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Acinetobacter baumannii ventilator-associated pneumonia: epidemiological and clinical findings

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Abstract *Objective:* To investigate prognostic factors and predictors of *Acinetobacter baumannii* isolation in ventilator-associated pneumonia (VAP). We specifically analyzed these issues for imipenem-resistant episodes. *Design and setting:* All episodes of VAP are prospectively included in a database. Information about risk factors was retrieved retrospectively. *Patients:* Eighty-one patients exhibiting microbiologically documented VAP: 41 by *A. baumannii* (26 by imipenem-resistant) and 40 by other pathogens. *Measurements and results:* The following variables were noted: underlying diseases, severity of illness, duration of mechanical ventilation and of hospitalization before VAP, prior episode of sepsis, previous antibiotic, corticosteroid use, type of nutrition, renal replacement therapy, reintubation, transportation out of the ICU, micro-organisms involved in VAP, concomitant bacteremia, clinical presentation, Sequential Organ Failure Assessment (SOFA) scale on the day of diagnosis, and adequacy of empirical antibiotic therapy. Prior antibiotic use was found to be associated with development of VAP by *A. baumannii* (OR 14). Prior imipenem exposure was associated with the isolation of imipenem-resistant strains (OR 4). SOFA score on the day of diagnosis was the only predictor of in-hospital mortality (OR 1.22); adequacy of empirical antibiotic therapy was a protective factor (OR 0.067). *Conclusions:* Our results confirm that prior exposure to antimicrobials is an independent predictor for the development of *A. baumannii* VAP, the prognosis of which is similar to that of infections caused by other pathogens. This study highlights the importance of initial antibiotic choice in VAP or whatever cause.

Keywords *Acinetobacter baumannii* · Ventilator-associated pneumonia · Severity of illness · Prognosis · Bacteremia · Initial antibiotic therapy

Introduction

In recent decades *Acinetobacter baumannii*, a micro-organism characterized by the rapid development of resistance to the majority of antimicrobials, has emerged as a pathogen frequently isolated in respiratory samples of patients with ventilator-associated pneumonia (VAP). This increasing problem is not confined to certain geographical areas and has been reported worldwide [1, 2, 3]. Outbreaks of nosocomial infection caused by multidrug-resistant *A. baumannii* have very recently reached the proportions of a national health problem causing great social alarm in several countries [4].

Many studies have examined various aspects of the epidemiology and outcome of VAP. Nevertheless, the information so far available about the risk factors and course of VAP caused by *A. baumannii* is scarce. Two previous studies analyzed the factors associated with the

isolation of *A. baumannii* in respiratory samples [5, 6]. Both focused in a small number of episodes (12 and 15, respectively) in nosocomial outbreaks. In addition, *A. baumannii* has been identified as a high-risk pathogen, although conflicting results have been published in relation to the impact which this pathogen has on the outcome of patients with VAP.

Nowadays imipenem is the gold standard therapy for *A. baumannii* infections, although the development of strains resistant to imipenem is becoming an increasing universal problem. The International Network for the Study and Prevention of Emerging Antimicrobial Resistance has recently defined the emergence of imipenem resistance as a "sentinel event" that warrants a coordinated response to control this multiresistant pathogen [7]. Since the first large outbreak of imipenem-resistant *A. baumannii* occurred in New York City at the beginning of the 1990s [8], many investigations have been carried out to elucidate the risk factors associated with infections caused by imipenem-resistant *A. baumannii* [9, 10]. However, to our knowledge, no previous investigation has examined potential predictors of VAP caused by imipenem-resistant strains.

Uncertainties still remain about the potential risk and prognostic factors of *A. baumannii*. The present investigation therefore compared cases of VAP caused by *A. baumannii* to those caused by other pathogens. We also analyzed potential predictors for isolation of imipenem-resistant *A. baumannii* and the clinical cause of these episodes. This research has been presented in part at a recent international meeting [11].

