SURGICAL INFECTIONS
Volume 12, Number 4, 2011

DOI: 10.1089/sur.2010.052

Multidrug-Resistant Pathogens and Pneumonia: Comparing the Trauma and Surgical Intensive Care Units

Robert D. Becher, J. Jason Hoth, Lucas P. Neff, Jerry J. Rebo, R. Shayn Martin, and Preston R. Miller

Abstract

Background: As acute care surgery evolves, more trauma surgeons are caring for critically ill general surgery as well as trauma patients. However, these two populations are unique, and infectious complications may need to be addressed differently, as the causative organisms may not be the same in the two groups. To study this, we evaluated ventilator-associated (VAP) and hospital-acquired (HAP) pneumonia in the trauma (TICU) and general surgical (SICU) intensive care units to investigate differences in the causative pathogens. Our hypothesis was that SICU patients would have a higher incidence of multi-drug-resistant (MDR) organisms causing VAP/HAP, possibly contributing to inadequate empiric antibiotic (IEA) coverage.
Methods: Retrospective review of 116 patients admitted with VAP or HAP over a one-year period to the TICU ($n = 72$) or SICU ($n = 44$) at a tertiary medical center. Culture was followed by initiation of empiric antibiotics on the basis of an antibiotic algorithm derived from trauma patients. Demographics, illness, and pneumonia characteristics were assessed; MDR organisms were identified.
Results: Multi-drug-resistant organisms caused 30.6% of first pneumonias in the TICU vs. 65.9% in the SICU ($p = 0.0002$). Subsequent pneumonias were seen in 31.8% of SICU patients and 16.7% of TICU patients ($p = 0.0576$). Inadequate empiric antibiotic coverage was documented in 38.6% of SICU pneumonias vs. 26.4% in the TICU ($p = 0.12$).
Conclusions: Multiply-resistant pathogens cause a significantly greater number of VAP/HAPs in the SICU than in the TICU. Associated with this, when using an antibiotic algorithm based on TICU bacterial pathogens, there is a trend toward a greater likelihood of subsequent pneumonias and toward more IEA coverage in the SICU population compared with TICU patients. Our results indicate that these distinct patient populations have different pathogens causing VAP/HAP and affirm the necessity for population-specific algorithms to tailor empiric coverage for presumed VAP/HAP.

The field of trauma surgery is evolving into "acute care surgery," which is the union of three disciplines: Trauma surgery, critical care, and emergency general surgery [1, 2]. An institution's establishment of an acute care surgery service has broad implications for the management of critically ill trauma and surgical patients [3]. This is because traumatologists, who historically have cared solely for trauma intensive care unit (TICU) patients, are now managing surgical intensive care unit (SICU) patients on a daily basis. Although the principles of critical care medicine remain the same, their application to a new patient population presents substantial new challenges [4].

One of these is the management of infectious complications, which is driven often by local treatment algorithms [5]. The use of such guidelines is good clinical practice, as there is great variability in the microbiology of infections within hospitals [6]. If an ICU's specific pattern of microbiologic variability is not accounted for in its treatment algorithms, inappropriate choice of initial empiric antibiotics (IEA) can lead to a higher mortality rate [7]; this has been shown in the management of ventilator-associated pneumonia (VAP) in the trauma population [8].

In comparison with the TICU patient-population, the SICU population appears to be unique, given its older age, higher prevalence of co-morbidities, and history of more previous hospitalizations. This means that infectious complications may need to be addressed differently in the SICU than in the

Acute Care Surgery Service, Department of General Surgery, Wake Forest University School of Medicine, Winston-Salem, North Carolina.
Presented at the Thirtieth Annual Meeting of the Surgical Infection Society, Las Vegas, Nevada, April 17–20, 2010.

TICU, as the causative organisms may not be the same in both groups. In particular, the SICU population harbors many risk factors for multi-drug-resistant (MDR) organisms [9], and this difference in microbiology may need to be incorporated into management guidelines for hospital-acquired pneumonia (HAP) and VAP [10,11]. No SICU-based antibiotic algorithm was in place on September 1, 2008, when our dedicated Acute Care Surgery Service took over daily management of SICU patients from their individual surgeons. Therefore, our trauma-based algorithm was used to guide empiric therapy of suspected pneumonia in the SICU during this one-year transitional period, after which the microbiology findings were to be assessed and an appropriate SICU-specific algorithm was to be developed.

