ORIGINAL ARTICLE

Clinical and Economic Impact of Multidrug Resistance in Nosocomial *Acinetobacter baumannii* Bacteremia

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OBJECTIVE. To investigate the impact of antimicrobial resistance on clinical and economic outcomes among hospitalized patients with multidrug-resistant (MDR) *Acinetobacter baumannii* bacteremia.

DESIGN. A retrospective, matched-cohort study.

SETTING. A tertiary care university teaching hospital

METHODS. A matched case-control (1 : 1) study was conducted to compare the differences in clinical and economic outcomes of patients with MDR *A. baumannii* bacteremia and patients with non-MDR *A. baumannii* bacteremia. Case patients were matched to control patients on the basis of sex, age, severity of underlying and acute illness, and length of hospital stay before onset of bacteremia.

RESULTS. Forty-six (95.8%) of 48 cases with MDR *A. baumannii* bacteremia were eligible for the study and matched with appropriate controls. The sepsis-related mortality rate was 34.8% among cases and 13.0% among controls, for an attributable mortality rate of 21.8% (adjusted odds ratio, 4.1 [95% confidence interval, 1.1-15.7]; $P = .036$). After the onset of bacteremia, cases and controls had a significantly different length of hospital stay (54.2 vs 34.1 days; $P = .006$), hospitalization cost (US$9,349 vs US$4,865; $P = .001$), and antibiotic therapy cost (US$2,257 vs US$1,610; $P = .014$). Thus, bacteremia due to MDR *A. baumannii* resulted in 13.4 days of additional hospitalization and US$3,758 of additional costs, compared with bacteremia due to non-MDR *A. baumannii.*

CONCLUSIONS. Patients with MDR *A. baumannii* bacteremia had a higher mortality rate and incurred greater medical costs than patients with non-MDR *A. baumannii* bacteremia.

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Antibiotic resistance is a recognized clinical issue and a major public health threat. Infections caused by antibiotic-resistant bacteria are believed to result in higher mortality rates, longer hospitalization durations, and higher healthcare costs than infections caused by antibiotic-susceptible bacteria.[1,2] The development of resistance to all available antibiotics in some organisms may preclude the effectiveness of many antibiotic regimens against other organisms.[1,2]

Acinetobacter baumannii is primarily a healthcare-associated pathogen and is increasingly reported as the cause of outbreaks of nosocomial infections, such as bloodstream infection, ventilator-associated pneumonia, urinary tract infection, and wound infection.[3] Moreover, of particular concern is the increasing prevalence of *A. baumannii* isolates with resistance to commonly prescribed antimicrobial agents.[4,5] Isolation of multidrug-resistant *A. baumannii* has been increasingly reported worldwide, and it is now one of the gram-negative pathogens that cause nosocomial infections that are difficult to treat.[3]

Nosocomial bacteremia is a leading cause of death, particularly among critically ill patients. The clinical course of *A. baumannii* bacteremia may range from benign transient bacteremia to fulminant septic shock, with a crude mortality rate as high as 52%.[6,7] Increasing reports of multidrug-resistant *A. baumannii* bacteremia in different healthcare settings were recently noted,[5-7] but the health and economic impact of multidrug resistance on patients with multidrug-resistant *A. baumannii* bacteremia has not been clearly defined. Therefore, the objective of the present case-control study was to investigate the impact of multidrug resistance on the clinical and economic outcomes of hospitalized patients with multidrug-resistant *A. baumannii* bacteremia.

METHODS

Setting and Study Design

A retrospective study was conducted in National Cheng Kung University Hospital, a university-affiliated medical center in

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Tainan, Taiwan. The hospital has approximately 900 beds, including a 67-bed intensive care unit (ICU), and serves a population of approximately 2,000,000 people. Patients with *A. baumannii* bacteremia hospitalized between April 1996 and August 2001 were identified from the records of the clinical microbiology laboratory. Demographic information abstracted from the charts included age, sex, hospital service, and dates of hospital admission and discharge. Medical histories were reviewed for underlying illnesses, diagnosis at admission, and invasive procedures performed within 1 week or antimicrobial therapy received within 4 weeks before the development of *A. baumannii* bacteremia. The severity of underlying medical conditions was stratified on the basis of the McCabe score as fatal, ultimately fatal, or nonfatal.[8] The severity of illness was evaluated on the first day of bacteremia onset by means of the Simplified Acute Physiology Score (SAPS) II[9] and the Pittsburgh bacteremia score.[10] Clinical presentations, presumed or documented source of bacteremia, radiographic findings, prescribed antimicrobial agents, clinical response to therapy, and clinical outcome were also recorded. For patients with more than 1 episode of *A. baumannii* bacteremia, only the first episode was considered.

