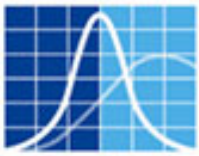

ORIGINAL ARTICLE

Epidemiology of Ventilator-Associated Pneumonia in a Long-Term Acute Care Hospital

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OBJECTIVE. To characterize the epidemiology and microbiology of ventilator-associated pneumonia (VAP) in a long-term acute care hospital (LTACH).

DESIGN. Retrospective study of prospectively identified cases of VAP.

SETTING. Single-center, 207-bed LTACH with the capacity to house 42 patients requiring mechanical ventilation, evaluated from April 1, 2006, through January 31, 2008.

METHODS. Data on the occurrence of VAP were collected prospectively as part of routine infection surveillance at Radius Specialty Hospital. After March 2006, Radius Specialty Hospital implemented a bundle of interventions for the prevention of VAP (hereafter referred to as the VAP-bundle approach). A case of VAP was defined as a patient who required mechanical ventilation at Radius Specialty Hospital for at least 48 hours before any symptoms of pneumonia appeared and who met the Centers for Disease Control and Prevention criteria for VAP. Sputum samples were collected from a tracheal aspirate if there was clinical suspicion of VAP, and these samples were semi-quantitatively cultured.

RESULTS. During the 22-month study period, 23 cases of VAP involving 19 patients were associated with 157 LTACH admissions (infection rate, 14.6%), corresponding to a rate of 1.67 cases per 1,000 ventilator-days, which is a 56% reduction from the VAP rate of 3.8 cases per 1,000 ventilator-days reported before the implementation of the VAP-bundle approach ($P < .001$). Microbiological data were available for 21 (91%) of 23 cases of VAP. Cases of VAP in the LTACH were frequently polymicrobial (mean number $\pm$ SD, 1.78 $\pm$ 1.0 pathogens per case of VAP), and 20 (95%) of 21 cases of VAP had at least 1 pathogen (*Pseudomonas* species, *Acinetobacter* species, gram-negative bacilli resistant to more than 3 antibiotics, or methicillin-resistant *Staphylococcus aureus*) cultured from a sputum sample. LTACH patients with VAP were more likely to have a neurological reason for ventilator dependence, compared with LTACH patients without VAP (69.6% of cases of VAP vs 39% of cases of respiratory failure; $P = .014$). In addition, patients with VAP had a longer length of LTACH stay, compared with patients without VAP (median length of stay, 131 days vs 39 days; $P = .002$). In 6 (26%) of 23 cases of VAP, the patient was eventually weaned from use of mechanical ventilation. Of the 19 patients with VAP, 1 (5%) did not survive the LTACH stay.

CONCLUSIONS. The VAP rate in the LTACH is lower than the VAP rate reported in acute care hospitals. Cases of VAP in the LTACH were frequently polymicrobial and were associated with multidrug-resistant pathogens and increased length of stay. The guidelines from the Centers for Disease Control and Prevention that are aimed at reducing cases of VAP appear to be effective if applied in the LTACH setting.

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Ventilator-associated pneumonia (VAP) is the second most common nosocomial infection in the critical care setting.[1] It is associated with increased morbidity and increased use of healthcare resources.[2] The epidemiology of VAP in intensive care units (ICUs) of acute care hospitals has been widely characterized,[1,3-6] resulting in the implementation of guidelines[1,5,7] that have been associated with significant reductions in the incidence of VAP in the ICU.[4,8] Although long-term acute care hospitals (LTACHs) have been increasingly used to provide post-ICU care to patients who require prolonged mechanical ventilatory support,[9,10] little is known about the epidemiology or the microbiology of VAP in the LTACH setting. Given the common characteristics of patients who require mechanical ventilatory support, we hypothesized that VAP rates in LTACHs would be similar to the VAP rates in acute care hospitals and that current Centers for Disease Control and Prevention (CDC) guidelines for preventing VAP could apply to the LTACH population. Therefore, our study examined the characteristics of patients with VAP and the incidence and microbiology of VAP in an LTACH population after the institution of CDC guidelines for VAP prevention.

