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ARTICLE

Impact of multi-drug-resistant *Acinetobacter baumannii* on clinical outcomes

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Abstract We conducted a retrospective matched cohort study to examine the impact of isolation of multi-drug-resistant (MDR) *Acinetobacter baumannii* on patient outcomes. Cases from whom MDR *A. baumannii* was isolated in a clinical culture (n=118) were compared with controls from whom MDR *A. baumannii* was not isolated (n=118). Cases and controls were matched according to ward, calendar month of hospitalization, and duration of hospitalization before culture. The following outcomes were compared in multivariable analysis: in-hospital mortality, length of stay, need for mechanical ventilation, and functional status at discharge. MDR *A. baumannii* was determined to be a pathogen in 72% of cases. In 36% of cases, the patient died, versus 21% of controls (odds ratio [OR] 2.21, 95% confidence interval [CI] 1.17–4.16, P=0.014). Median length of stay for surviving cases was 17 days, versus 11 for surviving controls (multiplicative effect 1.55, 95% CI 0.99–2.44, P=0.057). Fifty-two percent of cases required mechanical ventilation, versus 25% of controls (OR 3.72, 95% CI 1.91–7.25, P<0.001); 60% of surviving cases were discharged with reduced functional status, versus 38% of controls (OR 4.4, 95% CI 1.66–11.61, P=0.003). In multivariable analysis, clinical isolation of MDR *A. baumannii* remained a significant predictor of mortality (OR 6.23, 95% CI 1.31–29.5, P=0.021), need for mechanical ventilation (OR 7.34, 95% CI 2.24–24.0, P<0.001), and reduced functional status on discharge (OR 7.93, 95% CI 1.1–56.85, P=0.039). Thus, MDR *A. baumannii* acquisition is associated with severe adverse outcomes, including increased mortality, need for mechanical ventilation, and reduced functional status.

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Multi-drug-resistant (MDR) *Acinetobacter baumannii* is a nosocomial pathogen of increasing importance. Once considered an opportunistic pathogen of relatively low virulence affecting mostly patients in intensive care units (ICUs) [1], this organism has a selective advantage over many other nosocomial bacteria beause of its hardiness [2, 3], which allows cross-transmission, and its intrinsic and acquired resistance to many antimicrobial agents. Whereas multi-drug resistance is rarely found in community isolates of *A. baumannii*, the prevalence of the MDR phenotype among hospital isolates has increased during the last decade, and MDR *A. baumannii* has become a leading pathogen in many hospitals worldwide [4, 5]. Hospital outbreaks have been described from various geographical areas [6–9], and in some areas, this organism has become endemic [9]. It has been reported to be an important pathogen in wounded soldiers returning from Iraq and Afghanistan [10–12]. It has also been described infecting Iranian soldiers wounded during the Iran-Iraq conflict [13] and in trauma patients from mass casualty situations, such as suicide bombings [14], patients affected by the tsunami in Southeast Asia in December 2004 [15], and survivors of the earthquake in Turkey in 1999 [16]. Since these patients are often transferred to tertiary care centers, sometimes in

distant geographic areas, they may become a source of transmission in previously non-endemic hospitals.

Since the late 1990s, MDR *A. baumannii* has been an important nosocomial pathogen in several Israeli hospitals, including ours [17, 18]. We have recently reported its complex epidemiology and individual risk factors for infections with MDR *A. baumannii* [18]. Infections caused by resistant organisms are thought to result in higher morbidity and mortality, prolonged hospitalization, and increased costs compared with infections caused by antibiotic-susceptible strains [19–21]. Data concerning the impact of MDR *A. baumannii* are insufficient and controversial. Although the reported crude mortality of patients with these organisms reaches 50%, the attributable mortality and other effects on patient outcomes are difficult to study, since the affected patients are often severely ill and have prolonged spells of hospitalization, and poor prognoses, irrespective of their infection. Indeed, reported attributable mortality ranges from 7% to 36% [1, 22–27].