Definitions

All patients with microbiologically documented nosocomial multidrug-resistant *A. baumannii* bacteremia were enrolled as case patients. Multidrug resistance in *A. baumannii* was defined as resistance to commonly available antibiotics (antipseudomonal penicillins, antipseudomonal cephalosporins, antipseudomonal fluoroquinolones, aminoglycosides, or trimethoprim-sulfamethoxazole) but susceptibility to carbapenems, and non–multidrug resistance was defined as susceptibility to carbapenems and other alternative antipseudomonal antimicrobial agents (eg, penicillins, cephalosporins, fluoroquinolones, or aminoglycoside).[11]

Nosocomial infections were defined according to the criteria of the Centers for Disease Control and Prevention.[12] Polymicrobial infection was defined as the isolation of 2 or more microorganisms during an infectious episode, excluding cases in which specimens and/or cultures were contaminated. Immunosuppressive therapy was defined as corticosteroid treatment (10 mg per day or an equivalent dosage) received for more than 2 weeks or as antineoplastic chemotherapy or antirejection medication received within 1 month before admission.

Previous antibiotic therapy was defined as the receipt of a systemic antimicrobial agent for at least 72 hours during the 4 weeks preceding admission. Antimicrobial therapy was considered to be appropriate if the organism was susceptible in vitro to at least 1 of the drugs administered within 5 days after the onset of bacteremia. Sepsis-related death was defined as the death of a patient with a clinical course that suggested persistently active infection and had no other explanation. The attributable mortality rate was defined as the excess mortality rate related to multidrug resistance and was calculated by subtracting the sepsis-related mortality rate of the control group from that of the case group.[13] Excess ICU stay and hospital stay were calculated by subtracting the mean ICU stay and hospital stay of controls from those of cases.[13] Clinical events associated with organ system failure were assessed by the criteria specified in the organ dysfunction and/or infection score.[14]

The lengths of hospital stay and costs of hospitalization in US dollars were compared between case patients and control patients. In Taiwan, the national health insurance program pays $170 per day of ICU stay and $30 per day of general ward stay in medical centers. Data on the costs of hospitalization were retrieved from the central financial service at National Cheng Kung University Hospital and included information about the total cost of each hospital stay, as well as costs of accommodation, medication, laboratory procedures, and materials and services. The latter included the cost of catheters, implanted devices, procedures and operations, rehabilitation programs, respiratory care, dialysis and other special services, physician care, nursing care, and consultations.

Matching and Selection of Controls

The control group comprised patients with nosocomial bacteremia caused by non–multidrug-resistant *A. baumannii* who were hospitalized in the same unit and during the same period as the matched cases. Only adults (age, $\geqslant$18 years) were included in the study. For each case, the best matched control was selected in a stepwise manner by means of a previously described scoring system.[13] Controls were matched with cases at a ratio of 1 : 1 according to the following criteria: sex (1 point), age (3 points if the age difference was <5 years, 2 points if the age difference was 5-10 years, and 0 points if the age difference was >10 years), SAPS II score (3 points if the score difference was <5 points, 1 point if the score difference was <10 points, and 0 points if the score difference was >10), McCabe score of underlying disease severity (3 points for concordant scores and 0 points for discordant scores), source of bacteremia (3 points), and the length of stay from admission to onset of bacteremia (3 points if the duration was within 20% of that for the potential matched patient). If several controls with the same score were available for matching, one of them was chosen at random. Selection of controls was performed without knowledge of the matched cases' survival status. If a case was missing any of these data, matching was not performed, and the patient was not further analyzed. Of 48 patients with multidrug-resistant *A. baumannii* bacteremia identified in the study, only 46 (95.8%) were available for the case-control study. Overall, on the 16-point matching scale, 46 controls had a mean score of 12.9 points (match accuracy, 80.6%).

