

Risk Factors for Early-onset, Ventilator-associated Pneumonia in Critical Care Patients

Selected Multiresistant versus Nonresistant Bacteria

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Background: Ventilator-associated pneumonia is the leading nosocomial infection in critically ill patients. The frequency of ventilator-associated pneumonia caused by multidrug-resistant bacteria has increased in recent years, and these pathogens cause most of the deaths attributable to pneumonia. The authors, therefore, evaluated factors associated with selected multidrug-resistant ventilator-associated pneumonia in critical care patients.

Methods: The authors prospectively recorded potential risk factors at the time of intensive care unit admission. An endotracheal aspirate was obtained in all patients who met clinical criteria for pneumonia. Patients were considered to have ventilator-associated pneumonia only when they met the clinical criteria and aspirate culture was positive for bacteria 48 h or more after initiation of mechanical ventilation. Pediatric patients were excluded. Adult patients with ventilator-associated

pneumonia were first grouped as "early-onset" (< 5 days) and "late-onset," determined by episodes of ventilator-associated pneumonia, and then, assigned to four groups based on the bacteria cultured from their tracheal aspirates: *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, methicillin-resistant staphylococci, and all others. The first three bacteria were considered to be multidrug resistant, whereas the others were considered to be antibiotic susceptible. Potential risk factors were evaluated with use of univariate statistics and multivariate regression.

Results: Among 486 consecutive patients admitted during the study, 260 adults underwent mechanical ventilation for more than 48 h. Eighty-one patients (31%) experienced 99 episodes of ventilator-associated pneumonia, including *Pseudomonas* (36 episodes), methicillin-resistant staphylococci (17 episodes), *Acinetobacter* (9 episodes), and nonresistant bacteria (40 episodes). Sixty-six of these episodes were early onset and 33 episodes were late onset. Logistic regression analysis identified three factors significantly associated with early-onset ventilator-associated pneumonia caused by any one of the multidrug-resistant bacterial strains: emergency intubation (odds ratio 6.4; 95% confidence interval, 2.0–20.2), aspiration (odds ratio

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12.7; 95% confidence interval, 2.4–64.6), and Glasgow coma score of 9 or less (odds ratio, 3.9; 95% confidence interval, 1.3–11.3). *A. baumannii*-related pneumonia cases were found to be significantly associated with two of these factors: aspiration (odds ratio, 14.2; 95% confidence interval, 1.5–133.8) and Glasgow coma score (odds ratio, 6.0; 95% confidence interval, 1.1–32.6).

Conclusions: The authors recommend that patients undergoing emergency intubation or aspiration or who have a Glasgow coma score of 9 or less be monitored especially closely for early-onset multidrug-resistant pneumonia. The occurrence of aspiration and a Glasgow coma score of 9 or less are especially associated with pneumonia caused by *A. baumannii*. (Key words: Anesthesia; antibiotic resistance; infection; intensive care; nosocomial.)

PNEUMONIA is a frequent and serious complication in patients undergoing mechanical ventilation. Mechanical ventilation increases the incidence of pneumonia in patients in the hospital 6- to 20-fold.^{1–3} A consensus statement from the American Thoracic Society identified an incidence of approximately 35 episodes per 1,000 patient-days.⁴ Consequently, ventilator-associated pneumonia is the leading nosocomial infection in critical care patients.⁵ Although, the cause of pneumonia is well-known and prevention guidelines have been established, treatment of these infections is challenging, and these infections account for a substantial mortality.^{6,7}

Distal airways are usually colonized by upper respiratory tract flora after a few days of mechanical ventilation. The flora are mostly endogenous bacterial strains from the gastrointestinal tract, although some result from inhaled contaminants or are transmitted from healthcare workers.⁶ The specific epidemiology depends on numerous factors, including the patient's underlying disease and previous antibiotic use.⁸

The frequency of ventilator-associated pneumonia caused by multidrug-resistant bacteria has increased in recent years.^{6,9,10} Among the most important multidrug-resistant bacteria are *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and methicillin-resistant staphylococci. These pathogens cause most of the deaths attributable to pneumonia.^{9–11} Additionally, timing of the onset of pneumonia is an important factor in predicting causative organisms, complications, and prognosis of the illness.^{9,12–14} Accordingly, we prospectively evaluated factors associated with selected multidrug-resistant, early-onset, ventilator-associated pneumonia in critical care patients.

