Association of Facility Level Factors and Outcomes from Hospital-Acquired Pneumonia in Patients with Isolated Severe Traumatic Brain Injury

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Abstract

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Introduction

Traumatic brain injury (TBI) is a major public heath problem and leading cause of death and disability worldwide. While secondary brain injuries are known to worsen mortality in TBI, very little literature exists on the role of hospital-acquired infections in isolated TBI. Among adults with isolated severe TBI, we describe the cumulative incidence of hospital-acquired pneumonia and analyze the association between hospital characteristics and the development of hospital-acquired pneumonia.

Methods

We examined data from the National Trauma Databank (NTDB), excluding children, patients with non-isolated TBI, and patients hospitalized for less than one week. We describe clinical and demographic characteristics of patients, stratified by facility characteristics and the presence of hospital acquired pneumonia. We used multivariable Poisson regression to analyze the association between hospital characteristics and the development of hospital-acquired pneumonia.

Results

20,604 patients were included in our analysis. The cumulative incidence of hospital-acquired pneumonia was 17.3%. Among patients that developed hospital-acquired pneumonia, the cumulative mortality was 18.2%. On multivariate analysis, compared to small hospitals ($\leq$200 beds), patients at medium hospitals (201-400 beds) had a 28% reduced risk of hospital-acquired pneumonia (Relative risk 0.72, 95% CI: 0.53 – 0.96) and patients at large hospitals (>400 beds) had a 34% reduced risk of hospital-acquired pneumonia (Relative risk 0.66, 95% CI: 0.49 – 0.88).

Conclusion

Hospital-acquired pneumonia is common in patients with isolated severe TBI, and larger hospitals conferred a decreased risk for the development of hospital-acquired pneumonia. Future research should aim to explore the mechanism of the impact of facility characteristics on infectious complications, examine the utility of pneumonia prevention measures in the TBI

population, and determine the impact of in-hospital infectious complications on patient-level outcomes in isolated severe TBI.

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Introduction

Traumatic brain injury (TBI) is a major public health problem, affecting more than 1.7 million patients annually in the United States alone[1]. Severe TBI, representing the greatest level of injury, has been associated with several extracranial complications during the acute care hospitalization, which can adversely impact outcome[2]. One such complication is hospital-acquired pneumonia, which has been shown to increase mortality in TBI patients with polytrauma[3,4] and may be preventable[5]. Furthermore, there is strong evidence demonstrating that better hospital processes of care can decrease infectious complications and improve outcomes in hospitalized patients[6-8]. Knowledge of the underlying characteristics of hospitals with a decreased incidence of hospital-acquired pneumonia can lead to an improved understanding of the impact of hospital characteristics on TBI complications and outcomes.

While the impact of hospital-acquired pneumonia on mortality has been studied in patients with non-isolated TBI in the setting of polytrauma, no large studies have examined the impact of hospital-acquired pneumonia in purely isolated TBI. Furthermore, no studies have examined the association between hospital characteristics with the development of hospital-acquired pneumonia. In addition, the largest of the prior studies of complications after severe TBI, based on the National Traumatic Coma Data Bank, explored prospective data collected from 1983-1988[3], a time since progress has made in both TBI-specific surgical care, as well as intensive care unit (ICU) care[9]. Thus, the burden, risk factors, and outcomes of hospital-acquired pneumonia in the current era of isolated TBI care represent a gap in the current TBI literature. To address this, the aims of our study were to: 1.) Describe the cumulative incidence of hospital-acquired pneumonia in adult patients admitted to the hospital following isolated severe TBI, 2.)

Examine the association between specific hospital characteristics and development of hospital-acquired pneumonia, and 3.) Describe the mortality experience of patients with isolated severe TBI who develop hospital-acquired pneumonia. We hypothesized that the burden of hospital-acquired pneumonia among patients with severe isolated TBI would be significant, and certain characteristics of hospitals caring for adults with severe isolated TBI would be associated with the development of hospital-acquired pneumonia. A better understanding of hospital-acquired pneumonia in isolated severe TBI patients can help guide implementation of evidence-based practices for prevention, reduce the burden of secondary brain injuries, and improve outcomes in this vulnerable patient population.