Microbiological Analysis

All blood cultures were processed by the clinical microbiology laboratory, using the Bactec 9240 system (Becton Dickinson). *A. baumannii* isolates were identified by both standard mi-

crobiological techniques[15] and the Vitek system (bioMérieux). Antimicrobial susceptibility testing was determined by the disk diffusion technique, in accordance with the criteria established by the Clinical and Laboratory Standards Institute (formerly known as the National Committee for Clinical Laboratory Standards).[16]

Statistical Analysis

The results were analyzed with SPSS software for Windows, version 10.0 (SPSS). Continuous variables were expressed as mean values ± SD, and categorical variables were expressed as a percentage of the total number of patients analyzed. The categorical variables were compared using the Fisher exact test or the χ^2 test, as appropriate, and the continuous variables were compared using the Mann–Whitney *U* test or the Student *t* test. All tests for statistical significance were 2-tailed; *P* values less than .05 were considered statistically significant. Independent predictors for sepsis-related mortality were identified by means of logistic regression analysis. Matched analyses were conducted by using a conditional logistic regression model. Variables with a *P* value of .05 or less on univariate matched analysis were included in a multiple conditional logistic regression model.

RESULTS

From 1996 through 2001, a total of 275 (9.2%) of 2,983 episodes of nosocomial bacteremia were due to *A. baumannii;* the incidence of *A. baumannii* bacteremia increased from 94.8 episodes per 100,000 discharges in 1996 to 245 episodes per 100,000 discharges in 2001. Of 275 episodes of *A. baumannii* bacteremia, 48 (17.5%) caused by multidrug-resistant *A. baumannii* were identified. The annual incidence of nosocomial multidrug-resistant *A. baumannii* bacteremia increased from 8.61 episodes per 100,000 discharges in 1996 to 55.6 episodes per 100,000 discharges in 2001 ($P < .001$) (Figure 1).

Matched Cohort Study

Forty-six (95.8%) of 48 cases were available for matching. At the onset of bacteremia, 31 (67.4%) of 46 case-control pairs were treated in the ICU, 11 (23.9%) were treated in medical wards, and 4 (8.7%) were treated in surgical wards. Clinical characteristics and results of matched univariate analysis of cases and controls are summarized in Table 1. Of 46 case-control pairs, 29 (63.0%) were successfully matched for sex, 47 (87%) were matched for the McCabe score, 41 (89.1%) were matched for the SAPS II score, 38 (82.6%) were matched for the length of stay before bacteremia onset, and 40 (87.0%) were matched for the source of bacteremia. Overall, on the 16-point matching scale, 46 controls had a score of 12.9 ± 1.9 points (range, 10-16 points). Twenty-one matched pairs had a concordant outcome.

Treatment and Outcome

Of patients with *A. baumannii* bacteremia, fewer cases (39 [84.8%]) than controls (44 [95.7%]) received appropriate antimicrobial therapy ($P = .05$). The time from the onset of bacteremia to the initiation of appropriate antimicrobial therapy was longer for cases than it was for controls (2.8 ± 1.9 days vs 1.7 ± 2.0 days; $P = .01$). However, the prevalence of acute organ failure at the onset of bacteremia was not significantly different between cases and controls (Table 2).

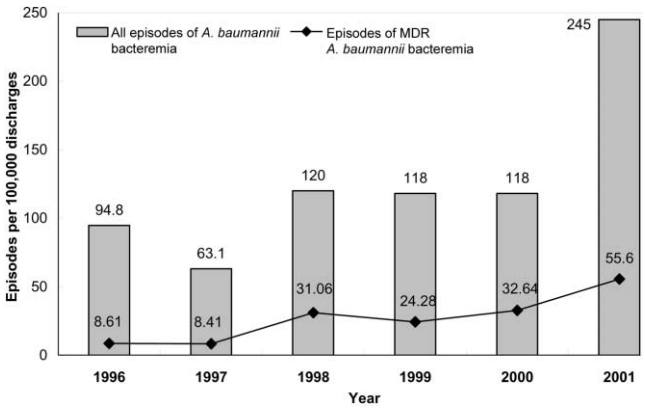

FIGURE. Annual incidences of *Acinetobacter baumannii* bacteremia and multidrug-resistant (MDR) *A. baumannii* bacteremia in a tertiary care hospital in southern Taiwan, 1996-2001.