At the completion of this transitional phase, we evaluated the patients in the TICU and SICU to investigate differences in the microbiology of VAP/HAP pathogens. Our hypothesis was that SICU patients would have a higher incidence of MDR organisms, and that this would contribute to IEA coverage.

Patients and Methods

Approval for this retrospective study was obtained from the Internal Review Board at Wake Forest University Medical Center. Over a one-year period, from September 1, 2008, to September 1, 2009, we identified patients who developed pneumonia while in our TICU or SICU. Data collected included patient demographics, MDR organism risk factors, Injury Severity Score (ISS) in TICU patients and Acute Physiology and Chronic Health Evaluation (APACHE II) score in SICU patients, and outcome variables including in-hospital death, length of stay (LOS), days of mechanical ventilation, VAP/HAP pathogens, and details of antibiotic coverage. Comorbid conditions were defined using the APACHE II method of classifying chronic health conditions [12]. We were unable to assess accurately the broad-spectrum antibiotic use in the three months before admission because the data were unavailable.

Pneumonia was suspected on clinical grounds: Systemic inflammatory response syndrome (SIRS) response, worsening respiratory function, and new or progressive infiltrates on chest radiograph. The diagnosis was confirmed with quantitative cultures of lower respiratory secretions; the majority of the cultures were obtained by bronchoalveolar lavage (BAL), with a small number of quantitative deep endotracheal aspirates. Identification of a primary causative pathogen was based on final culture results; a diagnosis of pneumonia was made if a threshold concentration of $>10^5$ colony-forming units (CFU)/mL was reached; growth below this threshold was considered colonization or contamination.

For the purposes of this study, an MDR pathogen was defined as any organism resistant to at least three classes of antibiotics [13]. The definition of MDR pathogens varies considerably in the literature, from the broadly defined taxonomy of microorganisms resistant to one or more class of antimicrobials [14], often used in epidemiologic studies, to the much more rigorously defined classification schemes that are complex and pathogen-specific [15].

After cultures were obtained, empiric antibiotics were initiated for suspected pneumonia in both units on the basis of an antibiotic algorithm derived from TICU patients (Fig. 1) [8]. During the study period, no SICU-specific antibiotic algorithm existed to guide empiric treatment. Antibiotic therapy was modified on the basis of the final microbiologic culture and sensitivity results. Inadequate empiric antibiotic coverage was defined as the use of initial empiric antibiotics with either no or intermediate activity against the microorganisms identified as the etiologic pathogens on culture.

Hospital-acquired pneumonia was defined as pneumonia that occurred 48 h or more after admission; VAP was defined as pneumonia that appeared more than 48–72 h after endotracheal intubation [11]. We also diagnosed VAP if the patient had been intubated previously for more than 48 h and the pneumonia occurred within seven days after extubation. Subsequent pneumonia was defined as a pneumonia following a first pneumonia but caused by a different organism.

The TICU and the SICU are 11-bed units located on different floors of our hospital. Although both are open units, meaning they occasionally admit patients from other services, a majority of patients in the TICU are victims of trauma, and a majority of patients in the SICU have undergone an operation. On the attending surgeon level, patients are managed by one surgical critical care service; on the resident level, there is one team managing TICU patients and a separate team managing SICU patients. Nursing and ancillary staff are unique to each unit, with no overlap in patient care.

For VAP prevention, the TICU and SICU follow the Institute for Healthcare Improvement's Ventilator Bundle [16]. Oral care with chlorhexidine is provided to all ventilated patients on any 12 h basis.

Patient characteristics were compared using chi-square analysis for categorical variables and the Student *t*-test for continuous variables, using commercial statistics software (SAS; SAS Institute Inc, Cary, NC). A p value <0.05 was considered statistically significant.

Results

Demographics and illness characteristics

A total of 116 patients were studied, 72 in the TICU and 44 in the SICU (Table 1); a majority in both groups was male. In comparison with the TICU group, the SICU patients were significantly older, had more co-morbidities, and had spent more time in a hospital or nursing home in the 90 days prior to admission. The average hospital length of stay (LOS) in the

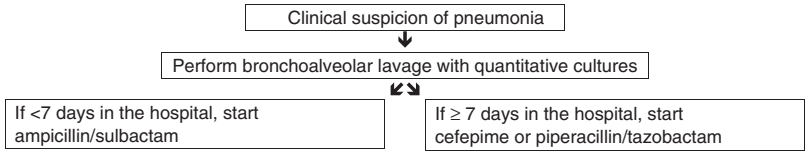

FIG. 1. Selection of treatment for pneumonia.

