Influence of Genospecies of *Acinetobacter baumannii* Complex on Clinical Outcomes of Patients with Acinetobacter Bacteremia

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Background. *Acinetobacter baumannii* complex infections are increasing in prevalence and are associated with a high mortality. Biochemical classification tests cannot differentiate *A. baumannii* (genospecies 2) from other genospecies. Genospecies typing offers a potential tool to determine whether there are major differences in pathogenicity among the genospecies.

Methods. Adult patients with *A. baumannii* complex bacteremia in intensive care units were prospectively observed from January 2007 through July 2009. *A. baumannii* complex was identified by biochemical methods and the Phoenix bacterial identification system. Genospecies were identified by 16S-23S ribosomal RNA intergenic-spacer sequencing.

Results. Among the 135 patients with *A. baumannii* complex bacteremia, 87 (64.4%) had isolates that belonged to genospecies 2, 36 (26.7%) had isolates that belonged to genospecies 13TU, and 12 (8.9%) had isolates that belonged to genospecies 3. Patients with *A. baumannii* (genospecies 2) bacteremia were more likely to have pneumonia than were patients with bacteremia due to genospecies 13TU (63.2 % vs 27.8%; *P* =.001), whereas patients with bacteremia due to genospecies 13TU were more likely to have primary bacteremia (69.4% vs 20.7%; *P* <.001). Genospecies 2 was less susceptible to antibiotics than were other genospecies. It was associated with a higher rate of mortality than was genospecies 13TU (58.6% vs 16.7%; *P* < .001). On multivariate analysis, genospecies 2 was an independent predictor of mortality (odds ratio, 5.46; 95% confidence interval, 2.00–14.91; *P* = .001).

Conclusions. Genospecies 2 of the *A. baumannii* complex was associated with greater resistance to antibiotics and higher mortality among bacteremic patients, compared with other genospecies, especially genospecies 13TU. These findings emphasize the need to focus on genospecies to better understand the pathogenesis and epidemiology of infections caused by the *A. baumannii* complex.

Acinetobacter baumannii is a nonfermenting gram-negative aerobic coccobacillus that can contaminate health care instruments and environmental surfaces [1]. The prevalence of health care–associated infections caused by *A. baumannii* is increasing among patients in intensive care units (ICUs) [2, 3] and among immunocompromized populations [4, 5]. These infections are associated with a high mortality and a prolonged length of hospital stay [6, 7].

Acinetobacter genospecies 1 (*Acinetobacter calcoaceticus*), genospecies 2 (*A. baumannii*), genospecies 3, and genospecies 13TU are phenotypically similar and are referred to as the *A. calcoaceticus–A. baumannii* complex (ACB complex) [8]. Genospecies 2 is primarily associated with human diseases [9]. The clinical manifestations and outcomes for the other genospecies within

the ACB complex need additional clarification. Identification limited to the ACB complex can be misleading, because the ACB complex genospecies differ in their biological and pathological characteristics. For example, genospecies 1 is considered to be an environmental pathogen and has been rarely implicated as a cause of severe disease [10, 11]. There are also differences among the ACB complex genospecies in their ability to colonize human skin [12, 13], antimicrobial susceptibility [14–19], and mechanisms of resistance to antimicrobial agents [15, 20, 21]. We hypothesized that patients infected with genospecies 2 of ACB complex may have a poorer outcome than those infected with other genospecies, because genospecies 2 tends to be more resistant to antimicrobial agents [14–19] and is more commonly isolated from patients than other genospecies [22]. The current prospective observational study was designed to test this hypothesis by comparing the clinical characteristics, microbiological findings, and final outcomes for patients with bacteremia caused by genospecies 2, compared with patients with bacteremia due to other members of the ACB complex.

METHODS

Study Population

This study was conducted among patients admitted to ICUs at the National Taiwan University Hospital (NTUH). NTUH is a 2200-bed teaching hospital located in Taipei, Taiwan. It provides both primary and tertiary medical care. ACB complex bacteremia was defined as the presence of ≥1 positive blood culture results for patients with signs and symptoms of infection. Patients with ACB complex bacteremia were prospectively enrolled from January 2007 through July 2009. Patients <18 years of age or with incomplete medical records were excluded. For patients with multiple episodes of ACB complex bacteremia, only the first episode was included. The study was approved by the Institutional Review Board of National Taiwan University Hospital.

