premature mortality, are also critical to the patient population as we assess the burden of this disease.

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Managing Ventilator Complications in a "VACuum" of Data

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Ventilator-associated pneumonia (VAP) has been a major complication of mechanical ventilation that in years past has led to excess morbidity and mortality and has led to vigorous efforts at prevention. In the past decade, we have seen a dramatic decline in the reported frequency of VAP in the United States, with the advent of the "ventilator bundle" and with a belief that this simple, multimodality intervention could result in "zero VAP," making pneumonia in patients on mechanical ventilation a potentially nonreimbursable medical error. However, a number of investigators have pointed out that the concept of zero VAP is biologically implausible and is the result of the manipulation of an imperfect clinical definition of pneumonia.[1] In an effort to avoid this "gaming" of publicly reported data, the Centers for Disease Control and Prevention and multiple professional organizations have proposed a more "objective" process to monitor, namely that of ventilator-associated events (VAEs), which includes ventilator-associated conditions (VACs), infection-related ventilator-associated complications (IVACs), and VAP.[2]

The definition of a VAC requires a stable or decreasing positive end-expiratory pressure (PEEP) and supplemental F_{IO_2} for at least 2 days, followed by an increase in F_{IO_2} of at least 0.2 or an increase in PEEP of at least 3 cm H_2O, for a minimum of 2 days. When a VAC is accompanied by signs of infection (fever, elevated WBC count, or neutropenia) and the addition of antibiotics for at least 4 days, an IVAC is present. Based on culture data, patients with an IVAC are further divided into possible or probable VAP. The putative "advantages" of the VAE concept are its objectivity, its lack of reliance on a chest radiograph (which is not used in the definition), and the ability to collect data rapidly with an electronic medical record, rather than through the laborious efforts of an infection control practitioner.

Despite these well-meaning intentions, the practical clinical validity of VACs has not been established, and it is quite surprising that we have been asked to monitor for these events. For example, although not all VACs are VAP, we do not know how many cases of VAP are defined as VACs. In an early study of 600 patients in six US centers, Klompas et al[3] found that 135 had VACs, whereas 55 had VAP. Similarly, an Australian study found that 153 of 543 patients had VACs, whereas only 40 patients with VACs had positive respiratory cultures and were treated with antibiotics,[4] so that both studies found VACs to be more common than VAP. In contrast to these data are the findings of a Canadian study of 1,320 patients who were mechanically ventilated, of which the prevalence of VACs was 10.5%, whereas the prevalence of VAP was 11.2%.[5] Of the patients with VAP, 79% had neither a VAC nor an IVAC. Similarly, Klein Klouwenberg et al[6] found that the prevalence of

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VACs and the prevalence of VAP were similar in a group of 2,080 patients, but that the VAE algorithm identified only 32% of the patients with VAP. In the current issue of *CHEST* (see page 68), Boyer et al[7] report their experience with a VAC in a prospective 1-year study of 1,209 patients who were mechanically ventilated. Their study had 67 VACs but 86 episodes of VAP, making VAP a more common event. In addition, most of the 86 episodes of VAP were not VACs, with only 15 probable cases of VAP and six possible cases of VAP being classified as IVACs.

In addition to questions about the frequency of infection as a cause of VACs, there are many other issues related to the definition of a VAC. Concerns include the fact that a VAC can be diagnosed only after a 2-day period of stability, followed by 2 days of worsened oxygenation, making diagnosis only possible after a minimum of 4 days. In the study by Boyer et al,[7] the median time of VAC onset was 6.2 days, even though the researchers used an adjudication method to include patients who died before the 2 calendar days of deterioration were met. Another concern with the definition of a VAC is that it depends on changes in FIO_2 and PEEP (physician behavior) and not on a physiologic parameter, even though prior studies have shown that the PaO_2/FIO_2 ratio is a good predictor of the clinical course of VAP.[8] Presumably the ventilator settings were chosen for the VAC definition to facilitate easy monitoring via electronic means. However, it is easy to eliminate most VACs by deciding to initially ventilate all patients with a higher FIO_2 and PEEP than is needed, and thus it would not be necessary to increase the PEEP or FIO_2 when the patient had a physiologic decline in oxygenation.

Although most studies do show that there is an adverse outcome for patients with VAEs, few convincing data exist that show we currently have the means to prevent these episodes. Boyer et al[7] found that patients with VACs had a mortality rate of 66%, compared with 14% in those without VACs, whereas Hayashi et al[4] found a 20.3% mortality rate that was not higher than that of patients without VACs. In both of these studies, the duration of mechanical ventilation was longer for patients with VACs than for those without, but the real impact of a VAC probably needs to be measured from the day of its onset and not from the first day of ventilation. The currently available data do not show that it is possible to prevent VACs by existing ICU care strategies, and that if there is a "VAC bundle," it should be defined, developed, and tested before we agree to monitor for VACs. Muscedere et al[5] found that over a 24-month period, the application of VAP-prevention recommendations increased, with a drop in the rate of VACs but with no change in the frequency of IVACs. In their current study in *CHEST*, Boyer et al[7] defined the "preventability" of VACs, based on diagnosis, and as assessed by an adjudication committee.[7] They judged that only 37.3% were preventable, but this dropped to 14.9% if probable VAP (which occurred despite documented adherence to a VAP-prevention bundle) was excluded. The preventable diagnoses included infection with inappropriate therapy, insufficient PEEP, excess IV fluids, aspiration, iatrogenic esophageal perforation, and postoperative bleeding necessitating resuscitation.

