlying diseases or comorbid conditions. Patients who died of *A. baumannii* bacteremia were more likely to have immunosuppression, a recently performed surgery, or previous shock. Use of corticosteroids and recently performed abdominal surgery were associated with a higher mortality rate (4/7 vs 29/142, $p=0.043$ and

5/9 vs 28/140, $p=0.026$, respectively). Presence of malignant solid tumors was not a significant prognostic factor while malignancy with distant metastasis was associated with a very high mortality rate of 42.9% (6/14), compared with 8.7% (2/23) in those without metastasis ($p=0.032$). The average number of underlying conditions was 4.6 (range, 0-11) for each patient. Mortality was more likely in patients with more underlying conditions (median: 5 underlying conditions in the mortality group and 4 in survivors, $p=0.016$).

Most patients (79.9%) had undergone 1 or more invasive procedures, with an average number of 2.8 in each patient (range, 0-8). A significant positive association was found between the number of invasive procedures and mortality (median: 4 vs 1, $p<0.001$). Mechanical ventilation, which had been given to 73 patients (49.0%) before the first bacteremic episode, was significantly associated with mortality (33.3% [26/78] vs 9.9% [7/71], $p=0.035$). The duration of mechanical ventilation prior to the first bacteremic episode was significantly shorter in patients who died of bacteremia than in survivors (10 vs 26 days, $p=0.001$). Other procedures significantly associated with mortality included central venous catheterization, urinary

Table 2. Univariate analysis of underlying diseases and invasive procedures associated with mortality in 149 episodes of *Acinetobacter baumannii* bacteremia

Underlying condition or invasive procedure	Percentage of deaths (no. of deaths/no. of cases)		p
	With risk factor	Without risk factor	
Alcoholism	16.7 (1/6)	22.4 (32/143)	1.0
Burn	0 (0/2)	22.4 (33/147)	1.0
Congestive heart failure	12.1 (4/33)	25.0 (29/116)	0.182
Chronic lung diseases	27.8 (5/18)	21.4 (28/131)	0.55
Diabetes mellitus	25.0 (10/40)	21.1 (23/109)	0.775
Autoimmune diseases	60.0 (3/5)	20.8 (30/144)	0.072
End-stage renal diseases	29.4 (10/34)	20.0 (23/115)	0.354
Liver cirrhosis	8.3 (1/11)	23.4 (32/137)	0.302
Leukemia or lymphoma	20.0 (1/5)	22.2 (32/144)	1.0
Immunosuppressive status	38.2 (13/34)	17.4 (20/115)	0.019
Solid tumor	21.6 (8/37)	22.3 (25/112)	1.0
Major trauma	35.7 (5/14)	20.7 (28/135)	0.195
Previous shock status	44.8 (13/29)	16.7 (20/120)	0.002
Recent surgery	47.6 (10/21)	18.0 (23/128)	0.008
Abdominal catheterization	29.2 (7/24)	20.8 (26/125)	0.525
Arterial catheterization	31.4 (16/51)	17.3 (17/98)	0.092
Central venous catheterization	34.3 (23/67)	12.2 (10/82)	0.002
Urinary catheterization	32.8 (21/64)	14.1 (12/85)	0.012
Nasogastric tube placement	35.6 (26/73)	9.2 (7/76)	<0.001
Pulmonary artery catheterization	54.5 (6/11)	19.6 (27/138)	0.015
Thoracic drainage	50.0 (2/4)	21.4 (31/145)	0.213
Total parenteral nutrition	21.4 (3/14)	22.2 (30/135)	1.0
Previous mechanical ventilation	33.3 (26/78)	9.9 (7/71)	0.035

Table 3. Univariate analysis of clinical features and treatment associated with mortality in 149 episodes of *Acinetobacter baumannii* bacteremia (ABB) episodes