Microbiological Studies

Blood cultures were processed by the hospital microbiology laboratory using the Bactec 9240 system (Becton Dickson). The ACB complex was primarily identified by biochemical methods [23], and the Phoenix bacterial identification system (BD Diagnostics). Antimicrobial susceptibility was determined by the disk diffusion method for gentamicin, amikacin, ciprofloxacin, levofloxacin, cefepime, ceftazidime, aztreonam, ticarcillin-clavulanate, meropenem, and ampicillin-sulbactam according to Clinical and Laboratory Standards Institute (CLSI) criteria [24]. Genospecies of blood isolates enrolled were identified according to 16S–23S ribosomal RNA (rRNA) gene intergenic spacer (ITS) region, as previously described [16]. Minimum inhibitory concentrations (MICs) of amikacin, ciprofloxacin, imipenem, and

ampicillin-sulbactam were determined by agar dilution methods according to CLSI criteria [24]. The Etest was used for colistin [24, 25]. MICs of tigecycline were determined by agar dilution test. Isolates with MIC ≤2 μg/mL to tigecycline were considered to be susceptible [26].

Data Collection

Demographic data, data on underlying diseases, and data on the site of infection were collected prospectively. The Charlson comorbidity index [27] was used to adjust for underlying conditions. Immunosuppressive therapy was defined as receipt of antineoplastic drugs, cyclophosphamide, or other immunosuppressive agents within 6 weeks after onset of ACB complex bacteremia or receipt of corticosteroids at a dosage equivalent to or higher than 20 mg of prednisolone daily for at least 2 weeks or 30 mg of prednisolone daily for at least 1 week before a positive blood culture for ACB complex bacteremia was obtained [28]. Sites of primary infection were identified according to definitions of the Centers for Disease Control and Prevention [29]. If no infectious focus could be identified, the bacteremia was classified as primary. Initial blood tests included white blood cell and platelet counts; determination of hemoglobin, C-reactive protein, and creatinine levels; and liver function tests (ie, determination of aspartate aminotransferase and total bilirubin levels). The severity of illness was determined by the Acute Physiology and Chronic Health Evaluation II (APACHE II) score [30], Sequential Organ Failure Assessment (SOFA) score [31], and the Pitt bacteremia score [32].

Appropriate empirical antimicrobial therapy was defined as the administration of an antimicrobial agent to which the patient's isolate had been shown to be susceptible in vitro within 24 h after the first positive blood culture for the ACB complex had been obtained. All-cause in-hospital mortality was recorded. Bacteremia-related death (attributable mortality) was defined as a blood culture positive for the ACB complex and death before resolution of signs and symptoms of bacteremia. Attributable mortality was used in the outcome analysis. Patients who remained alive following the episode of ACB complex bacteremia were classified as the survivor group.

Statistical Analysis

Median values and interquartile ranges (IQRs) were calculated for continuous variables, and percentages were used for categorical variables. The associations between the clinical presentations of ACB complex genospecies 2, genospecies 13TU, and genospecies 3 were compared using Kruskal–Wallis one-way analysis of variance (ANOVA), or Fisher's exact test. Post hoc analysis using Mann–Whitney U test or Fisher's exact text used a Bonferroni-adjusted α for pair-wise comparisons if the result of the initial Kruskal–Wallis one-way ANOVA or Fisher's exact test was statistically significant.

Multivariate logistic analysis and multivariate Cox proportional hazards models were used for outcome analysis. Variables included sex, age, length of hospital stay before the onset of bacteremia, infection focus, carbapenem resistance, appropriate use of empirical antibiotics, Charlson comorbidity index, use of immunosuppressive drugs, and genospecies. Variables with a P value <.2 in the univariate regression were added in a stepwise manner and selected to determine the final model for multiple variables analysis. A P value <.05 was considered statistically significant. Data were analyzed using Stata software, version 10 (StataCorp).