Methods

This study was conducted with approval from the Institutional Review Board at Istanbul University, Istanbul

Medical Faculty; consent was waived because the protocol was observational. All 483 adult patients in this 18-bed multidisciplinary intensive care unit (ICU) who underwent mechanical ventilation between January and September of 1996 were prospectively enrolled in the study.

We did not use prophylactic systemic antibiotics or selective digestive decontamination. All patients were administered either sucralfate or ranitidine to reduce the risk of stress ulcer formation. Unless the position was contraindicated, all patients were kept semirecumbent.

All patients underwent mechanical ventilation with the ventilator set in either pressure-controlled or pressure-support mode. Mechanical ventilation nearly always initiated a fraction of inspired oxygen (FiO_2) of 1.0, with complete muscular relaxation. Subsequently, muscular strength was allowed to return and the FiO_2 was appropriately reduced unless acute respiratory distress syndrome (ARDS) developed in patients, in which case the patients were kept paralyzed and given a high FiO_2 .^{15,16} (General management strategies are outlined in the Appendix.) Heat- and moisture-exchanging bacterial filters (Gibeck, Inc., Stockholm, Sweden) were inserted between the endotracheal tube and the ventilator circuit. The filters were changed daily and the breathing circuit was changed weekly, unless copious secretions mandated more frequent exchanges.

We prospectively recorded potential risk factors at the time of ICU admission. These included age, gender, admission source or type (medical or surgical); history of thorax trauma; need for emergency surgery; history of diabetes mellitus type II, chronic obstructive pulmonary disease (COPD), aspiration of oral or gastric content, renal failure, neurologic deficit, and antibiotic use within the seven preceding days; need for emergency intubation, acute physiology and chronic health evaluation (APACHE II) score;¹⁷ and Glasgow coma score.¹⁸ Aspiration and need for emergency intubation were similarly recorded from the clinical notes of the initial caregivers. *Emergency intubation* was defined as the need for immediate intubation during the initial inspection of the patient. The *need* was defined as respiratory or cardiac arrest or decreased level of consciousness. Emergency intubations were performed by the responsible consultant anesthesiologist, who also determined whether the patients had aspirated. Renal failure was determined as having occurred if blood creatinine concentrations that exceeded 1.5 mg/dl for two consecutive measurements.

The clinical criteria for a suspected diagnosis of ventilator-associated pneumonia was a new or persistent

opacity, seen during radiography, and any two of the following factors: (1) purulent endotracheal aspirate; (2) core temperature more than 38°C or less than 36°C; (3) leukocyte count more than 10,000 cells/mm³ or less than 4,000 cells/mm³; or (4) exudative pleural effusion.^{2,9} An endotracheal aspirate was obtained in all patients who met clinical criteria for pneumonia. The aspirates were quantitatively cultured; those yielding more than 10⁵ colony-forming units (cfu)/ml were considered to be positive for bacteria. Patients were considered to have ventilator-associated pneumonia only when they met the clinical criteria and if the aspirate culture was positive for bacteria 48 h after initiation of mechanical ventilation.^{2,9}

Patients with suspected ventilator-associated pneumonia were observed for development of ARDS. ARDS was diagnosed using the following criteria: partial pressure of arterial oxygen (PaO₂)-FIO₂ less than 200 mmHg (regardless of positive end-expiratory pressure [PEEP]), bilateral infiltrates seen on chest radiograph, a pulmonary artery occlusion pressure less than 18 mmHg (when available), and no clinical evidence of left atrial hypertension.¹⁹ It was not always easy to determine whether ventilator-associated pneumonia developed as a result of ARDS or whether the syndrome facilitated development of pneumonia. Consequently, we did not consider ARDS to be a specific complication of pneumonia.

Data Analysis

Patients with ventilator-associated pneumonia were compared with the remaining ICU population with use of unpaired, two-tailed *t* tests or a nonparametric analog of the *t* test (Kruskal-Wallis).

Patients with ventilator-associated pneumonia were first grouped as "early-onset" (< 5 days) and "late-onset,"^{13,14} and then assigned to four groups based on the bacteria cultured from their tracheal aspirates: *P. aeruginosa*, *A. baumannii*, methicillin-resistant staphylococci, and all others. The first three were considered to be multidrug-resistant, whereas the other bacteria were considered to be antibiotic susceptible. This decision was made prospectively in collaboration with the Infectious Diseases and Clinical Microbiology consultants and was based on clinical data collected during the previous year.^{20,21} We used one-way analysis of variance, unpaired, two-tailed *t* or Kruskal-Wallis tests to compare patients infected with sensitive or resistant species.