Table 1. Demographic and Illness Characteristics of Patients in TICU vs. SICU

Characteristic	*TICU (n = 72)*	*SICU (n = 44)*	P *value*
Male gender	57 (79.2%)	34 (77.3%)	0.8098
Age (years)	48 ± 18	65 ± 11	<0.0001
Patients with co-morbidities (%)	13 (18.0)	23 (52.3)	0.0001
Hospitalized or nursing home >2 days in the 90 days prior (%)	2 (2.8)	27 (61.4)	<0.0001
APACHE II score	–	24.7 ± 7.7	–
Blunt trauma (%)	68 (94.4%)	–	–
Mean Injury Severity Score ± standard deviation (SD)	29.1 ± 10.7	–	–
Traumatic chest injury (%)	48 (66.7)	–	–
Chest Abbreviated Injury Scale score	2.5 ± 0.5	–	–
Mean hospital length of stay (days) ± SD	25.6 ± 17.0	34.6 ± 24.0	0.0270
Deaths (%)	18 (25.0)	22 (50.0)	0.0060

APACHE II = Acute Physiologic and Chronic Health Evaluation II; ICU = intensive care unit; SICU = Surgery ICU; TICU = Trauma ICU.

SICU group was significantly longer than in the TICU group. In the SICU, the average APACHE II score was 24.7 points (range 10–51 points). The majority of TICU patients had suffered blunt trauma as the mechanism of injury, with an average ISS of 29.1 points (range 4–59 points).

Pneumonia characteristics in patients in trauma vs. surgical intensive care unit

A total of 116 patients were found to have either VAP or HAP during the study period (Table 2). Compared with the TICU group, the SICU patients were significantly more likely to develop pneumonia later in their hospitalization. There was a trend toward IEA coverage in more SICU pneumonias than TICU pneumonias using the trauma-based antibiotic algorithm, but this difference was not statistically significant ($p = 0.1205$). Similarly, SICU patients had a borderline higher rate of subsequent pneumonias than TICU patients ($p = 0.0576$).

Significantly more SICU patients than TICU patients had VAP/HAP caused by MDR organisms (Table 3). The most common MDR pathogens in the SICU were methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β-lactamase-producing (ESBL) *Klebsiella pneumoniae*, *Acinetobacter* spp., and *Enterobacter* spp. In contrast, no patients in the TICU developed pneumonia with MDR extended-spectrum beta-lactamase (ESBL) producing *K. pneumoniae*, *Acinetobacter*, or *Enterobacter*. In addition to MRSA, the most common MDR pathogens in the TICU were *Pseudomonas aeruginosa* and *Streptococcus pneumoniae*.

In IEA coverage cases, the microbiology was evenly distributed in the SICU; the most common pathogens were *Acinetobacter* spp., *Enterobacter* spp., MRSA, *P. aeruginosa*, *Stenotrophomonas maltophilia*, *E. coli*, and ESBL *Klebsiella* species (Table 4). In the TICU, the most common pathogen in the IEA coverage cases was MRSA; *Enterobacter* spp. and *P. aeruginosa* were the next most common.

Outcomes by site of care

Outcomes and pneumonia characteristics are described in Table 2. All patients in both units required mechanical ventilation during the treatment of their pneumonias. The TICU patients spent, on average, significantly fewer days on the ventilator than did the SICU patients. There was no significant difference in the rate of pneumonia per 1,000 ventilator days in the two ICUs. However, the probability of pneumonia for a patient admitted to the TICU was significantly higher than for a patient admitted to the SICU (0.14 vs. 0.09; $p = 0.0285$).

Overall, significantly more SICU patients than TICU patients died during their hospitalization (see Table 1). For those

Table 2. Pneumonia Characteristics in TICU vs. SICU

Characteristic	*TICU (n = 72) (%)*	*SICU (n = 44) (%)*	P *value*
VAP as first pneumonia	60 (83.3)	31 (70.5)	0.1017
HAP as first pneumonia	12 (16.7)	13 (29.5)	0.1017
Subsequent pneumonia	12 (16.7)	14 (31.8)	0.0576
Pneumonia diagnosis ≥5 days after admission	37 (51.4)	36 (81.8)	0.0010
Hospital day of pneumonia diagnosis	7 ± 5	12 ± 10	0.0002
MDR pathogen-caused pneumonias	22 (30.6)	29 (65.9)	0.0002
Patients with IEA coverage	18 (25.0)	17 (38.6)	0.1205
Death with inadequate coverage (IEA)	6 (33.3)	6 (35.3)	0.9028
Required mechanical ventilation	72 (100)	44 (100)	–
Multiple intubations	12 (16.6)	20 (45.5)	0.0008
Mean ventilator days	12.2 ± 7.6	16.2 ± 13.5	0.0428
Pneumonia rate/1,000 ventilator days	29.5	20.9	0.0732
Probability of pneumonia per ICU admission	0.14	0.09	0.0285