The current study was designed to examine the impact of MDR *A. baumannii* acquisition on the outcomes of patients at our institution. The impact of resistant organisms may be related to two separate phenomena: replacement and addition of infections, i.e., in certain cases, resistant organisms merely replace the susceptible form as causative pathogens (replacement), whereas in other cases, resistant organisms cause additional infections (addition). In our institution, non-MDR *A. baumannii* rarely causes nosocomial infections. Thus, infections caused by MDR *A. baumannii* are additive and do not replace infections caused by a susceptible variant of the organism. We therefore elected to analyze the impact of MDR *A. baumannii* by using the additive model and to compare patients from whom MDR *A. baumannii* was isolated, with similar patients at risk from whom it was not [28]. On the basis of our earlier findings, we considered clinical isolation of *A. baumannii* as indicative of acquisition in the hospital [18].

Methods

Hospital setting, data collection, and microbiology

This study was performed at the Tel Aviv Sourasky Medical Center, Israel, an 1100-bed tertiary-care teaching hospital with 70,000 admissions annually. Approximately 82,500 clinical microbiological cultures are processed annually. This is a retrospective matched cohort study designed to identify the effect of clinical isolation of MDR *A. baumannii* on patient outcomes.

Cases were defined as patients from whom MDR *A. baumannii* was isolated from any clinical culture during the 6-month period from January 1st through June 30th, 2001. A control patient was matched to each case patient based on temporo-spatial factors according to the scheme described by Carmeli et al. [29]. Controls were randomly chosen from the list of patients who stayed on the same ward in the same calendar month as the matched case and who had been hospitalized for at least the same number of days as the matched case had been at the time of culture. Controls did not have MDR *A. baumannii* isolated in any clinical culture. As we wanted the cohort to include the entire population at risk for MDR *A. baumannii* isolation, we did not exclude patients from whom non-MDR *A. baumannii* had been previously isolated from either the case or the control group. Random control selection was performed as follows: a list of all possible controls was created, each candidate was assigned a random number, and the highest random number was chosen.

Cases and control patients were included only once. Data were collected from the patients' records and from hospital computerized databases and entered into a prepared electronic abstraction sheet. The following information was recorded for each patient: age, sex, use of tobacco and alcohol prior to hospitalization, cause and ward of hospitalization, transfer from another institution or ward within our institution, ICU stay, underlying disorders, immunosuppressive therapy, severity of illness, functional capacity and neurological condition at the time of isolation of *A. baumannii* or matching and at discharge, placement of a Foley catheter, invasive devices, surgery, mechanical ventilation, dialysis, infection versus colonization (cases only), and antibiotic therapy. *A. baumannii* was isolated from clinical specimens submitted to the clinical microbiology laboratory and identified by using the Gram-Negative Identification Panel (Microscan, Dade Behring, Sacramento, Calif.). Susceptibilities were determined by automated microdilution broth testing (Neg/Urine Combo panel, Dade Behring). Resistance to imipenem and meropenem was confirmed by using the Kirby-Bauer disk diffusion method performed according to CLSI guidelines [30].

Definitions

We defined *A. baumannii* as MDR when the organism was resistant to all of the following agents: piperacillin/tazobactam, cefepime, ceftazidime, aztreonam, ciprofloxacin, gentamicin, and tobramycin). Isolates susceptible to amikacin, ampicillin-sulbactam, imipenem, meropenem, minocycline, and colistin could still be considered MDR. Infection was defined according to CDC definitions and modified to include community-acquired infections and to exclude asymptomatic bacteriuria [31]. Patients with MDR *A. baumannii* who did not fulfill criteria for infection were classified as being colonized.