The influence of potential risk factors on subsequent development of various types of ventilator-associated pneumonia was evaluated by one-way analysis of vari-

ance and with use of the Dunnett test, with nonresistant bacteria considered as the reference group. These univariate results are presented as the mean ± SD. Potential risk factors were further evaluated with use of multivariate regression. Logistic regression results are presented as odds ratios and 95% confidence intervals. In all cases, a two-tailed *P* < 0.05 was considered to be statistically significant.

Results

The ICU admitted 486 patients during the study period, and 260 adult patients underwent mechanical ventilation for more than 48 h. Most of the patients underwent elective surgical procedures and were admitted for planned postoperative care (47%; the remainder were medical multidisciplinary [31%] and trauma [22%] patients. There were many more men than women (166 vs 94, table 1)

Among these patients, 81 (28%) experienced 99 episodes of ventilator-associated pneumonia. Overall, 33 episodes of *P. aeruginosa*, 17 episodes of methicillin-resistant staphylococci, and 9 episodes of *Acinetobacter* species were diagnosed, along with 40 episodes attributed to nonresistant bacteria. There were only two mixed infections according to the quantitative culture results. One was *P. aeruginosa* and *Klebsiella*, and the other was *P. aeruginosa* and *A. baumannii*. Patients with ventilator-associated pneumonia were younger (41 ± 21 yr) than the remaining ICU population (50 ± 20 yr, *P* < 0.001). Admission APACHE II scores of patients with ventilator-associated pneumonia were minimally higher than the patients without; the Glasgow coma score of patients with ventilator-associated pneumonia was minimally lower.

Admission diagnosis of 33% of the patients with ventilator-associated pneumonia was thorax trauma. In contrast, thorax trauma was present in only 7% of the patients without ventilator-associated pneumonia (*P* < 0.001). The rate of COPD was higher in the patients with ventilator-associated pneumonia (20 vs. 13%), but this difference was not statistically significant. Emergency intubation, aspiration during intubation, and the need for emergency surgery were more common in patients with ventilator-associated pneumonia. Duration of ICU stay and mechanical ventilation were significantly longer in the patients with ventilator-associated pneumonia. Similarly, sepsis (26 vs. 11%) and ARDS (32 vs. 9%) were most common in patients with ventilator-associated

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Table 1. Diagnoses

		Diagnosis	No. of Patients
Surgical cases			122
	Thorax surgery	Pneumonectomy, lobectomy	40
	Esophagus surgery	Esophagectomy (thoracotomy)	7
	Upper GI surgery	Gastrectomy, cholecystectomy, and others	18
	Liver and pancreas surgery	Whipple, liver resection, and others	7
	Colon surgery	Hemicolectomy, subtotal-total colectomy, and others	12
	Vertebra surgery		12
	Vascular surgery	Aortobifemoral bypass, abdominal aortic aneurism	8
	Other	Abdominal hysterectomy, thyroid surgery, prostatectomy, and others	14
Trauma			58
	Polytrauma	Thorax + abdomen	12
		Thorax + head	19
	Thorax trauma		10
	Abdominal trauma		2
	Head trauma		15
Medical			80
	COPD		7
	Congestive heart failure		11
	Chronic renal failure		3
	CNS infection	Encephalitis, meningitis	5
	Cerebrovascular accident		4
	Intoxication		12
	Neurologic and neuromuscular illnesses	Guillion-Barre, myasthenia gravis, myelofibrosis	9
	Tetanus		4
	Sepsis		4
	Other	Pulmonary emboli, HELLP syndrome, botulism, and others	21
Total			260

GI = gastrointestinal; COPD = chronic obstructive pulmonary disease; CNS = central nervous system; HELLP = hemolysis, elevated liver enzymes, low platelet count.

pneumonia. A smaller percentage of patients with ventilator-associated pneumonia had been administered antibiotics during the first 48 h of admission than of patients without pneumonia (44 vs. 57%). Although, mortality rate was greater in the patients with ventilator-associated pneumonia than in the remaining critical care population (31 vs. 23%), this difference was not statistically significant (table 2).

When patients with early-onset ventilator-associated pneumonia were compared with the patients without pneumonia, significant differences were observed regarding emergency intubation (44 vs. 12%), aspiration (33 vs. 3%), thorax trauma (33 vs. 7%), emergency surgery (9 vs. 1%), and renal failure (24 vs. 14%). Similar to the general pneumonia population, early-onset pneumonia developed in fewer patients (44 vs. 59%; table 3) administered antibiotics during the first 48 h.

