

CONCISE COMMUNICATION

Mortality Rates Associated With Multidrug-Resistant *Acinetobacter baumannii* Infection in Surgical Intensive Care Units

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A retrospective, propensity-matched cohort study was conducted to determine the mortality rate in patients with healthcare-associated infection (HAI) due to multidrug-resistant (MDR) *Acinetobacter baumannii*. The 28-day mortality rate for patients with MDR *A. baumannii* HAI was not significantly different than that for patients with non-MDR *A. baumannii* HAI. The median length of hospital stay before diagnosis of HAI was 4.5 days longer for patients with MDR *A. baumannii* infection than for patients with non-MDR *A. baumannii* infection ($P < .001$).

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Multidrug-resistant (MDR) *Acinetobacter baumannii* infections have been increasingly reported throughout the world.¹⁻⁴ As MDR *A. baumannii* becomes more prevalent coupled with limited development of new antibiotics active against drug-resistant gram-negative organisms, clinicians will be increasingly challenged with the decision of whether to use older, more toxic antibiotics. Providing clinicians with outcome data associated with MDR *A. baumannii* infections will facilitate informed decisions and the discussion of prognoses with patients and their families.

METHODS

A matched, retrospective cohort study was conducted from July 2003 through June 2006 in a large, university-affiliated, tertiary care facility. The primary objective was to determine the 28-day mortality rate associated with MDR *A. baumannii* infection, compared with that associated with non-MDR *A. baumannii* infection. Patients at least 18 years of age who were hospitalized for at least 24 hours in 1 of 3 intensive care units (burn, surgical, and trauma) were included in the study. Transplant recipients were excluded.

Prospective surveillance for healthcare-associated infections (HAIs) was performed by trained infection control practitioners. HAIs were defined in accordance with criteria established by the Centers for Disease Control and Prevention.⁵ Multidrug resistance was defined as resistance to 3 or more classes of antibiotics, as tested in accordance with the guidelines of the Clinical and Laboratory Standards Institute. Classes were defined as follows: penicillins (ampicillin and piperacillin), cephalosporins (cefepime and cefotaxime), ami-

noglycosides (amikacin, gentamicin, and tobramycin), imipenem-cilastatin, levofloxacin, minocycline, and trimethoprim-sulfamethoxazole. Resistance to all agents within a class was required for the isolate to be considered resistant to the class. Polymyxins were not routinely included in susceptibility testing and, therefore, were not included in these criteria.

The infection control database was queried to identify cases of *A. baumannii* ventilator-associated pneumonia, healthcare-associated primary bloodstream infection, and healthcare-associated urinary tract infection occurring in patients from the target intensive care units from July 2003 through June 2006. For each patient, only the first episode of *A. baumannii* HAI was included in the study. The department of finance database (Transition Systems) provided patient-specific data on demographic characteristics, procedures, pharmacy data, and diagnoses. Procedure and pharmacy data were restricted to dates at least 48 hours before the diagnosis of infection.

Medical records were reviewed to collect data on vital signs, laboratory data, and microbiological data corresponding to the period 48 hours (range, 42–54 hours) before the diagnosis of infection, to mitigate confounding from physiologic parameters recorded at the time of infection identification. Microbiological data were reviewed to confirm the date and site of infection reported in the infection control database. Antimicrobial susceptibility information was also recorded.

An online Social Security Death Index⁶ was accessed to identify relevant deaths that occurred during the 28-day follow-up period. To assess the validity of this database, all deaths that occurred during the index hospitalization were cross-checked against the online data. All of the in-hospital deaths were also identified by the online death database.

A propensity matched-pairs sample was constructed to account for the large number of potential confounders.⁷ A logistic regression was fit that related MDR *A. baumannii* infection status to baseline variables including age, sex, type of intensive care unit, medications, procedures, and diagnoses. The propensity score was the predicted probability of acquiring infection due to MDR *A. baumannii*. Each patient infected with non-MDR *A. baumannii* was matched to the MDR *A. baumannii*-infected patient with the nearest propensity score, resulting in 42 matched pairs. The remaining patients were excluded from the matched-pairs analysis.

The propensity matched-pairs dataset was constructed using SAS, version 9.1 (SAS Institute), and analyzed using Stata software (StataCorp). The Cox proportional hazards regression model was used to compare mortality rates between the MDR *A. baumannii*-infected group and the non-MDR *A. baumannii*-infected group, with adjustment for preinfection length of stay, which was considered a likely risk factor for the development of infection with a multidrug-resistant strain. To account for correlation induced by matching MDR

A. baumannii-infected patients and non-MDR *A. baumannii*-infected patients, robust standard errors were used.⁸ The Fisher exact test and the Wilcoxon rank sum test were used to compare variables in the full cohort, and the McNemar χ^2 test and the signed rank test were used to compare variables in the matched groups. All statistical tests were 2-tailed. This study was exempt from scrutiny by the Vanderbilt Medical Center institutional review board.