RESULTS

During the study period, 149 ICU patients were found to have ACB complex bacteremia by phenotypic identification. Fourteen (9.4%) were excluded from the study according to the 16S–23S rRNA gene ITS region sequencing results. The distribution of ACB complex genotypes among the remaining 135 patients consisted of 87 patients (64.4%) with genospecies 2 isolates, 36 (26.7%) with genospecies 13TU isolates, and 12 (8.9%) with genospecies 3 isolates.

The demographic characteristics and underlying diseases of the 135 patients with ACB complex bacteremia are shown in Table 1. There were no significant differences among patients with different genospecies with respect to age, sex, or length of hospital stay. The Charlson scores were significantly different among the 3 groups ($P = .003$). Patients with genospecies 3 bacteremia had significantly higher Charlson scores and more metastatic malignancies than did patients with genospecies 2 bacteremia ($P = .004$ and .005, respectively). Patients with genospecies 13TU bacteremia had more frequent hypertension and were more likely to have a history of coronary artery disease but had less immunosuppressive therapy than did patients with bacteremia due to the other genospecies. Seventy-one patients had repeat blood cultures. Of these, 21 (29.6%) had persistent bacteremia. The median duration of persistent bacteremia was 3.5 days (range, 1–28 days).

The sources of infection for ACB complex bacteremia are shown in Table 2. Pneumonia was the most frequent source of bacteremia for those with genospecies 2 isolates (63.2% vs 27.8%; $P = .001$ for genospecies 2 vs 13TU, respectively). In contrast, primary bacteremia was the most frequent source of bacteremia for those with genospecies 13TU isolates (69.4% vs 20.7%; $P < .001$ for genospecies 13TU vs 2, respectively).

The clinical characteristics of the study patients are summarized in Table 3. There were no significant differences in APACHE II scores among the groups. The Pitt bacteremia score was significantly higher for those with genospecies 2 isolates than it was for those with genospecies 13TU isolates

on the day when the ACB complex bacteremia was first noted ($P = .002$). The laboratory findings were similar among the 3 groups. The only exception was a lower platelet count among patients with genospecies 2 than among patients with genospecies 13TU ($P = .006$). Genospecies 2 blood isolates exhibited more carbapenem resistance than did genospecies 13TU and genospecies 3 isolates ($P < .001$ and .002, respectively). There were also higher rates of appropriate empirical antimicrobial therapy among patients with genospecies 13TU and genospecies 3 isolates than there were among those with genospecies 2 isolates ($P < .001$ and .003, respectively).

The all-cause in-hospital mortality was 59.3% for the 135 patients with ACB complex bacteremia. The highest rate was 67.8% for patients with genospecies 2 isolates, followed by 58.3% for those with genospecies 3 isolates and 38.9% for those with genospecies 13TU isolates ($P = .01$). The attributable mortality was also higher for patients with genospecies 2 isolates than it was for the other patient groups.

The attributable mortality rates were similar between patients who did and those who did not receive appropriate empirical antimicrobial therapy (40.5% vs 47.3%; $P = .58$). Of 93 patients with inappropriate empirical antimicrobial therapy, there were mortality difference among these 3 groups ($P = .05$), especially between the genospecies 2 group and the 13TU group (53.4% vs 20%; $P = .02$). Of 42 patients with appropriate empirical antimicrobial therapy, the mortality rate among those with genospecies 2 isolates was significantly higher than the mortality rate among those with genospecies 13TU isolates (85.7% vs 14.3%; $P < .001$) (Table 3). Of the 12 patients who died due to genospecies 2 bactemiea and received appropriate empirical antimicrobial treatment, 5 received a combination of 2 antimicrobial agents. The antimicrobial agents included carbapenems ($n = 6$), anti-pseudomonas β-lactams ($n = 6$), fluoroquinolones ($n = 2$), colistin ($n = 2$), and tigecycline ($n = 1$).

