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ORIGINAL ARTICLE

Ventilator-Associated Pneumonia in a Neurologic Intensive Care Unit Does Not Lead to Increased Mortality

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Abstract
Background Ventilator-associated pneumonia (VAP) is the most common nosocomial infection among medical intensive care unit (ICU) patients and is associated with increased mortality and length of stay (LOS). Neurologic disease is a risk factor for VAP development, but the relationship between VAP and outcomes in patients admitted to the ICU for neurologic reasons remains largely unknown.
Methods All mechanically ventilated patients over a 2-year period with neurovascular disease were included in a retrospective study. Data collected included patient demographics, dates of admission and discharge, LOS, and ventilator hours. Comparisons between neurologic patients who did and did not develop VAP were made using univariate and multivariate analysis.
Results Of 585 intubated neurovascular patients, 24 (4.1%) developed VAP. Compared with those who did not develop VAP, those with VAP were younger (51.8 ± 13.9 years vs. 58.8 ± 15.9 years, $P = 0.03$), had increased LOS (32.6 ± 29.2 days vs. 14.5 ± 7.8 days, $P < 0.001$), and more ventilator hours (272 ± 257 h vs. 85.9 ± 140 h, $P < 0.001$). There was no difference in mortality between patients with and without VAP (25.0% vs. 28.3%, $P = 0.72$). VAP was not an independent predictor of mortality in a multivariate model (OR 1.11, 95% CI 0.37–3.30, $P = 0.855$).
Conclusions VAP in neurocritical care patients is associated with increased LOS and ventilator hours, but is not associated with increased mortality, contrary to prior studies in medical ICU patients.

Keywords Ventilator-associated pneumonia · Mortality · Outcome · Neurologic intensive care · Quality

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Introduction

Ventilator-associated pneumonia (VAP) is the most common nosocomial infection among patients treated in medical intensive care units (ICUs) and has been associated with a two-fold increased mortality, longer length of stay (LOS), and increased hospital costs [1, 2]. Multiple strategies have been developed by hospitals in order to prevent VAP, as increasing scrutiny develops over VAP rates as a marker for quality of care [3]. VAP is being considered for addition to the list of the Centers for Medicare & Medicaid Services' (CMS) preventable conditions acquired during the hospital stay that lead to stoppage of payment to hospitals for associated costs, leading to even more attention to this problem in recent years [3, 4].

The presence of neurologic disease has been previously identified as an independent risk factor for the development of VAP as well as for failure of VAP resolution with initial antibiotic therapy [2, 5]. Despite the fact that this neurologic population is at elevated risk for VAP development, the relationship between VAP and morbidity and mortality in neurologically ill patients remains largely unknown [6].

Research to date has mainly focused on quantifying the burden of disease and preventing VAP in this vulnerable population of patients [7–12].

It would seem likely, given the unique relationship between VAP and neurologic illness, that risk factors for VAP and consequences of developing VAP in neurologically ill ICU patients would be different from those in the more commonly studied medical population. In order to understand predictors and consequences of VAP in these patients, we conducted a retrospective review of neurologically ill ICU patients at a large tertiary care institution.

Methods

As part of a quality improvement project, all mechanically ventilated patients at UCSF Moffitt-Long Hospital over a 2-year period from January 1, 2006 to December 31, 2007 were included in the study. Patient characteristics were collected including dates of admission and discharge, LOS, age, gender, and duration of intubation. Patients with neurovascular diseases were identified as a subset of neurology ICU patients using the discharge International Classification of Diseases version 9 (ICD-9) and diagnosis-related group (DRG) codes for ischemic stroke, intracranial hemorrhage, unruptured aneurysm, dural sinus thrombosis, subdural hematoma, and subarachnoid hemorrhage.

Ventilator-associated pneumonia was defined using a standard published definition and criteria [13]. In immunocompetent adults, this definition includes (1) radiographic criteria (including a new or progressive and persistent infiltrate, consolidation, or cavitation), (2) signs and symptoms (including fever; leukopenia or leukocytosis; or altered mental status of unknown cause in adults older than 70 years coupled with either new or purulent sputum or increasing secretions/suction requirements; new cough, dyspnea or tachypnea; rales or bronchial breath sounds; or worsening gas exchange), and (3) laboratory requirements (including positive culture data or histology in various specific types of pulmonary specimens) all in the setting of a patient who has a device to continuously control respiration via tracheostomy or endotrachial intubation within the 48-h period before the onset of infection.

