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ORIGINAL SCIENTIFIC REPORT

Factors Predictive of Ventilator-associated Pneumonia in Critically Ill Trauma Patients

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Abstract

Background Ventilator-associated pneumonia (VAP) is a serious complication of mechanical ventilation. We sought to investigate factors associated with the development of VAP in critically ill trauma patients.

Methods We conducted a retrospective review of trauma patients admitted to our trauma intensive care unit between 2016 and 2018. Patients with ventilator-associated pneumonia were identified from the trauma database. Data collected from the trauma database included demographics (age, gender and race), mechanism of injury (blunt, penetrating), injury severity (injury severity score "ISS"), the presence of VAP, transfused blood products and presenting vital signs.

Results A total of 1403 patients were admitted to the trauma intensive care unit (TICU) during the study period; of these, 45 had ventilator-associated pneumonia. Patients with VAP were older ($p = 0.030$), and they had a higher incidence of massive transfusion ($p = 0.015$) and received more packed cells in the first 24 h of admission ($p = 0.028$). They had a higher incidence of face injury ($p = 0.001$), injury to sternum ($p = 0.011$) and injury to spine ($p = 0.024$). Patients with VAP also had a higher incidence of acute kidney injury (AKI) ($p < 0.001$) and had a longer ICU ($p < 0.001$) and hospital length of stay ($p < 0.001$). Multiple logistic regression models controlling for age and injury severity (ISS) showed massive transfusion ($p = 0.017$), AKI ($p < 0.001$), injury to face ($p < 0.001$), injury to sternum ($p = 0.007$), injury to spine ($p = 0.047$) and ICU length of stay ($p < 0.001$) to be independent predictors of VAP.

Conclusions Among critically ill trauma patients, acute kidney injury, injury to the spine, face or sternum, massive transfusion and intensive care unit length of stay were associated with VAP.

Introduction

Ventilator-associated pneumonia (VAP) is the most common nosocomial infection among trauma patients requiring prolonged mechanical ventilation [1]; it is associated with prolonged mechanical ventilation, intensive care unit stay and hospital length of stay [2]. Because of reported mortality from VAP reaching as high as 30–50% [3], preventive measures like the ventilator bundle have been implemented.

Despite the fact that hospitals have reported prolonged periods of decreased VAP rates and periods free of VAP

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[4, 5], Cook et al. in a prospective cohort study involving 16 ICUs and 1014 mechanically ventilated patients in Canada found the incidence of ventilator-associated pneumonia was 17.5% [6], and other authors reported an incidence of 8% among trauma patients admitted to the ICU [7].

Chastre et al., in a review of the literature, found VAP to be associated with increased hospital length of stay, intensive care unit stay and cost [8], and other authors found similar results in different patient populations [9–11]. Because of this increased morbidity, Hyde et al. in a retrospective review of 106 trauma patients with VAP and found early tracheostomy (mean hospital day 4) significantly decreased both pulmonary morbidity and critical care resource utilization [12].

VAP is associated with increased mortality. Magnotti et al. reported an associated mortality of 16% with VAP being an independent predictor [7], and Cavalcanti et al., in a case-control study, reported a mortality of 23% in patients with VAP who did not respond to antimicrobial treatment [13]. Because of the associated morbidity and mortality of VAP, implementation of the ventilator bundle gained popularity in intensive care units with some authors reporting up to 50% decrease in incidence of VAP [14–16].

Known risk factors for VAP are existing such as lung disease, aspiration, emergency endotracheal intubation, prolonged mechanical ventilation [6, 13, 17] and coagulopathy [18]. We hypothesized that other factors exist that are associated with development of VAP in critically ill trauma patients.

Materials and methods

Patient selection and variable definition

We performed a retrospective review of trauma patients admitted to our intensive care unit between January 2016 and October 2018 after institutional review board (IRB) approval was obtained. Patients with ventilator-associated pneumonia (VAP) were identified from the trauma database.