The antimicrobial susceptibility profiles of the 3 genospecies are shown in Table 4. Genospecies 2 exhibited the highest frequency of resistance to all antibiotics tested, with the exception of colisitin. There were significantly different rates of resistance to ciprofloxacin, amikacin, imipenem, ampicillin-sulbactam, and tigecycline among the 3 groups. Genospecies 2 isolates had significantly higher rates of resistance to ciprofloxacin, amikacin, imipenem, and ampicillin-sulbactam (all $P < .001$) and tigecycline ($P = .008$) than did genospecies 13TU isolates. Genospecies 2 isolates also had significantly higher rates of resistance to ciprofloxacin and ampicillin-sulbactam than did genospecies 3 isolates ($P < .001$ and .003, respectively). All isolates of these 3 groups were susceptible to colistin.

The logistic regression analysis for the factors that significantly predicted mortality is shown in Table 5. In univariate analysis, pneumonia, isolates with carbapenem resistance,

Table 1.   Demographic Characteristics and Underlying Diseases of Patients with *Acinetobacter baumannii* Complex Bacteremia

Characteristic	*A. baumannii* (Genospecies 2) (n = 87)	Genospecies 13TU (n = 36)	Genospecies 3 (n = 12)	Overall	Genospecies 2 vs 13TU	Genospecies 2 vs 3
Demographic characteristic						
Age, years	61.8(48.7–74.5)	73.7(52.0–80.7)	71.8(48.9–80.7)	.20		
Sex, male/female	53/34	26/10	6/6	.34		
Days of prior hospitalization[a]	17 (8–31)	19 (10–31.5)	21 (9–50.5)	.63		
Days of prior ICU stay[a]	10 (1–17)	10 (4–20.5)	3 (0.5–8)	.11		
Past history and underlying disease						
Charlson score	3 (2–6)	5.5 (3–7)	6 (4.5–8)	.003	.02	.004
Diabetes mellitus without end organ damage	28 (32.2)	16 (44.4)	2 (16.7)	.20		
Diabetes mellitus with end organ damage	13 (14.9)	9 (25.0)	0 (0)	.13		
Liver cirrhosis	18 (20.7)	11 (30.6)	5 (41.7)	.18		
Hypertension	31 (35.6)	22 (61.1)	6 (50.0)	.03	.016	.36
Coronary artery disease	6 (6.9)	9 (25.0)	0 (0)	.01	.012	>.99
Congestive heart failure	13 (14.9)	9 (25.0)	1 (8.33)	.37		
Chronic renal insufficiency	27 (31.0)	14 (38.9)	3 (25.0)	.63		
Chronic obstructive pulmonary disease	12 (13.8)	6 (16.7)	1(8.3)	.86		
Autoimmune disease	9 (10.3)	0 (0)	1 (8.3)	.11		
Usage of immunosuppressive agent	41 (47.1)	8 (22.2)	6 (50.0)	.03	.015	>.99
Leukemia	10 (11.5)	0 (0)	0 (0)	.07		
Lymphoma	4 (4.6)	1 (2.8)	1 (8.3)	.64		
Solid malignancies	15 (17.2)	10 (27.8)	2 (16.7)	.39		
Metastatic malignancy	11 (12.6)	5 (13.9)	6 (50.0)	.01	>.99	.005

NOTE.   Data are median value (interquartile range) for continuous variables and number of cases (%) for categorical variables. ICU, intensive care unit.

[a] Days of hospitalization and ICU stay prior to onset of bacteremia.

immunosuppressive agents, low platelet counts, high APACHE II scores at ICU admission, and genospecies 2 were significant predictive factors of mortality. On multivariate logistic regression analysis, platelet count, high APACHE II score, and genospecies 2 bacteremia were significant independent predictors for mortality. In multivariable Cox proportional hazards model analysis, genospecies 2 bacteremia (adjusted hazard ratio

[AHR], 3.04; 95% confidence interval [CI], 1.47–6.26; P = .003) was an independent factor for rapid mortality.