Methods

Patients

The present study was conducted in the intensive care unit of Virgen del Rocío Hospital, a 40-bed medical-surgical unit in a large university hospital. The study was performed in an 8-bed polyvalent unit that admits preferentially patients with serious infections. All episodes of VAP between July 1998 and December 2003 were included in the present investigation. Several episodes of VAP caused by *A. baumannii* included in the present study have been reported previously [12, 13]. Our ICU has suffered several sustained outbreaks of *A. baumannii* since 1993. For this reason, when a patient is colonized or infected by *A. baumannii*, strict isolation precautions are taken to prevent the cross-transmission of this pathogen.

During the 54-month period of the study 88 consecutive episodes of clinically defined VAP were diagnosed. Microbiological examination confirmed the pulmonary infection in 83 episodes. Two episodes were not included in this study: one patient who had been transferred to our ICU from another institution and whose data for risk factor analysis were not available; in the case of the other patient the medical record was not available for reviewing. This study thus included 81 episodes of VAP (20 diagnosed by protected specimen brush and 61 by quantitative tracheal aspirate).

All patients on mechanical ventilation were placed in semirecumbent position, with a nasogastric tube in place, and received ranitidine or pantoprazole for stress-ulcer prophylaxis. Oral (nonnasal) intubation was used in all cases. Selective decontamination of the digestive tract was not performed in our ICU. Ventilator circuits were not replaced unless they became soiled or experienced mechanical malfunction.

Study design

All episodes of VAP are prospectively included in a database. As this database does not contain information about risk factors, it was retrieved retrospectively from the medical record of each patient. Pneumonia was considered ventilator associated when onset occurred within 48 h after initiating mechanical ventilation and was judged not to have been incubated before starting mechanical ventilation. VAP diagnosis required radiographic image of a new and persistent pulmonary infiltrate and at least two of the following criteria: temperature above 38°C or below 35.5°C, leukocytosis with a count higher than 12,000 cells/mm^3 or leukopenia with a count less than 4,000 cells/mm^3, and purulent bronchial secretions.

Lower respiratory tract samples (protected specimen brush or tracheal aspirate) were cultured quantitatively. To be accepted for culture, tracheal aspirates were required to have more than 25 neutrophils present on Gram's stain with ten or fewer epithelial cells per high-power field. The cause of pulmonary infections was considered to have been determined if the protected specimen brush yielded more than 10^3 colony-forming units (cfu) per milliliter, or if the tracheal aspirate culture yielded more than 10^6 cfu/ml. Two or more sets of blood culture were obtained in all cases of suspected pneumonia.

The microbiology laboratory determined antimicrobial susceptibility of isolates by means of the microdilution method (MicroScan system, Baxter Health Care, West Sacramento, Calif., USA). Results were interpreted according to breakpoints defined by the National Committee for Clinical Laboratory Standards [14]. Imipenem resistance was defined as minimal inhibitory concentration of 16 μg/ml or above.

Empirical therapy was considered adequate when at least one effective antimicrobial was included in the initial antibiotic treatment. After culture results were known, the antimicrobial regimen was maintained or adapted on the basis of sensitivity testing. All patients were followed up until death or hospital discharge.

Data collection

The following variables were recorded as predisposing factors for the development of VAP: age, sex, severity of illness at ICU admission as evaluated by the Acute Physiology and Chronic Health Evaluation (APACHE) II score considering the worst data point of the first 24 h in the ICU [15], chronic organ insufficiencies as defined by the APACHE II scale, other comorbidities (alcoholism, smoking habit, diabetes mellitus, uncured malignancy, and previous surgery) [16], duration of hospitalization before pneumonia, length of mechanical ventilation before pneumonia, prior episodes of sepsis, previous antibiotic use from admission to hospital, type of antimicrobial administered, use of corticosteroids as previously defined [17], enteral or parenteral nutrition, renal replacement therapy, reintubation, and transportation out of the ICU.