Currently, there are not enough data to endorse the measurement of VACs as a reflection of quality of care, particularly because most episodes of a VAC are not VAP, and we do not have a prevention strategy that is able to prevent IVACs. In addition, the new data from Boyer et al[7] have nicely defined the causes of VACs and have shown that very few episodes are preventable using our current prophylactic strategies. Until this "VACuum" of data is filled with convincing information about the preventability of VACs, the methods for prevention, and the relation of VACs to quality of care, we urge a reevaluation of the VAC concept and consideration of a moratorium on its measurement.

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A Prospective Evaluation of Ventilator-Associated Conditions and Infection-Related Ventilator-Associated Conditions

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BACKGROUND: The Centers for Disease Control and Prevention has shifted policy away from using ventilator-associated pneumonia (VAP) and toward using ventilator-associated conditions (VACs) as a marker of ICU quality. To date, limited prospective data regarding the incidence of VAC among medical and surgical ICU patients, the ability of VAC criteria to capture patients with VAP, and the potential clinical preventability of VACs are available.

METHODS: This study was a prospective 12-month cohort study (January 2013 to December 2013).

RESULTS: We prospectively surveyed 1,209 patients ventilated for ≥ 2 calendar days. Sixty-seven VACs were identified (5.5%), of which 34 (50.7%) were classified as an infection-related VAC (IVAC) with corresponding rates of 7.0 and 3.6 per 1,000 ventilator days, respectively. The mortality rate of patients having a VAC was significantly greater than that of patients without a VAC (65.7% vs 14.4%, $P < .001$). The most common causes of VACs included IVACs (50.7%), ARDS (16.4%), pulmonary edema (14.9%), and atelectasis (9.0%). Among IVACs, 44.1% were probable VAP and 17.6% were possible VAP. Twenty-five VACs (37.3%) were adjudicated to represent potentially preventable events. Eighty-six episodes of VAP occurred in 84 patients (10.0 of 1,000 ventilator days) during the study period. The sensitivity of the VAC criteria for the detection of VAP was 25.9% (95% CI, 16.7%-34.5%).

CONCLUSIONS: Although relatively uncommon, VACs are associated with greater mortality and morbidity when they occur. Most VACs represent nonpreventable events, and the VAC criteria capture a minority of VAP episodes. CHEST 2015; 147(1):68-81

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ABBREVIATIONS: APRV = airway pressure release ventilation; CDC = Centers for Disease Control and Prevention; IVAC = infection-related ventilator-associated condition; NHSN = National Healthcare Safety Network; PEEP = positive end-expiratory pressure; VAC = ventilator-associated condition; VAP = ventilator-associated pneumonia

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Clinical criteria are known to be nonspecific for the diagnosis of ventilator-associated pneumonia (VAP).[1-10] The Centers for Disease Control and Prevention (CDC)/National Healthcare Safety Network (NHSN) has established a surveillance definition for probable nosocomial pneumonia, including VAP.[11] Unfortunately, these diagnostic criteria were not validated clinically.[12] We previously compared the observed rates of VAP using the CDC/NHSN surveillance method with the CHEST criteria and found that the agreement between the two sets of criteria was poor.[13] Others have also noted that US surveillance rates of VAP are decreasing compared with rates in Europe and Asia, whereas clinical diagnoses of VAP in the United States remain prevalent.[14,15]

Given that VAP surveillance is time consuming and potentially less accurate than clinical/microbiologic criteria and that the use of quantitative lower respiratory tract cultures for the establishment of VAP is not universal, the CDC/NHSN has recently supported efforts aimed at shifting ICU surveillance away from VAP. The CDC/NHSN has focused instead on the occurrence of ventilator-associated "conditions" (VACs) that may circumvent the subjectivity and inaccuracy of the

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VAP definition, facilitate electronic assessment, and make interfacility comparisons more meaningful.[16] This policy shift toward using VACs as a more objective marker of ICU quality has occurred without robust prospective clinical validation for this purpose and served as the impetus for this study. The goals of this study were to prospectively determine the incidence of VACs among patients in medical and surgical ICUs, to assess the potential preventability of VACs, and to assess the ability of the VAC criteria to identify VAP.

Materials and Methods

Study Population and Data Collection

The study was conducted in the surgical (36 beds) and medical (29 beds) ICUs of Barnes-Jewish Hospital, a 1,250-bed teaching hospital in St. Louis, Missouri. During a 12-month period (January 2013 to January 2014), ICU patient rosters were screened daily. Patients who were mechanically ventilated for ≥ 2 calendar days were monitored daily for the development of either a VAC or an infection-related VAC (IVAC). The Washington University Human Research Protection Office approved the protocol (HRPO number 201209071). The following baseline characteristics were recorded at the time of VAC determination: age, sex, race, cause of respiratory failure, comorbid conditions, APACHE (Acute Physiology and Chronic Health Evaluation) II score[17] at ICU admission, and cause of the VAC. Patients with a VAC were followed until hospital discharge or death. Additionally, a determination was made as to whether the VAC represented a potentially preventable event.

