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ORIGINAL ARTICLE

Comparison between bacteremia caused by *Acinetobacter pittii* and *Acinetobacter nosocomialis*

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Background/purpose: Patients with *Acinetobacter pittii* and *Acinetobacter nosocomialis* bacteremia have lower mortality rates than those with *Acinetobacter baumannii* bacteremia. However, it is unknown whether these organisms differ in outcomes of bacteremic patients. We conducted this study to answer this question.
Methods: In this retrospective study conducted at a teaching hospital in Taiwan, we enrolled all 86 patients who had developed *A. pittii* bacteremia and those with *A. nosocomialis* bacteremia from 2000 to 2008 while matching for age, sex, Acute Physiology and Chronic Health Evaluation II score, and appropriate antimicrobial therapy. After adjustment, we accessed the clinical characteristics and 14- and 28-day mortalities.
Results: We found that the patients with *A. pittii* bacteremia had multiple comorbidities less often and received invasive procedures less frequently. The 14-day mortality rate of patients with *A. pittii* or *A. nosocomialis* bacteremia was 14% and 7%, respectively, whereas their 28-

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day mortality rate was 17% and 9%, respectively. Using the mortality rate in patients with *A. nosocomialis* bacteremia as a reference, the odds ratios for the 14- and 28-day crude morality in those with *A. pittii* were 2.16 [95% confidence interval (CI), 0.77—6.05] and 2.06 (95% CI, 0.82—5.15), respectively, whereas the adjusted odds ratios for 14- and 28-day mortality were 1.89 (95% CI, 0.56—6.14) and 1.67 (95% CI, 0.59—4.78) respectively.

Conclusion: Our 8-year study showed that the mortality rate of *A. pittii* bacteremia was higher but the difference was not statistically significant.

Introduction

The *Acinetobacter calcoaceticus—baumannii* (Acb) complex has emerged as an important nosocomial pathogen. Among the members of this family, the phenotypically undifferentiated *A. baumannii*, *A. pittii*, and *A. nosocomialis* are the three most common *Acinetobacter* species isolated in clinical settings.[1—4] *A. baumannii* has been extensively studied because it has been associated with a high mortality rate (29.8—36.9%).[4—8] However, *A. pittii* and *A. nosocomialis* are increasingly identified as causative agents of nosocomial infections.[3,8] Recent studies have determined that the two species accounted for 29% of Acb complex bacteremia in the USA, 24—45% in Taiwan, 50% in Korea, and 66% in Norway.[4,8—11]

Previous studies demonstrated that *A. pittii* and *A. nosocomialis* were less multidrug resistant and associated with lower mortality rates than *A. baumannii*.[8,11] However, it was still unknown whether patients infected with *A. pittii* and *A. nosocomialis* had different clinical presentations, risk factors, and outcomes. Because the mortality of patients can be greatly affected by host factors such as the disease severity and the appropriateness of antimicrobial therapy, we compared the clinical outcomes of patients with monomicrobial *A. pittii* or *A. nosocomialis* bacteremia after matching for age, sex, disease severity, and the appropriateness of treatment in this study.

Materials and methods

Study design and data collection

During 2000—2008, all adult patients with monomicrobial *A. pittii* bacteremia at Taipei Veterans General Hospital, Taipei, Taiwan were included. The patients' charts were reviewed and those without complete clinical data were excluded. Demographic characteristics, the Acute Physiology and Chronic Health Evaluation (APACHE) II score within 24 hours of the onset of bacteremia, the origin of bacteremia, any underlying disease, any concurrent invasive procedures, and the concurrent use of intravenous antimicrobials were all recorded for each participant.

