A Multicentered Prospective Analysis of Diagnosis, Risk Factors, and Outcomes Associated With Pediatric Ventilator-Associated Pneumonia

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Objective: To assess risk factors and outcomes associated with pediatric ventilator-associated pneumonia.

Design: Multicentered prospective observational cohort.

Setting: Children's hospitals in the United States.

Patients: Mechanically ventilated patients less than 18 years old.

Measurements and Main Results: Prospective evaluation of the prevalence, risk factors, and outcomes of pediatric ventilator-associated pneumonia along with evaluation of diagnostic criterion for pediatric ventilator-associated pneumonia. The prevalence of pediatric ventilator-associated pneumonia was 5.2% ($n = 2,082$), for a rate of 7.1/1,000 ventilator days. Patients with ventilator-associated pneumonia had a longer unadjusted ICU length of stay ($p < 0.0001$) and increased length of mechanical ventilation by more than 11 days ($p < 0.0001$). After adjustment for patient factors, ICU length of stay ($p = 0.03$) and mechanical ventilation days ($p = 0.001$) remained significant. Patients with ventilator-associated pneumonia were almost three times more likely to die ($p = 0.007$). Independent risk factors for ventilator-associated pneumonia were reintubation and part-time ventilation.

Conclusions: Pediatric ventilator-associated pneumonia is common in mechanically ventilated pediatric patients. These patients have longer length of stay, longer duration of mechanical ventilation, and increased risk for mortality. (*Pediatr Crit Care Med* 2015; XX:00–00)

Key Words: hospital-acquired infections; pediatrics; pneumonia; ventilator-associated pneumonia

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Ventilator-associated pneumonia (VAP) is one of the most common hospital-acquired infections in PICUs and has significant patient and economic effects. The 2009 National Healthcare Safety Network (NHSN) reported PICU VAP rates of 1.1 per 1,000 ventilator days (1). Recent literature demonstrates that VAP occurs in 3–19% of ventilated pediatric patients (2–4), with rates between 1.1 and 27.1 per 1,000 ventilator days (5–7). VAP is associated with increased morbidity, including increased mechanical ventilation days and increased PICU length of stay (4, 8, 9). Pediatric patients with VAP demonstrate higher unadjusted mortality rates of 10–20% (3, 4, 8) that lose statistical significance once severity adjusted. Pediatric VAP is also associated with direct cost of $51,157 to $56,000 per patient (8, 10). Pediatric VAP is a common reason for the initiation of empiric antibiotic therapy and comprises almost half of all PICU antibiotic days (11).

Risk factors for developing VAP have been described in multiple studies. Almuneef et al (2) described increased VAP rates in patients with witnessed aspiration, reintubation,

prior antibiotic therapy, continuous enteral nutrition, and bronchoscopy. Elward et al (3) found that genetic syndromes, reintubation, and transport out of the PICU were independent predictors of VAP. Srinivasan et al (4) and Casado et al (7) identified enteral nutrition, sedative/narcotic usage, presence of a gastric tube, female sex, prolonged mechanical ventilation, and postsurgical admission as independent risk factors for VAP or healthcare-associated pneumonia in PICUs. Other reported risk factors include immunodeficiency, neuromuscular blockade, blood product usage, or medications such as steroids, H2 blockers, and metoclopramide (3, 4, 12).

The accurate diagnosis of VAP in children and adults has been a persistent problem due to inconsistent methodologies (13).A recent review by Venkatachalam et al (14) highlights the concern regarding variable diagnostic methods in pediatrics. The Centers for Disease Control and Prevention (CDC) provides three pediatric VAP diagnostic algorithms: clinical pneumonia (PNU-1), pneumonia + laboratory findings (PNU-2), and pneumonia in immunocompromised patients (PNU-3). Most pediatric VAP diagnoses are performed noninvasively. In 2009, the National Healthcare Safety Report demonstrated that the majority of pediatric VAPs were diagnosed using the clinical PNU-1 criteria (71–83% in medical and surgical PICUs; 40% in cardiac ICUs) (5). In addition to the multiple algorithms, the current CDC guidelines allow for significant detection and definition heterogeneity across institutions.

In the initial assessment of need (15 PICUs surveyed), we found significant diagnostic variability for pediatric VAP. Only 53% of the institutions used the most recent 2008 CDC VAP criteria, 33% performed daily surveillance, 27% used the chest radiograph (CXR) as the screening tool for VAP, and 27% used tracheal aspirates obtained from endotracheal or tracheostomy tubes. These variations in detection and disease definitions prevent rate comparisons, epidemiologic understanding, and reliable evaluation of reduction efforts.

We conducted a prospective, multicentered, observational cohort study to obtain reliable VAP prevalence rates and identify the risk factors and outcomes using standardized methodology for surveillance and diagnosis: the CDC PNU-1 age-based criteria. Additionally, we provide assessment of the diagnostic criterion.