Definitions for VAC and IVAC

The definitions used for VAC and IVAC were taken from the recently published update from the CDC.[16] To meet the VAC definition, a patient who was mechanically ventilated must have had at least 2 calendar days of stable or decreasing daily minimum positive end-expiratory pressure (PEEP) or FIO_2 followed by at least 2 days of increased daily minimum PEEP or FIO_2, in which the increase in the daily minimum PEEP is ≥ 3 cm H_2O or the increase in the daily minimum FIO_2 is ≥ 0.20 (or 20 percentage points in oxygen concentration). We modified the CDC VAC definition with clinical judgment based on ventilator mode, and in some cases mortality, in the 2-day window of VAC eligibility. We included potentially salvageable patients achieving the requirement of an increased daily minimum PEEP or FIO_2, but expiring before the 2-calendar day requirement was met. We excluded patients who met the strict interpretation of the CDC VAC criteria but whose deterioration was clinically judged to be consistent with expected impending mortality from their underlying illness. Moreover, although only the FIO_2 component of the CDC definition can be applied to patients receiving airway pressure release ventilation (APRV), we included those with a sustained increase in mean airway pressure of ≥ 3 cm H_2O. IVACs represent the subset of VACs that are potentially infection related, as evidenced by an abnormal WBC count ($\geq 12{,}000$ cells/mm^3 or $\leq 4{,}000$ cells/mm^3) or temperature (> 38°C or < 36°C) and a new antimicrobial start. IVACs were defined so as to be likely to capture patients with pulmonary and extrapulmonary infections of sufficient severity to trigger respiratory deterioration. The definitions used for possible and probable VAP were taken from the CDC update.[16]

VAP Definition

The CHEST definition for VAP includes a new or progressive consolidation on chest radiographs plus at least two of the following clinical criteria: fever >38°C, leukocytosis or leukopenia, and purulent secretions.[13] The presence or absence of a new or progressive radiographic infiltrate was based on the interpretation of the chest radiograph by board-certified radiologists who were blinded to the study. The diagnosis of VAP was considered to be microbiologically confirmed if either BAL or protected specimen brush cultures had significant growth using a semiquantitative culture technique ($\geq 10^4$ and $\geq 10^3$ colony-forming units/mL, respectively).

Adjudication

For each case, two physician investigators (A. F. B., M. H. K., or N. S.) independently classified each VAC and IVAC as to its preventability. Rater disagreements were resolved by consensus. A preventable VAC was defined as an event resulting in injury to the patient caused by a nonintercepted medical error, either through an act of omission or commission, rather than the underlying illness.[18] A nonpreventable VAC was defined as an unavoidable injury caused by the patient's underlying disease process, associated with appropriate medical care. For example, a pneumothorax associated with central line placement in a patient with severe ARDS was considered preventable, whereas worsening oxygenation in a patient with intraabdominal sepsis despite adequate source control and appropriate antibiotic treatment was considered nonpreventable. Potentially preventable events screened for daily included inappropriate antibiotic therapy (ie, an antibiotic regimen not active against the causative pathogen based on in vitro testing); procedure-related adverse events (eg, pneumothorax, hemorrhage); aspiration of enteral feedings; ventilation with potentially injurious tidal volumes (>6 mL/kg predicted body weight); pulmonary edema from excess IV fluid; effects of excess sedation (eg, atelectasis, aspiration, hypotension); and catheter-associated blood stream infection, wound infection, urinary catheter-associated infection, or probable VAP per CDC criteria.

Statistical Analysis

All comparisons were unpaired, and all tests of significance were two tailed. Continuous variables were compared using the Student *t* test for normally distributed variables and the Mann-Whitney *U* test for nonnormally distributed variables. The χ^2 or Fisher exact tests were used to compare categorical variables. For all analyses, a two-tailed *P* value $< .05$ was considered statistically significant. Statistical analyses were performed using SPSS, version 11.0 for Windows (IBM).

Results

Over 1 year, 1,209 patients met the inclusion criteria (Fig 1). Of these, 67 VACs were identified (5.5%), of which 34 (50.7%) were classified as an IVAC, with corresponding rates of 7.0 and 3.6 per 1,000 ventilator days, respectively. The baseline characteristics of the patients with VACs and IVACs are shown in Table 1. In addition to IVACs, other common causes of VACs included ARDS (16.4%), pulmonary edema (14.9%), and atelectasis (9.0%). Probable VAP was the most common cause of an IVAC (44.1%), followed by possible VAP (17.6%), and six IVACs without clinical or microbiologic confirmation (17.6%). Extrapulmonary infection or inflammation accounted for three IVACs (pancreatitis = 2, *Clostridium difficile* infection = 1). Three patients met the criteria for an IVAC; they were ultimately thought to have lung inflammation secondary to ARDS with negative cultures as the cause of fever and/or leukocytosis. The median day of mechanical ventilation during which a VAC occurred was 6.2 (SD, 4.3 days) (Fig 2). The mortality rate of patients having a VAC was significantly greater than that of patients without a VAC (65.7% vs 14.4%, $P < .001$). Similarly, the duration of mechanical ventilation was significantly longer for patients with a VAC than for patients without a VAC (14.7 ± 8.9 days vs 7.5 ± 6.3 days, $P < .001$).

Twenty-five VACs (37.3%) were adjudicated to represent potentially preventable events. Table 2 lists the VACs and IVACs according to their preventability. The 15 cases of probable VAP were considered preventable and occurred despite investigator-documented adherence to the hospital's VAP prevention bundle. The 10 additional potentially preventable events resulted from inappropriate antimicrobial coverage (2), insufficient PEEP (2), excessive administration of IV fluids (2), significant aspiration related to endotracheal intubation (2), esophageal perforation from nasogastric tube placement (1), and resuscitation for postoperative femoral artery bleeding (1). Among patients adjudicated to have a nonpreventable VAC, the most common causes were progressive ARDS (11), pulmonary edema in the setting of septic shock (8), and atelectasis despite appropriate ventilator settings (4).