The in-hospital mortality rate was not significantly different between cases and controls (47.8% vs 39.1%; odds ratio, 1.43 [95% confidence interval, 0.62-3.3]; $P = .53$) (Table 2). However, the sepsis-related mortality rate was higher for cases (16 [34.8%]), compared with controls (6 [13%]). Conditional logistic regression analysis revealed that multidrug resistance was associated with an increased risk of sepsis-related death for patients with *A. baumannii* bacteremia (odds ratio, 3.6 [95% confidence interval, 1.2-10.2]), after adjustment for the severity of illness and comorbidities. Thus, the mortality rate attributable to multidrug resistance among patients with *A. baumannii* bacteremia was 21.8%.

Duration and Cost of Hospitalization

After the onset of multidrug-resistant *A. baumannii* bacteremia, 22 cases and 18 controls died during hospitalization; their matches were excluded, leaving only 21 case-control pairs for the following cost analysis. The duration of ICU stay (±SD) was 21.2 ± 23.3 days for cases and 5.2 ± 7.3 days for controls ($P = .001$); the duration of hospital stay (±SD) was 54.2 ± 42.8 days for cases and 34.1 ± 30.5 days for controls ($P = .006$) (Table 3). The cost of hospitalization (±SD) was $9,348 ± $6,323 for cases and $4,865 ± $4,015 for controls; the cost of antibiotic therapy (±SD) was $2,257 ± $1,361 for cases and $1,610 ± $1,315 for controls. Thus, bacteremia due to multidrug-resistant *A. baumannii* resulted in 13.4 days of additional hospitalization and US$3,758 of additional costs, compared with bacteremia due to non–multidrug -resistant*A. baumannii.*

TABLE 1. Clinical Characteristics and Matched Univariate Analysis of Patients With Bacteremia Caused by Multidrug-Resistant (MDR) *Acinetobacter baumannii* (Case Group) or Non-MDR *A. baumannii* (Control Group)

Characteristic	Case group (n = 46)	Control group (n = 46)	P
Age, years	61.0 ± 17.8	59.6 ± 18.3	.7
Severity of critical illness			
SAPS II score	49.0 ± 19.4	42.0 ± 15.7	.1
Pittsburgh bacteremia score ⩾4	26 (56.5)	19 (41.3)	.2
Time from admission to onset of *A. baumannii* bacteremia, days	18.0 ± 18.2	17.2 ± 7.3	.8
Male sex	31 (67.4)	29 (63.0)	.3
Comorbidity			
Malignancy	18 (39.1)	18 (39.1)	1.0
Diabetes mellitus	17 (37.0)	17 (37.0)	1.0
Heart failure	5 (10.9)	8 (17.4)	.5
Immunosuppression	4 (8.7)	8 (17.4)	.4
Chronic obstructive pulmonary disease	2 (4.3)	0 (0)	.5
Liver cirrhosis	2 (4.3)	8 (17.4)	.09
None	6 (13.0)	5 (10.9)	1.0
Severity of underlying disease (McCabe classification)			1.0
Rapidly fatal	4 (8.7)	3 (6.5)	
Ultimately fatal	21 (45.7)	24 (52.2)	
Nonfatal or none	21 (45.7)	19 (41.3)	
Source of bacteremia			
Pneumonia	20 (43.5)	18 (39.1)	.8
Catheter-related infection	1 (2.2)	7 (15.2)	.6
Urinary tract infection	1 (2.2)	0 (0)	1.0
None (primary bacteremia)	23 (50.0)	20 (43.5)	.7
Polymicrobial bacteremia	18 (39.1)	16 (34.8)	.8

NOTE. Data are no. (%) of patients or mean value ± SD. SAPS, Simplified Acute Physiology Score.