To assess the impact of VAP on the outcome, the following variables were analyzed: age, sex, APACHE II score at admission to the ICU, previous comorbidities (see above), concomitant bacteremia, clinical presentation of infection classified as sepsis, severe sepsis, or septic shock [18], APACHE II score on the day of diagnosis, Sequential Organ Failure Assessment (SOFA) scale on the day of diagnosis, adequacy of empirical antibiotic therapy, and micro-organisms involved in the lung infection: imipenem-sensi-

tive *A. baumannii*, imipenem-resistant *A. baumannii*, and other pathogens.

Statistical analysis

Categorical variables were evaluated using the χ^2 test and Fisher's test when appropriate. We expressed continuous variables as mean (±SD) or median and interquartile range if their distributions were skewed. We compared groups using the unpaired Student's *t* test for normally distributed variables and the Mann-Whitney *U* test for nonnormally distributed continuous variables. Multivariate analysis using the forward stepwise logistic regression method was performed, including all variables with *p* value of 0.05 or lower in the bivariate analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each variable. Survival curves and estimates were calculated using the Kaplan-Meier method. The comparison between survival functions for different strata was assessed with the log-rank statistics [19]. Data were analyzed using the SPSS version 12 statistical package (SPSS, Chicago, Ill., USA). Statistical significance was set as $p<0.05$.

Results

Of the 81 episodes of VAP included in this study *A. baumannii* was isolated in 41 and other pathogens in 40. Of these, 21 episodes were reported in a previous manuscript describing the clinical and microbiological efficacy of intravenous colistin in *A. baumannii* VAP [12]. Only five episodes of imipenem-sensitive *A. baumannii* and one episode of imipenem-resistant *A. baumannii* were included in a multicenter case-control study designed to evaluate the attributable mortality of *A. baumannii* VAP [13]. *A. baumannii* was isolated together with other micro-organisms in three episodes (7.3%): *Pseudomonas aeruginosa*, *Serratia marcescens*, and methicillin-resistant *Staphylococcus aureus* (polymicrobial pneumonia). Four episodes (10%) of VAP caused by other pathogens were also polymicrobial. The micro-organisms isolated in the episodes caused by other pathogens were: *P. aeruginosa* (*n*=10), methicillin-susceptible *S. aureus* (*n*=7), Methicillin-resistant *S. aureus* (*n*=6), *Proteus mirabilis* (*n*=4), *Enterobacter* spp. (*n*=4), *S. marcescens* (*n*=3), *Haemophilus influenzae* (*n*=3), *Escherichia coli* (*n*=2), *Klebsiella pneumoniae* (*n*=2), *Stenotrophomonas maltophilia* (*n*=2), and *Streptococcus pneumoniae* (*n*=1).

Table 1 shows the bivariate analysis of predisposing factors for pulmonary infection development. The two groups of patients whose pneumonia was or was not caused by *A. baumannii* were similar with regard to age (59.5±12.4 vs. 62.4±9.8 years, $p=0.24$), sex, and severity of illness at admission measured by the APACHE II score (19.5±7.1 vs. 18.3±6.6, $p=0.69$). Factors associated with the development of VAP caused by *A. baumannii* were: prior sepsis ($p<0.0001$), previous antibiotic use ($p<0.0001$), reintubation ($p<0.005$), length of hospital stay before infection ($p<0.0001$), length of mechanical ventilation before diagnosis ($p<0.0001$), exposure to imipenem ($p<0.0001$), and exposure to fluoroquinolones ($p<0.05$). More details on prior antimicrobial treatment of patients included in the present study are shown in Table 2. However, multiple logistic regression analysis revealed that only prior antibiotic use as an independent variable associated with the development of *A. baumannii* VAP (OR 14, 95% CI 4.1–91, $p<0.0001$).