The onset of bacteremia was defined as the day when the blood culture that eventually grew *A. pittii* or *A. nosocomialis* was obtained. The episodes of bacteremia were categorized as intensive care unit (ICU)-acquired if the blood culture yielded a pathogen within 48 hours after ICU admission. The origin of bacteremia was clarified as previously suggested.[12] Chronic lung diseases included chronic obstructive pulmonary disease, asthma, bronchiectasis, pulmonary fibrosis, and old pulmonary tuberculosis.[7] We defined chronic renal disease as an estimated glomerular filtration rate < 60 mL/min/1.73 m^2 and end-stage renal disease as glomerular filtration rate < 10 mL/min/1.73 m^2. Immunosuppressant therapy was defined as treatment with cytotoxic agents for malignancy, autoimmune disease, or organ transplantation or as treatment with corticosteroids at a dosage equivalent to > 10 mg of prednisolone daily for 5 days within 4 weeks of the onset of bacteremia. We defined appropriate antimicrobial therapy as the administration of at least one effective antimicrobial agent according to susceptibility tests, at an appropriate dose and route within 48 hours of the onset of bacteremia.

Patients with monomicrobial *A. pittii* bacteremia were matched 1:1 to those with monomicrobial *A. nosocomialis* bacteremia based on age, sex, APACHE II score, and the appropriateness of antimicrobial therapy. The pool of patients with monomicrobial *A. nosocomialis* was adopted from the same hospital and study period.[13] The outcome measurement was 14- and 28-day mortality. The protocol was approved by the Institutional Review Board of Taipei Veterans General Hospital.

Bacterial isolates and identification

After testing with the API ID 32 GN system (bioMérieux, Marcy l'Etoile, France) or the Vitek 2 system (bioMérieux), the Acb complex were subjected to the multiplex polymerase chain reaction (PCR) method to identify *A. baumannii* to the genomic species level.[14] *A. pittii* or *A. nosocomialis* was confirmed using sequence analysis of the 16S—23S ribosomal DNA intergenic space.[15] The susceptibility results were tested and interpreted using the agar dilution test according to the Clinical and Laboratory Standards Institute.[16]

Statistical analysis

The differences between *A. nosocomialis* and *A. pittii* groups were analyzed using the Student *t* test or the Mann—Whitney *U* test depending on the distribution of the data. The nominal variables were assessed using the Chi-square test with Yate's correction or the Fisher's exact test. Logistic regression was used to model the effect of the two different species on mortality. All variables were entered in a single step to gauge the 14- and 28-day

Table 1 Clinical characteristics of patients infected by *Acinetobacter pittii* and matched cohorts infected by *Acinetobacter nosocomialis*

	A. nosocomialis		*A. pittii*		*p*
	No.	%	No.	%	
Male	58	67.4	58	67.4	>0.99
Age	59.3	18.8	57.8	18.8	0.607
APACHE II score	17	7.6	17.1	7.6	0.944
Respiratory origin	28	32.6	16	18.6	0.054
ICU admission	38	44.2	23	26.7	0.025
Underlying diseases					
Alcoholism	5	5.8	10	11.6	0.28
Chemotherapy	13	15.1	25	19.1	0.042
Chronic pulmonary diseases	5	5.8	4	4.7	>0.99
Chronic renal diseases	11	12.8	12	14	>0.99
ESRD	9	10.5	0	0	0.003
Autoimmune diseases	7	8.1	4	4.7	0.535
Congestive heart failure	7	8.1	6	7	>0.99
Coronary artery diseases	11	12.8	5	5.8	0.188
Cerebrovascular diseases	15	17.4	5	5.8	0.03
Haematological malignancy	5	5.8	13	15.1	0.079
Solid tumor	36	41.9	40	46.5	0.645
Hypertension	25	19.1	25	19.1	>0.99
Immunosuppresant	18	20.9	22	25.6	0.589
Liver cirrhosis	6	7	14	16.3	0.094
Neutropenia	4	4.7	9	10.5	0.248
Surgery	36	41.9	22	25.6	0.036
PAOD	3	3.5	1	1.2	0.621
Shock	11	12.8	17	19.8	0.302
Smoking	12	14	15	17.4	0.676
Trauma	5	5.8	3	3.5	
Diabetes	17	19.8	22	25.6	0.467
Invasive procedures					
Abdominal drainage	5	5.8	8	9.3	0.566
Arterial catheterization	8	9.3	3	3.5	0.211
Central venous catheterization	17	19.8	18	20.9	>0.99
Urinary catheter	27	31.4	13	15.1	0.018
Hemodialysis	5	5.8	2	2.3	0.443
Nasogastric tube	27	31.4	14	16.3	0.031
Pulmonary arterial line	1	1.2	3	3.5	0.621
Thoracic drainage	2	2.3	1	1.2	>0.99
Total parental nutrition	5	5.8	5	5.8	>0.99
Tracheostomy	9	10.5	0	0	0.003
Mechanical ventilator	22	25.6	6	7	0.002
Antimicrobial agents					
Penicillins	8	9.3	2	2.3	0.099
Sulbactam-containing	12	14	10	11.6	0.82
Cephalosporin	14	16.3	14	16.3	>0.99
Carbapenem	5	5.8	8	9.3	0.566
Aminoglycosides	11	12.8	10	11.6	>0.99
Tigecycline	1	1.2	1	1.2	>0.99
Sulfamethoxazole/trimethoprim	0	0	1	1.2	>0.99
Appropriate therapy	33	38.4	33	38.4	>0.99