We modified the CDC VAC definition with clinical judgment based on ventilator mode, and in some cases mortality, in the 2-day window of VAC eligibility. We included five potentially salvageable individuals who met the minimum PEEP or FIO_2 thresholds but expired before meeting the 2-calendar day requirement and four individuals who had significant increases in mean airway pressure (≥ 3 cm H_2O) while on APRV. Excluding

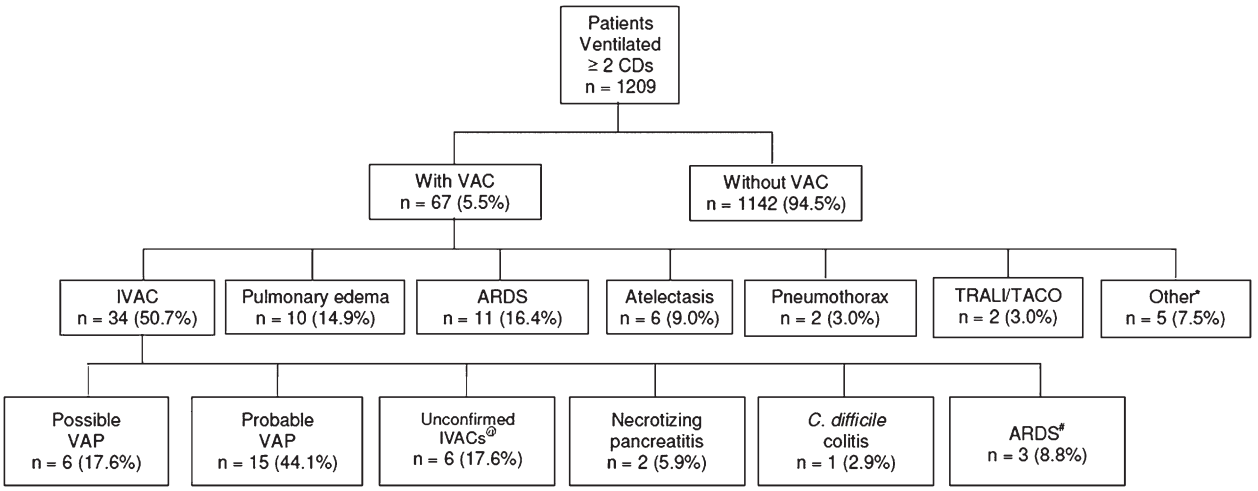

Figure 1 – *Analysis of patients with VACs and IVACs. Three VACs had more than one cause. *Other causes included untreated pneumonia, acute lung allograft rejection, malignant airway compression, and metastatic Hodgkin's lymphoma; #three cases met the technical criteria for an IVAC, but the reason for worsening oxygenation was thought to be ARDS; @patients meeting IVAC criteria without a clear source of infection were identified despite having clinical, radiographic, and microbiologic evaluations performed.* C. difficile = Clostridium difficile*; CD = calendar day; IVAC = infection-related ventilator-associated condition; TACO = transfusion-associated circulatory overload; TRALI = transfusion-related acute lung injury; VAC = ventilator-associated condition; VAP = ventilator-associated pneumonia.*

TABLE 1] Baseline Characteristics

Characteristic	Patients (N = 67)
Age, mean (SD), y	55.7 (15.5)
Male	38 (56.7)
Race	
White	52 (77.6)
Black	14 (20.9)
Asian	1 (1.5)
Medical ICU	42 (62.7)
Surgical ICU	25 (37.3)
APACHE II score, mean (SD)	19 (6.0)
Cause of respiratory failure	
Altered mental status	5 (7.5)
ARDS/ALI	4 (6.0)
Aspiration	3 (4.5)
Cardiopulmonary arrest	3 (4.5)
Congestive heart failure	1 (1.5)
Elective surgery	5 (7.5)
Heart failure	1 (1.5)
ILD	1 (1.5)
Obstructive lung disease	1 (1.5)
Pneumonia	15 (22.4)
Sepsis	15 (22.4)
Trauma	8 (11.9)
Other[a]	6 (9.0)
Comorbidities	
Cerebrovascular accident	3 (4.5)
Chronic kidney disease	8 (11.9)
Chronic lung disease	26 (38.8)
Congestive heart failure	8 (11.9)
Connective tissue disease	2 (3.0)
Coronary artery disease	11 (16.4)
Diabetes mellitus	23 (34.3)
Hepatic cirrhosis	6 (9.0)
Solid organ transplant	4 (6.0)
Malignancy	13 (19.4)

Data are presented as No. (%) unless indicated otherwise. ALI = acute lung injury; APACHE = Acute Physiology and Chronic Health Evaluation; ILD = interstitial lung disease.
[a]Other causes include lymphangitic carcinomatosis, acute lung allograft rejection, metastatic Hodgkin's lymphoma, hemothorax after thoracentesis, malignant airway compression, and anaphylaxis.

these nine individuals resulted in corresponding rates of VAC and IVAC of 4.3 and 2.2 per 1,000 ventilator days, respectively. We also excluded 11 patients who met the surveillance criteria because of impending and expected mortality from their underlying condition and who died very early on calendar day 2. Including these 11 patients would have made our overall VAC rate 6.5% and mortality among VAC patients 70.5%.

Eighty-six episodes of microbiologically confirmed VAP occurred in 84 patients (10.0 of 1,000 ventilator days) during the study period. The sensitivity of VAC for detection of VAP was 25.9% (95% CI, 16.7%-34.5%).

Discussion

We demonstrated that VACs and IVACs occurred in 5.5% and 2.8% of all medical and surgical patients requiring mechanical ventilation for 2 or more calendar days. Of all the VACs included, 37.3% were adjudicated to represent potentially preventable events, with the remaining VACs representing nonpreventable disease progression. The most common cause of a VAC was possible or probable VAP, and the most common preventable cause of a VAC was probable VAP. The VAC criteria identified a minority of patients with microbiologically confirmed VAP.