Table 1 Predictors of Acinetobacter *baumannii* (Ab) isolation in ventilator-associated pneumonia (*VAP*). (*APACHE* Acute Physiology and Chronic Health Evaluation, *COPD* chronic obstructive pulmonary disease, *NA* not applicable, *MV* mechanical ventilation, *parentheses* interquartile range)

	VAP due to Ab	VAP by other pathogens	*p*
Age	59.5±12.4	62.4±9.8	0.24
Sex: male	27±65.9	28±70	0.69
APACHE II	19.5±7.1	18.3±6.6	0.45
Hepatic cirrhosis	0±0	4±10	0.06
Immunosuppression	5±12.2	3±7.5	0.71
COPD	7±17.1	7±17.5	0.95
End-stage renal disease	1±2.4	3±7.5	0.2
Chronic cardiac failure	3±7.3	2±5	1
Diabetes mellitus	7±17.1	14±35	0.06
Uncured malignancy	1±2.4	3±7.5	0.36
Alcoholism	5±12.2	6±15	0.71
Smoking habit	8±19.5	12±30	0.27
Previous surgery	18±43.9	14±35	0.41
Length of stay before VAP	16 (10–21.5)	8 (4–15.7)	<0.0001
Length of MV before VAP	11 (7–16)	4 (3–8)	<0.0001
Prior episode of sepsis	33±80.5	14±35	<0.0001
Previous antibiotic therapy	39±95.1	20±50	<0.0001
Use of corticosteroids	10±24.4	8±20	0.63
Enteral nutrition	34±82.9	30±75	0.38
Parenteral nutrition	8±19.5	10±25	0.55
Renal replacement therapy	4±9.8	3±7.5	1
Reintubation	19±46.3	7±17.5	<0.001
Transportation from ICU	10±24.4	8±20	0.63

We also sought predictors for the development of VAP caused by imipenem-resistant *A. baumannii*, comparing patients with infection caused by imipenem-sensitive *A. baumannii*, patients with pulmonary infection caused by imipenem-resistant *A. baumannii*, and patients with pneumonia caused by other pathogens (Table 3). Multivariate analysis identified prior imipenem exposure as the only variable associated with the isolation of imipenem-resistant *A. baumannii* (OR 4, 95% CI 1.1–29.8, $p<0.005$).

Table 4 summarizes the clinical presentation of the episodes of VAP included in the present study. Those caused by *A. baumannii* and those caused by other pathogens differed neither in ICU mortality (24/41, 58.5%, vs. 19/40, 47.5%, $p=0.32$) nor in-hospital mortality (27/41, 65.9%, vs. 25/40, 62.5%, $p=0.3$). We compared the frequency of adequate antimicrobial therapy between

Table 2 Antibiotic use among the three groups of patients: ventilator-associated pneumonia caused by imipenem-sensitive (*IS*) *Acinetobacter baumannii* (*Ab*), imipenem-resistant (*IR*) *A. baumannii*, and other pathogens

	IS-Ab (*n*=15)	IR-Ab (*n*=26)	Other pathogens (*n*=40)	*p*
Nonpseudomonal cephalosporins	7±46.7	2±7.7	4±10	0.001
Pseudomonal cephalosporins	1±6.7	5±19.2	3±7.5	0.27
Piperacillin-tazobactam	4±26.7	8±30.8	8±20	0.6
Fluoroquinolone	5±33.3	4±15.4	2±5	0.02
Imipenem	2±13.3	12±46.2	0±0	<0.0001

Table 3 Predictors for isolation of imipenem-sensitive (*IS*) and imipenem-resistant (*IR*) *Acinetobacter baumannii* (*Ab*) strains (*APACHE* Acute Physiology and Chronic Health Evaluation, *COPD* chronic obstructive pulmonary disease, *NA* not applicable, *MV* mechanical ventilation, *VAP* ventilator-associated pneumonia, *parentheses* interquartile range)