The subgroups of early-onset pneumonia were also compared with each other. Morphometric and demographic characteristics of the patients in each pathogen group were similar. Age and gender were also similar in each pathogen group, and there were no significant

differences in APACHE II scores or the incidence of thorax trauma, diabetes mellitus, or acute renal failure. The types of procedures for which patients were admitted (medical vs. surgical) were also comparable among the groups. Aspiration was found to occur significantly less frequently in the nonresistant group, compared with the *A. baumannii* and *P. aeruginosa* groups (8 vs. 83 and 47%, respectively). Emergency intubation rate was also significantly less in the nonresistant group compared with the *A. baumannii* group (21 vs. 75%). The *P. aeruginosa* group stayed in the ICU significantly longer than did the nonresistant group (23 ± 13 vs. 12 ± 7 days). The *P. aeruginosa* group experienced the highest rate of ARDS (41%); mortality rate was highest in the *A. baumannii* group (50%). However, these differences were not statistically significant (table 4).

When all patients with resistant bacteria were compared with those with nonresistant bacteria by use of logistic regression, emergency intubation (odds ratio, 6.42; confidence interval, 2.04–20.22), aspiration (odds ratio, 12.69; confidence interval, 2.49–64.58), and Glasgow coma score of 9 or less (odds ratio, 3.86; confidence

Table 2. Morphometric and Demographic Characteristics and Potential Confounding Variables

Risk Factors	Patients with Ventilator-associated Pneumonia	Patients without Ventilator-associated Pneumonia	P
n	81	179	—
Age (yr)	41 ± 21	50 ± 20	<0.001
Gender (F/M)	28/56	66/121	0.309
Aspiration (%)	31	4	<0.001
Emergency intubation (%)	45	12	<0.001
Thorax trauma (%)	33	7	<0.001
Age > 60 yr (%)	26	42	0.00
Emergency surgery (%)	8	1	0.006
ARF (%)	24	14	0.05
Previous antibiotics (%)	44	57	0.05
Glasgow coma score	11 ± 4	12 ± 5	0.08
Diabetes mellitus (%)	9	4	0.16
COPD (%)	20	13	0.18
Type (M/S)	29/55	47/140	0.21
APACHE II score	14 ± 6	13 ± 8	0.27
Duration of ICU stay (days)	17 ± 15	5 ± 6	<0.001
Mechanical ventilation (days)	14 ± 11	4 ± 5	<0.001
ARDS (%)	32	9	<0.001
Sepsis (%)	26	11	0.00
Mortality (%)	31	23	0.16

Data are presented as mean ± SD, counts, and percentages.

ARF = acute renal failure; COPD = chronic obstructive pulmonary disease; APACHE = acute physiology and chronic health evaluation; ICU = intensive care unit; ARDS = adult respiratory distress syndrome.

interval, 1.31–11.34) were found to be statistically significant risk factors. Finally, a Glasgow coma score of 9 or less correlated significantly with early-onset pneumonia caused by *A. baumannii* (odds ratio, 6.00; confidence interval, 1.10–32.60), whereas it was not a significant predictor for the other two resistant strains (table 5).

Table 3. Risk Factors for Patients with Early-onset Ventilator-associated Pneumonia: Logistic Regression Model

Risk Factors	Odds Ratio	95% CI	P
Emergency intubation	6.02	3.26–11.12	<0.001
Aspiration	11.51	4.70–28.21	<0.001
Thorax trauma	3.10	1.71–5.63	<0.001
Age > 60 yr	0.98	0.97–0.99	0.001
Emergency surgery	8.13	1.69–39.09	0.009
Previous antibiotics	0.53	0.32–0.88	0.014
ARF	1.98	1.05–3.73	0.035
Diabetes mellitus	2.24	0.83–6.00	0.109
Gender (male vs. female)*	1.54	0.90–2.64	0.119
COPD	1.64	0.86–3.13	0.134

Entry criteria, $P < 0.15$. Data are presented as odds ratio and 95% upper and lower confidence intervals.

* Chi-square test.

ARF = acute renal failure; COPD = chronic obstructive pulmonary disease.