HAP = hospital-acquired pneumonia; ICU = intensive care unit; IEA = inadequate empiric antibiotic; MDR = multidrug resistant; SICU = surgery ICU; TICU = trauma ICU; VAP = ventilator-associated pneumonia.

Table 3. Number of Multiply Resistant Organisms by Intensive Care Unit Type

MDR pathogen	*TICU (n = 23)*	*SICU (n = 34)*	*Total (n = 57)*
Methicillin-resistant *Staphylococcus aureus* (MRSA)	10	10	20
Pseudomonas aeruginosa	4	3	7
Escherichia coli	2	3	5
Klebsiella pneumoniae ESBL	0	4	4
Acinetobacter spp.	0	4	4
Enterobacter spp.	0	4	4
Stenotrophomonas maltophilia	1	3	4
Streptococcus pneumoniae	4	0	4
Serratia marcescens	0	2	2
Citrobacter freundii	0	1	1
Methicillin-sensitive *S. aureus* (MSSA)	1	0	1
Burkholderia cepacia	1	0	1
Total MDR pathogens	23	34	57
Total MDR-caused pneumonias	22	29	51

MDR = multi-drug resistant; ESBL = extended-spectrum β-lactamase-producing; ICU = intensive care unit; SICU = Surgery ICU; TICU = Trauma ICU.

patients who received IEA coverage, the mortality rate was not significantly different in the groups (see Table 2).

Discussion

Our study confirms that the microbiology of HAP and VAP is significantly different in the TICU and SICU. Such infectious complications therefore need to be addressed differently according to the populations and should be guided by ICU-specific algorithms. This finding is consistent with those of previous studies, which have shown significant variability in the causative agents of hospital-acquired infections in locations within the same hospital [6,17].

Table 4. Pathogens Causing Pneumonia in IEA Coverage Cases

Pathogen	*TICU (n = 21)*	*SICU (n = 24)*	*Total (n = 45)*
Methicillin-resistant *Staphylococcus aureus* (MRSA)	8	3	11
Enterobacter spp.	4	4	8
Pseudomonas aeruginosa	4	3	7
Acinetobacter spp.	0	4	4
Stenotrophomonas maltophilia	1	3	4
Escherichia coli	0	3	3
Klebsiella spp. ESBL	0	3	3
Streptococcus pneumoniae	2	0	2
Serratia marcescens	0	1	1
Methicillin-sensitive *S. aureus (MSSA)*	1	0	1
Burkholderia cepacia	1	0	1
Citrobacter freundii	0	0	0
Total inadequately covered pathogens	21	24	45
Total pneumonias with IEA coverage	18	17	35

ESBL = extended-spectrum β-lactamase-producing; IEA = inadequate empiric antibiotics; ICU = intensive care unit; SICU = Surgery ICU; TICU = Trauma ICU.

Intuitively, one would assume that SICU patients would be at higher risk than TICU patients for MDR pathogens as the causative agents for VAP/HAP, although previous studies have never come to this conclusion. One recent study compared the differences between all early and late VAP in trauma vs. nontrauma patients [18], although the focus was not MDR risks or pathogens. In their mixed trauma/surgery ICU setting, the trauma VAP patients were significantly younger, had lower APACHE II scores, and had fewer comorbidities than the nontrauma patients; a majority of patients in both groups had late-onset VAP. However, specific MDR risk factors were either not assessed or not reported.

In our analysis, the SICU group had statistically significantly more risk factors for MDR pathogens than the TICU group. These included older average age, higher rate of comorbidities, more hospitalizations or nursing home stays of greater than two days in the 90 days prior to admission, and a greater likelihood of hospitalization for five days or greater prior to a diagnosis of VAP/HAP.

These multiple risk factors for MDR pathogens translated into SICU patients having a higher incidence of MDR pneumonias. Of the first episodes of VAP/HAP, 66% in the SICU were caused by MDR pathogens as opposed to 31% in the TICU ($p = 0.0002$). Perhaps because of this significant number of MDR pneumonias, SICU patients had a trend toward significantly higher rates of subsequent pneumonia than TICU patients ($p = 0.0576$). The lack of statistical significance may be attributable to an underpowered analysis (as discussed below).