	IS-Ab	IR-Ab	Other pathogens	*p*
Age	64.6±9.6	56.5±12.4	62.4±9.8	0.24
Sex: male	12±80	15±57.7	28±70	0.31
APACHE II	20.1±6.7	19.1±7.3	18.3±6.6	0.7
Hepatic cirrhosis	0±0	0±0	4±10	NA
Immunosuppression	1±6.7	4±15.4	3±7.5	NA
COPD	4±26.7	3±11.5	7±17.5	NA
End-stage renal disease	0±0	1±3.8	3±7.5	NA
Chronic cardiac failure	1±6.7	2±7.7	2±5	NA
Diabetes mellitus	2±13.3	5±19.2	14±35	0.17
Uncured malignancy	1±6.7	0±0	3±7.5	NA
Alcoholism	2±13.3	3±11.5	6±15	0.5
Smoking habit	3±20	5±19.2	12±30	NA
Previous surgery	7±46.7	11±42.3	14±35	0.69
Length of stay before VAP	14 (11–19)	17 (9.7–26.7)	8 (4–15.7)	<0.0001
Length of MV before VAP	5 (11–14)	11 (7–17.2)	4 (3–8)	<0.0001
Prior episode of sepsis	12±80	21±80.8	14±35	<0.0001
Previous antibiotic therapy	14±93.3	25±96.2	20±50	<0.0001
Use of corticosteroids	5±33.3	5±19.2	8±20	0.52
Enteral nutrition	12±80	22±84.6	30±75	0.65
Parenteral nutrition	3±10	5±19.2	10±25	0.83
Renal replacement therapy	3±20	1±3.8	3±7.5	NA
Reintubation	5±33.3	14±53.8	7±17.5	0.008
Transportation from ICU	4±26.7	6±23.1	8±20	0.8

Table 4 Clinical manifestations of episodes of ventilator-associated pneumonia (*VAP*) included in the present study. (*Ab Acinetobacter baumannii*, *SOFA* Sequential Organ Failure Assessment)

	VAP due to Ab	VAP by other pathogens	*p*
Bacteremia	5±12.2	8±20	0.34
Polymicrobial VAP	3±7.3	4±10	0.71
Clinical presentation			0.8
Sepsis	6±14.6	5±12.5	
Severe sepsis	15±36.6	17±42.5	
Septic shock	20±48.8	18±45	
SOFA score (day of VAP)	7±4.1	8±3.6	0.23
Worst SOFA (after VAP)	9.8±4.8	10.5±4.3	0.52
Empirical antibiotic therapy			0.0001
Inadequate	26±63.4	7±17.5	
Adequate	15±36.6	33±82.5	

Table 5 Correlation between adequacy of empirical antibiotic therapy and mortality depending on the type of pathogen responsible for ventilator-associated pneumonia

	Survivors	Nonsurvivors	*p*
A. baumannii			0.049
Inadequate	6	20	
Adequate	8	7	
Imipenem-sensitive			
Inadequate	0	5	
Adequate	5	5	
Imipenem-resistant			
Inadequate	6	15	
Adequate	3	2	
Other pathogens			0.03
Inadequate	0	7	
Adequate	15	18	

patients with *A. baumannii* pneumonia and those with other pathogens and related these findings to mortality to analyze the relationship between bacteriology, adequacy of empirical antibiotic therapy, and mortality (Table 5). Imipenem-resistant strains were susceptible only to colistin, and these episodes were treated with this antimicrobial intravenously.

Potential prognostic factors for in-hospital mortality were evaluated by means of univariate analysis, comparing survivors and nonsurvivors (Table 6). Only APACHE II score at admission ($p<0.01$), SOFA score on

Table 6 Prognostic factors for in-hospital mortality: bivariate analysis (*APACHE* Acute Physiology and Chronic Health Evaluation, *COPD* chronic obstructive pulmonary disease, *NA* not applicable, *MV* mechanical ventilation, *VAP* ventilator-associated pneumonia, *Ab A. baumannii*, IS imipenem-sensitive, *IR* imipenem-resistant)

