ORIGINAL ARTICLE

Ventilator-associated Events Surveillance in a Trauma Intensive Care Unit: A Prospective Study of Incidence, Predictive Values, Sensitivity, Specificity, Accuracy, and Concordance with Ventilator-associated Pneumonia

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ABSTRACT

Introduction: The Centers for Disease Control and Prevention (CDC) introduced a new definition of ventilator-associated events (VAEs) in 2013 in place of longstanding ventilator-associated pneumonia (VAP) definition. Three entities under VAE, ventilator-associated condition (VAC), infection-related ventilator-associated complication (IVAC), and possible ventilator-associated pneumonia (PVAP), were introduced.

Objectives: To assess the incidence of all VAEs in a tertiary care trauma ICU and to find the predictive value of VAE and sensitivity of VAE definitions for VAP.

Design: Cohort prospective study at trauma intensive care unit (ICU) of PGIMER, Chandigarh, from July 2018 till June 2019.

Materials and methods: Patients admitted in trauma ICU were checked for VAP and VAE criteria defined by CDC.

Results: Four hundred and sixty five patients were observed. Around 378 patients were included in the study with 4046 patient days and 3031 mechanical ventilation (MV) days. Incidence rate of PVAP, IVAC, VAC, and VAP was 2.97, 6.60, 10.23, and 9.24 per 1000 ventilator days, respectively. Sensitivity, specificity, positive predictive value, and negative predictive value (NPV) of diagnosing VAP were 0.61, 0.97, 0.68, and 0.97 for VAC; 0.80, 0.97, 0.57, and 0.99 for IVAC; and 0.78, 0.94, 0.25, and 0.9 for PVAP, respectively. Kendall’s W test showed that there was very poor concordance between VAP and VAE.

Keywords: Infection-related ventilator-associated complication, Possible ventilator-associated pneumonia, Ventilator-associated condition, Ventilator-associated events, Ventilator-associated pneumonia.
**Materials and Methods**

**Design**  
A prospective study was done at the Trauma ICU of PGIMER, Chandigarh, from July 2018 till June 2019.

**Inclusion and Exclusion Criteria**  
All the patients who were admitted in the Trauma ICU and mechanically ventilated for more than two days were recruited in the study. The patients who were not mechanically ventilated or mechanically ventilated for less than 2 days or organ donors were excluded from the surveillance.

**Data Collection**  
The data collection forms were made and finalized by the study group. One dedicated infection control nursing officer visited the ICU every day at same time of the day for data collection. The denominator data were collected for all the patients present at the Trauma ICU. The patients were prospectively followed up for the development of VAP (NHSN definition) and VAEs (Flowchart 1 and Table 1) based on criteria defined by CDC. Daily monitoring of positive-end expiratory pressure (PEEP), fraction of inspired oxygen (FiO₂), fever, total leukocyte count, mental status deterioration, increase in volume and change in character of secretions, tachypnea, bronchial breath sounds, worsening gas exchange, and progressive or new infiltrates/consolidation/cavitation, along with new antibiotics and positive microbiology cultures. All the patients who fit into the criteria of VAP and VAE were recognized and discussed with the study group and included in numerator data.

**Statistical Analysis**  
Kendall’s coefficient of concordance was calculated using the Statistical Package for Social Sciences software version 20 to find the agreement between VAE (VAC, IVAC, and PVAP) and VAP. MEDCALC statistical software was used to calculate the PPV, NPV, sensitivity, specificity, and accuracy of the VAE (VAC, IVAC, and PVAP) for the diagnosis of VAP.