RESULTS

Table 1 summarizes the demographic and clinical characteristics of all patients before matching. Compared with patients in the non-MDR *A. baumannii* group, patients in the MDR *A. baumannii* group had significantly greater exposure to aminoglycosides (64.3% vs 80.1%; $P = .04$) and quinolones (16.7% vs 34.2%; $P = .02$). For the MDR *A. baumannii* group, patients were ventilated a median of 9.5 days (interquartile range [IQR], 6.5–15.5 days), compared with 6.8 days (IQR, 4–9.5 days) for the non-MDR *A. baumannii* group ($P < .01$). There was a trend toward more exposure to anti-

biotics and invasive procedures in the MDR *A. baumannii* group. Ventilator-associated pneumonia was the most common HAI, representing more than 75% of infections in both groups.

Patients in the MDR *A. baumannii* group were hospitalized a median of 4.5 days longer prior to HAI diagnosis than those in the non-MDR *A. baumannii* group (11.5 days [IQR, 7–19 days] vs 7 days [IQR, 5–10 days]; $P < .001$); there were no significant differences in the median total length of stay (32.5 days [IQR, 22–51 days] vs 26.5 days [IQR, 16–43 days]; $P = .11$) or postinfection length of stay (18 days [IQR, 10–28 days] vs 17.5 days [IQR, 9–33 days]; $P = .93$).

Table 2 shows the demographic and clinical characteristics of the propensity-matched patients. There remained a trend toward more exposure to antibiotics, vasopressor agents, and procedures in the MDR *A. baumannii* group, compared with the non-MDR *A. baumannii* group. Bronchoscopy was more commonly performed for the MDR *A. baumannii* group than for the non-MDR *A. baumannii* group (92.9% vs 76.2% of patients; $P = .04$).

In the matched cohort, a total of 10 patients died (4 [9.5%]

TABLE 1. Demographic and Clinical Characteristics of All Patients Before Matching

Characteristic	Patients with non-MDR <i>A. baumannii</i> HAI ($n = 42$)	Patients with MDR <i>A. baumannii</i> HAI ($n = 146$)	P
Age, median (IQR), years	41.5 (27–59)	48 (34–59)	.21
Male sex	29 (69.0)	106 (72.6)	.70
Died	4 (9.5)	23 (15.8)	.45
Antibiotics received ^a			
Aminoglycosides	27 (64.3)	117 (80.1)	.04
Antipseudomonal penicillins	10 (23.8)	46 (31.5)	.44
Carbapenems	22 (52.4)	77 (52.7)	.99
Cephalosporins	25 (59.5)	83 (56.8)	.86
Penicillins	5 (11.9)	22 (15.1)	.30
Quinolones	7 (16.7)	50 (34.2)	.02
Vasopressor agents received ^a	33 (78.6)	131 (89.7)	.06
Procedures undergone ^a			
Bronchoscopy	32 (76.2)	126 (86.3)	.15
Central venous catheter	33 (78.6)	114 (78.1)	.99
Tracheostomy	28 (66.7)	102 (69.9)	.71
Ventilator-days, median (IQR)	6.8 (4–9.5)	9.5 (6.5–15.5)	<.01
Diagnosis received ^b			
Acute renal failure	10 (23.8)	44 (30.1)	.56
Coronary artery disease	9 (21.4)	21 (14.4)	.34
Congestive heart failure	6 (14.3)	31 (21.2)	.38
Diabetes mellitus	6 (14.3)	20 (13.7)	.99
COPD	4 (9.5)	8 (5.5)	.47
Type of infection			
Ventilator-associated pneumonia	33 (78.6)	110 (75.3)	.42
Bloodstream infection	8 (19.0)	26 (17.8)	.51
Urinary tract infection	1 (2.4)	10 (6.8)	.25

NOTE. Data are no. (%) of patients, unless otherwise specified. COPD, chronic obstructive pulmonary disease; HAI, healthcare-associated infection; IQR, interquartile range; MDR, multidrug-resistant.

^a Received before the date of infection.

^b Received any time during the index hospitalization.