To the best of our knowledge, this study represents the first prospective surveillance study to evaluate the occurrence of VACs and IVACs and the clinical conditions captured, and to assess their potential preventability. Our results are consistent with those of retrospective studies demonstrating that the presence of VACs and IVACs is associated with greater hospital mortality. Muscedere et al[19] recently evaluated 1,320 patients ventilated for > 48 h over four defined time periods. VACs developed in 10.5%, and IVACs developed in 4.9%. Patients who developed a VAC or an IVAC had significantly more ventilator days, hospital days, and antibiotic days, and greater hospital mortality. They also showed that increased concordance with VAP prevention guidelines during the defined time periods was associated with decreased VAP and VAC rates but no change in IVAC rates. An Australian study performed in a single hospital found the prevalence of VAC to be 28%, with hospital mortality being 20.3% in patients with VAC and 28.2% in those without VAC.[20] Similarly, a retrospective US study of three hospitals found the VAC rate to be 23%, with an associated hospital mortality of 38%.[21] A recent prospective electronic surveillance for VAC observed that detection of VAP was poor and that small differences in electronic implementation could considerably affect the incidence and mortality rates associated with VACs.[22]

Our results differ from these previous studies in that our results demonstrate a lower rate of VAC and greater

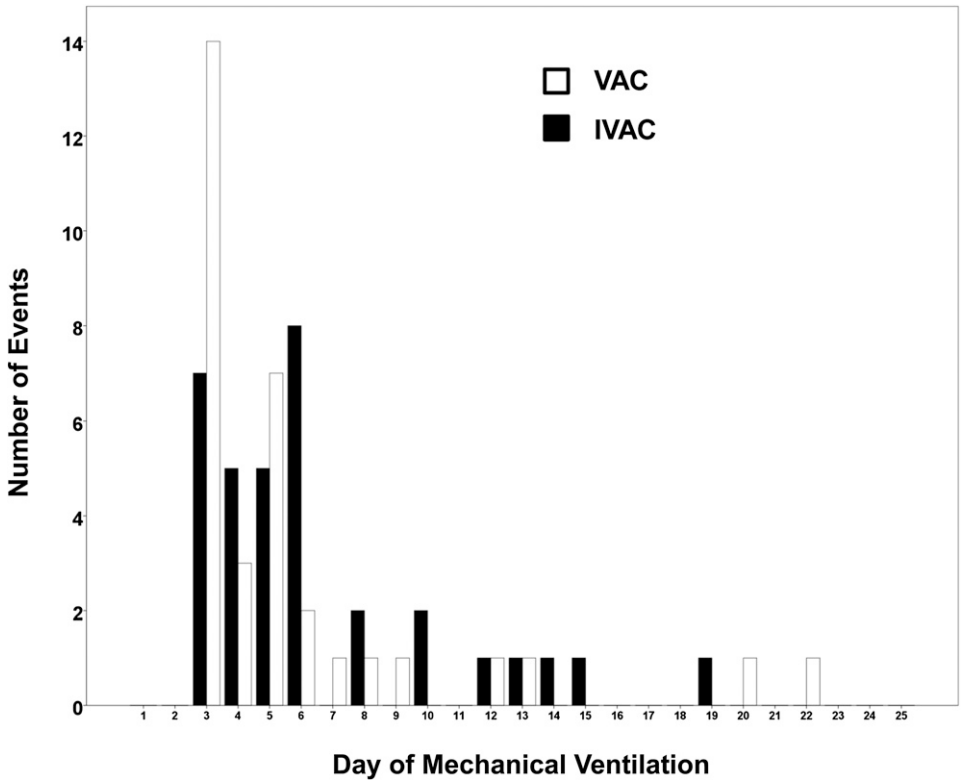

Figure 2 – *Occurrence of VAC and IVAC relative to the start of mechanical ventilation. See Figure 1 legend for expansion of abbreviations.*

hospital mortality. One explanation for this discrepancy is that we used the most recent CDC recommendation for defining VAC, as opposed to the retrospective studies, which used smaller changes in PEEP and F_{IO_2}.[20,21] Additionally, our prospective evaluation allowed us to more accurately determine the presence of VAC according to the calendar day requirement. Interestingly, our VAC rate would have been even lower had we excluded the five patients who died prior to reaching the 2-calendar day requirement for PEEP or F_{IO_2} deterioration and the four patients ventilated with APRV, but higher if we included patients whose ventilator changes were caused by their impending death (all 11 considered not preventable).

Our findings demonstrate that most VACs are nonpreventable events. However, the high mortality associated with VAC suggests that any and all opportunities to prevent these events when possible should be undertaken. Ahmed et al[23] conducted a retrospective 10-year study to determine the association between specific hospital exposures and the rate of ARDS development among at-risk patients. These investigators evaluated patients who developed ARDS and, thus, presumably would have gone on to be classified as having a VAC. Several potentially preventable hospital exposures were markedly more common among patients developing ARDS, including inadequate antimicrobial therapy, medical and surgical adverse events, hospital-acquired aspiration, ventilation with potentially injurious tidal volumes, and greater volumes of blood product transfusion and fluid administration. Our investigation also suggests that many events can contribute to the development of worsening respiratory failure. These represent events of both omission and commission, rather than simply deterioration of the underlying illness, and thus may be potentially preventable. Like VAP, it is likely that some type of prevention bundle[24,25] or prevention protocol[26,27] will have to be developed and tested to see if VAC rates can be reduced with concomitant improvement in patient outcomes.