In addition to risk factors, the type of MDR organisms causing pneumonia also differed according to the ICU (see Table 3). The most common MDR organism causing VAP/HAP in the SICU was MRSA, which was isolated from 34% of all MDR SICU pneumonias. Whereas MRSA was the only gram-positive organism causing pneumonia in the SICU, three gram-positive bacteria caused pneumonia in the TICU: MRSA, *S. pneumoniae*, and methicillin-sensitive *S. coccus aureus* (MSSA). Two of these pathogens—*S. pneumoniae* and MSSA—are not traditionally thought of as MDR organisms. Their inclusion is related specifically to the definition we used to classify MDR pathogens. If we removed these two gram-positive organisms from consideration as MDR pathogens, our conclusion would be made stronger because the percentage of MDR pneumonias in the TICU would decrease, whereas the number in the SICU would stay the same, thus increasing the statistical significance of the difference between MDR-caused pneumonias in the TICU and SICU.

Among the MDR gram-negative pathogens causing pneumonia, six of them caused VAP/HAP at roughly equal rates in the SICU; these organisms were ESBL *K. pneumoniae*, *Acinetobacter* spp., and *Enterobacter* spp., as well as *P. aeruginosa*, *E. coli*, and *S. maltophilia*. Of these six, three (ESBL *K. pneumoniae*, *Acinetobacter* spp., and *Enterobacter* spp.) caused no VAP/HAP in the TICU, and one (*P. aeruginosa*) caused more TICU pneumonias than the other two organisms (*E. coli* and *S. maltophilia*) combined.

We were concerned that the differences in VAP/HAP microbiology in the TICU vs. the SICU, coupled with the use of a

trauma-based antibiotic algorithm, would increase the risk of IEA coverage in SICU patients. This is of concern, as IEA coverage, or a delay in appropriate coverage, leads to adverse outcomes in ICU patients, including a higher in-hospital mortality rate and greater LOS [7,19,20]. Additionally, stopping the IEA and changing to the appropriate antibiotics does not appear to reduce the risk of in-hospital death [21]. The differences we found in IEA coverage were not significant statistically, although this may simply be related to an underpowered analysis (see discussion of limitations below). Furthermore, although there was a significant difference in the overall in-hospital mortality rate in the two groups (25% in the TICU vs. 50% in the SICU; $p = 0.0060$) as well as in the hospital LOS (25.6 days for TICU vs. 34.6 days for SICU group; $p = 0.0270$), there was no mortality rate or LOS difference by IEA coverage.

Our study has a number of limitations. First, our conclusions are drawn from a small sample of 116 cases of VAP/HAP over a one-year period. Therefore, we lack the necessary power to show potentially significant differences in the TICU and SICU populations in terms of IEA coverage and subsequent pneumonias. Second, both the trauma and surgical ICUs at our institution are open units. Only 489 of the 832 admissions to the surgical ICU (58.8%) were true SICU patients, and only 516 of the 755 admissions to the trauma ICU (68.3%) were true TICU patients. The rest of the patients in these ICUs during the study period came from other services. Although these patients were not included in our analysis, exposure to these patients from other services (including medicine patients in particular) could contribute to the presence of MDR pathogens not generally seen in trauma or surgical patients. Therefore, in addition to specific differences between the trauma and surgery patient populations, other factors may have contributed to our conclusions. Lastly, this study is a retrospective analysis, and therefore is prone to biases that can be avoided with a prospective study.

One final important limitation deserves mention, which is germane to all studies on MDR pathogens: there is no generally accepted definition of an MDR organism, which makes studying this field difficult. In fact, many studies in the literature do not define what they mean by MDR pathogen. This is troubling, as the definition can differ considerably. We decided to use any organism resistant to at least three classes of antibiotics [13] as the definition for two main reasons: (1) It was more inclusive than the traditional epidemiologic definition [14], avoiding defining relatively easy-to-treat bacteria as MDR; and (2) it was less stringent than organism-specific definitions [15], which can make practical application in clinical practice difficult.