**Results**  
Five hundred and nine admissions were enrolled over a period of 1 year in the trauma ICU. One hundred and thirty-one patients were excluded from the study. Three hundred and seventy-eight patients who were mechanically ventilated for more than two days were recruited as study population for surveillance of VAP and VAE. The majority of patients were male (76.2%) and around 70% of the patients were less than 40 years of age without any co-morbidity. Most of them (73.3%) were received after average 2–3 days stay in emergency unit and 50% of the patients were intubated either in emergency or outside PGIMER (Table 2). The total patient days in the study were 4046 and mechanical ventilation days were 3031. The MV utilization ratio was 0.75. Out of total study population 40 (10.6%) patients developed VAE and/or VAP-NHSN (Table 3). The incidence of VAC ranged from 0 to 24 in 12 months with a peak in April (20), while that of VAP ranged from 0 to 18.96 with a peak in March (9.48) (Fig. 1). The mortality was 21.4% overall, 66.7% in patients who developed VAP and 73.4% in those with VAC (Table 2).

**Discussion**  
VAE surveillance has not been widely adopted beyond the United States. One of the reasons may be that there exists uncertainty about the overlap between VAP and VAE, thereby with implications of the same on clinical utility. We sought to determine the accuracy of VAC for the diagnosis of VAP and vice versa in a setting of trauma ICU in our tertiary care hospital in India.

As previous studies have also reported,6,7 we found a higher incidence of VAP compared to VAE (10.2 vs 9.2 per 1000 MV days). However, the incidence of VAP was more than IVAC (6.6/1000 MV days) and much higher than PVAP (2.97/1000 MV days). Here was therefore a poor concordance of VAP with VAC (0.005), IVAC (0.095), and PVAP (0.374) in our patients. The PPV of VAC and IVAC for VAP-NHSN was 67.9 and 57.1%, respectively, while that of PVAP for VAP was only 25%. The sensitivity of VAC and IVAC for VAP-NHSN was 61.3 and 80.0%, respectively.

Table 6 lists the previous studies conducted to compare VAP and VAE in different study populations. The results of these studies also show poor relation between both definitions. V-associated event surveillance did not accurately detect cases of traditionally defined VAP in ICUs.

As the study was conducted in trauma intensive care, the majority of the cohort comprised severe head injury. In such patient profile, it may be worth noting that certain trauma-related factors like depressed consciousness, loss of protective reflexes, reduced muscle strength, and delayed presentation may contribute to higher infectivity and mortality.

**Comparison of Challenges Faced during VAP and VAE Surveillance**  
To meet VAP definition, subjective criteria [amount of endotracheal (ET) secretions, change in character of ET secretions, progressive/new and persistent X-ray changes] are applied, which for some patients, clinicians and surveillance team might find difficult to agree on. Ventilator-associated event is more objective, easy to use, and has less chances of disagreement on case definition. However, there is a strict definition for window period in VAE which sometimes excludes some cases if the definition criteria meet ± few days of that period. For example, if a tracheal aspirate (TA) culture has come positive 1–4 days before worsening PEEP/FiO₂, clinicians sometimes do not repeat the TA for surveillance purposes. Our study found a low concordance found between VAP and VAE (including VAC, IVAC, and PVAP). It is possible that the new VAE definitions are missing out on the patients who would fit into VAP criteria.

Klompas and Berra8 found that a screening ventilator setting for VAC captures a similar set of complications to traditional VAP.
Flowchart 1: Ventilator-associated events (VAE) surveillance algorithm

Patient has a baseline period of stability or improvement on the ventilator, defined by ≥ 2 calendar days of stable or decreasing daily minimum* FiO₂ or PEEP values. The baseline period is defined as the 2 calendar days immediately preceding the first day of increased daily minimum PEEP or FiO₂

Daily minimum defined by lowest value of FiO₂ or PEEP during a calendar day that is maintained for > 1 hour.

After a period of stability or improvement on the ventilator, the patient has at least one of the following indicators of worsening oxygenation:
1) Increase in daily minimum *FiO₂ of ≥ 0.20 (20 points) over the daily minimum FiO₂ of the first day in the baseline period, sustained for ≥ 2 calendar days.
2) Increase in daily minimum *PEEP values of ≤ 3 cmH₂O over the daily minimum PEEP of the first day in the baseline period, sustained for ≥ 2 calendar days.