Methods

Study Design and Population

We conducted a retrospective cohort study, using the National Trauma Data Bank (NTDB), a centralized national trauma registry created and operated by the American College of Surgeons. The NTDB represents the largest aggregation of United States trauma registry data ever assembled, with the mission to provide the trauma community with accessible and "consistent, quality data."[10] The study did not require institutional review board approval, as the data was de-identified and did not meet the regulatory definition of human subjects research. We used NTDB data from 2008-2012, with linkage (using the de-identified patient number) of multiple data files (demographic, facility, admission, injury, complications, discharge diagnoses, and outcomes). We identified all admissions to participating trauma centers with severe isolated TBI. All patients less than 18 years of age at admission were excluded. We ascertained our TBI cohort in the injury file by keeping every patient with a head abbreviated injury score (AIS). We then dropped any patient with AIS scores for other body regions (other than head) to narrow the cohort to only isolated TBI patients. After this procedure, we excluded all patients with a head AIS score of less than 4, patients with and AIS Score of 6, and patients admitted to the hospital for less that one week, based on the rationale that a facility-level exposure would require time to exert its effect on hospital-acquired infections. Lastly, we excluded patients at facilities that did not report at least one complication of hospital-acquired pneumonia, a method for ascertainment of complications in the NTDB dataset that is previously described[11].

Exposures, Outcomes, and Confounders

Our primary facility-level exposures of interest were hospital size (≤200 beds, 201-400 beds, >400 beds), teaching status (teaching versus non-teaching), and American College of Surgeons trauma level designation (trauma designated versus non-trauma designated facility); this data was ascertained from the "facilities" file of the NTDB dataset. The outcomes of hospital-acquired pneumonia and in-hospital mortality were ascertained from the "complications" and "discharge" data files, respectively. Our analysis was adjusted for the following variables, a minimum set which has been previously published for the NTDB dataset[12]: age at admission, heart rate at admission, the presence of hypotension at admission (defined as a systolic blood pressure < 90), the injury severity score (ISS), and admission total Glasgow Coma Scale (GCS) score.

Statistical Analysis

We described the clinical and demographic characteristics of our patient cohort, stratified by the facility characteristics and the development of hospital-acquired pneumonia, as described above. Continuous variables are reported as means, standard deviation, and range; and categorical variables are reported as counts and percentages. We calculated the cumulative incidence of hospital-acquired pneumonia based on the proportion of cases of pneumonia among the entire severe isolated TBI cohort.

We calculated univariate and multivariate estimates of the association between facility characteristics and development of pneumonia using a Poisson regression model with clustered robust sandwich standard error estimates relaxing the assumption that observations from the

same hospital are independent. In our multivariable model, we included age, admission heart rate, ISS score, and total GCS score as continuous variables; and we included the presence of hypotension at admission and the need for mechanical ventilation as binary variables. To test the robustness of our assumption that hospitalization for at least one week was necessary for a facility characteristic to have an impact on infectious complications, we conducted sensitivity analyses restricting the duration of hospitalization of the population to >5 days, >6 days, and >8 days. We report our point estimates as a relative risk, with 95% confidence intervals. All analyses were conducted using STATA statistical software, version 12 (College Station, Texas).

Results

We initially narrowed our cohort to a sample of severe isolated TBI patients from the 2008-2012 NTDB (n=118,512). We then excluded patients at facilities that did not report at least one complication of hospital-acquired pneumonia (n=37,111) and patients with an AIS Score of 6 (n=156). Lastly, we excluded all patients who were admitted to the hospital for less than one week (n=60,641). After all of the above procedures were fully completed, we had 20,604 patients remaining for our analysis.

Patient Characteristics Based on Facility Type

Characteristics of patients treated at non-teaching hospitals (n=8,895) were generally similar to those treated at teaching hospitals (n=11,709) [Table 1]. Non-teaching and teaching hospitals had similar initial physiologic values, and patients were predominantly male (65.9% and 67.6%, respectively), white (43.8% and 42.5%, respectively), and funded through public insurance (57.5% and 58.3%, respectively). Teaching hospitals had a greater proportion of patients that were transferred to the facility (51.9% versus 38.7%).