Data are presented as mean value (SD) for continuous variables and the number of cases (%) for categorical variables.
APACHE II = Acute Physiology and Chronic Health Evaluation II; ESRD = end-stage renal disease; ICU = intensive care unit; PAOD, peripheral artery occlusive disease.

Table 2 Crude and adjusted risk of 14-day mortality in patients with *Acinetobacter pittii* compared to a matched cohort

	No. of events	No. of patients	Crude		Adjusted[a]	
			Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*
A. nosocomialis	6	86	Reference		Reference	
A. pittii	12	86	2.16 (0.77–6.05)	0.142	1.89 (0.56–6.14)	0.292

[a] Adjusted for variables listed in Table 1.
CI = confidence interval.

adjusted odds ratio. All analyses were processed with SPSS software version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

During the study period, 86 patients with monomicrobial *A. pittii* bacteremic met the inclusion criteria. The demographic data, underlying comorbidities, invasive procedures performed and antimicrobial agents prescribed for the *A. pittii* and *A. nosocomialis* patients are summarized in Table 1. The mean age of patients was 59 years, and males were predominant (67.4%). The average Apache II score was 17. The most common underlying condition was a solid tumor, followed by diabetes, surgery, and the receipt of immunosuppresants. Most patients had not undergone invasive procedures other than surgery. The proportion of patients who received adequate antimicrobial therapy within 48 hours of the onset of bacteremia was 38.4%.

There was no difference between patients with *A. pittii* or *A. nosocomialis* bacteremia regarding age, sex, appropriateness of antimicrobial therapy, and APACHE II score. However, fewer patients with *A. pittii* bacteremia had been admitted to ICU (26.7% vs. 44.2%, $p = 0.025$). There were no significant intergroup differences for most underlying diseases, except that patients with *A. pittii* bacteremia did have a lower rate of end-stage renal disease (0% vs. 10.5%, $p = 0.003$), cerebral vascular disease (5.8% vs. 12.8%, $p = 0.188$), and history of surgery (25.6% vs. 41.9%, $p = 0.036$). However, more patients with *A. pittii* bacteremia had received chemotherapy (19.1% vs. 15.9%, $p = 0.042$), and more patients with *A. nosocomialis* bacteremia had undergone invasive procedures. These invasive procedures included urinary catheter (31.4% vs. 15.1%, $p = 0.018$), nasogastric tube (31.4% vs. 16.3%, $p = 0.031$), tracheostomy (10.5% vs. 0%, $p = 0.003$), and mechanical ventilator (25.6% vs. 7%, $p = 0.002$). The 14-day mortality rate of patients with *A. pittii* or *A. nosocomialis* bacteremia was 14% (12/86) and 7% (6/86), respectively (Table 2), whereas their 28-day mortality rate was 17% (15/86) and 9% (8/86), respectively (Table 3); these differences were not statistically significant. For the differences among the underlying diseases and procedures, the variables in Table 1 were used for the adjustment. However, patients with *A. pittii* bacteremia still had similar 14- and 28-day mortality rate compared to those with *A. nosocomialis* (adjusted odds ratio 1.89, 95% confidence interval, 0.56–6.14 and 1.67, 95% confidence interval, 0.59–4.78).