METHODS

This is a prospective, observational, multi-institutional cohort analysis of pediatric VAP conducted at 16 PICUs. The 16 participating PICUs represented various geographic regions, hospital size, and configurations (large academic quaternary-care centers and smaller community-based programs housed within an adult hospital). The study period was from January 2009 to November 2009, and each institution collected data for six consecutive months during the study period. The inclusion criteria were all invasively (intubated or tracheostomy dependent) mechanically ventilated patients who were admitted to the PICU.

Exclusion criteria were patients who were 18 years old or older. Informed consent was waived by all participating institutions' institutional review boards.

Study Design
Participating institutions agreed to 6 months of prospective data collection for all mechanically ventilated patients and training for standardized pediatric VAP diagnosis. Interrater reliability testing was performed for all individuals designated to perform VAP surveillance using three standardized cases. A minimum score of 85% was required for individuals to be approved for VAP surveillance. Sites were given reference manuals detailing answers to common questions regarding diagnosis as well as specific information on methods for evaluating criteria for diagnosis. The steering committee was also available throughout the study period to assist with difficult patient scenarios. Data collected at each institution was de-identified and sent electronically to a central database. Diagnosis of VAP was made by using the age-specific PNU-1 criteria (**Fig. 1**) provided by National Nosocomial Infections Surveillance and the CDC (15). Prospective VAP surveillance was performed daily (Monday through Friday); weekend (Saturday and Sunday) surveillance was performed on the following Monday. Surveillance refers to the assessment of screening criteria (CXR) and then, if needed, other patient factors for diagnosis of clinical VAP. Mechanically ventilated patients were evaluated daily until one of four endpoints: 1) 48 hours after extubation, 2) 48 hours after transfer to an intermediate care level within the same institution, 3) discharge from the PICU, home for chronically ventilated patients, or to another institution (inpatient rehabilitation, another PICU), or 4) death. Patients reintubated within 48 hours of extubation were analyzed as a single mechanical ventilation episode. For patients who remained mechanically ventilated at the end of the study period, only the data up until the study end was included in the analysis.

Surveillance
Individuals not responsible for patient care were selected at each institution to perform surveillance. Screening was performed by reviewing CXR reports. CXR frequency was not dictated by study protocol. Each institution worked with their radiologist to standardize CXR reports to assist with surveillance. When patients met the screening criteria, further evaluation using the CDC PNU-1 criteria was performed to determine if patients met the clinical diagnosis of VAP. An incident form was completed for each instance a patient met CXR criteria until the patient either no longer met CXR criteria or was diagnosed with VAP. Once VAP was diagnosed, CXR evaluation and incident form completion (for VAP occurrence) ceased for 14 days. Progression through the PNU-1 algorithm was driven by clinical data from the prior 24 hours.

Data Collection
Prospective data collection from each site was conducted using Adobe Data collection forms (Adobe Systems, http://www.adobe.com). Patient demographics and a priori risk factors—age,
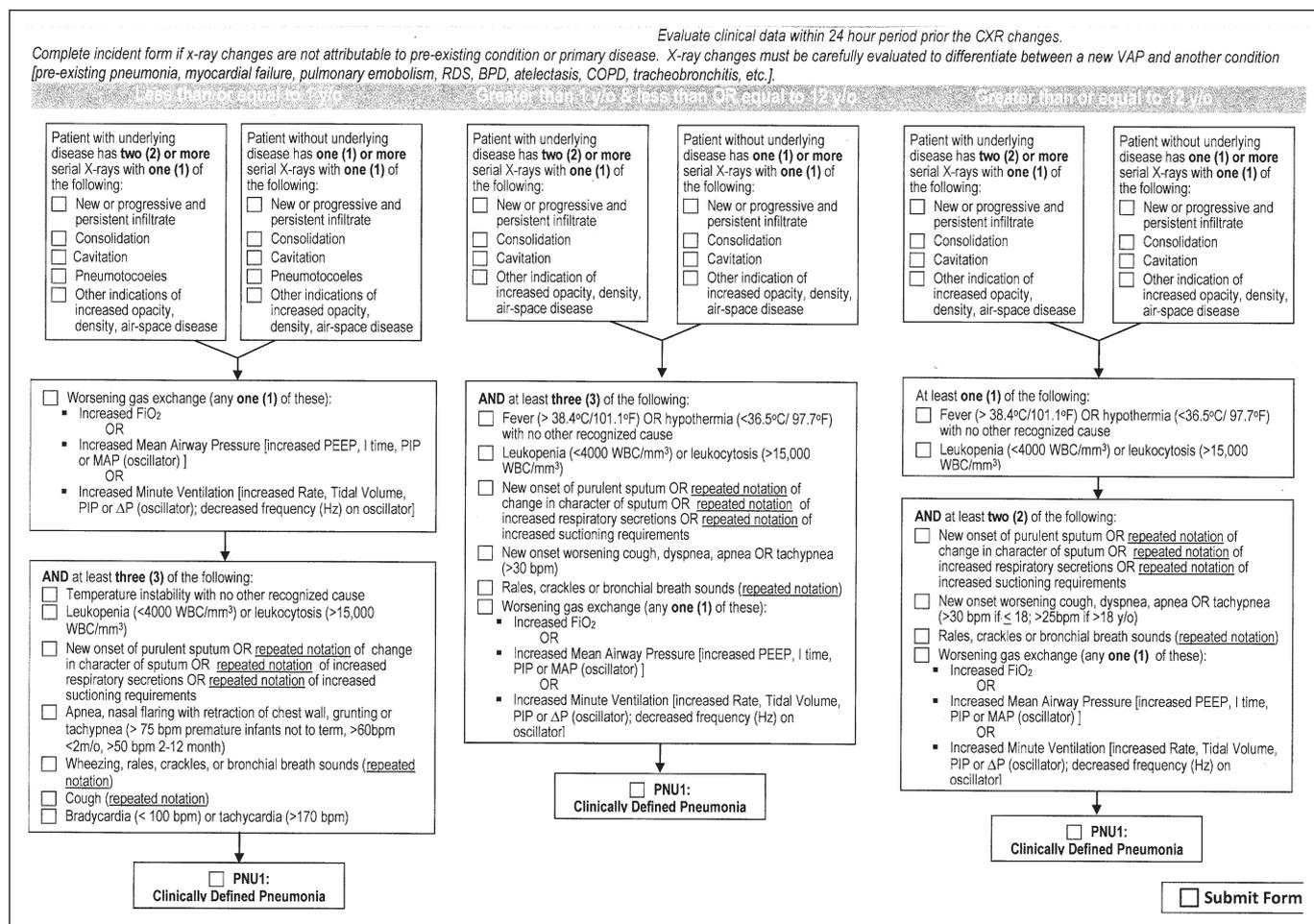
Figure 1. Diagnostic flowchart used to determine ventilator-associated pneumonia (VAP). BPD = bronchopulmonary dysplasia, COPD = chronic obstructive pulmonary disease, CXR = chest radiograph, MAP = mean arterial pressure, PEEP = positive end-expiratory pressure, PIP = peak inspiratory pressure, PNU = pneumonia, RDS = respiratory distress syndrome..