DISCUSSION

Antimicrobial resistance is a growing threat to public health. Infection due to antibiotic-resistant organisms is associated with an increased mortality rate, morbidity rate, and cost, compared with infection due to antibiotic-susceptible organisms.[2] Recent epidemiological data show that the frequency of isolation of bacteria that are resistant to antimicrobial agents is increasing.[17,18] Awareness of antimicrobial resistance is growing, and the impact of antimicrobial resistance on clinical and economic outcomes is important.[19] Information about and outcomes associated with infection caused by drug-resistant organisms may be targeted for patients with infection, clinicians, hospitals, and uninfected persons in the community to define the prognosis of infection, to improve infection control and antibiotic prophylaxis to prevent such infections, and to make decisions about funding of measures to track and prevent the spread of antimicrobial-resistant organisms.[19,20]

In this study, the mean total duration of hospitalization for cases (67 days) was much longer than the national average for patients in medical centers covered under Taiwan's national health insurance program (range, 8.3-10.2 days), longer than that for patients with nosocomial bloodstream infections in a medical center in Taiwan (40 days),[21] and much longer than that for patients in Western countries (range, 28.5-40 days).[22-24] To our knowledge, our study is the first to focus on the economic impact of multidrug-resistant *A. baumannii* bacteremia. Our study showed that multidrug-resistant *A. baumannii* bacteremia was associated with an excess attributable mortality rate of 21.8%, an excess length of hospital stay of 13.4 days, and excess hospital costs of $3,758, compared with non–multidrug-resistant *A. baumannii* bacteremia. These findings are consistent with those of earlier studies, which reported that antibiotic-resistant *A. baumannii* infections resulted in increased mortality and morbidity rates, longer hospitalization durations, and increased costs, compared with nosocomial infections caused by antibiotic-susceptible *A. baumannii*.[22,24,25]

Resistance to multiple classes of antimicrobials among nosocomial pathogens has become a major problem for the clinical management of nosocomial infections. Duration and cost of hospitalization were reported to be significantly increased

TABLE 2. Clinical Manifestations in, Antimicrobial Treatment for, and Outcome of Patients With Bacteremia Caused by Multidrug-Resistant (MDR) *Acinetobacter baumannii* (Case Group) or Non-MDR *A. baumannii* (Control Group)

Characteristic	Case group (n = 46)	Control group (n = 46)	P
Organ failure–related comorbidity at onset of bacteremia	39 (84.8)	39 (84.8)	1.0
Respiratory failure	30 (65.2)	27 (58.7)	.7
Shock	22 (47.8)	14 (30.4)	.1
Hepatic failure	19 (41.3)	16 (34.8)	1.0
Renal failure	16 (34.8)	16 (34.8)	1.0
Hematological failure	12 (26.1)	8 (17.4)	.5
Neurological failure	7 (15.2)	2 (4.3)	.2
Acute respiratory distress syndrome	3 (6.5)	7 (15.2)	.3
Number per patient, mean ± SD	1.8 ± 2.0	1.6 ± 1.5	.7
Treatment			
Received appropriate antimicrobial therapy	37 (80.4)	44 (95.7)	.05
Time from bacteremia onset to start of appropriate therapy, days	2.8 ± 1.9	1.7 ± 2.0	.01
Duration of any therapy, days	12.8 ± 5.7	14.3 ± 6.0	.4
Time from initiation of any therapy to defervescence, days	6.6 ± 4.6	6.1 ± 4.1	.8
Mortality rate, % of patients			
Sepsis related	34.8	13.0	.026
Crude	47.8	39.1	.53

NOTE. Data are no. (%) of patients or mean value ± SD, unless otherwise indicated.

for patients infected with drug-resistant bacteria.[26,27] On the contrary, a recent study has shown that antibiotic resistance in nosocomial bacteremia caused by gram-negative organisms did not increase the need for hospital resources and did not adversely affect the outcome for critically ill patients.[24] However, the findings of that study were not persuasive because the authors used a subjective assessment of the causes of death as the primary outcome measure and did not control for disease severity and because the study was underpowered.

