Bacteremic nosocomial pneumonia caused by *Acinetobacter baumannii* and *Acinetobacter nosocomialis*: a single or two distinct clinical entities?

Y.-T. Lee[1,2,3], S.-C. Kuo[1,4], S.-P. Yang[2,5], Y.-T. Lin[1,2,5], D.-H. Chiang[2,6], F.-C. Tseng[4], T.-L. Chen[1,2,5] and C.-P. Fung[1,2,5]

1) *Institute of Clinical Medicine,* 2) *School of Medicine, National Yang-Ming University, Taipei,* 3) *Department of Medicine, Chutung Veterans Hospital, Hsinchu County,* 4) *National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, Miaoli County,* 5) *Division of Infectious Diseases and* 6) *Department of Critical Care Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*

Abstract

The phenotypically indistinguishable *Acinetobacter baumannii* and *Acinetobacter nosocomialis* have become leading pathogens causing nosocomial pneumonia in critically ill patients. *A. baumannii* and *A. nosocomialis* nosocomial pneumonias were grouped as a single clinical entity previously. This study aimed to determine whether they are the same or a different clinical entity. A total of 121 patients with *A. baumannii* and 131 with *A. nosocomialis* bacteremic nosocomial pneumonia were included during an 8-year period. Despite the similar Charlson co-morbidity scores at admission, patients with *A. baumannii* pneumonia were more likely to have abnormal haematological findings, lobar pneumonia, significantly higher Acute Physiology and Chronic Health Evaluation II scores and higher frequency of shock at the onset of bacteraemia than those with *A. nosocomialis* pneumoni. *A. baumannii* isolates were resistant to more classes of antimicrobials, except colistin, and therefore the patients with *A. baumannii* pneumonia were more likely to receive inappropriate antimicrobial therapy. The 14-day mortality was significantly higher in patients with *A. baumannii* pneumonia (34.7% vs. 15.3%, p 0.001). *A. baumannii* was an independent risk factor for mortality (OR, 2.03; 95% CI, 1.05–3.90; p 0.035) in the overall cohort after adjustment for other risk factors for death, including inappropriate antimicrobial therapy. The results demonstrated the difference in clinical presentation, microbial characteristics and outcomes between *A. baumannii* and *A. nosocomialis* nosocomial pneumonia, and supported that they are two distinct clinical entities.

Keywords: *Acinetobacter baumannii*, *Acinetobacter nosocomialis*, antimicrobial therapy, mortality, pneumonia
Original Submission: 4 May 2012; **Revised Submission:** 2 July 2012; **Accepted:** 8 July 2012
Editor: M. Paul
Article published online: 12 July 2012
Clin Microbiol Infect 2013; **19:** 640–645
10.1111/j.1469-0691.2012.03988.x

Corresponding author: T.-L. Chen, Division of Infectious Diseases, Taipei Veterans General Hospital, No. 201, Section 2, Shih-Pai Road, Taipei, 11217, Taiwan
E-mail: tecklayyy@yahoo.com.tw

Introduction

The phenotypically indistinguishable *Acinetobacter baumannii*, *Acinetobacter nosocomialis* (formerly *Acinetobacter* genomic species 13TU) and *Acinetobacter pittii* (formerly *Acinetobacter* genomic species 3) are grouped as the *A. baumannii* (Ab) group [1,2] and have emerged as leading pathogens of nosocomial pneumonia in critically ill patients [3,4]. To date, there is controversy over whether Ab group pneumonia results in higher mortality [5–7] or inappropriate antimicrobial therapy affects the mortality of patients with Ab group pneumonia [8,9].

The pneumonia caused by phenotypically identified '*A. baumannii*' described in many studies actually comprises pneumonia caused by either one of the *Acinetobacter* species in the Ab group [8,10]. Recently, several studies reported that there are differences in antimicrobial resistance and outcome between *A. baumannii* and other *Acinetobacter* species in the Ab group [11–13]. It is unclear whether pneumonia caused by these different *Acinetobacter* species can be considered as a single clinical entity, or they are different in clinical presentation, microbial characteristics and outcomes.

Acinetobacter baumannii and *A. nosocomialis* are the two most commonly isolated *Acinetobacter* species in clinical settings [14] and account for more than 80% of infections caused by the Ab group [11,12,15,16]. In this study, the clinical

characteristics, microbiological findings and final outcomes of a large number of patients with bacteraemic nosocomial pneumonia caused by *A. baumannii* and *A. nosocomialis* were analysed to determine whether nosocomial pneumonia caused by these two *Acinetobacter* species is a single or distinct clinical entity.