previous antibiotic use, recent hospitalization, transport, reintubation, bronchoscopy, use of high-frequency oscillatory ventilation, prior thoracic disease (defined as lung pathology such as new or progressive infiltrate, consolidation, cavitation, or pneumatoceles noted on CXR in the 48 hr prior to mechanical ventilation in the PICU), recent mechanical ventilation, part-time ventilation (defined by > 8 hr/d of mechanical ventilation but < 24 hr as defined through consultation with the CDC), type of intubation, length of mechanical ventilation, and immunosuppression status—were collected. Further individual patient information, such as Pediatric Index of Mortality (PIM)-2, ICU length of stay, and mortality, were obtained from the VPS^{LLC} (https://portal.myvps.org/Contact.aspx), a PICU-specific, validated clinical database that facilitates data sharing, benchmarking, and quality improvement among PICUs (16).

Data Analysis

The primary outcome was to determine a pediatric VAP rate per 1,000 ventilator days defined by the CDC age-specific PNU-1 criteria using a prospective surveillance method. Secondary outcomes were to assess associations between pediatric VAP and ICU length of stay, length of mechanical ventilation,

and mortality. Outcomes were corrected by predetermined demographic and patient-based factors that were present prior to PICU mechanical ventilation of: age, weight, PIM-2, immunosuppressed status, prior thoracic disease, and admission on a home ventilator. Other analyses to be performed included determining patient factors associated with pediatric VAP, examining survival time in days from ventilation to first VAP event, and assessing the frequency of diagnostic criterion used in VAP diagnosis. Data analysis was performed using SAS 9.3 (SAS Institute, Cary, NC). Categorical variables were summarized as frequencies with percentages. Continuous variables were summarized as means, SDs, 95% CIs for means, medians, and ranges. As all of the continuous variables were nonparametric, medians were more robust measures of central tendency. Kaplan-Meier method was used to compute survival estimates and produce survival curves of time to first VAP event analysis, with survival times regarded as censored observations for patients without VAP events. Comparisons of patient characteristics were conducted using chi-square, or Fisher exact tests on categorical variables, and Wilcoxon-Mann-Whitney tests on nonnormally distributed continuous variables. p Value less than or equal to 0.05 was considered

statistically significant, and all tests of significance were two-tailed. A generalized estimating equation (GEE) model, which accounts for the intrainstitutional correlation among cases from the same hospital, was used to calculate crude unadjusted odds ratio (OR) estimates with 95% CIs in univariate analyses, adjusted OR estimates with 95% CIs in multivariable analyses, and to investigate the associations of VAP events with each of secondary outcomes, respectively. Multivariable GEE modeling was also used to identify the independent predictors (i.e., risk factors) of VAP events. Variables associated with VAP at an $\alpha = 0.10$ significance level in univariate analyses, and PIM-2, were entered into the GEE regression models. The quasi-likelihood information criterion (QIC) was used for selecting predictor variables and a working correlation matrix. The chosen best model fit had the smallest value of the QIC. Model assessment based on cumulative residuals was examined to investigate if a continuous variable was correctly specified in the model as p greater than or equal to 0.05 would indicate correct specification. Results are reported as VAP versus non-VAP, and medians (95% CI) or mean (range), unless otherwise stated.