Comparisons between those patients with neurovascular conditions who did and did not develop VAP were made using students' *t*-test for continuous variables and Fisher's exact test for dichotomous variables. Those variables found to have a *P*-value < 0.2 were entered into a multivariable model to test their independence; those variables with $P < 0.05$ were considered independent predictors of VAP development. An additional multivariate model was used to test if patient variables, including VAP, predicted mortality. In order to explore the hypothesis that patient transportation, with associated ventilator disconnection and supine posturing, influences the development of VAP in these patients similar to that demonstrated in other populations, a case–control study was performed matching cases of VAP and non-VAP controls by age, LOS, diagnosis, and ventilator duration [14].

Results

A total of 585 patients with neurovascular conditions were admitted to the ICU and tracheally intubated at least once during the study period. Of these, 24 (4.1%) developed VAP, leading to a yearly rate of VAP of around 2%. Of the six deaths in patients with VAP, five were unrelated to VAP including four from family decision to withdraw care due to lack of neurologic recovery and one sudden death in the setting of a clear chest radiograph and no signs of infection. A single death may have been attributed partially to VAP in a patient with stroke, multifactorial respiratory failure (including ARDS and pulmonary edema), and inability to wean off mechanical ventilation; the family withdrew care rather than pursue tracheostomy per previously stated patient wishes.

Comparisons between those neurovascular patients developing and those not developing VAP are found in Table 1. We found no significant difference in mortality between patients with and without VAP. Compared with those who did not develop VAP, those with VAP tended to be significantly younger, had an increased LOS (more than double), and spent more time on the ventilator. The average number of ventilator days prior to development of VAP was 10.0 (±9.0).

Although VAP is associated with increased LOS and increased duration of ventilation in this cohort, it remains unclear if these factors are the result of, or the cause of, VAP. Using multivariate modeling, only ventilator days, calculated as ventilator days prior to onset of VAP in those with VAP (OR, 1.079, 95% CI 1.04–1.11, $P < 0.001$) and age (OR 0.752, 95% CI 0.573–0.986, $P = 0.039$) were

Table 1 Comparison between all neurovascular patients in the study and those with and without VAP

	All patients	VAP	Non-VAP	*P*-value
Number	585	24	561	
Age (years) (SD)	58.6 (15.9)	51.8 (13.9)	58.8 (15.9)	0.03
LOS (days)	15.2 (18.7)	32.6 (29.2)	14.5 (17.8)	<0.001
Mortality (%)	28.2	25.0	28.3	0.72
Ventilator (h)	93.6 (151)	272 (257)	85.9 (140)	<0.001

P-values are for differences between VAP patients and non-VAP patients

Table 2 Multivariate model of mortality in all study patients ($n = 585$)

Variable	Odds ratio	95% CI	*P*-value
Age (decade)	1.23	[1.08–1.39]	0.001
Length of stay (days)	0.92	[0.90–0.95]	<0.001
Vent days	1.11	[1.07–1.15]	<0.001
VAP	1.11	[0.37–3.30]	0.855

independently associated with the development of VAP likely because the variables LOS and duration of intubation are highly collinear.

We found that VAP in these neurologically ill ICU patients does not lead to an increased mortality, and in order to explore this further, we constructed a multivariable model of mortality in the entire cohort (Table 2). Age, LOS, and ventilator days, but not VAP, were independently associated with mortality suggesting that VAP by itself does not account for mortal outcomes.

We further explored risk factors for the development of VAP using a case–control method comparing VAP ($N = 24$) and non-VAP ($N = 24$) neurovascular patients matched for age, LOS, and ventilator days. This revealed that transports for cross-sectional imaging were significantly higher in those patients who developed VAP (Table 3). A non-significant trend was demonstrated for total trips outside the ICU.