Standard criteria were used to define underlying disorders. Disease was considered to be active if signs of disease were clinically apparent or if the patient received treatment for the disease. A patient was considered to be under immunosuppressive therapy if he had received chemotherapy within 3 weeks, if he was treated with at least 20 mg prednisone daily for at least 2 weeks before entering the study, or if he recently received anti-rejection or other immunosuppressive therapy.

Severity of illness attributable to co-morbidities was defined according to the McCabe score [32]. Functional capacity during the index hospitalization was divided into two categories: independent or requiring significant assistance in activities of daily living. Renal failure was defined as a serum creatinine level above 2 mg/dl. Neurological function was classified according to three conditions: fully conscious, confused/demented, or unconscious.

We recorded the number of antibiotics that each patient received from the time of admission until study inclusion; home antibiotic therapy was recorded separately. Recent hospitalization was defined as hospital stay up to 3 months before the index hospitalization. Surgery, mechanical ventilation, and any invasive procedure that took place up to 1 month prior to inclusion in the study were recorded.

Statistical analysis

Statistical analysis was performed by using Stata version 7 (Stata, College Station, Tex.). All analyses were matched in order to correspond to the study design. Univariate analysis was performed by using the McNemar and paired Student's *t* tests. Variables with a *P*-value of <0.2 in univariate analysis were included in the multivariate model. Multivariate analysis was performed by using conditional (fixed effect) logistic regression for dichotomized outcomes (in-hospital mortality, mechanical ventilation after inclusion in the study, surgery after inclusion in the study, functional status at discharge, and discharge disposition). For length of stay after inclusion in the study, matched linear regression (linear regression with absorbed variable) of the log-transformed length of stay was performed. The effect estimate in the mortality model was reported as the odds ratio (OR) and in the length-of-stay model as the multiplicative effect (ME; the anti-log of the β-coefficient [33]).

Variables with a *P*-value of <0.1 were retained in the multivariable model. Variables that were not retained in the model by this procedure were then tested for confounding by adding them one at a time to the model and examining their effects on the β-coefficients. Variables that caused substantial confounding (change in the β-coefficient of greater than 10%) were included in the final model.

In addition to examining statistical significance and confounding, effect modification between variables was evaluated by testing appropriate interaction terms for statistical significance. Colinearity was examined by interchanging variables and examining the effect on the model. All statistical tests were two-tailed. In the final multivariable models, a *P*-value of ≤0.05 was considered significant.

Results

Demographics and clinical characteristics

We identified 133 patients with a clinical culture of MDR *A. baumannii*. Four patients were not hospitalized adults (one was a child, and three were adult outpatients) and were therefore excluded. Charts were available for review for 120 cases. For two, no controls could be matched. Thus, a total of 236 patients were included in the study (118 cases and their matched controls). Of these, six (2.5%) had non-MDR *A. baumanii* isolated prior to inclusion in the study. MDR *A. baumannii* was initially isolated from the following sites: respiratory tract, 38 (32%); wounds, 23 (19.5%); urine, 22 (19%); blood 19, (16%); sterile fluids or catheter tips, 16 (13.5%).

Patients' characteristics are displayed in Table 1. Cases were similar to their matched controls with respect to age (average 67.7 versus 64.4 years old) and sex distribution (60% versus 50% male). The groups were also similar with respect to tobacco and alcohol use and to the prevalence of lung disease, diabetes, kidney disease, liver disease, malignancy, and transplantation. The prevalence of ischemic heart disease was higher among cases than among controls (69% versus 52%, OR 2.33, $P=0.006$), and cases tended to have been transferred from another institution more often than controls (20% versus 10%, OR 2.12, $P=0.065$).