RESULTS

Over the 6-month collection period, 2,082 mechanically ventilated patients were followed up for the development of VAP. One hundred eight patients (5.2%) developed a VAP during the study period and five had a second occurrence of VAP during the hospitalization. Only the first VAP occurrence was used for statistical analysis. The study group accounted for 16,147 ventilator days for an aggregate VAP prevalence rate of 7.00 VAP/1,000 ventilator days. PICU length of stay and severity of illness analysis were available on the 1,448 patients (69.6%) who were enrolled in institutions that submit data to VPS[LLC], this included 50 of the VAP-positive patients and 1,398 patients who did not develop a VAP (Fig. 2). VAP rate for the

non-VPS hospitals was 6.74 VAP/1,000 ventilator days versus 8.51 VAP/1,000 ventilator days for the VPS hospitals. There were 41 patients still mechanically ventilated at study end.

Secondary Outcomes
There were 13 deaths and a nonsignificant trend toward increased unadjusted mortality (12.04% vs 6.99%; $p = 0.056$) in those that developed VAP. VAP events were associated with over a 2.5-fold increased unadjusted mechanical ventilation days (11.00 [9.0, 13.0] vs 3.0 [3.0, 3.0]; $p < 0.0001$) and increased PICU length of stay (13.94 d [11.17, 19.89] vs 5.61 d [5.11, 5.89]; $p < 0.0001$). After severity adjustment, the significant increase persisted in length of mechanical ventilation (12.21 d [4.93, 19.49]; $p = 0.001$) and PICU length of stay (10.8 d [0.92, 20.68]; $p = 0.032$). VAP events were associated with higher severity-adjusted PICU mortality (OR, 3.07; CI, 1.36, 6.90; $p = 0.007$). See **Supplemental Tables 1–3** (Supplemental Digital Content 1, http://links.lww.com/PCC/A141) for multivariate analysis.
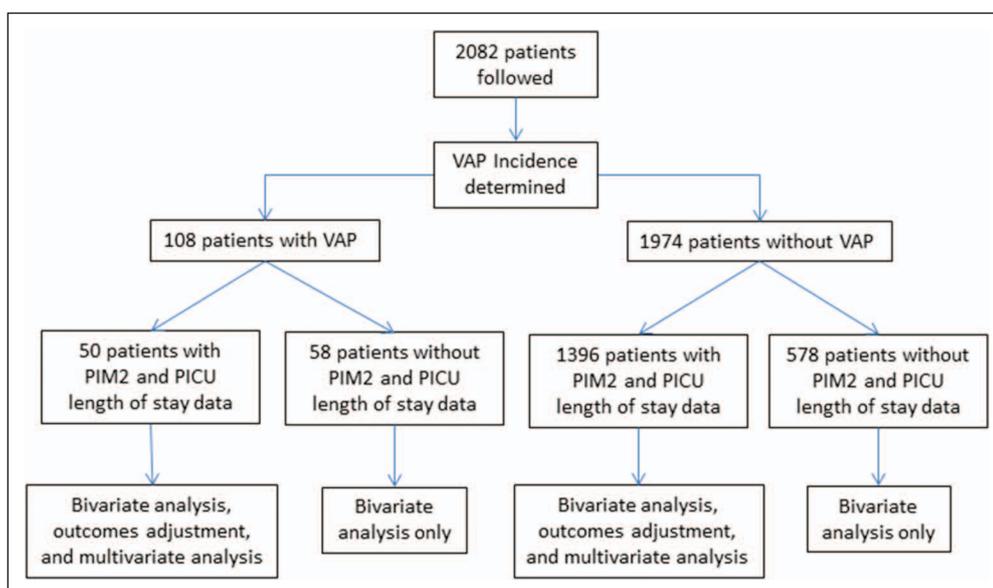
Risk Factor Analysis
Bivariate analysis (**Table 1**) demonstrated that patients who received chemotherapy before ($p = 0.048$) or during mechanical ventilation ($p = 0.004$), received a bone marrow transplant prior to mechanical ventilation ($p = 0.002$), had their endotracheal tube replaced ($p = 0.0001$), received high-frequency oscillatory ventilation ($p = 0.0001$), and underwent flexible bronchoscopy ($p = 0.0006$) were all at higher risk for a VAP event. Greater length of mechanical ventilation was also positively associated with the likelihood of a VAP event ($p = 0.001$). The only factor that was found to be protective against VAP diagnosis was admission on a home ventilator. Additional Kaplan-Meier analysis of group differences in days from mechanical ventilation until first VAP event (**Fig. 3**) demonstrated significance for mechanical ventilation in last 30 days being protective from VAP ($p = 0.003$) and bone marrow transplant prior to mechanical ventilation being associated with VAP ($p = 0.011$).