Several limitations of our study should be noted. First, our findings may not be generalizable. This would be especially true for ICUs caring for patients with less disease acuity. Moreover, our data reflect the practices within the ICUs of Barnes-Jewish Hospital and may not apply to hospitals using different ICU staffing models. Second, we used clinical and microbiologic criteria to define the occurrence of VAP, which may have resulted in an underestimation of the number of cases of VAP,

TABLE 2] Clinical Characteristics of Ventilator-Associated Events

Patient No.	Cause of Respiratory Failure	Cause of VAC	VAC Criteria	Preventable	Reason Preventable	Mortality	Cause of Death	Miscellaneous
1	Urosepsis	Pulmonary edema	Increase in PEEP from 5 to 10 cm H_2O	No	NA	Yes	Cardiogenic and septic shock	Patient presented with septic shock and subsequently developed acute systolic dysfunction
2	Trauma (motor vehicle collision)	IVAC[a]	Increase in PEEP from 5 to 10 cm H_2O	No	NA	No	NA	…
3	Sepsis (pneumonia)	IVAC, probable VAP	Increase in F_{IO_2} from 40% to 60%	Yes	Probable VAP	Yes	Septic shock and VAP	BAL positive for MSSA and MDR *Pseudomonas aeruginosa*
4	Surgery (abdominal aortic aneurysm repair)	IVAC, probable VAP	Increase in F_{IO_2} from 40% to 60%	Yes	Probable VAP	Yes	Septic shock and VAP	ETA positive for *P aeruginosa and Serratia marcescens*
5	Pneumonia	Untreated pneumonia	Increase in PEEP from 5 to 10 cm H_2O	Yes	Inappropriate antimicrobial coverage	No	NA	BAL positive for *Stenotrophomonas maltophilia*, organism not treated initially
6	Burn injury	IVAC, possible VAP	Increase in PEEP from 5 to 12.5 cm H_2O	No	NA	Yes	Septic shock	Blood culture positive for *P aeruginosa* at time of VAC
7	Cardiopulm onary arrest	IVAC, probable VAP	Increase in PEEP from 5 to 10 cm H_2O	Yes	Probable VAP	Yes	Respiratory failure due to metastatic adenoid cystic carcinoma	ETA positive for *Acinetobacter calcoaceticus-baumanii* complex
8	Aspiration/seizure	ARDS	Increase in F_{IO_2} from 40% to 80%	No	NA	Yes	Anoxic encephalopathy	…
9	Sepsis (suspected intraabdominal source)	ARDS	Increase in F_{IO_2} from 60% to 80%	No	NA	Yes	Septic shock	…
10	Urosepsis	IVAC, possible VAP	Increase in MAP from 12 to 24 cm H_2O	No	NA	No	NA	…

(Continued)

TABLE 2] *(continued)*

Patient No.	Cause of Respiratory Failure	Cause of VAC	VAC Criteria	Preventable	Reason Preventable	Mortality	Cause of Death	Miscellaneous
11	Small cell lung cancer	Atelectasis and pulmonary edema	Increase in PEEP from 5 to 10 cm H_2O	No	NA	No	NA	…
12	Pneumonia	Pulmonary edema	Increase in PEEP from 5 to 10 cm H_2O	No	NA	No	NA	…
13	Sepsis (scrotal abscess)	Atelectasis and pulmonary edema	Increase in F_{IO_2} from 40% to 60%	No	NA	No	NA	…
14	Acute lung allograft rejection	Allograft dysfunction	Increase in PEEP from 5 to 10 cm H_2O	No	NA	Yes	Allograft rejection	Lung transplantation in June 2012
15	Sepsis (pneumonia)	Pulmonary edema	Increase in F_{IO_2} from 40% to 60%	No	NA	Yes	Disseminated *Rhizopus* infection confirmed by autopsy	…
16	Ruptured abdominal aortic aneurysm	Pulmonary edema	Increase in PEEP from 5 to 10 cm H_2O	No	NA	Yes	Septic shock	…
17	Pneumonia	ARDS	Increase in PEEP from 5 to 8 cm H_2O	No	NA	Yes	ARDS	…
18	Pneumonia and pulmonary embolism	IVAC, possible VAP	Increase in F_{IO_2} from 50% to 80%	No	NA	Yes	ARDS	…
19	ARDS	Worsening ARDS	Increase in MAP from 15 to 26 cm H_2O	No	NA	Yes	ARDS	…
20	Subarachnoid and intraventricular hemorrhage	IVAC[a]	Increase in PEEP from 5 to 10 cm H_2O	Yes	Difficult intubation resulting in emergent cricothyroidotomy	Yes	Subarachnoid and intraventricular hemorrhage	…

(Continued)