Discussion

Our aim was to identify specific risk factors associated with early-onset ventilator-associated pneumonia caused by bacteria that are typically multidrug-resistant. The reason for performing this risk analysis was that approximately 60% of ventilator-associated pneumonia is caused by multidrug-resistant bacteria.^{6,9,10} More importantly, ventilator-associated pneumonia caused by resistant bacteria is associated with a more serious clinical course and a higher mortality rate. Our results identify three independent risk factors for early-onset ventilator-associated pneumonia caused by resistant bacteria: emergency intubation, aspiration, and a Glasgow coma score of 9 or less. The latter two of these factors were also found to be independent risks for the *A. baumannii* subgroup of early-onset ventilator-associated pneumonia.

There is considerable regional variability in critical care populations and treatment strategies. The specific relative risks we identify must therefore be applied with considerable caution to other populations. Nonetheless, factors related to patient health and preadmission history should be considered seriously when planning clinical treatment and assessing individual risk. For example, intensivists started to develop predictive models for nosocomial pneumonia more than a decade ago and were

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Table 4. Morphometric and Demographic Characteristics and Potential Confounding Variables for Early-onset Ventilator-associated Pneumonia: Multidrug Resistant versus Nonresistant

Risk Factors	<i>Pseudomonas aeruginosa</i>	<i>Acinetobacter baumannii</i>	MRSA	All-resistant Ventilator-associated Pneumonia	Nonresistant Ventilator-associated Pneumonia
n	17	8	10	35	31
Age	47 ± 19	35 ± 21	38 ± 18	42 ± 20	40 ± 23
Gender (F/M)	3/14	1/7	4/6	8/27	8/23
Type (M/S)	8/9	1/7	4/6	13/22	14/17
APACHE II score	15 ± 6	18 ± 6	14 ± 8	15 ± 7	13 ± 6
Glasgow coma score	10 ± 5	8 ± 4	10 ± 5	10 ± 5	12 ± 4
Thorax trauma (%)	24	50	40	34	32
Diabetes mellitus (%)	12	0	20	11	6
COPD (%)	29	25	10	23	19
ARF (%)	40	14	0	22	27
Aspiration (%)	47	83	38	54	8
Emergency intubation (%)	59	75	63	64	21
Duration of MV before ventilator-associated pneumonia (days)	4 ± 1	3 ± 1	3 ± 1	4 ± 1	4 ± 1
Emergency surgery (%)	12	13	0	9	10
Previous antibiotics (%)	44	14	33	34	55
Duration of ICU stay (days)	23 ± 23	11 ± 11	14 ± 4	17 ± 18	12 ± 7
Duration of mechanical ventilation (days)	14 ± 16	10 ± 9	11 ± 3	12 ± 12	11 ± 7
ARDS (%)	41	25	0	26	26
Sepsis (%)	24	33	35	29	25
Mortality (%)	24	50	10	26	39

Data are presented as mean ± SD, counts, and percentages.

MRSA = methicillin-resistant *Staphylococcus aureus*; APACHE = acute physiology and chronic health evaluation; COPD = chronic obstructive pulmonary disease; ARF = acute renal failure; MV = mechanical ventilation; ICU = intensive care unit; ARDS = adult respiratory distress syndrome.

able to identify numerous risk factors.²²⁻²⁴ The risks determined in these studies improved clinical practice by identifying treatments that have since become routine for critical care. These include maintaining patients in a semirecumbent position and use of drugs that protect the gastric-mucosal barrier.

More recently, investigators have focused on specific risk factors for multidrug-resistant bacteria.⁹⁻¹¹ These studies mostly identified *P. aeruginosa*, *A. baumannii*, methicillin-resistant staphylococci, and *Stenotrophomonas maltophilia* as multidrug-resistant bacteria. In a prospective study of 135 episodes of ventilator-associated

pneumonia, Talon *et al.*¹⁰ found that duration of hospital stay, duration of mechanical ventilation exceeding 7 days, previous use of third-generation cephalosporins with poor effectiveness against *P. aeruginosa*, and COPD significantly increased the risk of ventilator-associated pneumonia caused by *P. aeruginosa*. Additionally, Celis *et al.*,²⁵ Talon *et al.*,¹⁰ and Rello *et al.*^{2,23,26} identified preexisting COPD as one of the most important predictors of infection by *P. aeruginosa*.^{10,23,26} Consistent with the findings of Talon *et al.*,¹⁰ we observed that *P. aeruginosa* was more frequently observed as a late-onset episode. Although only 26% of early-onset