Clinical feature, treatment or response to treatment	Percentage of deaths (no. of deaths/no. of cases)		p
	With risk factor	Without risk factor	
Fever	21.4 (30/140)	33.3 (3/9)	0.415
Hypothermia	50.0 (1/2)	21.8 (32/147)	0.395
Catheter-related infection	3.8 (1/26)	26.0 (32/123)	0.027
Respiratory tract infection	39.2 (20/51)	13.3 (13/98)	0.001
Unknown sources	18.2 (10/55)	24.5 (23/94)	0.492
Previous bacteremia	29.4 (5/17)	21.2 (28/132)	0.534
Polymicrobial bacteremia	21.2 (7/33)	22.4 (26/116)	1.0
Superinfection	22.8 (13/57)	21.7 (20/92)	1.0
Carbapenem-resistant ABB	44.4 (4/9)	20.7 (29/140)	0.11
Pandrug-resistant ABB	50.0 (3/6)	21.0 (30/143)	0.123
Empiric antibiotic appropriate ^a	11.6 (5/43)	27.8 (27/97)	0.07
Delayed appropriate treatment ^b	20.5 (8/39)	16.3 (7/43)	1.0
Inappropriate or no antibiotic treatment	28.4 (19/67)	17.1 (14/82)	0.197
Removal of catheter	0 (0/20)	25.6 (33/129)	0.007
Defervescence	7.9 (7/89)	43.3 (26/60)	<0.001
Acute renal failure	70.0 (14/20)	13.7 (16/117)	<0.001
Acute respiratory failure	60.7 (17/28)	8.5 (8/94)	<0.001
Septic shock	56.5 (26/46)	6.8 (7/103)	<0.001

^aNine bacteremic episodes during which empiric antimicrobial therapy was not administered were excluded from analysis.

^bSixty seven bacteremic episodes during which appropriate antibiotics were not used were excluded from analysis.

catheterization, placement of a nasogastric tube and pulmonary catheterization.

Clinical symptoms and signs

The results of univariate analysis of the association between mortality and symptoms, treatment, or response to treatment are shown in Table 3. The majority (94.0%) of patients had fever at the onset of symptoms. The presence of fever on the day of the first isolation of *A. baumannii* was not significantly related to mortality. The percentages of patients with leukocytosis, neutropenia, and anemia were not significantly different between the mortality and survival groups. However, patients who died of the *A. baumannii* bacteremia had a significantly lower platelet count (112 ± 86 vs $181 \pm 114 \times 10^9/L$, $p=0.001$) and a lower concentration of serum albumin (2.9 ± 0.5 vs 3.2 ± 0.5 g/dL, $p=0.005$). Systolic blood pressures at the onset of bacteremic episodes were significantly lower in patients who died of the bacteremia (89.8 ± 27.7 vs 109 ± 24 mm Hg, $p=0.015$).

Source of bacteremia and previous, concurrent or superinfections

The most common source of *A. baumannii* bacteremia was the respiratory tract (34.2%), followed by

intravascular catheters (18.0%). Only a minority of patients had other sources, including the urinary tract (1.3%), gastrointestinal tract (2.0%), wounds (2.7%) and others (4.9%). There were 55 bacteremic episodes (36.9%) for which the source of bacteremia could not be identified. Origin of bacteremia from the respiratory tract was associated with a higher mortality rate compared to other sources (Table 3). By contrast, catheter-related bacteremia was associated with fewer deaths than bacteremia originating elsewhere. Polymicrobial bacteremia, previous bacteremia, and superinfection after *A. baumannii* bacteremia were not associated with mortality. Microorganisms involved in polymicrobial bacteremic episodes included *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, methicillin-resistant *Staphylococcus aureus*, *Serratia marcescens*, *Enterobacter* spp. (5 episodes for each organism), and enterococci (4 episodes). Five patients had concurrent candidemia. The involvement of different organisms in polymicrobial bacteremic episodes was not related to outcome (data not shown).

Antibiotic resistance

The results of in vitro susceptibility tests for antimicrobial agents are shown in Table 4. Imipenem

Table 4. Antimicrobial susceptibility of *Acinetobacter baumannii* isolates determined by agar dilution tests

Antimicrobial agent	MIC ^a (µg/mL)			No. of isolates (%)			Susceptibility ^b breakpoint (µg/mL)
	Range	MIC ₅₀	MIC ₉₀	Susceptible	Intermediately resistant	Resistant	
Amikacin	2~>32	>32	>32	69 (46.3)	1 (0.7)	79 (53.0)	≤4
Ampicillin-sulbactam	≤8~>16	16	>16	59 (39.6)	31 (20.8)	59 (39.6)	≤8/4
Aztreonam	8~>16	>16	>16	9 (6.0)	31 (20.8)	109 (73.2)	≤8
Ceftazidime	≤1~>32	32	>32	47 (31.5)	27 (18.1)	75 (50.3)	≤8
Chloramphenicol	4~>16	>16	>16	2 (1.3)	1 (0.7)	146 (98.0)	≤8
Ciprofloxacin	≤0.06~>2	2	>2	72 (48.3)	7 (4.7)	70 (47.0)	≤1
Ceftriaxone	4~>32	>32	>32	13 (8.7)	38 (25.5)	98 (65.8)	≤8
Cefepime	1~>16	16	>16	73 (49.0)	20 (13.4)	56 (37.6)	≤8
Gentamicin	0.5~>8	>8	>8	69 (46.3)	1 (0.7)	79 (53.0)	≤4
Imipenem	≤0.25~>8	2	4	135 (90.6)	5 (3.4)	9 (6.0)	≤4
Trimethoprim-sulfamethoxazole	≤0.5~>2	>4	>4	47 (31.5)	0 (0)	102 (68.5)	≤2/38
Tobramycin	≤0.5~>8	>8	>8	68 (45.6)	1 (0.7)	80 (53.7)	≤4
Piperacillin-tazobactam	≤2~>64	64	>64	45 (30.2)	34 (22.8)	70 (47.0)	≤16/4