Clinical outcome of isolation of MDR *A. baumannii*

Mortality

A total of 42 case patients (36%) died in hospital. Among the 85 cases with clinical infection caused by *A. baumannii*, 41 (48%) died, and among the 33 patients in whom *A. baumannii* was classified as a colonizer, only one (3%) died. Among 118 control patients, 25 (21%) died. The crude fatality ratio was significantly higher among cases than among controls (OR 2.21, 95% CI 1.17–4.16, $P=0.014$)

Other variables identified by univariate analysis as risk factors for in-hospital mortality included age >70 years (OR

Table 1 Baseline characteristics of cohort and comorbid conditions

Parameter	Cases n=118 (%)	Controls n=118 (%)	OR	95% confidence interval	P-value
Demographic parameters					
Average age (SD)	67.7 (16.4)	64.4 (19.2)	1.01	0.996–1.03	0.13
Male sex	71 (60)	59 (50)	1.48	0.89–2.45	0.13
Smoking	35 (30)	43 (36)	0.72	0.41–1.27	0.26
Alcohol usage	7 (6)	5 (4)	1.50	0.42–5.31	0.53
Admission from another institution	23 (19)	12 (10)	2.12	0.96–4.76	0.07
Comorbid conditions					
Ischemic heart disease	82 (69)	61 (52)	2.33	1.27–4.27	0.006
Lung disease	59 (50)	50 (42)	1.58	0.82–2.72	0.18
Diabetes	39 (33)	28 (24)	1.58	0.88–2.8	0.12
Liver disease	10 (8)	18 (15)	0.56	0.25–1.2	0.14
Renal disease	35 (30)	27 (23)	1.39	0.76–2.54	0.29
Post transplantation	7 (6)	3 (3)	2.33	0.6–9.02	0.22
Malignancy	35 (30)	38 (32)	0.92	0.53–1.6	0.78

3.2, P=0.023), unconsciousness (OR 2.8, P=0.048), a McCabe score of 3, indicating life expectancy of less than 6 months (OR27, P<0.001), malignancy (OR2.6, P=0.04), presence of a Foley catheter (OR5.5, P=0.027), and *A. baumannii* infection rather than colonization (OR6, P<0.001). Variables that approached statistical significance (0.05<P<0.1) as risk factors for mortality were surgery, mechanical ventilation, and poor functional status before isolation of *A. baumannii* (Table 2). In the multivariable analysis (Table 3), the following variables were included in the model for mortality: being a case patient (OR6.23, P=0.021), having malignant disease (OR6.49, P=0.064), and having a McCabe score of 3 (OR64.4, P=0.003).

Additional factors associated with mortality included need for mechanical ventilation after *A. baumannii* isolation, and need for antibiotic treatment after isolation. The fact that these covariates represent occurrences after the isolation of *A. baumannii* indicates that they are likely intermediate variables rather than confounders [34].

Length of hospital stay

The average hospital stay after study entry among surviving cases tended to be longer than that among surviving controls (28.34±43 versus 17.5±23.7 days, median 17 versus 11 days, P=0.057). Among the cases defined as having clinical infection with *A. baumannii* but who survived to discharge, the average hospital stay was significantly longer (36.5±53 days, P=0.024; median 20 days).

The following variables were found to be risk factors for prolonged hospital stay in univariate analysis (Table 2): infection rather than colonization (ME 1.92, P=0.02), male sex (ME 2.34, P=0.009), age (considered as a continuous variable; ME 1.02, P=0.03), unconsciousness (ME1.54, P=0.05), and mechanical ventilation before *A. baumannii* isolation (ME2.89, P=0.003).

In multivariable analysis (Table 3), only male sex was significantly associated with prolonged length of hospital stay (ME1.95, P=0.04). Other factors included in the model were age >70 years (ME1.75, P=0.08) and being a case (ME1.4, P=0.13).