Multivariate Analysis
The GEE model consisted of eight factors plus PIM-2. Factors associated with the development of VAP were replacement of endotracheal tube (OR, 2.12 [1.09, 4.14]; $p = 0.027$) and part-time mechanical ventilation (OR, 2.61 [1.11, 6.14]; $p = 0.028$). Ventilator days prior to VAP diagnosis was not found to be significant ($p = 0.96$).

Evaluation of Diagnostic Criterion
The CDC-PNU-1 criterion notation frequencies are displayed in **Table 2**. All criteria

Figure 2. Flowchart of the different patient populations represented in the analyses. PIM2 = Pediatric Index of Mortality 2, VAP = ventilator-associated pneumonia.

TABLE 1. Bivariate Analysis of Risk Factors Associated With Ventilator-Associated Pneumonia

Risk Factors		n	VAP (n = 108)	No VAP (n = 1,974)	p
Age (mo), median (CI)		2,081	16.00 (11.00, 27.00)	13.00 (11.00, 15.00)	0.3134
Weight (kg), median (CI)		2,081	10.55 (7.90, 12.70)	8.80 (8.30, 9.30)	0.2424
Admitted on a home ventilator (%)	Yes	162	3 (1.85)	159 (98.15)	0.0423
	No	1,920	105 (5.47)	1,815 (94.53)	
Transferred on a ventilator (%)	Yes	745	35 (4.70)	710 (95.30)	0.4523
	No	1,337	73 (5.46)	1,264 (94.54)	
Ventilated in last 30 d (%)	Yes	444	18 (4.05)	426 (95.95)	0.2248
	No	1,638	90 (5.49)	1,548 (94.51)	
Hospitalized in last 30 d (%)	Yes	740	42 (5.68)	698 (94.32)	0.4556
	No	1,342	66 (4.92)	1,276 (95.08)	
Antibiotics in last 7 d (%)	Yes	825	47 (5.70)	778 (94.30)	0.3956
	No	1,257	61 (4.85)	1,196 (95.15)	
Prior thoracic disease (%)	Yes	898	54 (6.01)	844 (93.99)	0.1388
	No	1,184	54 (4.56)	1,130 (95.44)	
Immunosuppressed (%)	Yes	163	14 (8.59)	149 (91.41)	0.0622
	No	1,919	94 (4.90)	1,825 (95.10)	
Bone marrow transplant within 90 d (%)	Yes	35	7 (20.00)	28 (80.00)	0.0017
	Off	2,047	101 (4.93)	1,946 (95.07)	
Replaced endotracheal tube (%)	Yes	325	31 (9.54)	294 (90.46)	0.0001
	No	1,757	77 (4.38)	1,680 (95.62)	
Flexible bronchoscopy (%)	Yes	139	17 (12.23)	122 (87.77)	0.0006
	No	1,943	91 (4.68)	1,852 (95.32)	
High-frequency oscillatory ventilation (%)	Yes	99	15 (15.15)	84 (84.85)	0.0001
	No	1,983	93 (4.69)	1,890 (95.31)	
Part-time ventilation (%)	Yes	156	14 (8.97)	142 (91.03)	0.0368
	No	1,926	94 (4.88)	1,832 (95.12)	
Tracheal intubation type (%)					
Oral	Yes	1,452	79 (5.44)	1,373 (94.56)	0.4286
	No	630	29 (4.60)	601 (95.40)	
Nasal	Yes	327	11 (3.36)	316 (96.64)	0.1054
	No	1,755	97 (5.53)	1,658 (94.47)	
Tracheostomy	Yes	342	20 (5.85)	322 (94.15)	0.5468
	No	1,740	88 (5.06)	1,652 (94.94)	
Pediatric index of mortality-2 score, median (CI)		1,448	−3.48 (−4.28, −3.20)	−3.44 (−3.48, −3.40)	0.2846
Ventilator days as risk for VAP, median (CI)		2,082	4.50 (4.00, 5.00)	3.00 (3.00, 3.00)	0.001