When the Pitt bacteremia score was included in the multivariate logistic analysis, both genospecies 2 (odds ratio [OR], 4.08; 95% CI, 1.61–10.31; P = .003) and Pitt bacteremia score (OR, 1.28; 95% CI, 1.07–1.54; P = .008) were independent predictors for mortality. In addition, both genospecies 2 (AHR,

Table 2.   Infectious Foci of Patients with *Acinetobacter baumannii* Complex Bacteremia

	No. (%) of patients			P		
Infection source[a]	*A. baumannii* (genospecies 2) (n = 87)	Genospecies 13TU (n = 36)	Genospecies 3 (n = 12)	Overall	Genospecies 2 vs 13TU	Genospecies 2 vs 3
Primary bacteremia	18 (20.7)	25 (69.4)	5 (41.7)	<.001	<.001	.14
Pneumonia	55 (63.2)	10 (27.8)	5 (41.7)	.001	.001	.21
Catheter-related infection	17 (19.5)	1 (2.8)	1 (8.3)	.04	.02	.69
Intra-abdominal infection	5 (5.8)	0 (0)	0 (0)	.44		
Surgical site infection	7 (8.1)	1 (2.8)	0 (0)	.51		

[a] Patients may have had >1 focus of infection.

Table 3. Clinical Characteristics of Patients with *Acinetobacter baumannii* Complex Bacteremia

Characteristic	*A. baumannii* (Genospecies 2) (n = 87)	Genospecies 13TU (n = 36)	Genospecies 3 (n = 12)	Overall	Genospecies 2 vs 13TU	Genospecies 2 vs 3
At ICU admission						
APACHE II	25 (20–31)	22.5 (16–28)	14.5 (9.0–29.5)	.09		
On day 0[a]						
Pitt bacteremia score	5 (4–7)	4 (2–5)	3.5 (2.0–5.5)	.005	.002	.09
SOFA score	13 (9–17)	8 (4–11)	8.5 (6–15)	.02	.008	.27
White blood cell count, cells/μL	9795 (4670–19480)	12035 (7970–18620)	7605 (3270–14360)	.22		
Hemoglobin level, g/dL	9.8 (8.6–10.8)	9.7 (9.0–10.6)	9.2 (7.8–10.4)	.52		
Platelet count, platelets ×10³/μL	86.5 (48–165)	133 (76–246)	103.5 (41–208)	.02	.006	.57
Aspartate aminotransferase level, U/L	45 (30–87)	59 (35–89)	59 (35.5–70.5)	.95		
Total bilirubin level, mg/dL	2.45 (.77–8.29)	2.10 (.71–6.55)	2.77 (1.02–3.6)	.99		
Creatinine level, mg/dL	1.6 (0.9–2.4)	1.2 (0.9–2.7)	1.3 (1–2.7)	.73		
C-reactive protein level, mg/dL	9.36 (4.22–16.12)	6.49 (2.48–10.38)	11.76 (9.93–16.79)	.21		
Carbapenem resistance[b]	63 (72.4)	7 (19.4)	3 (25.0)	<.001	<.001	.002
Appropriate empirical antimicrobial therapy[c]	14 (16.1)	21 (58.3)	7 (58.3)	<.001	<.001	.003
Mortality						
All cause in-hospital mortality	59 (67.8)	14 (38.9)	7 (58.3)	.01	.004	.53
Attributable mortality	51 (58.6)	6 (16.7)	4 (33.3)	<.001	<.001	.13

NOTE. Data are median value (interquartile range) for continuous variables and no. of cases (%) for categorical variables. APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment.

[a] Day 0 was the day on which blood was drawn, which was the day on which the first blood culture positive for *Acinetobacter baumannii* complex was obtained.

[b] Results of carbapenem resistance were determined by disk diffusion method according to Clinical and Laboratory Standards Institute criteria.

[c] Appropriate empirical antimicrobial therapy was defined as the administration of an antimicrobial agent to which the patient's isolate had been shown to be susceptible in vitro within 24 h after the first positive blood culture for the ACB complex had been obtained.