The adoption of an acute care surgery service has broad implications for the management of critically ill trauma and surgical patients. One facet is management of infectious complications. As this study demonstrates, TICU and SICU patient populations are unique, with the SICU patients having a significantly higher incidence of MDR pathogens as causative agents in VAP/HAP. Therefore, consistent with American Thoracic Society recommendations [11], each group requires its own antibiogram for management of VAP/HAP on the basis of local microbiology. Such protocol-directed therapy may reduce IEA coverage, thereby improving both the morbidity and mortality rate attendant on VAP/HAP in the TICU and SICU.

Author Disclosure Statement

No competing financial interests exist. No financial support was received for this study.

References

1. Committee to Develop the Reorganized Specialty of Trauma, Surgical Critical Care, and Emergency Surgery. Acute care surgery: Trauma, critical care, and emergency surgery. J Trauma 2005;58:614–616.
2. Kim PK, Dabrowski GP, Reilly PM, et al. Redefining the future of trauma surgery as a comprehensive trauma and emergency general surgery service. J Am Coll Surg 2004; 199:96–101.
3. Moore EE, Maier RV, Hoyt DB, et al. Acute care surgery: Eraritjaritjaka. J Am Coll Surg 2006;202:698–701.
4. Diaz JJ, Miller RS, May AK, Morris JA. Acute care surgery: A functioning program and fellowship training. Surgery 2007; 141:310–316.
5. Ibrahim EH, Ward S, Sherman G, et al. Experience with a clinical guideline for the treatment of ventilator-associated pneumonia. Crit Care Med 2001;29:1109–1115.
6. Namias N, Samiian L, Nino D, et al. Incidence and susceptibility of pathogenic bacteria vary between intensive care units within a single hospital: Implications for empiric antibiotic strategies. J Trauma 2000;49:638–645.
7. Alvarez-Lerma F. Modification of empiric antibiotic treatment in patients with pneumonia acquired in the intensive care unit. ICU-Acquired Pneumonia Study Group. Intensive Care Med 1996;22:387–394.
8. Miller PR, Partrick MS, Hoth JJ, et al. A practical application of practice-based learning: Development of an algorithm for empiric antibiotic coverage in ventilator-associated pneumonia. J Trauma 2006;60:725–729.
9. Chastre J, Fagon J. Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002;165:867–903.
10. Tablan OC, Anderson LJ, Besser R, et al. Guidelines for preventing health-care-associated pneumonia, 2003: Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. MMWR Recomm Rep 2004;53(RR-3):1–36.
11. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388–416.
12. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: A severity of disease classification system. Crit Care Med 1985;13:818–829.
13. Mammina C, Di Carlo P, Cipolla D, et al. Surveillance of multidrug-resistant gram-negative bacilli in a neonatal intensive care unit: Prominent role of cross transmission. Am J Infect Control 2007;35:222–230.
14. Siegel JD, Rhinehart E, Jackson M, Chiarello L. Management of multidrug-resistant organisms in health care settings, 2006. Am J Infect Control 2007;35(10 Suppl 2):S165–193.
15. Hidron AI, Edwards JR, Patel J, et al. NHSN annual update: Antimicrobial-resistant pathogens associated with healthcare-associated infections: Annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. Infect Control Hosp Epidemiol 2008;29:996–1011.
16. Institute for Healthcare Improvement: Implement the Ventilator Bundle. Cited April 29, 2010; available at www.ihi.org/IHI/Topics/CriticalCare/IntensiveCare/Changes/ImplementtheVentilatorBundle.htm

17. Rello J, Sa-Borges M, Correa H, et al. Variations in etiology of ventilator-associated pneumonia across four treatment sites: Implications for antimicrobial prescribing practices. Am J Respir Crit Care Med 1999;160:608–613.
18. Hedrick TL, Smith RL, McElearney ST, et al. Differences in early- and late-onset ventilator-associated pneumonia between surgical and trauma patients in a combined surgical or trauma intensive care unit. J Trauma 2008;64:714–720.
19. Iregui M, Ward S, Sherman G, et al. Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia. Chest 2002;122:262–268.
20. Garnacho-Montero J, Garcia-Garmendia JL, Barrero-Almodovar A, et al. Impact of adequate empirical antibiotic therapy on the outcome of patients admitted to the intensive care unit with sepsis. Crit Care Med 2003;31:2742–2751.
21. Luna CM, Vujacich P, Niederman MS, et al. Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia. Chest 1997;111:676–685.

Address correspondence to:
Dr. Preston R. Miller
Department of General Surgery
Wake Forest University School of Medicine
Medical Center Blvd.
Winston-Salem, NC 27157

E-mail: pmiller@wfubmc.edu