VAP = ventilator-associated pneumonia.
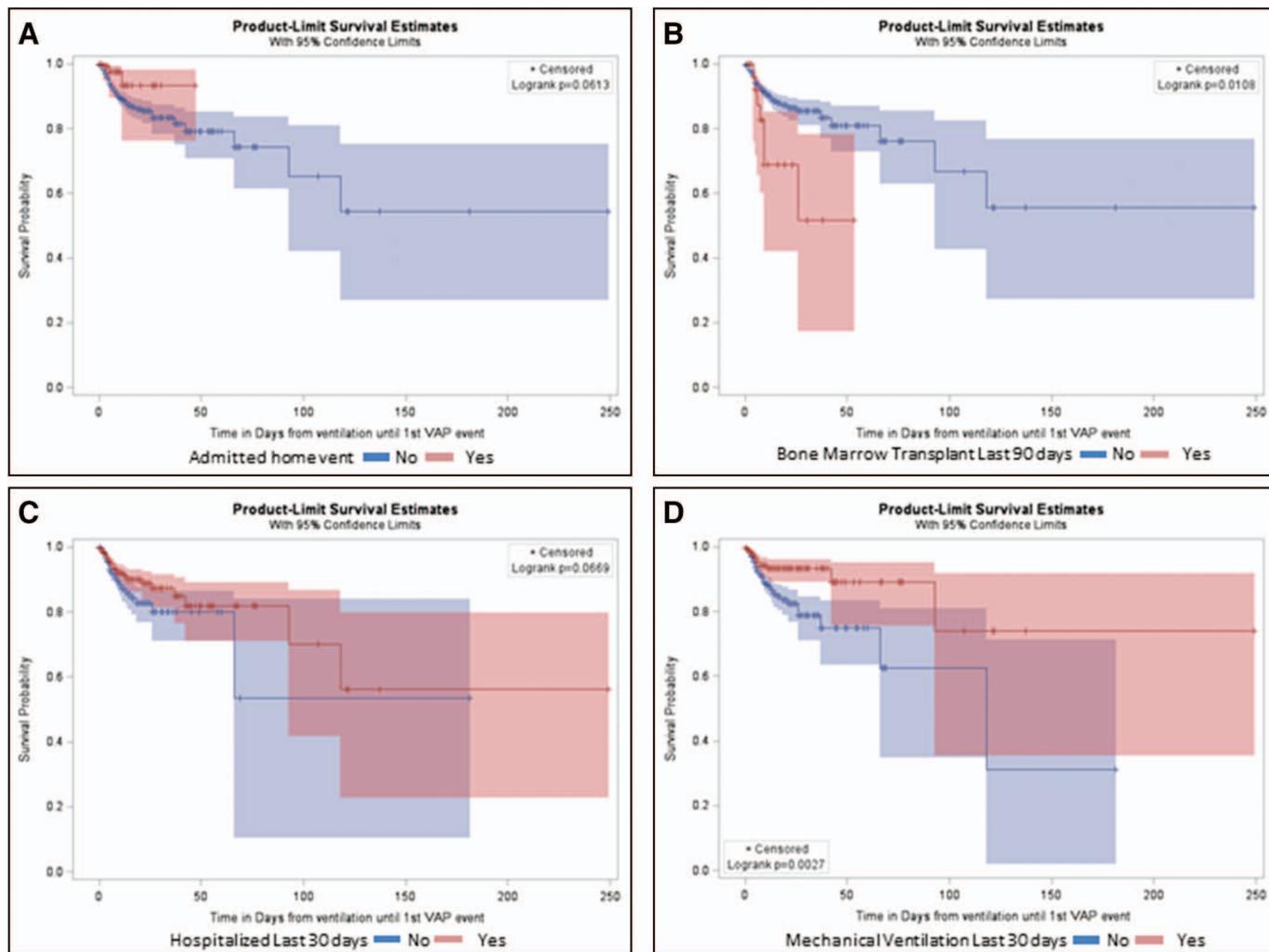
Figure 3. Survival analysis using Kaplan-Meier method with log-rank test to compare group difference in days from ventilation until 1st ventilator-associated pneumonia (VAP) event. **A**, When mechanical ventilator days before 1st VAP event are the same, "No" group has higher failure probability compared to "Yes" group. **B**, When mechanical ventilator days before 1st VAP event are the same, "Yes" group has higher failure probability compared to "No" group. **C**, When mechanical ventilator days before 1st VAP event are the same, "No" group has higher failure probability compared to "Yes" group. **D**, When mechanical ventilator days before 1st VAP event are the same, "No" group has higher failure probability compared to "Yes" group.

demonstrated greater frequency in the VAP patients when compared with those who did not develop VAP.

The vast majority of patients developed their VAPs within the first 10 days of mechanical ventilation. **Figure 4** demonstrates Kaplan-Meier VAP free survival as per mechanical ventilation days. More than 50% of the patients who developed VAP did so by the 5th day of mechanical ventilation and more than 90% by day 14.

DISCUSSION

We conducted a prospective, multicentered, observational assessment and external validation of the CDC PNU-1 VAP criteria for children. This study represents the largest multicentered evaluation of pediatric VAP to date. The use of severity of illness adjustment allowed for improved assessment of patient outcomes. The inclusion of tertiary and nontertiary hospitals allows for generalization of the results.

Our primary outcomes demonstrated a VAP rate and prevalence that is consistent with other reports of pediatric VAP in the literature, although it is still significantly higher than the NHSN rates that are reported by the CDC (1). The disparity may be due to the predominance of tertiary care centers in our hospital group as well as in other reports in the literature or due to the strict surveillance methodology that was used. Our methodology minimized clinical personnel bias by using objective criteria and having diagnosis performed by individuals not involved in the bedside care of the patient. Additionally, the use of prospective, daily surveillance has been shown to improve detection rates of nosocomial infections (17).