Mechanical ventilation

Ninety-one patients (38%) had to be mechanically ventilated after entering the study (52% of cases versus 25% of controls). In univariate analysis, the following variables were found to be statistically significant predictors of mechanical ventilation: being a case (OR3.72, P<0.001), having lung disease (OR3, P=0.02), being bed-ridden before *A. baumannii* isolation (OR5.3, P=0.008), unconsciousness (OR11.05, P<0.001), having a Foley catheter (OR6.33, P=0.003), or a McCabe score of 3 (OR3.23, P=0.005). In multivariate analysis (Table 3), the following variables were found to be statistically significant as risk factors for mechanical ventilation: being a case (OR7.34, P<0.001), having a Foley catheter (OR5.84, P=0.03), and having a McCabe score of 3 (OR11.4, P=0.005).

Functional status at discharge

Among surviving patients, cases were more likely than controls to be discharged with low functional status, i.e., requiring significant assistance in activities of daily living (60% versus 38%, OR4.4, P=0.003), and to be discharged to a nursing home (55% versus 42%, OR3.33, P=0.01).

In univariate analysis, the following variables were found to be predictors of poor functional status at discharge: having poor functional status before culture

Table 2 Univariate analysis of risk factors for mortality and length of hospital stay (*LOS* length of stay, *ICU* intensive care unit)

Parameter	Mortality in patients with the parameter, *n* (%)	Mortality in patients without the parameter, *n* (%)	OR	95% confidence interval	*P*-value	LOS multiplicative effect	95% confidence interval	*P*-value
Demographic parameters								
Status as case	42/118 (36)	25/118 (21)	2.21	1.17–4.16	0.014	1.55	0.99–2.44	0.057
Clinical infection with *A. baumannii*	41/85 (48)	26/151 (17)	6	2.32–15.46	<0.001	1.92	1.1–3.35	0.02
Male sex	(25) 32/130	35/106 (33)	0.72	0.35–1.47	0.37	2.34	1.25–4.4	0.009
Age>70 years	39/114 (34)	28/122 (23)	3.2	1.17–8.73	0.023	0.57	0.29–1.11	0.10
Admission from home	53/201 (26)	14/35 (40)	0.43	0.11–1.66	0.22	NA	NA	NA
Smoking	28/78 (36)	39/158 (25)	0.92	0.42–2.02	0.84	1.45	0.64–3.29	0.36
Alcohol use	3/12 (25)	64/224 (29)	1	0.14–7.09	1	2.29	0.49–10.73	0.28
Comorbid conditions								
Cardiovascular disease	50/143 (35)	17/93 (18)	2.2	0.76–6.33	0.14	0.76	0.37–1.54	0.44
Lung disease	41/109 (38)	26/127 (20)	1.2	0.52–2.77	0.67	1.41	0.61–3.27	0.41
Diabetes	20/67 (30)	47/169 (28)	0.61	0.25–1.45	0.28	0.62	0.29–1.31	0.21
Liver disease	7/28 (25)	60/208 (29)	0.37	0.01–1.41	0.15	0.41	0.15–1.13	0.09
Renal disease	25/62 (40)	42/174 (24)	1.33	0.56–3.16	0.51	1.15	0.48–2.76	0.73
Organ transplantation	5/10 (50)	62/226 (27)	1.33	0.29–5.95	0.7	3.9	0.34–44.62	0.27
Malignancy	7/73 (10)	40/163 (25)	2.6	1.04–6.81	0.04	0.76	0.37–1.54	0.44
Clinical parameters								
Unconsciousness	31/66 (47)	36/170 (21)	2.8	1.01–7.77	0.048	1.54	1–2.38	0.05
Surgery before culture	13/66 (20)	54/170 (23)	0.3	0.08–1.09	0.07	1.22	0.51–2.92	0.64
ICU stay before culture	21/69 (30)	46/167 (28)	1.1	0.71–1.7	0.65	1.04	0.99–1.09	0.16
Mechanical ventilation before culture	51/117 (44)	16/119 (13)	2.5	0.97–6.44	0.06	2.89	1.45–5.72	0.003
Dialysis before culture	11/15 (73)	56/221 (25)	2.66	0.7–10.05	0.14	NA	NA	NA
Immunosuppresion	23/56 (41)	44/180 (24)	1.71	0.67–4.35	0.25	1.07	0.48–2.4	0.85
Poor functional status before culture	58/167 (35)	9/69 (13)	2.75	0.87–8.63	0.08	1.80	0.96–3.35	0.07
McCabe 3	67/117 (57)	5/119 (4)	27.0	3.67–198.7	0.001	1.16	0.50–2.69	0.72
Procedures								
Foley catheter before culture	61/172 (35)	6/64 (9)	5.5	1.22–24.81	0.027	1.74	0.95–3.19	0.07
Central venous catheter	44/139 (32)	23/97 (24)	1.5	0.53–4.21	0.44	1.3	0.63–2.67	0.47
Arterial line	27/69 (39)	40/167 (23)	1.0	0.32–3.10	1.00	1.95	0.78–4.86	0.15
Other	43/141 (30)	24/94 (26)	0.54	0.2–1.47	0.23	0.86	0.41–1.8	0.69