Ventilator-associated condition (VAC)

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, the patient meets both of the following criteria:
1) Temperature > 38°C or <36°C, OR white blood cell count > 12,000 cells/mm³ or <4,000 cells/mm³ And
2) A new antimicrobial agent(s) (see appendix for eligible antimicrobial agents) is started, and is continued for ≥ 4 qualifying antimicrobial days (QAD)

Infection-related ventilator-associated complication (IVAC)

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met (taking into account organism exclusions specified in the protocol)
1) Criterion 1: positive culture of one of the following specimens, meeting quantitative or semiquantitative threshold as outlined in protocol, without requirement for purulent respiratory secretions:
   - Endotracheal aspirate, >105 CFU/mL or corresponding semiquantitative result
   - Bronchoalveolar lavage, >104 CFU/mL or corresponding semiquantitative result
   - Lung tissue, >104 CFU/g or corresponding semiquantitative result
   - Protected specimen brush, >103 CFU/mL or corresponding semiquantitative result

2) Criterion 2: purulent respiratory secretions (defined as secretions from the lungs, bronchi, or trachea that contain >25 neutrophils and <10 squamous epithelial cells per low power field [lpf, x100]) PLUS organism identified from one of the following specimens (to include qualitative culture, or quantitative/semiquantitative culture without sufficient growth to meet criterion #1):
   - Sputum
   - Endotracheal aspirate
   - Bronchoalveolar lavage
   - Lung tissue
   - Protected specimen brush

   If the laboratory reports semiquantitative results, those results must correspond to the quantitative thresholds see additional instructions for using the purulent respiratory secretions criterion in the VAE protocol

3) Criterion 3: one of the following positive tests:
   - Organisms identified from pleural fluid (where specimen was obtained during thoracentesis or initial placement of chest tube and NOT from an indwelling chest tube)
   - Lung histopathology, defined as: 1) abscess formation or foci of consolidation with intense neutrophil accumulation in bronchioles and alveoli; 2) evidence of lung parenchyma invasion by fungi (phyphae, pseudophyphae or yeast forms); 3) evidence of infection with the viral pathogens listed below based on results of immunohistochemical assays, cytology, or microscopy performed on lung tissue
   - Diagnostic test for Legionella species
   - Diagnostic test on respiratory secretions for influenza virus, respiratory syncytial virus adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus, coronavirus

Possible ventilator-associated pneumonia (PVAP)
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Table 1: VAP_PNEU1 criteria (CDC)

For ANY PATIENT, at least one of the following:
- Fever (>38.0°C or >100.4°F)
- Leukopenia (≤4,000 WBC/mm³) or leukocytosis (>12,000 WBC/mm³)
- For adults >70 years old, altered mental status with no other recognized cause

And at least two of the following:
- New onset of purulent sputum or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements
- New onset or worsening cough, or dyspnea, or tachypnea
- Rales or bronchial breath sounds
- Worsening gas exchange (for example: O₂ desaturations (for example: PaO₂/FiO₂ <240), increased oxygen requirements, or increased ventilator demand)

Two or more serial chest imaging test results with at least one of the following:
- New and persistent or
- Progressive and persistent
  - Infiltrate
  - Consolidation
  - Cavitation
  - Pneumatoceles, in infants ≤1-year-old

Table 2: Demographic data of study participants

| Categories            | Number (%) |
|-----------------------|------------|
| Admission units       |            |
| Neurosurgery          | 264 (69.8) |
| Orthopedics           | 43 (11.4)  |
| Others                | 71 (18.8)  |
| Gender                |            |
| Male                  | 288 (76.2) |
| Female                | 90 (23.8)  |
| Age (years)           |            |
| <18                   | 84 (22.2)  |
| 19–40                 | 183 (48.4) |
| 41–60                 | 76 (20.1)  |
| >61                   | 22 (5.8)   |
| No data               | 13 (3.4)   |
| Previous unit         |            |
| Emergency             | 277 (73.3) |
| Ward                  | 76 (20.1)  |
| No data               | 25 (6.6)   |
| Intubation             |            |
| Before ICU admission  | 189 (50)   |
| Intubated inside ICU  | 189 (50)   |
| End status            |            |
| Expired               | 81 (21.4)  |
| LAMA*                 | 10 (2.6)   |
| Transferred to another unit | 287 (76) |
| Trauma with head injury |          |
| Yes                   | 231 (61.1) |
| No                    | 84 (22.2)  |
| No data               | 63 (16.7)  |
| Comorbidity**         |            |
| Present               | 27 (7.1)   |
| Not present           | 181 (47.9) |
| No data               | 170 (45)   |