The significant increase in mechanical ventilation days and the increase in ICU length of stay are previously documented (4, 6, 8). These outcome differences persisted in our study when corrected for severity of illness and other patient factors. This is similar to the results demonstrated by Srinivasan et al (4), with increased duration of mechanical ventilation and

TABLE 2. Frequency of Diagnostic Criterion

Criteria	n	VAP Cases (%)	Non-VAP Cases (%)
Less than 1 yr (total)	926	48	878
Worsening gas exchange[a]	262	48 (18.32)	214 (81.68)
Temperature instability	88	25 (28.41)	63 (71.59)
Leukopenia or leukocytosis	135	23 (17.04)	112 (82.96)
Purulent sputum	96	26 (27.08)	70 (72.92)
Apnea	61	15 (24.59)	46 (75.41)
Wheeze	303	32 (10.56)	271 (89.44)
Cough	39	5 (12.82)	34 (87.18)
Bradycardia	63	21 (33.33)	42 (66.67)
1–12 yr (total)	498	58	440
Worsening gas exchange	134	42 (31.34)	92 (68.66)
Fever or hypothermia	90	41 (45.56)	49 (54.44)
Leukopenia or leukocytosis	96	34 (35.42)	62 (64.58)
Purulent sputum	4	3 (75.00)	1 (25.00)
Cough or dyspnea	125	31 (24.80)	94 (75.20)
Rales or crackles	108	37 (34.26)	71 (65.74)
> 12 yr (total)	176	9	167
Worsening gas exchange	68	6 (8.82)	62 (91.18)
Fever or hypothermia	39	5 (12.82)	34 (87.18)
Leukopenia or leukocytosis	22	7 (31.82)	15 (68.18)
Purulent sputum	0	0 (0)	0 (0)
Cough or dyspnea	27	3 (11.11)	24 (88.89)
Rales or crackles	30	8 (26.67)	22 (73.33)

VAP = ventilator-associated pneumonia.
[a]Worsening gas exchange is a prerequisite for all VAP cases < 1 year old.

ICU length of stay after correction for severity of illness, age, gender, race, and diagnosis. Increase in mortality is known to occur with VAP in adults, and pediatrics studies have demonstrated an association with VAP diagnosis, but adjustment for admission severity of illness had not previously demonstrated VAP as a predictor of mortality. After correction for severity of illness and other patient risk factors, we found that patients with VAP were three times more likely to die. These significant changes in patient outcomes continue to lend credence to the importance of VAP diagnosis and prevention.

We assessed factors that were previously noted to be independent or associated predictors of pediatric VAP. We did not find any difference in risk for VAP when comparing age or weight. Duration of mechanical ventilation prior to VAP diagnosis was found to be associated with VAP but was not found to be an independent association, although Casado et al (7) did recently demonstrate ventilator days as an independent risk factor for healthcare-associated pneumonia. The lack of an independent association between ventilator days and VAP

brings to light that patient factors may be large contributors to the risk of developing VAP.

We found that replacement of the endotracheal tube (defined in our study as reintubation within 24 hr from prior removal) was also associated with VAP. This may partially explain the worsened outcomes in patients with unplanned extubations (18). The relation of VAP to unplanned extubation has been previously noted in neonatal and adult populations (19, 20).

Another independent association with VAP was part-time ventilation. For the purpose of the study, this was defined as daily ventilation for periods of 8–23 hr/d without active weaning. This association with VAP may be due to the frequent ventilator circuit interruption which in most prevention bundles is avoided. Additionally, less continuous positive pressure may contribute to decreased airway clearance, increased atelectasis, and intermittent airway obstruction, which could all increase the likelihood for development of pneumonia.

More than 25% of the VAP-positive patients were diagnosed within the first 2 days after initiation of mechanical
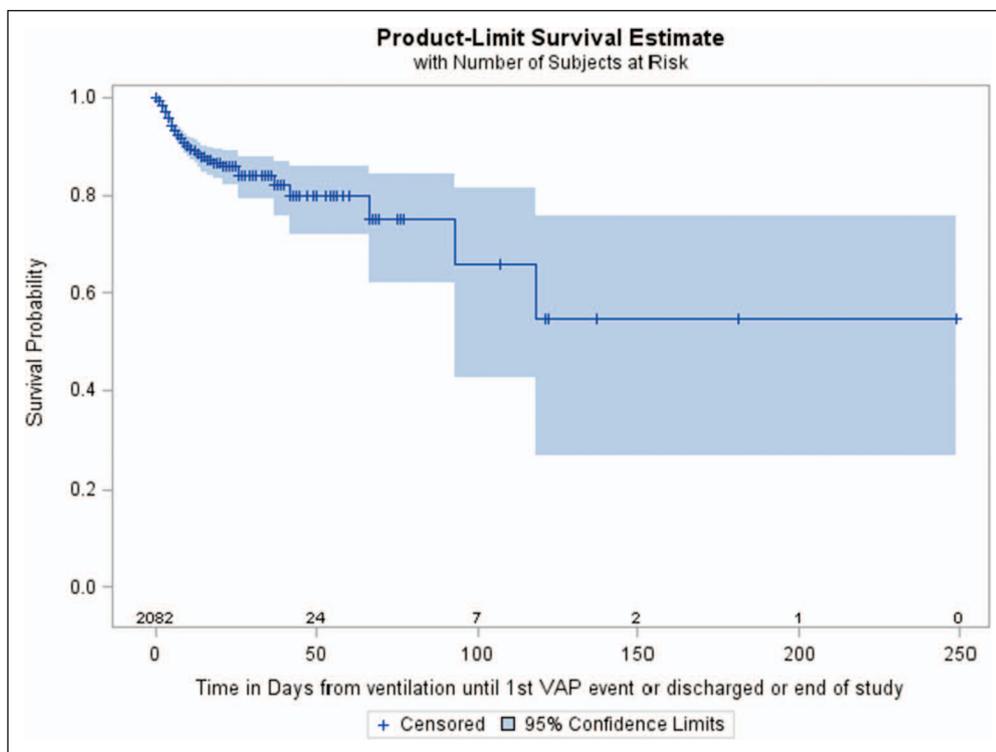
Figure 4. Kaplan-Meier survival plot of ventilator-associated pneumonia (VAP) diagnosis as compared to ventilator days.