TABLE 2] *(continued)*

Patient No.	Cause of Respiratory Failure	Cause of VAC	VAC Criteria	Preventable	Reason Preventable	Mortality	Cause of Death	Miscellaneous
21	Cardiopulmonary arrest	Atelectasis	Increase in F_{IO_2} from 40% to 60%	Yes	Reduction in PEEP resulting in worsening atelectasis	Yes	Cardiopulmonary failure due to suspected pulmonary embolism	…
22	Cardiopulmonary arrest	IVAC	Increase in F_{IO_2} from 40% to 80%	No	NA	Yes	Cardiogenic and septic shock	IVAC secondary to *Clostridium difficile* colitis
23	Sepsis (necrotizing pancreatitis)	IVAC	Increase in F_{IO_2} from 40% to 60%	No	NA	Yes	Septic shock	IVAC secondary to necrotizing pancreatitis
24	Trauma (motor vehicle collision)	IVAC, probable VAP	Increase in PEEP from 5 to 10 cm H_2O	Yes	Probable VAP	Yes	VAP	BAL positive for *Enterobacter aerogenes*
25	Intraoperative cardiopulmonary arrest	IVAC, probable VAP	Increase in F_{IO_2} from 40% to 100%	Yes	Probable VAP	Yes	Myocardial infarction and VAP confirmed by autopsy	Patient was being treated for *Escherichia coli* VAP when IVAC criteria met, additional cultures not obtained during window period
26	Sepsis (necrotizing pancreatitis)	IVAC	Increase in PEEP from 5 to 12.5 cm H_2O	No	NA	Yes	Septic shock	IVAC secondary to necrotizing pancreatitis
27	Idiopathic pulmonary fibrosis	IVAC[a]	Increase in PEEP from 5 to 10 cm H_2O	No	NA	Yes	Respiratory failure due to IPF	…
28	Drug overdose	IVAC, possible VAP	Increase in PEEP from 5 to 10 cm H_2O	Yes	Significant aspiration during intubation	No	NA	…
29	Metastatic Hodgkin's lymphoma	Worsening metastatic disease	Increase in F_{IO_2} from 50% to 70%	No	NA	Yes	Cardiogenic shock due to malignant pericardial effusion	…
30	Sepsis (abdominal wall abscess)	IVAC, probable VAP	Increase in PEEP from 5 to 12.5 cm H_2O	Yes	Probable VAP	Yes	Septic shock and VAP	ETA positive for *A calcoaceticus-baumanii* complex

(Continued)

TABLE 2] *(continued)*

Patient No.	Cause of Respiratory Failure	Cause of VAC	VAC Criteria	Preventable	Reason Preventable	Mortality	Cause of Death	Miscellaneous
31	Pneumonia	IVAC	Increase in F_{IO_2} from 40% to 60%	No	NA	Yes	Septic shock	Patient met IVAC criteria but cause of VAC likely related to organizing pneumonia
32	Aspiration/seizure	IVAC, probable VAP	Increase in F_{IO_2} from 40% to 70%	Yes	Probable VAP	No	NA	BAL positive for *P aeruginosa*
33	Pneumonia	Pulmonary edema	Increase in PEEP from 5 to 10 cm H_2O	No	NA	No	NA	…
34	Hemothorax after thoracentesis	TRALI/TACO	Increase in PEEP from 5 to 10 cm H_2O	No	NA	No	NA	…
35	Sepsis (pneumonia)	ARDS	Increase in MAP from 21 to 34 cm H_2O	No	NA	Yes	Septic shock	…
36	Interstitial lung disease	IVAC	Increase in PEEP from 10 to 20 cm H_2O	No	NA	Yes	AIP	Patient met IVAC criteria but cause of VAC likely related to AIP
37	Altered mental status	IVAC[a]	Increase in PEEP from 5 to 10 cm H_2O	Yes	Aspiration and esophageal perforation from nasogastric tube	Yes	ARDS	…
38	Surgery (excision of tubo-ovarian abscess)	Atelectasis	Increase in PEEP from 5 to 8 cm H_2O	Yes	Insufficient PEEP in obese patient	No	NA	…
39	Metastatic Ewing's sarcoma	Airway compression	Increase in PEEP from 5 to 12.5 cm H_2O	No	NA	No	NA	PEEP used to stent airway
40	Aspiration	ARDS and pneumothorax	Increase in PEEP from 5 to 14 cm H_2O	No	NA	Yes	ARDS	…
41	Pneumonia	Atelectasis	Increase in PEEP from 12 to 15 cm H_2O	No	NA	No	NA	…

(Continued)

TABLE 2] *(continued)*

Patient No.	Cause of Respiratory Failure	Cause of VAC	VAC Criteria	Preventable	Reason Preventable	Mortality	Cause of Death	Miscellaneous
42	Sepsis (cholangitis)	IVAC, probable VAP	Increase in F_{IO_2} from 40% to 70%	Yes	Probable VAP	Yes	Multifactorial shock and VAP	ETA positive for *E coli*
43	Sepsis (pneumonia)	IVAC, probable VAP	Increase in F_{IO_2} from 40% to 60%	Yes	Probable VAP	Yes	Septic shock and VAP	ETA positive for *Aspergillus niger*
44	Trauma (assault)	IVAC, probable VAP	Increase in MAP from 10 to 25 cm H_2O	Yes	Probable VAP	Yes	Subdural hematoma	BAL positive for *A calcoaceticus-baumanii*, *Serratia marcescens*, and MSSA
45	COPD exacerbation	Atelectasis	Increase in PEEP from 5 to 10 cm H_2O	No	NA	No	NA	…
46	Anaphylaxis	Pulmonary edema	Increase in PEEP from 5 to 10 cm H_2O	Yes	Excessive IV fluids	No	NA	…
47	Pneumonia	IVAC	Increase in F_{IO_2} from 70% to 100%	No	NA	Yes	ARDS	Patient met IVAC criteria but cause of VAC likely related to ARDS as revealed on autopsy
48	Pneumonia	IVAC, probable VAP	Increase in F_{IO_2} from 50% to 100%	Yes	Probable VAP	Yes	VAP	ETA positive for MSSA
49	Sepsis (suspected intraabdominal source)	Pulmonary edema	Increase in MAP from 13 to 20 cm H_2O	Yes	Excessive IV fluids	Yes	Cerebral edema	…
50	Trauma (motor vehicle collision)	IVAC, probable VAP	Increase in F_{IO_2} from 40% to 60%	Yes	Probable VAP	No	NA	ETA positive for *E aerogenes*
51	Pneumonia	IVAC, possible VAP	Increase in PEEP from 5 to 10 cm H_2O	No	NA	Yes	Rapidly progressive organizing pneumonia	Patient met IVAC criteria but cause of VAC likely related to organizing pneumonia as revealed on autopsy