Materials and Methods

Study population

The study was conducted at Taipei Veterans General Hospital (T-VGH) during an 8-year period from July 2000 to August 2008. T-VGH is a 2900-bed tertiary-care teaching hospital located in Taipei, Taiwan. Charts were reviewed for all patients with at least one positive blood culture for *A. baumannii* or *A. nosocomialis* who had symptoms and signs of infection. Only the first blood culture from patients with two or more positive blood cultures was included. The criteria for inclusion [17] in this study were (i) at least one positive respiratory sample (sputum, bronchoalveolar lavage or pleural effusion) for the Ab group obtained within 48 h before or after the first positive blood culture; (ii) a clinical course compatible with the diagnosis of pneumonia, including a new pulmonary infiltrate plus one additional criterion (fever ≥38°C, blood leukocytosis ≥10 000 cells/mm^3 or leucopenia ≤3000 cells/mm^3), together with one or more of the following conditions: new cough, change of color of sputum, chest pain, and dyspnoea; and (iii) that the positive blood culture was not related to another source of infection. Patients <18 years of age and those with incomplete medical records were excluded. The protocol was approved by the T-VGH Institutional Review Board with a waiver of informed consent.

Microbiological studies

The presumptive identification of the isolates to the level of the Ab group was performed with the API ID 32 GN system (bioMérieux, Marcy l'Etoile, France) or Vitek 2 system (bioMérieux). A multiplex-PCR method was used to identify *A. baumannii* to the genomic species level [18]. Isolates identified as non- *A. baumannii* species of *Acinetobacter* were identified to the genomic species level by 16S–23S ribosomal DNA intergenic spacer sequence analysis [19]. Antimicrobial susceptibilities were determined by the agar dilution method according to the Clinical Laboratory Standards Institute (CLSI) [20]. Multidrug resistance was defined as resistance to three or more of the following classes of antimicrobial agents: antipseudomonal cephalosporins, antipseudomonal carbapenems, ampicillin/sulbactam, fluoroquinolones and aminoglycosides [1].

Data collection

Medical records were reviewed to extract clinical information, including demographic characteristics, underlying diseases, Charlson [21] co-morbidity score, duration of stay in an intensive care unit (ICU), length of hospital stay, time of receipt, dose and route of administration of individual antimicrobials, the mechanical ventilation, central venous catheters, a nasogastric tube, or a foley catheter at the time of onset of bacteremi *A.* Community-acquired pneumonia (CAP), healthcare-associated pneumonia (HCAP), nosocomial pneumonia and ventilator-associated pneumonia (VAP) were defined according to the 2005 American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines [22]. Chronic lung diseases other than chronic obstructive pulmonary disease (COPD) included asthma, bronchiectasis, pulmonary fibrosis and old pulmonary tuberculosis [23]. Immunosuppressive therapy was defined as receipt of cytotoxic agents within 6 weeks, or corticosteroids at a dosage equivalent to or higher than 10 mg of prednisolone daily for more than 5 days within 4 weeks prior to the onset of bacteremi *A.* Neutropenia was defined as an absolute neutrophil count <500 per mm^3. Recent surgery was defined as operations performed within 4 weeks prior to the onset of bacteremi *A.* Chronic kidney disease was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2. Polymicrobial bacteraemia was defined as isolation of one or more microorganisms other than *A. baumannii* or *A. nosocomialis* from blood during the same bacteraemic episode. The illness severity was evaluated using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score [24] within 24 h prior to bacteraemia onset.

Appropriate antimicrobial therapy was defined as administration of at least one antimicrobial agent, to which the causative pathogen was susceptible, within 48 h after the onset of bacteraemia, with an approved route and dosage for end-organ(s) function. Antimicrobial therapy that did not meet this definition was considered as inappropriate. Monotherapy with an aminoglycoside was not considered as an appropriate therapy. The primary outcome measure was all-cause 14-day mortality following the onset of *A. baumannii* or *A. nosocomialis* bacteraemia, respectively.

Statistical analysis

To assess differences, the chi-square test with Yate's correction or Fisher's exact test was used to compare the discrete variables; the Student's *t*-test or Mann–Whitney rank sum test was used to analyse continuous variables. Logistic regression models were used to explore independent risk factors for 14-day mortality. Univariate analyses were per-