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METHODS

Setting

Data on the occurrence of VAP were collected prospectively as part of routine infection surveillance at Radius Specialty Hospital, an urban 207-bed LTACH with the capacity to house 42 patients requiring mechanical ventilation. This facility provides rehabilitative care, with a staff of 2 pulmonologists, as well as respiratory therapists, nurses, nutrition specialists, and occupational, physical, and speech therapists contributing to daily patient care. All patients were ventilated through a tracheostomy tube. During the study period, patients were referred to Radius Specialty Hospital from 10 medical centers, including academic and community-based hospitals.

After March 2006, Radius Specialty Hospital implemented a bundle of interventions for the prevention of VAP (hereafter referred to as the VAP-bundle approach). This bundle included a dedicated employee education program as well as the adoption of the CDC guidelines for the prevention of nosocomial pneumonia.[7] Central to the VAP-bundle approach at Radius Specialty Hospital was an order set that included the elevation of the head of the bed to an angle of 35°–40°, mouth care during each nursing shift, and prophylaxis against peptic ulcer and deep vein thrombosis. A daily break from sedative therapy was generally less applicable, because the majority of patients who required long-term mechanical ventilation were weaned from sedative therapy before or shortly after admission. Patients were artificially ventilated with the Puritan Bennett 740 ventilator (Puritan Bennett) or the Newport e360 series ventilator (Newport Medical), both of which were composed of heated ventilator circuits that required the use of a heat and moisture exchanger or a heated humidifier. The ventilator circuits were changed routinely every 7 days, and the heat and moisture exchangers were changed daily, unless a greater frequency of change was dictated by secretion load or equipment function. The suctioning of secretions was performed by use of a closed system (in-line suction catheter; Ballard).

Patients With VAP

Patients hospitalized at Radius Specialty Hospital were included in our study if they met the CDC criteria for VAP[11] during the study period, defined as April 1, 2006, through January 31, 2008. This time frame was selected because it reflected the period during which both the VAP-bundle approach and the CDC definitions for VAP were strictly adopted. In brief, a case of VAP was defined as a patient who required mechanical ventilation at Radius Specialty Hospital for at least 48 hours before any symptoms of pneumonia appeared. These included (1) one of the following: presence of fever, leukocytosis, leukopenia, or altered mental status (if more than 70 years of age); (2) two of the following: a change in sputum characteristics; the presence of a new cough, dyspnea, and/or tachypnea; a change in breath sounds; or increased oxygen and/or ventilation demands; and (3) the presence of a new and persistent (unless no underlying cardiopulmonary disease) radiographic infiltrate, consolidation, or cavitation.

Microbiologic Samples

At the discretion of the treating physician, sputum samples were collected from tracheal aspirate if there was clinical suspicion of VAP, and these samples were semiquantitatively cultured. Cultures were reviewed for the presence of *Pseudomonas* species, *Acinetobacter* species, gram-negative bacilli resistant to more than 3 antibiotics, and/or methicillin-resistant *Staphylococcus aureus*.[12] A multidrug-resistant isolate was defined as being resistant to more than 3 classes of antibiotics.

Data Collection and Analysis

All data collection was performed at Radius Specialty Hospital in Boston. Patients were prospectively identified as having VAP by use of a hospital epidemiology service, which included the hospital epidemiologist and a dedicated staff of epidemiology nurses. Study data on these VAP patients were then collected retrospectively by chart review. Data were collected on age, sex, duration of LTACH stay, duration of LTACH stay before VAP onset, antibiotic use before VAP, speciation of and resistance patterns for organisms from sputum samples, and adherence to the VAP-bundle approach. Data on length of stay and diagnosis for LTACH patients without VAP who were receiving mechanical ventilation were obtained by review of discharge face sheets. Because of the retrospective nature of the data collection, the need for informed consent was waived by the institutional review board of the affiliated academic medical center (ie, the Boston Medical Center) after review of the study protocol, and this waiver was accepted by Radius Specialty Hospital.