*Left against medical advice
**Diabetes mellitus, hypertension, asthma, alcoholism, coronary artery disease, hypothyroidism, and cerebrovascular accident

Table 3: Incidence of VAP and VAE in trauma ICU from July 2018 till June 2019

| Entity            | Number (%) | Incidence per 1,000 MV days |
|-------------------|------------|-----------------------------|
| VAP               | 28 (7.41)  | 9.24                        |
| VAC/VAE           | 31 (8.20)  | 10.23                       |
| IVAC              | 20 (5.29)  | 6.60                        |
| PVAP              | 9 (2.38)   | 2.97                        |
| VAP but no VAE    | 9 (2.38)   | 2.97                        |
| VAC but no VAP    | 12 (3.17)  | 3.96                        |
| IVAC but no VAP   | 4 (1.06)   | 1.32                        |
| PVAP but no VAP   | 2 (0.53)   | 0.66                        |
| Both VAC and VAP  | 19 (5.02)  | 6.26                        |

Limitation of the Study and Future Areas of Work

There are many extraneous variables that may have affected the incidence of VAP and VAC. First, the majority of patients in trauma ICU reach ICU after an average 2–3 days stay in emergency. Some of the patients even get initial first aid or sometimes get endotracheal intubation done at the local hospitals. The condition in which the initial intubation done and the care taken post intubation affects the chest status of patients. Second, patients in trauma ICU sometimes have conditions like fracture of ribs, hypoventilation, pneumothorax, aspiration, etc. These patients have higher chances of deteriorating post ventilation. So, it would be worthwhile to conduct studies to evaluate the role of these factors in this patient population in the future.

Conclusion

As a surveillance definition, VAC, IVAC, and PVAP have poor concordance with VAP-NHSN. Many extraneous factors as mentioned in the limitations in the study might have contribution to the change in trends. More studies are needed to study the role of pre ICU intervention factors in this population.
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Fig. 1: Incidence rate of VAC, IVAC, PVAP and VAP from July 2018 to June 2019

Table 4: Test characteristics of VACs for the diagnosis of VAP

|                      | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | Accuracy (95% CI) |
|----------------------|----------------------|----------------------|--------------|--------------|-------------------|
| VAC for VAP          | 61.3% (42.2–78.2)    | 97.4% (95.1–98.8)    | 67.9% (51.1–81.0) | 96.6% (94.8–97.8) | 94.4% (91.6–96.5) |
| IVAC for VAP         | 80.0% (56.3–94.3)    | 96.7% (94.2–98.3)    | 57.1% (42.4–70.8) | 98.9% (97.3–99.5) | 95.8% (93.2–97.6) |
| PVAP for VAP         | 77.8% (40.0–97.2%)   | 94.31% (91.4–96.4)   | 25.0% (16.2–36.5) | 99.4% (98.1–99.8) | 93.9% (91.0–96.1) |

Table 5: Antibiogram of pathogens found during VAP and IVAC surveillance in trauma ICU from July 2018 to June 2019