2.48; 95% CI, 1.18–5.21; P = .017) and Pitt bacteremia score (AHR, 1.29; 95% CI, 1.16–1.43; P < .001) were found to be independent risk factors in the multivariate Cox regression.

The Kaplan-Meier survival curves for ACB complex bacteremia caused by genospecies 2 and genospecies 13TU are shown in Figure 1. Nearly eighty percent of patients with genospecies 13TU bacteremia survived through day 28, compared with only 40% of patients with genospecies 2 bacteremia (P < .001, by log-rank test). There was no significant differences in survival between those with genospecies 2 and those with genospecies 3 bacteremia (P = .22).

DISCUSSION

We found that *A. baumannii* genospecies 2 accounted for approximately two-thirds (64.4%) of ACB bacteremias among critically ill patients. Genospecies 2 was significantly more often associated with pneumonia and severe infection and was associated with greater resistance to a wide variety of antimicrobial agents than were the other genospecies. It was a significant independent predictive factor for mortality.

A. baumannii infections are associated with a high mortality and increased length of hospital stay in critically ill patients [7]. The overall mortality of patients with *A. baumannii* bacteremia

is nearly 50% [33, 34]. The rate of antimicrobial resistance is increasing, and this limits treatment options [17, 35]. It is difficult to differentiate *A. baumannii* from the ACB complex by the classic biochemical typing methods that have been used in previous studies [7,33–35]. Biochemical typing tends to underestimate the virulence and severity of infections caused by the ACB complex, because it dilutes the effect of *A. baumannii*. Although the clinical characteristics and risk factors for mortality in patients with *A. baumannii* bacteremia have been examined in numerous studies [2, 5, 36, 37], few studies have included molecular methods to identify specific genospecies [11]. None of these studies compared the clinical impact of bacteremia caused by different genospecies among the ACB complex.

The current study demonstrates that specific genospecies within the ACB complex differ in their pathogenicity and in their frequency of antimicrobial resistance. Previous studies have revealed higher levels of antimicrobial resistance among *A. baumannii* than among genospecies 3 and genospecies 13TU isolates [14–16, 38, 39], especially to ciprofloxacin, ampicillin-sulbactam, and imipenem [14–16, 38]. The high rate of antimicrobial resistance to *A. baumannii* may be responsible for inappropriate selection of empirical therapy and poorer outcome. In the current prospective observational study, we found higher rates of

Table 4. Antimicrobial Susceptibility Tests of Clinical Isolates of *Acinetobacter baumannii* Complex

Variable	A. baumannii (genospecies 2) (n = 87)		Genospecies 13TU (n = 36)		Genospecies 3 (n = 12)		P[a]		
	Concentration, μg/mL	Susceptible isolates, %	Concentration, μg/mL	Susceptible isolates, %	Concentration, μg/mL	Susceptible isolates, %	Overall	Genospecies2 vs 13TU	Genospecies2 vs 3
Ciprofloxacin									
MIC_{50}	32	17.4	0.25	80.6	0.25	75.0	<.001	<.001	<.001
MIC_{90}	>128		8		128				
Range	0.06 to >128		0.06–64		0.06 to >128				
Amikacin									
MIC_{50}	>128	27.9	4	80.6	8	66.7	<.001	<.001	.017
MIC_{90}	>128		32		>128				
Range	2 to >128		2 to >128		2 to >128				
Imipenem									
MIC_{50}	8	48.8	0.25	94.3	0.25	66.7	<.001	<.001	.25
MIC_{90}	32		4		16				
Range	0.25–64		0.125–32		0.125–32				
Sulbactam									
MIC_{50}	16	29.1	1	80.7	1	75.0	<.001	<.001	.003
MIC_{90}	16		16		8				
Range	0.5–32		0.5–64		0.5–16				
Tigecycline									
MIC_{50}	2	65.1	0.25	88.9	0.25	83.3	.02	.008	.33
MIC_{90}	8		4		4				
Range	0.25–16		0.125–8		0.25–4				
Colistin									
MIC_{50}	0.25	100	0.19	100	0.25	100			
MIC_{90}	0.38		0.38		0.38				
Range	0.094–0.75		0.094–0.38		0.125–0.38				

NOTE. MIC_{50}, 50% minimum inhibitory concentration; MIC_{90}, 90% minimum inhibitory concentration.

