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Burn patients with infection-related ventilator associated complications have worse outcomes compared to those without ventilator associated events

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ABSTRACT

Background: The Centers for Disease Control and Prevention (CDC) replaced its definition for ventilator-associated pneumonia (VAP) in 2013. The aim of the current study is to compare the outcome of burn patients with ventilator associated events (VAEs).
Methods: Burn patients with at least two days of ventilator support were identified from the registry between 2013 and 2016. Kruskal-Wallis and Fisher's exact tests were utilized for continuous and categorical variables, respectively. A logistic regression was used for the association between VAE and in-hospital mortality.
Results: 243 patients were admitted to our burn center, of whom 208 had no VAE, 8 had a VAC, and 27 had an IVAC or PVAP. There was no difference in hospital length of stay, ICU length of stay and ventilator support days between those with no VAE and a VAC. Those with IVAC-plus had significantly worse outcomes compared to patients with no VAEs.
Conclusions: Burn patients with IVAC-plus had significantly longer hospital and ICU lengths of stay, days on ventilator compared with patients with no VAEs.

1. Introduction

The most significant complication after burn injury is pneumonia, with an incidence of 10–65%.[1] In D'Avignon's autopsy series,[2] bacterial pneumonia was a more common cause of mortality in burn patients than bacterial wound infections and second only to bacterial blood stream infections. Ventilator associated pneumonia (VAP) is also associated with a high mortality rate, with reports in the range of 30–50%[3,4]; as a result, multiple measures to decrease pneumonia incidence such as the VAP prevention bundle have been implemented.[5] The American Burn Association (ABA) consensus conference recommendations for pneumonia[6] are helpful to in the clinical diagnosis of pneumonia in burn patients; however, most of these guidelines involve subjective criteria such as chest x-ray interpretation and changes in character of sputum which can make more vulnerable to inaccuracies and bias. The Center for Disease Control and Prevention (CDC) replaced the old VAP definition with the new more objective ventilator-associated events (VAEs) algorithm in 2013,[7,8] the new algorithm allows for a fully automated electronic method for surveillance of VAEs.[9]

Klompas et al. (2014), using the new VAE algorithm, reported increased length of ventilator support, longer hospital stay, and higher mortality for patients with VAEs; however, their study population included all patients on mechanical ventilation and was not specific to the burn population. Stevens[9] and Boyer[10] reported similarly increased mortality rates among patients with ventilator associated conditions (VACs) were significantly higher than those without VACs; yet again the study population was not specific to the burn patient population. In light of the limitations of the prior research, we sought to determine the clinical outcomes of burn patients with VAC, infection related ventilator associated

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complication (IVAC), and no VAEs within the burn patient population.

2. Materials and methods

2.1. Study design and variable definitions

The study was approved by the University of Alabama at Birmingham (UAB) Institutional Review Board (IRB). The study population for this retrospective cohort study included patients aged 18 years or older admitted to a large, academic burn center between 2013 and 2016 that had at least two days of ventilator support.

Ventilator associated events (VAEs) were defined using NHSN criteria and were categorized as ventilator-associated condition (VAC), infection-related ventilator associated complication (IVAC), and possible ventilator-associated pneumonia (PVAP). The VAC criteria were met if one of two conditions occurred: 1) an increase in fraction of inspired oxygen (FiO2) of greater than or equal to 20% over the daily minimum FiO2 in the baseline period occurs and is sustained for two or more calendar days or 2) an increase in the daily minimum positive end-expiatory pressure (PEEP) values of $\geq$ 3 cm H_2O occurs over the daily minimum PEEP in the baseline period and is sustained for two or more days after a baseline period of at least two days of stable or improved FiO2 or PEEP while ventilated. The IVAC criteria were met if a patient with VAC in addition to a core temperature >38 °C or <36 °C or a WBC $\geq$12,000 or $\leq$4000 cells/mm3 and were administered eligible antimicrobial agents that were continued for four or more days. To meet the PVAP criteria, in addition to meeting the criteria for VAC and IVAC, patients had to have $>10^4$ colony forming units (CFU) of microorganism on cultures of broncho-alveolar lavage (BAL) specimens, $>10^5$ CFUs from tracheal aspirate specimens, or a positive gram stain from a respiratory culture. For purposes of the current analysis, IVAC and PVAP were combined into one category called IVAC-plus due to both being related to infections.