Our hospital is a level 1 academic trauma center and has 1032 beds. The trauma intensive care unit has 20 beds and is staffed by 2 surgical intensivists. There are 10 trauma intensive care specialists in our division who alternate between managing patients in the intensive care unit patients and regular floor.

Inclusion and exclusion criteria

The study included all adult trauma patients admitted to the intensive care unit. Variables collected from the patients' medical records and trauma database included age, race, gender (demographics), presenting vital signs, injury type and severity, the presence of ventilator-associated pneumonia, hospital and intensive care unit length of stay and survival data.

The attendings at our institution follow the center for disease control (CDC) criteria for diagnosing ventilator-associated pneumonia: "The presence of a new or progressive radiographic infiltrate plus at least two of three clinical features (fever greater than 38C, leukocytosis or leukopenia and purulent secretions) represent the combination of criteria for starting empiric antibiotic therapy" [19].

The massive transfusion protocol (MTP) at our institution is initiated by the attending trauma surgeon on-call; the first pack includes 5 units of packed red blood cells (pRBCs), 3 units of fresh frozen plasma (FFP) and 5 unit equivalent of platelets. The second pack includes 5 units of pRBCs, 5 units of FFP, 5 unit equivalent of platelets and 5 unit equivalent of Cryoprecipitate. Massive transfusion in this study was defined as massive transfusion protocol "initiated" and the patients receiving 10 units or more of packed red blood cells (pRBCs) in the first 24 h.

Statistical analysis

Demographics and clinical characteristics were summarized using descriptive statistics (mean and standard deviation for continuous variables; frequency and percentage for categorical variables).

T-test and Chi-square tests were used to detect differences between those with VAP and those without VAP (for continuous and categorical variables, respectively). Mann–Whitney *U* test was used to compare the Medians of ISS, ED SBP, ED HR and ED RR.

Multiple logistic regression models were used to assess association between VAP and variables of interest to detect associations, and each individual model examined the influence of a single predictor while controlling for injury severity (ISS) and age.

Analysis was performed using SPSS software version 25, IBM Company, Armonk, New York, 10,504.

Results

One thousand four hundred and three patients were admitted to the trauma intensive care unit (TICU) during the study period; of these, 45 had ventilator-associated pneumonia (VAP). The average age was 53.0 ± 22.5 years, and the median (IQR) for ISS was 14 (9–19). There were 948 (67.7%) men, 762 (54.5%) were white, and 1113 (79%) had blunt trauma. Mean ICU stay

Table 1 Demographic, injury and clinical characteristics of trauma patients admitted to the intensive care unit