ventilation in the PICU. Although it is possible to develop nosocomial pneumonia secondary to intubation/mechanical ventilation in this time period, a more plausible explanation is that these VAP events reflect initial disease progression and not a hospital-associated infection (21, 22). The current guidelines do not account for this common clinical phenomenon, so strict adherence to the current CDC criteria may lead to a falsely elevated VAP rate. Other adult guidelines, such as those from the American Thoracic Society, avoid these false positives by requiring 48–72 hours after intubation until the diagnosis of VAP can be made (23). In the current healthcare economy where nosocomial infections are being targeted for nonreimbursement, the potential for false positives must be minimized. An iterative, evidence-based process will optimize the latest guidelines.

There are several limitations to our report. The foremost is the debated accuracy of the clinical diagnosis of pediatric VAP as defined by the CDC. In our assessment of current practice, clinical diagnosis was the most common method used among pediatric hospitals as reported by NHSN data and our survey of interested institutions. The use of lower respiratory samples for microbiological assessment was inconsistent, and the CDC does not provide guidance for the use of tracheal aspirate cultures. Understanding the limitations of the PNU-1 criteria, we strove to harmonize the process of detection across the institutions in the study to ensure similar diagnosis and at least minimize variability in application of the PNU-1 criteria.

Another limitation associated with diagnosis was the variability in CXR frequency for patients. We did not dictate variables for CXR performance and left this to clinical decision making or hospital standard. Patient populations that require greater number of CXRs, such as those undergoing bronchoscopy or being immunosuppressed, may be biased toward a PNU-1 VAP diagnosis. Sites were asked to partner with their departments of radiology to encourage standardized language in CXR reports that would facilitate consistent interpretation for VAP screening. Because the CXR is the screening criteria for PNU-1 VAP diagnosis, this may have limited our ability to diagnose VAP effectively across all institutions, although the data garnered represents real-world analysis of pediatric VAP diagnosis by the rigorous application of the PNU-1 clinical criteria.

Another limitation was regarding data acquisition because only a subset of our patients (1,446) belonged to institutions that were submitting data to VPS[LLC], therefore limiting severity of illness correction and multivariate analysis to this group of patients. Additionally, a difference in ratios of VAP and non-VAP patients in the VPS subset as compared to the overall dataset was present. Therefore, our results are not generalizable to the entire group of institutions involved, although the institutions providing VPS data still represent a variety of PICUs.

Although the clinical diagnosis of VAP is debated, the outcomes we portray by strictly adhering to the PNU-1 CDC age-based criteria demonstrate clinical significance of the diagnosis even after adjustment for patient factors including severity of illness. The new ventilator-associated events surveillance in adults seeks to provide a more objective method of surveillance for mechanically ventilated patients, but is not related to infection. It maybe that the PNU-1 diagnostic criteria are also not specific to infection due to the many issues in regard to application and subjectivity of criteria, but the difference in clinical outcomes cannot be ignored. These clinical outcomes associated with VAP are generalizable to pediatric critical care populations throughout the United States. Standardization of surveillance and removal of ambiguity would improve accuracy of prevalence data and inform reduction strategies. New clinical diagnostic measures that are developed for pediatric ventilator-associated complications should continue to demonstrate clinical outcome differences with severity of illness adjustment.

CONCLUSIONS

Daily, prospective monitoring for VAP can be performed in children. Prospective monitoring of PNU-1 with strict criteria at these 16 hospitals yielded an average rate of 7.00 VAPs/1,000

patient ventilator days, much higher than the 1.1 VAPs/1,000 patient ventilator days reported by the NHSN during this time frame. VAPs were common in patients with airway manipulation (reintubation) and those that are ventilated part-time. Pediatric patients with VAP are more likely to die, have more days of mechanical ventilation, and longer ICU stays, and these outcomes persist after adjustment for patient factors.

ACKNOWLEDGMENTS

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