[a] The susceptibility of various antimicrobial agents among *Acinetobacter baumannii* complex were compared by Fisher's exact test

antimicrobial resistance and poorer outcome for patients infected with genospecies 2 (*A. baumannii*) than for those infected with other members of the ACB complex.

Newer-generation antimicrobial agents, such as tigecycline, and the older-generation antimicrobial agent colistin are now being used more often to treat infections caused by multidrug-resistant *Acinetobacter* species. In the current study, we found significantly higher MICs in *A. baumannii* than in other species for all of the antimicrobial agents that were tested, including tigecycline. Colistin was the only exception. Ko et al [14] found that 9 imipenem–intermediate susceptible and 13 imipenem-resistant isolates of *A. baumannii* were susceptible to tigecycline. In the current study, we found that only 64% of carbapenem-resistant *A. baumannii* isolates were susceptible to tigecycline. Ko et al [14] showed that MICs of colistin and tigecycline were similar among *A. baumannii* and other genospecies 3 isolates. We also found that all members of the ACB complex were highly susceptible to colistin, including carbapenem-resistant isolates of *A. baumannii*. However, *A. baumannii* was more resistant to tigecycline than were other genospecies.

The mortality in patients with genospecies 2 bacteremia who received appropriate empirical antimicrobial treatment was exceptionally high (85.7%). This may have been attributable to the irreversible severity of their disease. Patients infected with genospecies 2 strains had a significantly higher Pitt bacteremia score. This was independently associated with a higher mortality.

The ACB complex has been implicated in numerous nosocomial outbreaks [40]. Phenotypic typing systems are inadequate to differentiate *A. baumannii* from genospecies 3 and genospecies 13TU strains [8]. No single metabolic test can distinguish *Acinetobacter* species from other similar glucose non-fermenters [11]. For example, in the current study, 14 (9.4%) of the 149 blood culture isolates were phenotypically identified as ACB complex bacteremia but had to be excluded according to the 16S–23S rRNA gene ITS region sequencing results. Several studies have shown that 0.3% [14], 4.3% [16], and 8.6% [15] of

Table 5. Logistic Regression Analysis of Predictor of Mortality Among Patient with *Acinetobacter baumannii* Complex Bacteremia

Risk factor	Mortality[a](n = 61)	Survivor(n = 74)	Univariate analysis		Multivariate analysis	
			Odds ratio(95% CI)	P	Odds ratio(95% CI)	P
Age, years	61.3 (50.7–74.4)	69.1 (49.1–79.9)	0.99 (0.91–1.01)	.18		
Sex, male/female	37/24	48/26	0.84 (0.41–1.68)	.61		
Days of prior hospitalization[b]	20 (10–34)	17 (10–31)	1.00 (0.99–1.02)	.78		
Primary bacteremia	16 (26.2)	32 (43.2)	0.47 (0.22–.97)	.04		
Pneumonia	39 (63.9)	31 (41.9)	2.46 (1.22–4.94)	.01		
Catheter-related infection	9 (14.8)	10 (13.5)	1.11 (0.42–2.93)	.84		
Carbapenem resistance	44 (72.1)	29 (39.2)	4.02 (1.94–8.32)	<.001		
Appropriate empirical antimicrobial therapy[c]	17 (28.8)	25 (33.8)	0.75 (0.36–1.58)	.46		
Charlson score	4 (2–6)	4 (3–6)	1.00 (0.87–1.13)	.95		
Use of immunosuppressive agent	32 (52.5)	23 (31.1)	2.45 (1.21–4.94)	.01		
White blood cell count, cells/μL	8710(2210–18340)	12070(7490–17790)	1.00 (1.00–1.00)	.67		
Hemoglobin level, g/dL	9.1 (8.3–10.7)	10 (9.2–10.6)	0.84 (0.68–1.03)	.10		
Platelet count, platelets $\times 10^3$/μL[d]	64 (31–121)	160 (82–255)	0.99 (0.98–.99)	<.001	0.99 (.98–.99)	.001
APACHE II at ICU admission	26 (21–34)	21.5 (15–27.5)	1.07 (1.02–1.12)	.003	1.07 (1.01–1.13)	.013
Genospecies (genospecies 13TU as reference)						
Genospecies 2	51 (83.6)	36 (48.7)	7.08 (2.67–18.78)	<.001	5.46 (2.00–14.91)	.001
Genospecies 3	4 (6.6)	8 (10.8)	2.50 (0.57–11.05)	.23		