(Continued)

TABLE 2] *(continued)*

Patient No.	Cause of Respiratory Failure	Cause of VAC	VAC Criteria	Preventable	Reason Preventable	Mortality	Cause of Death	Miscellaneous
52	Sepsis (suspected intraabdominal source)	ARDS	Increase in MAP from 10 to 16 cm H_2O	No	NA	Yes	Septic shock	…
53	Sepsis (pneumonia)	Untreated pneumonia	Increase in PEEP from 5 to 12.5 cm H_2O	Yes	Inappropriate antimicrobial coverage	Yes	Pneumonia	BAL positive for *S maltophilia*, organism not treated initially
54	Constrictive pericarditis	IVAC, probable VAP	Increase in PEEP from 5 to 8 cm H_2O	Yes	Probable VAP	Yes	Constrictive pericarditis	ETA positive for *Enterobacter cloacea*
55	Trauma (motor vehicle collision)	IVAC, probable VAP	Increase in MAP from 12 to 19 cm H_2O	Yes	Probable VAP	No	NA	BAL positive for MSSA
56	ARDS (drug toxicity)	IVAC	Increase in F_{IO_2} from 80% to 100%	No	NA	Yes	ARDS	Patient met IVAC criteria but cause of VAC likely related to ARDS
57	Pneumonia	ARDS	Increase in PEEP from 5 to 10 cm H_2O	No	NA	No	NA	Lung transplant in September 2013
58	Sepsis (pneumonia)	ARDS	Increase in PEEP from 5 to 10 cm H_2O	No	NA	No	NA	…
59	ARDS	IVAC, probable VAP	Increase in PEEP from 7 to 12.5 cm H_2O	Yes	Probable VAP	Yes	ARDS and VAP	ETA positive for *P aeruginosa*
60	Trauma (bike accident)	IVAC, possible VAP	Increase in PEEP from 7.5 to 15 cm H_2O	No	NA	Yes	Septic shock	…
61	Trauma (motor vehicle collision)	IVAC[a]	Increase in F_{IO_2} from 40% to 60%	No	NA	No	NA	…
62	Influenza pneumonia	ARDS	Increase in PEEP from 5 to 10 cm H_2O	No	NA	No	NA	…

(Continued)

TABLE 2] *(continued)*

Patient No.	Cause of Respiratory Failure	Cause of VAC	VAC Criteria	Preventable	Reason Preventable	Mortality	Cause of Death	Miscellaneous
63	Surgery (abdominal aortic aneurysm repair)	TRALI/TACO	Increase in F_{IO_2} from 40% to 60%	Yes	Postoperative femoral artery bleed	…	…	…
64	Sepsis (spontaneous bacterial peritonitis)	Pulmonary edema	Increase in F_{IO_2} from 50% to 80%	No	NA	Yes	Decompensated liver failure	…
65	Drug overdose	IVAC[a]	Increase in PEEP from 5 to 15 cm H_2O	No	NA	No	NA	…
66	Pneumonia	Pneumothorax	Increase in F_{IO_2} from 40% to 60%	No	NA	No	NA	…
67	Influenza pneumonia	ARDS	Increase in F_{IO_2} from 40% to 60%	No	NA	Yes	ARDS	…

AIP = acute interstitial pneumonia; ETA = endotracheal aspirate; IPF = idiopathic pulmonary fibrosis; IVAC = infection-related ventilator-associated complication; MAP = mean airway pressure; MDR = multidrug resistant; MSSA = methicillin sensitive *Staphylococcus aureus*; NA = not applicable; PEEP = positive end-expiratory pressure; TACO = transfusion-associated circulatory overload; TRALI = transfusion-related acute ling injury; VAC = ventilator-associated condition; VAP = ventilator-associated pneumonia.

[a]Patients meeting IVAC criteria without a clear source of infection identified despite having clinical, radiographic, and microbiologic evaluations performed.

because we did not include patients diagnosed with endotracheal cultures. Third, possible VAP was classified as a potentially preventable infection despite the use of a VAP prevention bundle.[24] Although we assessed compliance with this bundle, it is possible that a more comprehensive bundle could have reduced the occurrence of VAP.[25] Moreover, not all cases of VAP are preventable, as demonstrated by various investigations.[24,25] Had we not classified probable VAP as a preventable event, our rate of potentially preventable VACs would have been only 14.9%.

Another limitation of our study is that we included nine cases of VAC that did not strictly meet the CDC/NHSN criteria. These nine cases were assessed to represent obvious respiratory deterioration despite either dying prior to the 2-calendar day requirement or being managed with APRV. Additionally, we excluded 11 patients who met the strict interpretation of the CDC VAC criteria but whose deterioration was clinically judged to be consistent with expected impending mortality from their underlying illness. Inclusion of these patients would have increased the overall rate of VACs observed. Finally, we did not define risk factors for VAC. Future studies should aim at identifying such risk factors to target interventions for their prevention. Our data suggest that the heterogeneity of VAC will limit any single intervention program, unless it targets the most common causes of VAC. This may also explain why the improved adherence to the VAP prevention program in the Canadian experience did not reduce rates of IVACs over time.[19]

Conclusions

In conclusion, although relatively uncommon, VAC is associated with greater mortality and morbidity when it occurs. Most VACs represent nonpreventable events and identify a minority of VAP episodes. Our data suggest that more study of the VAC criteria is needed before they can be routinely implemented as a comparative tool to assess the medical care provided in the ICU setting.

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