Abbreviations: MIC = minimum inhibitory concentration; MIC₅₀ = minimum concentration inhibiting 50% of isolates; MIC₉₀ = minimum concentration inhibiting 90% of isolates

^aMICs were determined using agar dilution method as described by the National Committee for Clinical Laboratory Standards (NCCLS) [16].

^bBreakpoints of susceptibility and resistance for individual agents were determined according to the NCCLS interpretive standards [16].

remained the most active agent (90.6% susceptible), followed by cefepime (49%) and ciprofloxacin (48.3%). Of the 9 imipenem-resistant isolates, 3 were susceptible or moderately susceptible to ampicillin-sulbactam and all were also resistant to cefepime. There were 6 isolates of pandrug-resistant *A. baumannii*. The mortality rate in patients with bacteremia caused by carbapenem- or pandrug-resistant isolates was higher than in patients with carbapenem-susceptible isolates, but this difference was not significant (Table 3).

Treatment and outcome

Empiric antimicrobial therapy was administered during 140 (94.0%) bacteremic episodes but was appropriate in only 43 (28.9%) of them. Antimicrobial therapy was adjusted in 94 bacteremic episodes (63.1%) because of failure to achieve apparent clinical response or according to the results of in vitro susceptibility tests. The antibiotic therapy was eventually appropriate in 82 bacteremic episodes (55.0%), while appropriate treatment was classified as delayed in 39 episodes (26.2%). Administration of appropriate antibiotics was associated with a lower mortality rate compared with episodes treated with inappropriate or no antibiotic therapy, although these differences were not significant (Table 3). Use of appropriate antimicrobial agents within 48 h of onset of symptoms was not associated with a higher chance of survival compared with delayed appropriate

antibiotic therapy. Removal of the presumed infected intravascular catheters was done in 21 bacteremic episodes (14.1%) and was associated with a higher survival rate ($p=0.007$). With or without appropriate antibiotic treatment, a defervescent response, noted in 89 bacteremic episodes (59.7%), was associated with a favorable outcome ($p<0.001$). Appropriate antimicrobial therapy was also associated with a higher rate of defervescence (56/82 vs 33/67, $p=0.037$). Among patients with defervescence, the median duration of fever was also significantly shorter for those who survived the bacteremia (2 vs 4 days, $p=0.003$).

Twenty patients (13.4%) had acute deterioration of renal function, 46 (30.9%) developed septic shock, and 28 (18.8%) developed respiratory failure requiring mechanical ventilation after the onset of *A. baumannii* bacteremia. The development of any of these 3 complications was a significant predictor of mortality. There were 71 bacteremic episodes (47.7%) during which the patient did not have any of these 3 complications and only 2 (2.8%) of them led to mortality. By contrast, all 8 patients who suffered from all 3 of these complications died of the bacteremic episode.

The results of stepwise logistic regression analysis of possible prognostic indicators are listed in Fig. 1. Multivariate analysis revealed that the average age of the fatality group was significantly older than that of the surviving group (odds ratio [OR], 1.10; 95%