All data analysis was performed at the Boston University School of Medicine. Data were analyzed by use of SPSS software, version 16.0 (SPSS), and SAS software, version 9.3.1 (SAS). The incidence rates of VAP were defined as the number of cases of VAP per 1,000 ventilator-days, according to CDC recommendations.[4] Continuous variables were compared by use of an independent Student t test. Data on duration of LTACH stay before VAP onset were reported as median values (interquartile ranges [IQRs]) and compared using Kaplan-Meier survival plots and log-rank testing. The χ^2 test or the Fisher exact test was used for comparisons of categorical variables. Comparisons of incidence rates of VAP before with those after the implementation of the VAP-bundle approach were analyzed with a Poisson regression model (by use of the "Genmod" procedure in SAS). A 2-tailed P value of less than .05 was chosen as the threshold for statistical significance for all analyses.

TABLE. Baseline Characteristics of 23 Cases of Ventilator-Associated Pneumonia (VAP) at a Long-Term Acute Care Hospital, April 1, 2006–January 31, 2008

Characteristic	Cases of VAP
Age, mean ± SD, years	63 ± 17.7
Diagnosis at admission	
Neurological injury[a]	10 (43.5)
Sepsis	4 (17.5)
Pneumonia	3 (13.0)
COPD and/or CRF	2 (8.7)
Gastrointestinal hemorrhage and sepsis	1 (4.3)
Metastatic cancer	1 (4.3)
Postoperative	1 (4.3)
Trauma	1 (4.3)
Indication for receipt of mechanical ventilation	
Neurological impairment	16 (69.6)
Respiratory failure	6 (26.1)
Other	1 (4.3)
Comorbidity	
Stroke and/or anoxic brain injury	13
COPD and/or asthma	7
Spinal cord injury and/or paralysis	6
Diabetes mellitus	5
Malignancy	4
CAD and/or CHF	3
Dementia	2
Substance abuse	1
HIV infection	1

NOTE. Data are no. (%) of VAP cases or no. of patients with a diagnosis of VAP, unless otherwise indicated. CAD, coronary artery disease; CHF, congestive heart failure, COPD, chronic obstructive pulmonary disease; CRF, chronic respiratory failure; HIV, human immunodeficiency virus; SD, standard deviation.

[a] Stroke, persistent vegetative state, multiple sclerosis, amyotrophic lateral sclerosis, or spinal cord injury.

RESULTS

During the 22-month study period (April 1, 2006–January 31, 2008), there were 157 LTACH admissions involving 88 patients who required mechanical ventilation (some patients were admitted on more than 1 occasion). A total of 23 CDC-defined cases of VAP occurred in 19 patients during 13,746 ventilator-days. The cumulative VAP incidence was 14.6% (23 of 157 admissions), and the incidence rate was 1.67 cases per 1,000 ventilator-days, which was a 56% reduction from the VAP rate of 3.8 cases per 1,000 ventilator-days before the implementation of a VAP-bundle approach (relative risk, 0.44 [95% confidence interval, 0.27–0.70]; $P < .001$).

The characteristics of patients with VAP can be seen in the Table. Neurological impairment was the primary etiology for prolonged mechanical ventilatory support in 16 (69.6%) of 23 VAP cases. This is in contrast to the significantly lower rate of neurological impairment among admissions during which VAP did not occur (39% [49 of 126; the reason for mechanical ventilation was not available for 8]; $P = .014$).

The timing of VAP onset did not appear to be related to any identifiable clinical characteristics. The median total duration of LTACH stay was 226 days (IQR, 78–391 days), the median duration of LTACH stay before VAP onset was 41 days (IQR, 13–131 days), and the median total duration of mechanical ventilation before VAP onset (for LTACH and acute care hospital patients) was 166 days (IQR, 66–450 days). However, the total length of LTACH stay was longer for patients with VAP (median, 131 days [IQR, 50–300 days]), compared with patients without VAP (median, 39 days [IQR, 12–105 days]; $P = .002$) (Figure 1). Patients with VAP who had a neurological etiology for respiratory failure had a longer length of stay than did patients with VAP who had a pulmonary etiology for respiratory failure (median, 300 days [IQR, 71–391 days] vs 127 days [IQR, 97–148 days]; $P = .034$) (Figure 2). This is in contrast to the relatively similar lengths of stay between patients without VAP who had a neurological etiology for respiratory failure (median, 39 [IQR, 7–105 days]) and patients without VAP who had a pulmonary etiology for respiratory failure (median, 29 days [IQR, 11–75 days]; $P = .45$).