Variable	Survivors (*n*=29)	Nonsurvivors (*n*=52)	*p*
Age	58.4±10.9	62.3±10.9	0.12
Sex: males	22±75.8	33±63.5	0.25
APACHE II	16.2±6.1	20.4±6.8	<0.001
Hepatic cirrhosis	1±3.4	3±5.8	0.55
Immunosuppression	1±3.4	7±13.5	0.14
COPD	4±13.8	10±19.2	0.53
End-stage renal disease	1±3.4	2±3.8	0.71
Chronic cardiac failure	1±3.4	4±7.7	0.41
Diabetes mellitus	6±20.4	15±28.8	0.42
Uncured malignancy	1±3.4	3±5.8	0.55
Alcoholism	3±10.3	8±15.4	0.65
Smoking habit	8±27.6	12±23.1	0.65
Previous surgery	18±43.9	14±35	0.41
Bacteremia	3±10.3	10±19.2	0.24
Micro-organisms			0.95
IS Ab	5±17.2	10±19.2	
IR Ab	9±31	17±32.7	
Other pathogens	15±51.7	25±48.1	
Clinical presentation			0.0001
Sepsis	7±24.1	4±7.7	
Severe sepsis	17±58.6	15±28.8	
Septic shock	5±17.2	33±63.5	
SOFA score (day of VAP)	5.8±3.8	8.4±3.7	0.0001
Empirical antibiotic therapy			0.006
Inadequate	6±20.7	27±51.9	
Adequate	23±79.3	25±48.1	

the day of VAP diagnosis ($p<0.01$), and the adequacy of empirical antibiotic therapy ($p<0.01$) differed significantly different between survivors and nonsurvivors. Moreover, there were no differences in mortality between patients with imipenem-sensitive *A. baumannii* pneumonia (10/15; 66.7%) and those with imipenem-resistant *A. baumannii* VAP (17/26; 65.4%).

Multivariate analysis by multiple regression confirmed that SOFA score on the day of diagnosis was the only independent predictor of in-hospital mortality (OR 1.22, 95% CI 1.03–1.43, $p<0.05$) whereas the adequacy of empirical antibiotic therapy was a protective factor for in-hospital mortality (OR 0.067, 95% CI 0.009–0.5, $p<0.01$). Using the Kaplan-Meier analysis found no statistically significant differences in survival curves between patients with imipenem-sensitive *A. baumannii* VAP, imipenem-resistant *A. baumannii* VAP, or lung infection caused by other pathogens (log rank test. $p=0.81$).

Discussion

The present study carried out in an institution with sustained outbreaks of *A. baumannii* found that prior exposure to antimicrobials is an independent predictor for the development of VAP caused by *A. baumannii*. In addition, previous treatment with imipenem is the only predisposing factor for the isolation of imipenem-resistant *A. baumannii* in VAP. We also conclude that the isolation of *A. baumannii* in respiratory samples of patients with VAP entail a similar prognosis as pneumonia caused by other virulent pathogens. However, the severity of illness at the moment of pneumonia diagnosis is an independent predictor of mortality whereas the adequacy of empirical antibiotic therapy is a strong protective factor.

Knowledge of predictors for the isolation a certain pathogen in patients with the clinical diagnosis of VAP has important practical implications since it determines which patients should receive active antimicrobials against this organism. Bivariate analysis identified several factors associated with the isolation of *A. baumannii* in respiratory samples of patients with lung infection: prior sepsis, previous antibiotic use, reintubation, length of hospital stay before infection, length of mechanical ventilation before diagnosis, exposure to imipenem, and exposure to fluoroquinolones. The presence of infection and the administration of previous antimicrobial therapy have been found to be predisposing factors for infection by *A. baumannii* [20, 21]. Otherwise, previous administration of third-generation cephalosporins or fluoroquinolones has been reported to be associated with *A. baumannii* infection [6, 22, 23]. Interestingly, one study carried out in critically ill patients with VAP did not identify prior antimicrobial therapy as a potential risk factor for *A. baumannii* isolation [5].

Previous reintubation was also significantly more frequent in patients with *A. baumannii*. It is well established that reintubation is a risk factor for VAP [24]. This may be explained by the aspiration of colonized oropharyngeal secretions into the lower respiratory tract taking place at the moment of reintubation. In the case of an ICU with an outbreak of *A. baumannii* these secretions may be colonized by this pathogen, explaining the occurrence of pulmonary infection after the intubation procedure.