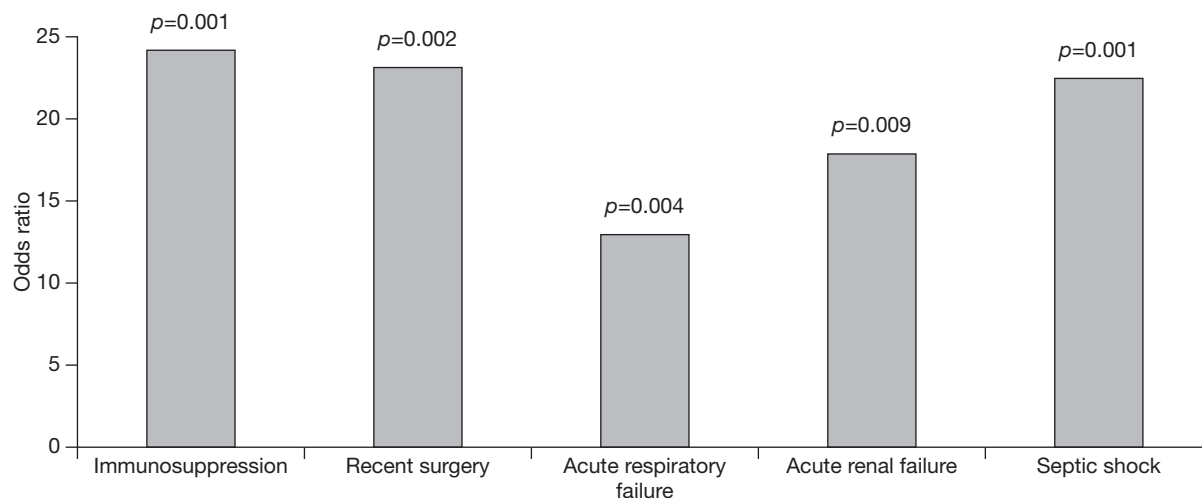


Fig. 1. Multivariate analysis of prognostic factors for *Acinetobacter baumannii* bacteremia.

confidence interval [CI], 1.03-1.18). Among other variables entered into the multivariate analysis, immunosuppression (OR, 24.1; 95% CI, 3.4-168.0), recent surgery (OR, 23.0; 95% CI, 3.1-168.7), development of acute respiratory failure (OR, 12.8; 95% CI, 2.3-72.3), acute renal failure (OR, 17.8; 95% CI, 2.1-154.4) and septic shock (OR, 22.4; 95% CI, 4.5-11.5) were independent predictors of mortality.

Discussion

In this study, patients who died of *A. baumannii* bacteremia acquired this infection more quickly than those who survived. The time intervals from ICU admission or initiation of mechanical ventilation to the development of *A. baumannii* bacteremia were both shorter in patients who died due to bacteremic episodes. The greater number of comorbid conditions and invasive procedures in the mortality group indicates that patients who died of the bacteremia had more risk factors associated with entry of this microorganism and the development of infection. Gross and colleagues demonstrated a positive correlation between the number of comorbid conditions and the length of ICU stay and the development of complications in patients with nosocomial infection [17].

Pittet et al studied the prognostic value of pre-existing comorbidities and concluded that the severity and number of comorbid conditions were strongly predictive of mortality [18]. These findings suggest the need for early stratification of these patients as needing a timely effective treatment and highlight the importance of a strategy of quick stratification based

simply on numbers of comorbid conditions and invasive procedures.

Data are limited on the difference in mortality rates between community-acquired and nosocomial *A. baumannii* bacteremia. A previous study from Taiwan found that the mortality rate associated with community-acquired *Acinetobacter* bacteremia was 58% [19] and that multiple clinical risk factors, including cigarette smoking, alcoholism, chronic obstructive airway diseases and diabetes mellitus, were more common in cases of fatal community-acquired *A.baumannii* bacteremic pneumonia [20]. In our study, the mortality rate of community-acquired bacteremia was just slightly higher (30% vs 23%) than that resulting from nosocomial infection. Differences in the underlying conditions of patients may be a possible reason for this discrepancy.

The underlying condition most significantly associated with increased mortality in this study was immunosuppression, which represented a heterogeneous group of several conditions. While a previous study found that the use of corticosteroids was unrelated to the outcome of *A. baumannii* bacteremia [21], in our study this risk factor was associated with a significantly higher mortality rate. Further analysis on our patients who received corticosteroids revealed that all 4 who died of this episode of bacteremia had been mechanically ventilated during the month prior to onset, suggesting that the severity of their underlying illnesses may have played an important role. Unlike previous studies which found that malignant tumors were related to a higher percentage of deaths [11,22], our study did not find this condition predictive of mortality. However, this was

probably attributable to the need to take different stages of malignant diseases into account when analyzing their influence on prognosis. Unlike some previous studies which suggested diabetes mellitus was a predictor for mortality from *A. baumannii* bacteremia [10,21], there was no difference in mortality between the diabetic and non-diabetic patients in our study. Further investigation based on status of glycemic control might be necessary to clarify the significance of this factor. In a study of traumatic patients with *Acinetobacter* bacteremia, Tilley and Roberts found that outcome was more favorable in young males suffering motor vehicle accidents [22]. Our traumatic patients had a slightly poorer outcome (5/14 vs 28/135, $p=0.195$) but most patients were older (mean age, 51.8 years old) and their trauma mainly consisted of intracranial hemorrhages resulting from falling accidents.