Microbiological data were available for 21 (91%) of the 23 cases with VAP. Sputum epithelial cell counts were available

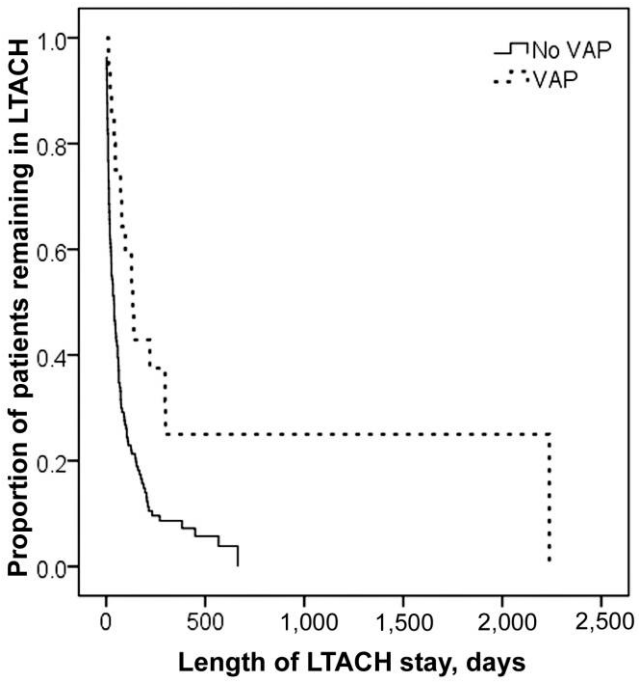

FIGURE 1. Kaplan-Meier survival curves that compare the length of long-term acute care hospital (LTACH) stay between patients with ventilator-associated pneumonia (VAP) and patients without VAP. During the 22-month study period (April 1, 2006–January 31, 2008), there were 157 LTACH admissions involving 88 patients who required mechanical ventilation (some patients were admitted on more than 1 occasion).

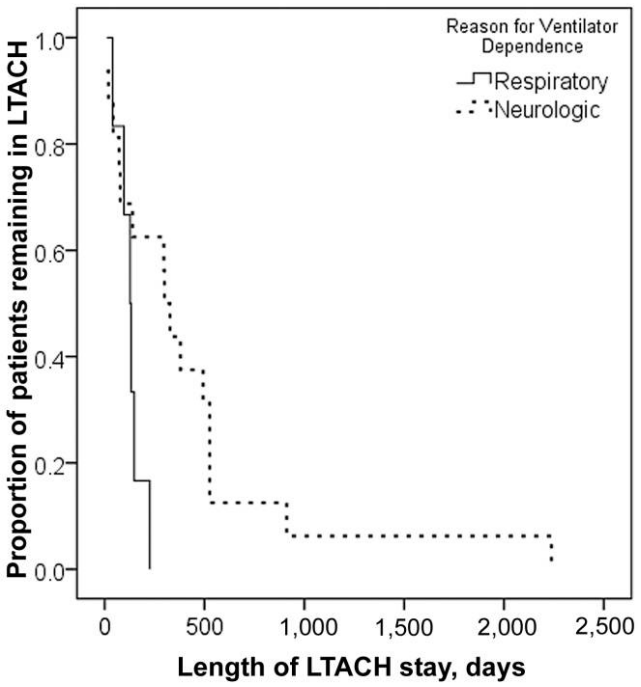

FIGURE 2. Kaplan-Meier survival curves that compare the duration of long-term acute care hospital (LTACH) stay associated with ventilator-associated pneumonia (VAP) between patients who had a neurological etiology for respiratory failure and patients who had a pulmonary etiology for respiratory failure. During the 22-month study period (April 1, 2006–January 31, 2008), there were 157 LTACH admissions involving 88 patients who required mechanical ventilation (some patients were admitted on more than 1 occasion).