	All patients (N = 1403)	Non-VAP patients (N = 1358)	VAP patients (N = 45)	p value
Demographics				
Mean age (Years)	53.0 ± 22.5	52.8 ± 22.6	58.9 ± 19.6	0.030*
Gender, n (%)				0.746
Male	948 (67.7)	916 (67.6)	32 (71.1)	
Female	452 (32.3)	439 (33.4)	13 (28.9)	
Race (%)				0.267
White	762 (54.3)	735 (54.1)	27 (60.0)	
Non-white	641 (45.7)	623 (45.9)	18 (40.0)	
Injury, n (%)				0.059
Blunt	1113 (79.8)	1072 (78.9)	41 (91.1)	
Penetrating	282 (20.2)	278 (20.5)	4 (8.9)	
ISS (injury severity score), median (IQR)	14 (9–19)	14 (9–19)	17 (10–25)	0.015*
Clinical				
ED systolic blood pressure, median (IQR)	130 (110–150)	130 (111–150)	146 (114–160)	0.053
ED heart rate, median (IQR)	88 (75–104)	88 (75–104)	94 (77–105)	0.122
ED respiratory rate, median (IQR)	18(16–20)	18 (16–20)	18 (17–22)	0.193
Massive transfusion, n (%)	31 (2.2)	27 (2.0)	4 (9.8)	0.015*
Packed red blood cells transfused in first 24 h	0.96 ± 4.99	0.9 ± 5.0	2.0 ± 4.9	0.028*
Tracheostomy, *n* (%)	226 (16.2)	215 (15.8)	11 (32.4)	0.146
Head injury, *n* (%)	667 (47.5)	642 (47.3)	25 (55.6)	0.291
Face injury, n (%)	206 (14.7)	191 (14.1)	15 (33.3)	0.001*
Chest injury, n (%)	463 (33.0)	445 (32.8)	18 (40.0)	0.335
Sternum injury, n (%)	44 (3.1)	39 (2.9)	5 (11.1)	0.011*
Spine injury, n (%)	295 (21)	279 (20.5)	16 (35.6)	0.024*
Surgeries				
Exploratory laparotomy, n (%)	117 (8.3)	113 (8.3)	4 (8.9)	0.785
Neurosurgical operations, n (%)	108 (7.7)	102 (8.6)	6 (14.3)	0.259
Face operations, n (%)	42 (2.9)	39 (3.3)	3 (6.9)	0.181
Orthopedic operations, n (%)	224 (15.9)	218 (18.2)	6 (15.0)	0.834
Thoracic operations, n (%)	20 (1.4)	18 (1.3)	2 (4.4)	0.133
Complications				
Cardiovascular events (CVA/MI), n (%)	14 (1.0)	12 (0.9)	2 (4.4)	0.079
Thromboembolic events (DVT/PE), n (%)	24 (1.7)	20 (1.7)	4 (9.7)	0.007
Acute kidney injury, n (%)	17 (1.2)	12 (0.9)	5 (11.1)	<0.001*
Outcomes				
ICU length of stay	3.8 ± 6.0	3.5 ± 5.4	14.9 ± 11.4	<0.001*
Hospital length of stay (days)	8.1 ± 8.3	7.6 ± 7.6	21.5 ± 14.6	<0.001*
Dead, n (%)	132 (9.4)	124 (9.1)	8 (17.8)	0.065

CVA cerebro-vascular accidents (stroke), *MI* myocardial infarction, *DVT* deep vein thrombosis, *PE* pulmonary embolism

p value for t test and Fisher's exact tests for continuous and categorical variables, respectively, between those with no VAP and those with VAP, and Mann–Whitney test was used to compare medians. A value less than 0.05 is considered significant (*)

was 3.8 ± 6.0 days, and mean total hospital length of stay (LOS) was 8.1 ± 8.3 days. Thirty-one patients received massive transfusion (2.2%), incidence of acute kidney injury (AKI) was 1.2% and 132 (9.4%) died.

Patients with VAP were older (p = 0.030) and had an average BMI of 28.8 ± 9.2. Their co-morbidities included CVAs (stroke) in 3 (6.7%), hypertension in 17 (37.8%), CKD (chronic kidney disease) in 3 (6.7%), smoking in 10 (22.2%), COPD (chronic obstructive pulmonary disease) in

Table 2 Multiple logistic regression* for variables predictive of VAP

	OR	95% CI	*p*
Massive transfusion	4.06	1.28–12.87	.017*
Acute kidney injury	12.02	3.97–36.43	<.001*
Injury to face	3.27	1.69–6.34	<.001*
Injury to sternum	3.91	1.45–10.56	.007*
Injury to spine	1.91	1.01–3.61	.047*
ICU length of stay	1.13	1.10–1.17	<.001*

*p value is <0.05, multiple logistic regression models controlling for age and injury severity (ISS)

7 (15.5%), diabetes in 9 (20%) and coronary artery disease in 3 (6.7%). These patients also had higher ISS ($p = 0.015$), and they had a higher incidence of massive transfusion ($p = 0.015$) and received more packed cells in the first 24 h of admission ($p = 0.028$). Among those with massive transfusion, the average number of packed red blood cells received in the first 24 h was 15 ± 6.7, while the average number of fresh frozen plasma units was 9.8 ± 7.1. VAP patients also had a higher incidence of face injury ($p = 0.001$), injury to sternum ($p = 0.011$) and injury to spine ($p = 0.024$). Patients with VAP also had a higher incidence of acute kidney injury (AKI) ($p < 0.001$) and had a longer ICU ($p < 0.001$) and hospital length of stay ($p < 0.001$). There were 8 deaths among patients with VAP; 2 were VAP-associated (Table 1).