Surgery performed within 2 weeks prior to the first episode of *A. baumannii* bacteremia was an independent predictor for bacteremia-related death in this study. Further analysis of the types of surgeries performed revealed that a recent abdominal surgery was a significant predictor of mortality. A similar result was suggested by Seifert et al [11]. The digestive tract has been suggested to be the major site for *A. baumannii* colonization [23]. Interestingly, all of the abdominal surgeries in our patients were associated with manipulation of the gastrointestinal tract, including hemicolectomy, gastrectomy, resection of the bowel tract, and feeding jejunostomy. Abdominal invasive procedures without direct breakdown of intestinal mucosa, such as percutaneous transhepatic cholangio-drainage, post-surgical abdominal drainage, peritoneal dialysis and abdominocentesis, were not associated with a higher risk of mortality related to *A. baumannii* bacteremia in this study.

Different sources of bacteremia may be associated with different outcomes. Previous study suggested that *Acinetobacter* bacteremia complicated with pneumonia was associated with a higher mortality rate while catheter-related bacteremia appeared to be less lethal [11,24,25]. Similar results were found in this study, with a fatality rate of 3.85% (1/26) in catheter-related bacteremia and 39.2% (20/51) in bacteremic pneumonia.

In vitro susceptibility tests showed that imipenem remained the most effective drug against *A. baumannii* isolates in Taiwan, while susceptibility to third- or fourth-generation cephalosporins, broad-spectrum penicillins, and ciprofloxacin varied considerably.

In recent years, the emergence of carbapenem-resistant or even pandrug-resistant *A. baumannii* has been an increasing problem for both control and treatment of nosocomial infections [5,7,26]. A recent study on pandrug-resistant *A. baumannii* bacteremia in Taiwan by Kuo et al showed a 60% crude mortality and a 40% mortality directly related to the bacteremic episode [5]. In our patients, carbapenem-resistant and pandrug-resistant isolates were associated with an attributable mortality rate of 44.4% (4/9) and 50.0% (3/6), respectively. Although the mortality rate was not significantly higher in *A. baumannii* bacteremia caused by isolates with carbapenem resistance, this difference may have been due to the small number of patients. In addition, 3 of 6 (50%) of pandrug-resistant *A. baumannii* bacteremic episodes were catheter-related infections, which was a condition associated with a favorable outcome.

Patients with *Acinetobacter* bacteremia are almost always treated with empirical antibiotics but are often treated inappropriately. Leibovici et al found that *Acinetobacter* sp. was among the 4 microorganisms which were independently associated with inappropriate antibiotic treatment [27]. Appropriate and early antimicrobial therapy had been shown to decrease the mortality related to bacteremia [25]. However, the impact of appropriate antibiotic treatment in *A. baumannii* bacteremia remains unclear. Reports showed controversial results on this issue, probably due to heterogeneous populations of patients included [11,21,24,28].

In our study, the mortality rate in patients without appropriate antibiotic treatment was substantially higher than in those with appropriate treatment, although this result was not significant. A delay in appropriate antimicrobial therapy, however, did not affect the outcome significantly. Excluding 6 patients who died within 48 h, the median survival after the onset of *A. baumannii* bacteremia in fatal cases was 10 days (range, 3-29 days), while the median duration of delay in administering appropriate antibiotics was 4 days (range, 3-8 days). It is possible that even in the mortality group, most patients still survived long enough to receive at least delayed appropriate antimicrobial therapy. Under this situation, other factors might play more important roles in prognosis compared with timing of treatment with appropriate antibiotics. This might explain why delayed administration of appropriate antibiotics was not associated with a worse outcome in this study.

In conclusion, this study found that advanced age, immunosuppressive status, recent surgery and development of complications such as septic shock, acute renal failure and acute respiratory failure were independently associated with mortality from *A. baumannii* bacteremia. Early identification of patients at high risk for mortality based on these factors is important on account of the high mortality and morbidity associated with this disease.

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