However, the multivariate analysis found prior antibiotic use to be a strong predictor of *A. baumannii* pulmonary infection, increasing 14 times the risk of infection by this pathogen. This result is another persuasive argument to discourage the overzealous use of antibiotics in critically ill patients whenever possible. The overuse of antimicrobials in the critical care setting is a well known problem. Highly revealing in this sense is a recent study reporting that only 26% of 529 patients with suspected infection fulfilled the Centers for Disease Control criteria for infection. More importantly, 80% of these patients

were on antibiotics, and this proportion remained unchanged over the 7 days of the study [25].

When we assessed episodes caused by imipenem-resistant *A. baumannii*, only previous use of imipenem was an independent risk factor, increasing 4 times the risk of VAP caused by an imipenem-resistant *A. baumannii*. Our finding further corroborates previous investigations [9, 10], although these studies did not specifically evaluate a cohort of critically ill patients with VAP.

The medical literature in hospital-acquired pneumonia is riddled with disagreements and uncertainties. A good example is the prognosis of VAP caused by *A. baumannii*. A case-control study, for example, reported significantly higher mortality in cases of VAP caused by *P. aeruginosa* or *A. baumannii* [26]. Similarly, Kollef et al. [27] found that VAP due to nonfermentative Gram-negative pathogens was an independent predictor of in-hospital mortality. In our study the prognosis of VAP caused by *A. baumannii* did not differ from that with other virulent pathogens. This finding is in agreement with a recent case-control study which concluded that VAP caused by *A. baumannii* was not associated with an increase in the risk of death, although imipenem-resistant episodes were associated with a tendency to higher mortality rates [13]. Intuitively, one could suppose that a pulmonary infection caused by multidrug resistant *A. baumannii* increases mortality. However, many variables are involved in the clinical course of critically ill patients. Two different methods (case-control study and multivariate analysis) have been used to demonstrate that episodes of pneumonia caused multidrug resistant *A. baumannii* do not carry a worse prognosis than other causes of pulmonary infection in ventilated patients.

Our results are consistent with those of previous studies demonstrating that the adequacy of initial antibiotic choice is a crucial factor in determining outcome in patients with VAP [28, 29, 30]; other authors, however, disagree on the importance of the initial antibiotic regimen [31, 32, 33]. We found that patients with *A. baumannii* received adequate empirical antibiotic therapy less frequently than those with other micro-organisms. However, as Luna and coworkers [34] have reported, outcome in both groups benefitted from the adequacy of initial therapy. We also observed that the severity of illness at the moment of pneumonia diagnosis measured by the SOFA scale is an independent predictor of fatality. Previous clinical studies have revealed that the severity of illness at the moment of diagnosis is a key prognostic factor [32, 35, 36].

We acknowledge that our study has several limitations. First, it was a retrospective analysis of predisposing factors, the sample is relatively small, and our study may have missed other important predictors or produced spurious findings. Second, we also cannot overlook the impact of the architectural design of the ICUs on the transmission of *A. baumannii* [37]. Third, it is well known that the incidence of multidrug resistant pathogens is closely linked to local factors and varies generally from one institution to another. Despite all these limitations we performed an extensive evaluation of potential risk factors and the outcome of *A. baumannii* VAP, including those episodes caused by imipenem-resistant *A. baumannii*, providing useful information especially for ICUs in which *A. baumannii* presents a major infection problem. Obviously all this information should be use to reinforce our strategies to prevent the appearance of this multiresistant pathogen despite the absence of a significant relationship to mortality in this study.

In summary, our study provides insights into predictors of *A. baumannii* isolation in respiratory samples of patients with VAP. Our findings reinforce the necessity of limiting antibiotic use in critically ill patients, especially broad-spectrum antimicrobials such as imipenem. Moreover, this study highlights the importance of initial antibiotic choice in pneumonias regardless of cause, including episodes caused by A. *baumannii*. VAP episodes caused by *A. baumannii* have a similar prognosis to pneumonia episodes caused by other virulent pathogens.

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