Table 5. Risk Factors for Patients with Early-onset Ventilator-associated Pneumonia: Subgroups Logistic Regression Model

	<i>Pseudomonas aeruginosa</i>	<i>Acinetobacter baumannii</i>	MRSA	All-resistant Bacteria
Emergency intubation	2.27 (0.73-7.10)	4.57 (0.84-24.83)	2.35 (0.51-10.87)	6.42 (2.04-20.22)*
Aspiration	2.36 (0.68-8.22)	14.17 (1.50-133.82)*	1.66 (0.33-8.43)	12.69 (2.49-64.58)*
Glasgow coma score ≤ 9	1.17 (0.38-3.61)	6.00 (1.10-32.60)*	2.25 (0.54-9.34)	3.86 (1.31-11.34)*
Previous antibiotics	0.97 (0.31-3.37)	0.18 (0.02-1.59)	0.58 (0.13-2.59)	0.43 (0.15-1.20)
Age > 60 yr	1.02 (0.99-1.05)	0.98 (0.95-1.02)	0.99 (0.96-1.02)	1.00 (0.98-1.03)
ARF	2.81 (0.80-9.95)	0.49 (0.05-4.41)	—	0.77 (0.24-2.47)
ARDS	4.72 (0.93-23.81)	1.24 (0.13-11.86)	—	2.42 (0.43-13.46)

Entry criteria, $P < 0.15$. Data presented as odds ratio and 95% confidence intervals.

* $P < 0.05$ compared with all other groups (including resistant subgroups and nonresistant group) of bacteria.

MRSA = methicillin-resistant *Staphylococcus aureus*; ARF = acute renal failure; ARDS = adult respiratory distress syndrome.

ventilator-associated pneumonia episodes are associated with *P. aeruginosa*, in the late-onset group, this rate was 48%. However, we were not able to identify other specific risk factors for *P. aeruginosa*. Unlike in our results, in a recent report by Rello *et al.*, it was shown that aspiration was a specific risk for early pneumonia (< 48 h) in patients who underwent mechanical ventilation.²⁶

The conclusions of recently published studies by Trouillet *et al.*⁹ and Rello *et al.*²⁶ differ. In the report of Trouillet *et al.*,⁹ previous use of broad-spectrum antibiotics was found to be an independent risk factor for ventilator-associated pneumonia. However, in a study published a year later, Rello *et al.*²⁶ showed previous antimicrobial use to be an independent protective factor. Our results are most consistent with those of Rello *et al.*²⁶ because prior antibiotic use was observed in 44% of the patients with ventilator-associated pneumonia *versus* in 57% of those without ventilator-associated pneumonia.

Data are not sufficient to suggest firm conclusions about prophylactic antibiotic use. It is likely that well-developed antibiotic-use policy within a unit based on experience and known patterns of resistance will reduce infection rates, whereas haphazard choice may increase risk. Rello *et al.*²⁶ makes the same point, suggesting that instead of following general recommendations, antimicrobial prescribing practices for ventilator-associated pneumonia should be based on up-to-date information of the pattern of multiresistant isolates from each institution.¹² *Acinetobacter baumannii* pneumonia has been described as having epidemiologic characteristics similar to *P. aeruginosa* and the Enterobacteriaceae family. In previous publications, for example, preexisting illness, including COPD, and duration of mechanical ventilation were not found to be associated with ventilator-associated pneumonia caused by *A. baumannii*. The important risk factors for this agent appear to be head trauma, neurosurgery, ARDS, and large-volume aspiration.¹¹ Our results are consistent in identifying a Glasgow coma score of 9 or less and aspiration as significant risk factors.

A limitation of our study is that we cultured endotracheal aspirates rather than samples obtained from bronchoalveolar lavage. The role of invasive *versus* noninvasive culture sampling is controversial.^{27-31,32} However, there has yet to be a study showing that mortality, morbidity, or any other outcome in patients with ventilator-associated pneumonia can be improved by invasive culture methods.^{31,33,34} Cultures from endotracheal aspirates are routine and have been used in numerous recent studies.

In summary, we identify aspiration, emergency intubation, and a Glasgow coma score of 9 or less as specific risk factors for early-onset ventilator-associated pneumonia caused by resistant organisms. Additionally, aspiration and a Glasgow coma score of 9 or less were significant risk factors for early-onset ventilator-associated pneumonia caused by *A. baumannii*. We recommend that patients with these risk factors be closely monitored for development of pneumonia caused by multidrug-resistant bacteria.

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