A. baumannii appears to have a propensity for developing antimicrobial resistance extremely rapidly.[5,7] Moreover, resistance involves multiple drugs and causes serious therapeutic problems. The reason that antibiotic resistance leads to adverse outcomes is presumably because of an increased like-

TABLE 3. Outcomes and Adjusted Analysis for Patients With Bacteremia Caused by Multidrug-Resistant (MDR) *Acinetobacter baumannii* (Case Group) or Non-MDR *A. baumannii* (Control Group)

			Adjusted analysis[a]	
Outcome	Case group (n = 46)	Control group (n = 46)	Attributable to MDR *A. baumannii*	P
Clinical				
Sepsis-related mortality	16 (34.8)	6 (13.0)	21.8	.036
Length of ICU stay, days[b]	21.2 ± 23.3	5.2 ± 7.3	13.4	.001
Length of hospital stay, days[b]	54.2 ± 42.8	34.1 ± 30.5	15.9	.006
Economic, US$[b]				
Antibiotics	2,257 ± 1,361	1,610 ± 1,315	865	.014
Hospitalization	9,349 ± 6,323	4,865 ± 4,015	3,758	.001

NOTE. Data are no. (%) of patients or mean value ± SD.

[a] Adjusted for the severity of underlying disease (McCabe score), acute illness (Simplified Acute Physiology Score II), and time from admission to onset of bacteremia.

[b] Twenty-one matched case-control pairs had concordant outcomes and were included in the analysis of economic outcome.

lihood that antibiotic therapy will be ineffective or suboptimal,[6,7] as evidenced in the present study. A higher sepsis-related mortality rate among patients with multidrug-resistant *A. baumannii* bacteremia, compared with that for patients with non–multidrug-resistant *A. baumannii* bacteremia, is likely associated with a lower probability that appropriate antibiotic therapy will be prescribed and with a longer delay in the initiation of appropriate therapy. In addition, the relationship between receipt of appropriate therapy and a favorable outcome for ICU patients with nosocomial bloodstream infections is clear.[28] Strategies to minimize the delay in the administration of appropriate antibiotic therapy are essential, as are techniques to facilitate the earlier identification of drug-resistant organisms.[19]

The limitation of this study is that, similar to other observational analyses, there may be additional confounding factors not captured or included in the models. To avoid confounding in case-control studies, it is essential to select the appropriate reference group by matching control patients on the basis of length of hospital stay and the severity of comorbidities before infection.[20] However, if these matching criteria are used, any deviation in outcome will be attributable to multidrug resistance, rather than to other inherent differences between the cases and controls. Thus, the attributable duration and cost of hospitalization will be overestimated to a certain extent.[13,26] Such an issue was cautiously addressed by matching cases and controls on the basis of several factors with a possible contribution to adverse outcomes. To minimize the confounding effects of other factors, we adopted the scoring system of Pittet et al.[13] to evaluate whether controls were appropriately matched to cases. In our study, 2 of 48 cases were unmatched simply because important variables were missing, not because there were no appropriate controls. In view of the difficulty in matching cases with appropriate controls and the significant deviations in several targeted end points among well-matched pairs, the credibility of our findings is strengthened. This outcome analysis provided a clear picture of the impact of multidrug resistance in *Acinetobacter* sepsis.

In summary, nosocomial bacteremia due to multidrug-resistant *A. baumannii* is associated with increased medical costs, prolonged hospitalization, and an increased mortality rate. Thus, efforts to minimize the emergence of antimicrobial resistance in all nosocomially acquired pathogens should be a priority.