for 16 (70%) of the 23 cases. The sputum samples were generally of good quality: in 13 (81%) of these 16 cases, there were less than 10 squamous epithelial cells per low-power field. Neutrophil counts were available for 18 (78%) of the 23 cases: in 17 (94%) of these 18 cases, there were more than 10 neutrophils per low-power field (in 12 cases [67%], there were more than 25 neutrophils per low-power field). In our LTACH, VAP tended to be associated with patients for whom culture yielded multidrug-resistant organisms. Forty-one pathogenic isolates were recovered from sputum samples in 23 VAP cases (mean ± SD, 1.78 ± 1.0 organisms per case). Of these isolates, 12 (29%) were enteric gram-negative bacilli (prevalence of multidrug resistance, 58% [7 isolates]), 12 (29%) were *Pseudomonas aeruginosa* (58% [7]), 11 (27%) were *Acinetobacter* species (90% [10]), 5 (12%) were *S. aureus* (80% [4]), and 1 was *Alicaligenes xylosidans* (100%). Of 21 cases for which microbiological data were available, culture yielded at least 1 isolate in 20 (95%). No difference existed between the patients transferred from community hospitals (5 [63%] of 8) and the patients transferred from tertiary hospitals (23 [74%] of 31) with respect to the presence of multidrug-resistant organisms. No difference existed in seasonal occurrence with respect to the 23 cases of VAP (7 cases occurred in the winter, 4 in the spring, 5 in the summer, and 7 in the fall; $P = .76$).

In 6 (26%) of the 23 cases of VAP, the patients were weaned from mechanical ventilation. If stratified by reason for long-term use of mechanical ventilation, patients with VAP who had a pulmonary etiology for respiratory failure were more likely to be weaned from mechanical ventilation than were patients with VAP who had a neurological etiology for respiratory failure (67% vs 12.5%; $P = .025$). One patient with VAP died in the LTACH. For this patient, who accounted for 3 cases of VAP, it was determined that the cause of death was not VAP. Data on adherence to the VAP-bundle approach showed that all patients with VAP had the head of the bed elevated to an angle of 35°–40° and received prophylaxis against peptic ulcer and that, in 22 of the 23 cases of VAP, the patient received food by use of a gastric tube.

DISCUSSION

Although the epidemiology of VAP in ICUs of acute care hospitals has been widely studied,[1,3-6] little is known about VAP in the growing LTACH population. The incidence rate of 1.67 cases per 1,000 ventilator-days cited in the present study indicates a lower incidence rate of VAP in the LTACH setting, compared with incidence rates cited in reports of VAP in adult ICU settings. For example, the 2004 National Nosocomial Infection Surveillance system report[4] determined that incidence rates of VAP for adult patients ranged from 4.4 case per 1,000 ventilator-days in coronary care units to 15.2 cases per 1,000 ventilator-days in trauma ICUs; the mean incidence rate in general medical and surgical ICUs was approximately 5 cases per 1,000 ventilator-days.

There are 2 likely reasons for this lower incidence rate of VAP in the LTACH: (1) all patients had a tracheostomy, and (2) there was a high level of compliance with the recently implemented VAP-bundle approach. A case-control study by Nseir et al.[13] that took place in an ICU demonstrated that having had a tracheostomy was associated with a 48% reduction in the incidence rate of VAP, from 9.2 to 4.8 cases per 1,000 ventilator-days. In addition, Zach et al.[8] have shown that, in their single-center, ICU-based study, the implementation of CDC guidelines aimed at preventing VAP reduced the incidence rate of VAP by 57%, from 12.6 to 5.7 cases per 1,000 ventilator-days. Similarly, the incidence rate of VAP at our LTACH before the implementation of the VAP-bundle approach (ie, 3.8 cases per 1,000 ventilator-days) resembles the incidence rate of VAP associated with having had a tracheostomy (ie, 4.8 cases per 1,000 ventilator-days) in the study by Nseir et al.,[13] and we found that the implementation of the VAP-bundle approach was associated with a 56% reduction in the incidence rate of VAP.