(OR 18, P=0.005), age >70 years (OR 4, P=0.03), and having a Foley catheter (OR 13, P=0.013). In multivariable analysis, after adjustment for functional status before culture, being a case remained an independent predictor of poor functional status at discharge (OR 7.93, P=0.039; Table 3).

Discussion

The literature regarding clinical outcomes of MDR *A. baumannii* acquisition among hospitalized patients is inconclusive regarding one principal question: are the adverse outcomes associated with the organism directly

Table 3 Outcomes of isolation of MDR *A. baumannii*; multivariable analysis (*OR* odds ratio, *LOS* length of stay)

Parameter	Adjusted OR	95% Confidence Interval	P Value
Mortality[a]	6.23	1.31–29.5	0.021
Mean LOS after culture[b]	1.41	0.9–2.22	0.13
Mechanical ventilation[c]	7.34	2.24–24.0	<0.001
Poor functional status at discharge[d]	7.93	1.1–56.85	0.039

[a] Also included in the mortality model: malignancy (OR 5.49, P=0.064), McCabe 3 (OR 64.4, P=0.003), mechanical ventilation after culture (OR 8.3, P<0.001), and antibiotics after culture (OR 3.75, P=0.019)
[b] Significant in the LOS model: male sex (multiplicative effect 1.95, P=0.04)
[c] Also significant in the mechanical ventilation model: Foley catheter (OR 5.84, P=0.03), McCabe 3 (OR 11.4, P=0.005)
[d] Also significant in the functional status model: poor functional status prior to culture (OR 33.88, P=0.013)

attributable to its acquisition, or is the presence of MDR *A. baumannii* merely a marker of poor outcome in patients with extensive comorbid conditions?

In an attempt to allay some of the confusion on the subject, Falagas et al. conducted a systematic review of published case-control studies and examined the effect of colonization or infection with *A. baumannii* on morbidity and mortality by comparing critically ill patients with *A. baumannii* with matched controls without *A. baumannii* [5]. Whereas their findings suggested increased attributable mortality and ICU stay in patients with *A. baumannii* infection and colonization, their ability to draw conclusions was limited by small sample sizes and by methodological heterogeneity in the included studies.

Our study, the largest to date on outcomes of MDR *A. baumannii* acquisition in hospitalized patients, adds to the currently limited supply of data on the topic. We have found that, after control for confounding variables, patients with MDR *A. baumannii* were significantly more likely to die, to require mechanical ventilation, and to be discharged with poor functional status than patients without MDR *A. baumannii*. Moreover, the findidng that the overwhelming majority of case patients who died and those mechanically ventilated had clinical infection with *A. baumannii* rather than just colonization (41 of 42 and 56 of 61, respectively) suggests that the organism is a cause, rather than a mere marker, of these deleterious outcomes. Furthermore, a certain proportion of colonized patients will ultimately develop infection and thereby potentially be at higher risk for adverse outcomes. Ideally, future analyses that can account for variation in status between colonization and infection over time will help to elucidate more clearly the precise effect of MDR *A. baumannii* isolation on outcomes.