| Pathogens                                      | No. of patients | AMK | MINO | CIPRO | CEFOTAX | IMI | PIP | CEFOSULB/CSL | CEFOTAZ/CTZ | DOXY | MERO | ERTA | COL | CEFEP |
|------------------------------------------------|-----------------|-----|------|-------|---------|-----|-----|-------------|------------|------|------|------|-----|-------|
| Acinetobacter baumannii                         | 10              | 0   | 3    | 0     | 0       | 0   | 1   | 0           | 0          | 0    | 0    | 0    | 0   | 0     |
| Klebsiella pneumoniae                           | 7               | 4   | 1    | 2     | 1       | 1   | 2   | 2           | 1          | 3    | 1    |      |     |       |
| Escherichia coli                                | 3               | 2   | 1    | 0     | 0       | 1   | 1   | 1           | 0          | 0    | 1    | 0    | 3   | 0     |
| Pseudomonas aeruginosa                          | 2               | 2   | 2    | 2     | 2       | 2   | 2   | 2           | 2          | 2    | 2    | 2    | 2   | 2     |
| Enterobacter Spp.                               | 2               | 2   | 1    | 2     | 0       | 0   | 0   | 0           | 0          | 0    | 0    | 0    | 1   |       |
| Methicillin resistant staphylococcus aureus      | 2               |     |      |       |         |     |     |             |            |      |      |      |     |       |

| Pathogens                                      | No. of patients | TIG | GENT | TETRA | LEVO | CHL | VANCO | TEICO | SAM | LNZ | CLIND | OXA | ERYTHRO |
|------------------------------------------------|-----------------|-----|------|-------|------|-----|-------|-------|-----|-----|-------|-----|---------|
| Acinetobacter baumannii                         | 10              | 4   | 0    | 2     | 1    |     |       |       |     |     |       |     |         |
| Klebsiella pneumoniae                           | 7               | 1   |      |       |      |     |       |       |     |     |       |     |         |
| Escherichia coli                                | 3               | 2   |      |       |      |     |       |       |     |     |       |     |         |
| Pseudomonas aeruginosa                          | 2               |     |      |       |      |     |       |       |     |     |       |     |         |
| Enterobacter Spp.                               | 2               |     |      |       |      |     |       |       |     |     |       |     |         |
Table 6: List of previous studies conducted to compare VAP and VAE in different study populations

| Author, country | Study setting                                                                 | Incidence of VAP/VAE | Sensitivity (%) of VAE to detect VAP | Specificity (%) | PPV (%) | NPV (%) | Conclusion |
|-----------------|-------------------------------------------------------------------------------|----------------------|--------------------------------------|-----------------|--------|--------|------------|
| Piriyapatsom et al., Massachusetts, USA | Retrospective, single-center, trauma subjects, IVAC compared to VAP | IVAC or VAP 35.6, VAP 29.6% Both 8.3% | IVAC 28.12 | 91.45 | 58.06 | 75.14 | IVAC criteria had a low accuracy for identifying VAP-NHSN in subjects with high-risk trauma |
| Klouwenberg et al., Netherlands | Prospective cohort study in two Dutch academic medical centers | VAC 10/1000 MV days IVAC 4.2 VAE–VAP 32. VAP 8.0/100 MV days | VAC 33% IVAC 17% | | | | Noted much poorer concordance between the novel VAE algorithm and VAP. The incidence rate of VAC, IVAC, VAE-VAP, and VAP in the present study was comparable (10.23, 6.60, 6.26, and 9.24, respectively). Poor concordance noted between VAP and VAE in the present study too |
| Fan et al., Wuhan, China | Meta-analysis of 18 studies | VAC 10.23 IVAC 6.6 | VAE <50% | >80% | <50% | >80% | VAE surveillance missed many cases of VAP, and the population characteristics identified by the two surveillance paradigms differed |
| Boyer et al., St Louis, Missouri | Prospectively surveyed 1,209 patients ventilated for 2 calendar days at medical surgical ICU | VACs 5.5% (7/1,000 MV days) IVAC 3.6%1,000 MV days VAP 10.0/1,000 MV days | VAC 25.9% | | | | VAC criteria captured a minority of VAP episodes |
| Meagher et al., USA | Retrospective study, adult trauma patients (2012–2017) | VAE 8.1% VAP 7.4% and Both 4.1% of patients | | | | | The proportions of individual entities were found to be comparable to the present study for VAC (8.2%), VAP (7.41%), and VAE + VAP (5.02%) |
| Younan et al., China | Retrospective study, trauma patients | “New”VAP 6.6% “Old”VAP 30.9% Both 5.8% | | | | | The concordance between new and old definitions was poor (kappa 0.22), similar to the present study |
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