Discussion

To the best our knowledge, this is the largest study to specifically describe the clinical characteristics of patients with monomicrobial *A. pittii* bacteremia and that addressed the difference in mortality among non-*baumannii* Acb complex infections. After matching, our study revealed similar mortality rates between patients with *A. pittii* or *A. nosocomialis* bacteremia.

The different bacterial genospecies that constitute the Acb complex are usually identified as *A. baumannii* in most laboratories where only phenotypic identification methods are applied.[4] Differentiation among species is important because of the differences in antimicrobial susceptibility, resistance mechanisms, and pathogenicity.[10,13,17,18] Therefore, a variety of methods have been proposed for the rapid identification and differentiation of the Acb complex,[10,14,19,20] especially for *A. baumannii* because early appropriate therapy for this virulent pathogen is crucial to improve clinical outcomes.[7] Although the clinical outcomes of non-*baumannii* Acb complex infections have not been worse than that of *A. baumannii*, the increasing incidence has also drawn additional clinical attention.

In 2011, Nemec et al[21] proposed the formal names of *A. pittii* and *A. nosocomialis* to replace the names for the names *Acinetobacter* genomic species 3 and genomic species 13TU, respectively, in order to echo their clinical relevance. However, there has been no conclusive evidence

Table 3 Crude and adjusted risk of 28-day mortality in patients with *Acinetobacter pittii* compared to a matched cohort

	No. of events	No. of patients	Crude		Adjusted[a]	
			Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*
Acinetobacter nosocomialis	8	86	Reference		Reference	
A. pittii	15	86	2.06 (0.82–5.15)	0.122	1.67 (0.59–4.78)	0.336

[a] Adjusted for variables listed in Table 1.
CI = confidence interval.

to support which species of the non-*baumannii* Acb complex has more favorable outcomes because of the complexity of the patient presentation and the relatively low mortality of *A. nosocomialis* and *A. pittii*, which would require more patients to demonstrate any differences.

A. nosocomialis bacteremia reportedly has higher mortality than *A. pittii* bacteremia. Wisplinghoff et al[4] observed that the mortality rate in patients with *A. nosocomialis* and *A. pittii* bacteremia were 16% and 13%, respectively. Lee et al[10] had similar findings in Taiwan—the 30-day mortality rates were 16% and 14%, respectively. However, patients with *A. pittii* bacteremia had fewer comorbidities and had received fewer invasive procedures. Wisplinghoff et al[4] reported that patients with *A. pittii* underwent hemodialysis less frequently and had fewer peripheral intravenous line and had urinary catheter insertions than those with *A. nosocomialis* bacteremia. These findings were consistent with ours. The 14- and 28-day adjusted mortality rate of *A. pittii* was not lower than that of *A. nosocomialis* (14% vs. 7% and 17% vs. 9% for 14- and 28-day mortality). The discrepant results of this study compared with previous studies may be the result of our unique study design. We matched important confounding factors including age, sex, APACHE II score, and the appropriateness of antimicrobial therapy and previous literature only looked at the raw mortality rate.

The limitation of this study was that it was a retrospective single-center study. The limited number did not allow us to assess the role of antimicrobial therapy on mortality. However, to the best of our knowledge, this study included the largest number of patients with monomicrobial *A. pittii* over an extended period of time. The study was strengthened by the matching of *A. nosocomialis* patients with similar severity and demographic characteristics.

In conclusion, our 8-year study showed the mortality rate of *A. pittii* bacteremia was higher than *A. nosocomialis* but the difference was not statistically significant. More patients needed to be included from a multicenter study to demonstrate the difference.

Conflicts of interest

T.-L.C. is a medical advisor of TTY Biopharm. No other authors reported disclosures.

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