Although, to our knowledge, no study has investigated VAP in the LTACH setting, the study by Chenoweth et al.[14] of young home care patients who required long-term receipt of mechanical ventilation determined a VAP incidence rate of

1.55 cases per 1,000 ventilator-days, a rate similar to our study of cases of VAP in an LTACH. Interestingly, these rates are not very different from the incidence rate of pneumonia reported in a nursing home whose patients do not require mechanical ventilation (ie, 1.5 cases per 1,000 patient-days).[15] This raises the intriguing possibility that the incidence rate of VAP for patients who require long-term receipt of mechanical ventilation could approach the incidence rate of pneumonia for chronically ill patients who do not require mechanical ventilation.

The timing of VAP onset was variable, ranging from as little as 2 days after LTACH admission to greater than 5 years after hospitalization. We could not demonstrate any pattern to the timing of VAP onset related to patient characteristics, season, or microbiologic profile. Cases of VAP in the LTACH were frequently polymicrobial; multidrug-resistant organisms were isolated from the majority of patients with VAP, regardless of prior antibiotic exposure, referring facility, clinical characteristics, or timing of VAP onset. In general, the LTACH patients with VAP for whom culture yielded multidrug-resistant organisms resembled the ICU patient with "late-onset VAP" described by Kollef et al.,[16] and the polymicrobial nature of VAP in these patients was similar to that in the ICU patients with VAP described by Combes et al.[17] Our LTACH patients had very-late-onset VAP: the median time from receipt of mechanical ventilation to VAP was approximately 5 months. The fact that 95% of the cases of VAP yielded multidrug-resistant organisms on culture (including *Pseudomonas* species [12 {29%} of 41 organisms] and *Acinetobacter* species [11 {27%} of 41 organisms]) deserves special mention and should be considered, along with a medical center's antibiogram for monitoring susceptibility patterns of isolates recovered from patients, during the selection of an antibiotic regimen for LTACH patients with VAP.

Compared with our LTACH patients without VAP, the LTACH population with VAP was found to have an increased likelihood of neurological impairment as the primary etiology of prolonged mechanical ventilatory support and longer lengths of LTACH stay. Central nervous system disease is a known risk factor for VAP,[18] possibly because patients with this disease have decreased airway reflexes and an increased risk of aspiration. Further studies on additional methods to prevent VAP in these high-risk patients are warranted. Stratified analysis that focused on patients without VAP who required prolonged mechanical ventilatory support did not reveal any difference in length of LTACH stay between those who had a pulmonary etiology for respiratory failure and those who had a neurological etiology for respiratory failure. This finding demonstrates that neurological disease alone is likely not responsible for the relationship between VAP and increased length of stay. Finally, in our study, VAP appeared to be associated with a slightly decreased incidence of successful ventilator weaning, compared with past studies of an LTACH population. It is unclear from our study whether the weaning rate of 26% among VAP cases, compared with the weaning rate of 40%–54% among cases cited in prior studies in a LTACH setting,[10,19] is attributable to VAP. To better investigate these questions, further studies, with appropriate control for confounding variables, are necessary.

The limitations of our study were the retrospective nature of the data collection with respect to the VAP patients, the single-center setting, and the lack of additional information on patients without VAP from this LTACH. Further investigation of these patients without VAP may help elucidate the additional risk factors for VAP and the differences in outcomes between patients with and patients without VAP in the LTACH setting.

In conclusion, the rate of VAP in our LTACH appears to be less than that in an ICU setting. After the implementation of the VAP-bundle approach in our LTACH, VAP occurred at a relatively low incidence rate of 1.67 cases per 1,000 ventilator-days, with the burden of VAP falling primarily on those patients with significant neurological impairment. Despite this low incidence, 95% of the cases of VAP were associated with patients for whom culture yielded multidrug-resistant organisms, and VAP was associated with longer lengths of LTACH stay. Our study highlights that adherence to the current CDC guidelines for prevention of VAP is important for reducing these types of infection in the LTACH setting.

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Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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