Discussion

The emergence of neurohospitalists and neurointensivists has increased attention toward quality of care in the neurologic inpatient setting [15]. With this increased focus, has come the realization that patients with neurologic disorders may differ in very fundamental ways from other medically ill patients, possibly requiring distinct metrics to adequately measure quality.

Table 3 Case–control study of patients with VAP ($N = 24$) versus those without VAP matched for age, LOS, and ventilator hours

Variable	VAP	Non-VAP	*P*-value
Age (years, SD)	51.8 (14.5)	57.7 (14.4)	0.2
LOS (days)	36.2	35	0.99
Mortality (%)	28.6	33.3	1
Ventilator hours, mean (SD)	344 (357)	290 (300)	0.6
OR trips (SD)	0.95	1.1	0.72
Imaging trips (SD)	6.8 (3.3)	4.9 (2.8)	0.03
Angiograms (SD)	1.7 (1.5)	1.2 (1.6)	0.24
Other transports (SD)	10 (3.8)	7.7 (5.1)	0.39
Total trips (SD)	6.3 (5.1)	5.2 (4.5)	0.05

We examined VAP, a measure commonly used to define safety and quality in the ICU, in an exclusively neurologically ill patient population. In contrast with multiple studies of medical ICU patients, we found no increased mortality in these neurologically ill ICU patients who developed VAP. Deaths in patients with VAP were due mainly to neurologic injury and withdrawal of care. We found that VAP was associated with younger age, duration of ventilation, and transports outside of the ICU for imaging. Coupled with the observation that neurologic disease leads to increased VAP rates, this finding calls into question whether VAP in this neurologic population might be a distinct disease from VAP in the medical or surgical population.

We used the currently accepted definition of VAP in this study that is commonly used by many hospitals for the purposes of reporting to national and state agencies [13]. This definition takes into account strict radiographic, clinical, and laboratory criteria for making a diagnosis of VAP and should be used as the standard for future studies of VAP in this patient population.

Our reported VAP rate of around 2% per year is lower than some previous studies of neurologically ill patients [8]. While some of our low incidence may reflect our adherence to the current strict VAP definition, specific characteristics of our ICU may also be driving this result including (1) a high adherence to an oral care "bundle" aimed at lowering VAP rates, (2) a trend toward earlier tracheostomy in those thought to likely remain intubated for a prolonged period, (3) a selection bias that includes some relatively healthy patients that are intubated for only a few days post-operatively, or (4) a different selection bias introduced by particularly neurologically ill patients with a high mortality being referred to our tertiary center who may die from neurologic disease prior to the development of VAP. Future prospective studies are needed that accurately define the incidence of VAP in a diverse set of neurologically ill ICU patients across multiple institutions controlling for these variables and baseline patient characteristics.

Patients with neurologic disorders may indeed have a naturally increased risk of VAP either due to pulmonary factors associated with nervous system disease or simply the consequences of altered mentation in the setting of prolonged intubation. These patients, in contrast with medical ICU patients, are often intubated for airway protection rather than for a pulmonary process. As a result, intubations last longer and this length of ventilation may in itself predispose to VAP as indicated in our multivariable model. In addition, many medically ill patients have an abnormal chest radiograph at the time of intubation, making them ineligible to develop VAP using current criteria; therefore, the true VAP rate in medical ICU patients is likely underreported. The clear chest radiograph that

accompanies most neurologic patients at the time of intubation for airway protection may naturally lead to higher rates of VAP simply because of the way VAP is defined.

Our finding that VAP may be an epiphenomenon in neurologically ill ICU patients has important consequences for hospital reimbursement. The consideration by CMS and others to use VAP as a quality measure and as a method to limit hospital reimbursement needs to account for the reason for patient hospitalization. Since the occurrence of VAP is dependent, to some extent, on the duration of intubation, and the duration of intubation is driven by the underlying neurological diagnosis, VAP may be a less robust measure of quality of care in neurologic patients compared with a medical ICU population. However, since VAP is associated with fever, which itself may cause secondary brain injury, methods to reduce the incidence of VAP are important. We plan to explore the impact of reducing transports in our patient population to better understand if this is a direct cause of VAP as suggested in our analysis. If indeed VAP is a different disorder in this specific patient population, then further research will be needed to define the optimal care of these patients.

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