NOTE. Data are median values (interquartile range) for continuous variables and no. of cases (%) for categorical variables. APACHE II, Acute Physiology and Chronic Health Evaluation II; CI, confidence interval; ICU, intensive care unit.

[a] Attributable mortality.

[b] Days of hospitalization and ICU stay prior to onset of bacteremia.

[c] Appropriate empirical antimicrobial therapy was defined asthe administration of an antimicrobial agent to which the patient's isolate had been shown to be susceptible in vitro within 24 h after the first positive blood culture for the ACB complex had been obtained.

[d] Per 1000 platelets/μL increment.

isolates were misclassified according to conventional phenotypic methods. For example, *Acinetobacter* genospecies 10, 11, and 14BJ [15, 16] have been misidentified as belonging to the ACB complex. Misidentification can also exclude some isolates that should belong to the ACB complex.
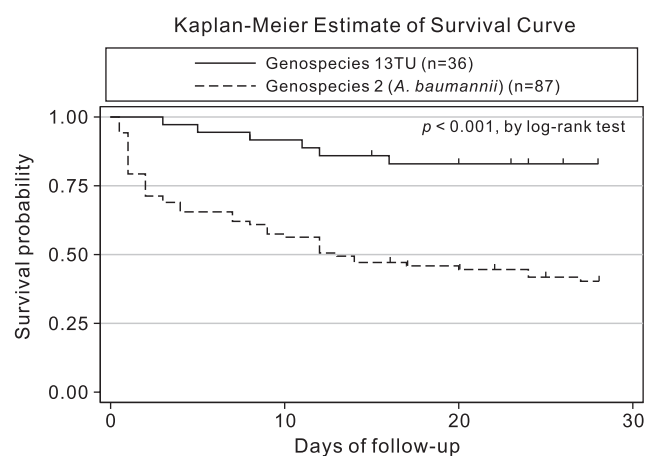

Kaplan-Meier Estimate of Survival Curve

Figure 1. Comparison of Kaplan–Meier survival curves, at 28 days, in patients with *Acinetobacter baumannii* complex bacteremia between *A. baumannii* (genospecies 2) group and genospecies 13TU group.

This study has several limitations. First, we only included patients in ICUs, where the ACB complex is most prevalent and is associated with the highest mortality rates [2, 3]. Therefore, our findings may not apply to patients with mild infections and those without bacteremia. Second, to our knowledge, this is the largest clinical comparison of the 3 molecularly identified genospecies, but the number of cases was relatively small, compared with the number of cases of bacteremia due to other causes. Third, the Pitt bacteremia score was used as an indicator of severity, but it is also a predictor for the outcome of bacteremia and may not be applicable in the multivariate analysis of mortality. Nevertheless, we found that both bacteremia due to genospecies 2 and the Pitt bacteremia score were independent predictors of mortality.

In conclusion, we found that *A. baumannii* (genospecies 2) bacteremia in critically ill patients exhibits higher levels of antimicrobial resistance and is associated with more-severe infections and greater mortality, compared with other members of the ACB complex, particularly genospecies 13TU. Patients with *A. baumannii* (genospecies 2) bacteremia were significantly more likely to have pneumonia. In contrast, patients with genospecies 13TU bacteremia were significantly more likely to have primary bacteremia. Additional studies are needed to identify

the putative virulence factors associated with individual geno-species of the ACB complex.

Acknowledgments

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