That MDR *A. baumannii* should lead to poor outcomes is certainly plausible for a number of reasons. First, the patient populations affected by the organism are largely debilitated [35]. The insult of a bacterial infection added to multiple comorbidities may certainly result in clinical deterioration. Moreover, the types of infections commonly caused by *A. baumannii*, particularly pneumonia or bacteremia (occurring in over 50% of infected patients in our study), may be particularly severe. In addition, the high degree of antimicrobial resistance found among these pathogens may result in a deleterious delay in an institution of effective therapy, as empiric coverage may not include the agents ultimately to be proven necessary when culture and susceptibility data become available [36, 37]. Finally, the emergence of pan-resistant and nearly pan-resistant strains of *A. baumannii* may result in an inability to treat infections caused by this pathogen optimally with currently available antibiotics [38].

Why have different investigators arrived at differing conclusions regarding the role of *A. baumannii* in causing poor outcomes [1, 22–27]? The reasons for the differences in results can be divided into four basic categories: methodological, population, therapeutic, and bacterial. Methodological differences include those of study design, choice of comparison group (if any), control for confounding variables such as severity of underlying illness and comorbid conditions, and decisions regarding the matching of cases and controls according to specific attributes. Whereas these types of differences could certainly account for differing results, there is a lack of accord in results, even among studies employing similar methodology [5, 39].

Population differences, including medical versus surgical patients, adults versus children, outpatients versus inpatients, and differences in underlying comorbidity, may play a causative role in outcome differences among studies. Nevertheless, population differences are unlikely a major cause of the heterogeneity in results observed in outcome studies of MDR *A. baumannii* acquisition, as this is an organism isolated primarily among inpatients with extensive contact with the healthcare system and significant underlying comorbidity and antimicrobial exposure [18, 35]. Moreover, as the review by Falagas demonstrates, even studies of critically ill patients alone fail to yield definitive outcome results [5]. In our study, even after extensive

efforts to control for differences in patient characteristics, we have found a significant and strong effect of MDR *A. baumannii* acquisition on outcomes.

Treatment differences among various cohorts of infected patients may likewise play a role in differing outcomes. Falagas et al. [37] have demonstrated worse outcomes in patients with *A. baumannii* bacteremia receiving inappropriate empirical therapy compared with those who received appropriate treatment. Even in established infection with an identified organism, and even when choices are within the susceptibility profile of the pathogen, differences in antibiotic selection may affect the outcome of treatment [40, 41]. Yet in MDR *A. baumannii* infection, the spectrum of susceptibility to presently available antibiotics is so narrow that little room is left for any variation in treatment options.

We postulate that the differences in observed outcomes of MDR *A. baumannii* infection and colonization reported in the literature are primarily attributable to differences in the bacteria themselves. In an earlier study at our institution, among 51 unique-patient MDR *A. baumannii* clinical strains available for genotyping, fully 10 distinct clones were identified [18]. A considerable degree of difference in genome has been observed between different genotypes of this organism. Moreover, the advent of whole-genome sequencing has allowed for quantitation and characterization of the wide array of resistance determinants that strains of *A. baumannii* are known to acquire [42]. While little is known about determinants of virulence in *A. baumannii*, there is evidence of virulence factors selectively present among resistant strains of other bacterial pathogens [43, 44]. Therefore, heterogeneity among genotypes, resistance determinants, and virulence factors might play the predominant role in the differences observed in outcome studies of MDR *A. baumannii* acquisition performed to date worldwide.

Our study adds to the growing body of data regarding the deleterious effects of MDR *A. baumannii* infection and supports the conclusion that this pathogen is independently associated with poor outcomes. Further studies are needed to elucidate the bacterial factors associated with differences in clinical outcomes.

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