TABLE 2. Demographic and Clinical Characteristics of Matched Patients

Characteristic	Patients with non-MDR	Patients with MDR	P
	<i>A. baumannii</i> HAI (n = 42)	<i>A. baumannii</i> HAI (n = 42)	
Age, median (IQR), years	41.5 (27–59)	40.5 (25–54)	.39
Male sex	29 (69.0)	32 (76.2)	.61
Died	4 (9.5)	6 (14.3)	.74
Antibiotics received ^a			
Aminoglycosides	27 (64.3)	34 (81.0)	.19
Antipseudomonal penicillins	10 (23.8)	13 (31.0)	.65
Carbapenems	22 (52.4)	25 (59.5)	.70
Cephalosporins	25 (59.5)	26 (61.9)	.99
Penicillins	3 (7.1)	6 (14.3)	.51
Quinolones	7 (16.7)	10 (23.8)	.55
Vasopressor agents received ^a	33 (78.6)	35 (83.3)	.79
Procedures undergone ^a			
Bronchoscopy	32 (76.2)	39 (92.9)	.04
Central venous catheter	33 (78.6)	34 (81.0)	.99
Tracheostomy	28 (66.7)	27 (64.3)	.99
Ventilator-days, median (IQR)	6.8 (4–9.5)	7.3 (5.5–11)	.30
Diagnosis received ^b			
Acute renal failure	10 (23.8)	11 (26.2)	.99
Coronary artery disease	9 (21.4)	9 (21.4)	.99
Congestive heart failure	6 (14.3)	8 (19.0)	.77
Diabetes mellitus	6 (14.3)	7 (16.7)	.99
COPD	4 (9.5)	3 (7.1)	.99
Type of infection			
Ventilator-associated pneumonia	33 (78.6)	37 (88.1)	.39
Bloodstream infection	8 (19.0)	4 (9.5)	.39
Urinary tract infection	1 (2.4)	1 (2.4)	.99

NOTE. Data are no. (%) of patients unless otherwise specified. COPD, chronic obstructive pulmonary disease; HAI, healthcare-associated infection; IQR, interquartile range; MDR, multidrug-resistant.

^a Received before the date of infection.

^b Received any time during the index hospitalization.

patients in the non-MDR *A. baumannii* group died, and 6 [14.3%] patients in the MDR *A. baumannii* group died). Kaplan-Meier curves of survival probability separated at approximately day 16, suggesting greater mortality in the MDR *A. baumannii*-infected group. However, there was no detectable difference in mortality rates between groups (adjusted hazard ratio, 1.43 [95% confidence interval, 0.42–4.89]).

DISCUSSION

A. baumannii is an important emerging pathogen occurring with ever greater frequency in healthcare institutions.^{1–4} This organism has a remarkable capacity to develop resistance to all currently available antimicrobial agents, which complicates treatment, often contributes to prolonged hospital stays, and leads to substantial economic burden.⁹

In the present study, a matched retrospective analysis was conducted to assess the mortality rates associated with HAIs caused by MDR *A. baumannii* compared with the mortality rates associated with HAIs caused by non-MDR strains of *A.*

baumannii. An increased mortality rate associated with MDR *A. baumannii* HAIs was not demonstrated, but this study was limited by the small sample size achieved after performing a matched analysis. Patients with MDR *A. baumannii* HAIs were hospitalized a median of 4.5 days longer before the diagnosis of infection than those with non-MDR *A. baumannii* HAIs. This did not translate into an increased total length of stay, however, and the length of stay after diagnosis of HAI did not differ significantly between the groups.

Sunenshine et al.¹⁰ conducted a retrospective, matched cohort study to assess the mortality rates associated with MDR *A. baumannii* infection. They reported an increase in hospital and intensive care unit lengths of stay for patients with MDR *A. baumannii* infection, compared with patients infected with non-MDR *A. baumannii*. However, the in-hospital mortality rate was not significantly different between the groups. Similarly, the present study failed to demonstrate an increase in 28-day mortality rates associated with infection with an MDR strain. However, this should be interpreted with caution, since this study was designed to detect large differences in mortality rates.

Though much attention has been given to antimicrobial resistance in gram-positive organisms, such as methicillin-resistant *Staphylococcus aureus*, resistance in gram-negative bacilli, such as *A. baumannii*, is rapidly emerging. *A. baumannii*, however, can express complex resistance patterns, such that treatment of the infections is severely hampered by the lack of effective antimicrobial agents. Thus, further study is essential to advance our understanding of the morbidity and mortality associated with MDR *A. baumannii* HAI and other similar infections that are due to multidrug-resistant gram-negative organisms.

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