Demographic (i.e., age, race, and sex) and injury characteristics (i.e., total burn surface area [TBSA], presence of inhalation injury) were collected from the burn registry. Electronic medical record data tables were queried to obtain clinical outcome (i.e., hospital length of stay [LOS] in days, intensive care unit [ICU] LOS in days, ventilator support days), PEEP, FiO2, white blood cell count (WBC), temperature, antimicrobial agents administered, and culture data (i.e., organism count, gram stain results, bacterial genus). The microbiological data were validated by a clinician to ensure the microorganism species, count of microorganism on gram stain and culture, WBC, and antimicrobial agent administered were classified appropriately and met CDC criteria for the various VAE classifications.

2.2. Statistical analysis

Demographic, injury, and clinical characteristics were compared among the No VAE, VAC and IVAC-plus groups using a Kruskal-Wallis and Fisher's exact test for continuous and categorical variables, respectively. For continuous variables, a Dwass, Steel, Critchlow-Fligner Method was used to pairwise comparisons to determine between which groups observed significant differences exist. A logistic regression model adjusted for age was used to estimate odds ratios (ORs) and associated 95% confidence intervals (CIs) for the association between VAE group and in-hospital mortality. Of note, nearly 20% of the patient population was missing TBSA, preventing including this variable in statistical models due to loss of sample size when doing so.

3. Results

From 2013 through 2016, a total of 243 patients were admitted to our burn center that had at least two days of ventilator support. Of these, 208 had no VAE, eight met the criteria for VAC, and 27 met the criteria for IVAC and PVAP combined.

There was no significant difference among the three groups in regards to age, race, gender, incidence of inhalation injury, TBSA, body temperature in the emergency department (ED) or respiratory rate in ED (Table 1). A significant difference was observed for hospital LOS ($p < 0.001$), ICU days ($p < 0.0001$), and ventilator support days ($p < 0.0001$). Examining pairwise comparisons, the significance was driven by the comparison of patients with no VAE to those with IVAC-plus. In particular, for those with no VAE, lower values were observed for hospital LOS (mean difference −28.1 days, $p < 0.0001$), ICU length of stay (mean difference −21.9 days, $p < 0.0001$), and ventilator support days (mean difference −20.1, $p < 0.0001$) (Table 2). There was no difference in mortality among the three groups (see Table 3).

Bacterial causes of PVAP included: *E. cloacae* (4.6%), *E. coli* (6.8%), methicillin-resistant *Staphylococcus aureus* (MRSA) (22.7%), *P. aeruginosa* (27.3%), methicillin-susceptible *S. aureus* (11.4%) and other bacteria in 27.2%.

4. Discussion

The main findings in this study are that patients with IVAC-plus had significantly longer hospital and ICU lengths of stay, and days on ventilator compared with patients with no VAEs. There was no difference in outcomes between patients with VAC and those with no VAE. These findings point towards worse outcomes in infection-related ventilator conditions compared with non-infection related conditions among burn patients.

Though not in burn patients, multiple studies demonstrated VAEs to be associated with worse outcomes. Hayashi et al., found that patients with VAC spent more time on mechanical ventilation and more days in intensive care compared to patients without VAC.[10] Klompas et al., observed that VAEs were associated with more days to extubation and hospital discharge[11] while Muscedere et al., in a retrospective study, found that both VACs and iVACs were associated with significant morbidity (including ventilator days, hospital days).[12] Our study has similar findings with these studies, observing worse outcomes in patients with IVAC-plus compared to those without VAE.

While there is a paucity of information on the incidence and outcomes of VAEs in burn patients, the incidence of all VAEs in our study was 14.4%, this is comparable to the incidence reported by other authors.[13,14] Our study shows that even in the ventilated burn population, VAP remains a major cause of morbidity and mortality.[15] Our study has confirmed similar findings in burn patients that show worse outcomes in patients with IVAC-plus compared to those without VAE. Early identification of ventilator associated conditions and infection-related ventilator associated complications in this patient population can result in earlier identification of their causes and potentially earlier treatment and better outcomes.

Contrary to published literature,[11] we did not find a difference in outcomes between the IVAC plus and VAC groups (despite the VAC group having a higher incidence of inhalation injury). The likely explanation for this difference is that the current study includes only burn patients. Burn patients are a critically ill population who might have disease characteristics that alter the severity between different groups of the VAEs and hence may be inadequate in differentiating these disease patterns in this population. Another possible explanation for the difference between the current study and prior literature's results is due to disease characteristics in each

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