Multiple logistic regression models controlling for age and injury severity (ISS) showed massive transfusion ($p = 0.017$), AKI ($p < 0.001$), injury to face ($p < 0.001$), injury to sternum ($p = 0.007$), injury to spine ($p = 0.047$) and ICU length of stay ($p < 0.001$) to be independent predictors of VAP (Table 2).

Discussion

We found that, among critically ill trauma patients admitted to the intensive care unit, injury to the spine, face or sternum, massive transfusion, acute kidney injury and intensive care unit length of stay were associated with ventilator-associated pneumonia (VAP). These findings have significant consequences on the care of these critically ill patients.

Published risk factors for VAP include head and neck trauma, hypotension, craniotomy, pre-existing pulmonary disease, witnessed aspiration, emergency intubation, prolonged mechanical ventilation [6, 13, 17] and more recently coagulopathy [18]. We identified other associative factors in this study including ICU length of stay and hospital length of stay, injury severity score and acute kidney injury. It is not entirely clear why acute kidney injury predicts VAP, and it might be a measure of the severity of the injury and illness.

In this study, certain injuries were associated with development of VAP in these patients, including face fractures, sternum fracture and injury to the spine. While chest trauma was found to be predictive of VAP in previous studies [20], and some authors advocated early broncho-alveolar lavage to identify it in patients with chest trauma [21], sternal fractures by themselves—although often associated with significant pain and underlying pulmonary contusions—have not. Chest wall trauma (without sternum) in this study was not associated with development of VAP.

Spine trauma was associated with VAP in this study, and multiple previous studies have described this association. Aarabi et al. indicated a significant relationship between pulmonary complications and spinal cord injury [22], and other authors even advocated performing early tracheostomy in patients with spinal cord injury [23]. Our data are in agreement with published literature.

While Gursel et al. and others noted a high incidence of acute renal failure during episodes of ventilator-associated pneumonia in the intensive care unit and showed an association with VAP [24, 25], in this study, acute kidney injury (AKI) was an independent predictor of VAP on multivariable analysis. The higher incidence of AKI in patients with VAP is a marker of the high injury severity these patients sustained.

We also found the length of intensive care unit stay to be associated with VAP. While other authors similarly found VAP to be associated with ICU stay [8], Tsakiridou et al., in a prospective observation study performed at a tertiary care hospital, found that delayed (>24 h) ICU admission was an independent risk factor for VAP [26]. We also found massive transfusion to be associated with development of VAP in this study, and others have noted that transfusion was associated with augmentation of the inflammatory response with resultant increased susceptibility to nosocomial infections [27].

Our study has limitations. First, the study is retrospective and performed at a single center. Second, the clinical diagnosis of VAP in an intensive care unit setting is not an easy one to make and will differ between providers depending on experience and practice patterns. It is important to note that differences in physician practice patterns may result in differences in the observed incidence of VAP. Third, we did not have data on the existing pulmonary disease or witnessed aspiration, and these have been identified as predictive factors for VAP in the past and would have helped shed more light on the associations and predictive factors of VAP.

Conclusion

Among critically ill trauma patients admitted to the intensive care unit, acute kidney injury, injury to the spine, face or sternum, massive transfusion and intensive care unit length of stay were associated with VAP. Further studies are needed to confirm these findings.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict interests.

Informed consent Informed consent was waived by the institution review board.

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