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REFERENCES

1. Acar JF. Consequences of bacterial resistance to antibiotics in medical practice. *Clin Infect Dis* 1997; 24(suppl 1):S17-S18.
2. Holmberg SD, Solomon SL, Blake PA. Health and economic impacts of antimicrobial resistance. *Rev Infect Dis* 1987; 9:1065-1078.
3. Urban C, Segal-Maurer S, Rahal JJ. Considerations in control and treatment of nosocomial infections due to multidrug-resistant *Acinetobacter baumannii. Clin Infect Dis* 2003; 36:1268-1274.
4. Bergogne-Berezin E, Towner KJ. *Acinetobacter* spp. as nosocomial pathogens: microbiological, clinical, and epidemiological features. *Clin Microbiol Rev* 1996; 9:148-165.
5. Cisneros JM, Rodriguez-Bano J. Nosocomial bacteremia due to *Acinetobacter baumannii:* epidemiology, clinical features and treatment. *Clin Microbiol Infect* 2002; 8:687-693.
6. Seifert H, Strate A, Pulverer G. Nosocomial bacteremia due to *Acinetobacter baumannii:* clinical features, epidemiology, and predictors of mortality. *Medicine (Baltimore)* 1995; 74:340-349.
7. Cisneros JM, Reyes MJ, Pachon J, et al. Bacteremia due to *Acinetobacter baumannii:* epidemiology, clinical findings, and prognostic features. *Clin Infect Dis* 1996; 22:1026-1032.
8. McCabe WR, Jackson GG. Gram-negative bacteremia. I. Etiology and ecology. *Arch Intern Med* 1962; 110:847-855.
9. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA* 1993; 270:2957-2963.
10. Yu VL, Chiou CC, Feldman C, et al. An international prospective study of pneumococcal bacteremia: correlation with in vitro resistance, antibiotics administered, and clinical outcome. *Clin Infect Dis* 2003; 37: 230-237.
11. Paterson DL. The epidemiological profile of infections with multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter* species. *Clin Infect Dis* 2006; 43(suppl 2):S43-S48.
12. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control* 1988; 16:128-140.
13. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients: excess length of stay, extra costs, and attributable mortality. *JAMA* 1994; 271:1598-1601.
14. Fagon JY, Chastre J, Novara A, Medioni P, Gibert C. Characterization of intensive care unit patients using a model based on the presence or absence of organ dysfunctions and/or infection: the ODIN model. *Intensive Care Med* 1993; 19:137-144.
15. VonGraevenitz A. *Acinetobacter, Alcaligenes, Moraxella,* and other nonfermentative gram-negative bacteria. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, eds. *Manual of Clinical Microbiology.* 6th ed. Washington, DC: American Society for Microbiology; 1995:520-532.
16. National Committee for Clinical Laboratory Standards (NCCLS). *Methods for Dilution: Antimicrobial Susceptibility Testing for Bacteria That Grow Aerobically.* 4th ed. Villanova, PA: NCCLS; 1997. NCCLS document M7-A3.
17. National Nosocomial Infections Surveillance (NNIS) report, data summary from October 1986–April 1996, issued May 1996. *Am J Infect Control* 1996; 24:380-388.
18. National Nosocomial Infections Surveillance (NNIS) System report, data summary from January 1990–May 1999, issued June 1999. *Am J Infect Control* 1999; 27:520-532.
19. Cosgrove SE, Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis* 2003; 36:1433-1437.
20. Cosgrove SE. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. *Clin Infect Dis* 2006; 42(suppl 2):S82-S89.

21. Sheng WH, Chie WC, Chen YC, Hung CC, Wang JT, Chang SC. Impact of nosocomial infections on medical costs, hospital stay, and outcome in hospitalized patients. *J Formos Med Assoc* 2005; 104:318-326.
22. Wilson SJ, Knipe CJ, Zieger MJ, et al. Direct costs of multidrug-resistant *Acinetobacter baumannii* in the burn unit of a public teaching hospital. *Am J Infect Control* 2004; 32:342-344.
23. Jellison TK, McKinnon PS, Rybak MJ. Epidemiology, resistance, and outcomes of *Acinetobacter baumannii* bacteremia treated with imipenem-cilastatin or ampicillin-sulbactam. *Pharmacotherapy* 2001; 21:142-148.
24. Blot S, Vandewoude K, De Bacquer D, Colardyn F. Nosocomial bacteremia caused by antibiotic-resistant gram-negative bacteria in critically ill patients: clinical outcome and length of hospitalization. *Clin Infect Dis* 2002; 34:1600-1606.
25. Raymond DP, Pelletier SJ, Crabtree TD, Evans HL, Pruett TL, Sawyer RG. Impact of antibiotic-resistant gram-negative bacilli infections on outcome in hospitalized patients. *Crit Care Med* 2003; 31:1035-1041.
26. Digiovine B, Chenoweth C, Watts C, Higgins M. The attributable mortality and costs of primary nosocomial bloodstream infections in the intensive care unit. *Am J Respir Crit Care Med* 1999; 160:976-981.
27. Carmeli Y, Troillet N, Karchmer AW, Samore MH. Health and economic outcomes of antibiotic resistance in *Pseudomonas aeruginosa. Arch Intern Med* 1999; 159:1127-1132.
28. Zaragoza R, Artero A, Camarena JJ, Sancho S, Gonzalez R, Nogueira JM. The influence of inadequate empirical antimicrobial treatment on patients with bloodstream infections in an intensive care unit. *Clin Microbiol Infect* 2003; 9:412-418.