Hospital size was stratified between small ($\leq$ 200 beds), medium (201-400 beds), and large (>400 beds) hospitals (n=476, n=4,225, and n=15,903, respectively) [Table 1]. Patients were similar across hospital sizes with respect to age, gender, and initial physiologic variables. Large and medium sized hospitals had a greater proportion of patients on ventilators (43.7% and 46.9%, respectively) as compared to small hospitals (37.4%). Large and medium sized hospitals had a greater proportion of white patients (42.7% and 45.1%, respectively) compared to small hospitals (37.2%). Small hospitals had a greater proportion of patients with private insurance

(26.7%) compared to large and medium sized hospitals (17.3% and 19.8%, respectively). The proportion of patients that were transferred to the facility increased from small (27.9%) to medium (36.5%) to large (49.3%) hospitals.

Characteristics of patients treated at non-trauma designated hospitals (n=6,831) were similar to patients treated at American College of Surgeons verified trauma hospitals (n=13,597) with respect to age, gender, and initial physiologic variables (Table 1). A greater proportion of patients at non-trauma hospitals had public insurance (62.6%) as compared to trauma hospitals (55.2%). Non-trauma and trauma hospitals were similar with regard to the proportion of patients that were transferred to the facility (44.1% and 47.2%, respectively.)

Patient Characteristics Based on the Development of Hospital-Acquired Pneumonia

Hospital-acquired pneumonia occurred in 3,563 patients in our cohort, giving a cumulative incidence of 17.3%. Characteristics of patients who developed hospital acquired pneumonia (n=3,563) and patients who did not develop hospital-acquired pneumonia (n=17,041) are shown it Table 2. Patients who developed hospital-acquired pneumonia had a lower mean age (59.2 years versus 64.2 years), had a higher mean injury severity score (18.1 versus 16.8), had a lower mean admission GCS score (9.6 versus 12.0), and had a higher proportion of patients requiring mechanical ventilation (78.4% versus 37.1%). Among patients who developed hospital-acquired pneumonia, the cumulative mortality was 18.2%.

Relationship Between Facility Characteristics and Hospital-Acquired Pneumonia

The association between facility characteristics and the development of hospital-acquired pneumonia is shown in Table 3. Univariate statistics demonstrated a possible protective effect for teaching hospitals and larger hospitals. After multivariate analysis, the data provides evidence that increasing hospital size is associated with a lower incidence of hospital-acquired pneumonia among patients with isolated severe TBI who are hospitalized for at least one week. As compared to small hospitals, patients at medium sized hospitals (201-400 beds) had a statistically significant 28% decreased risk of developing hospital-acquired pneumonia (Relative Risk 0.72, 95% CI: 0.53 – 0.96). As compared to small hospitals, patients at large hospitals (>400 beds) had a statistically significant 34% decreased risk of developing hospital-acquired pneumonia (Relative Risk 0.66, 95% CI: 0.49 – 0.88). Multiple sensitivity analyses revealed no meaningful change to our regression point estimates or statistical significance.

Discussion

Overall, the results of our study demonstrate that among patients with isolated severe TBI hospitalized for greater than one week, hospital-acquired pneumonia is common (cumulative incidence of 17.3%) and increasing hospital size is associated with a lower incidence of hospital-acquired pneumonia. Furthermore, among patients hospitalized for greater than one week with isolated severe TBI and hospital-acquired pneumonia, the cumulative morality is 18.2%. Thus, among isolated severe TBI patients, the development of hospital-acquired pneumonia is common, associated with a high burden of mortality, and potentially modifiable based on facility characteristics.

To our knowledge, no prior studies have examined the relationship of facility-level factors and the development of hospital-acquired pneumonia in the isolated TBI population. In our study, larger hospitals (as compared to small hospitals) exerted a significant protective effect against the development of hospital-acquired pneumonia among patients hospitalized for greater than one week. Although the effect of hospital size on complications has not been previously demonstrated in the TBI literature, this effect has been shown in other disease paradigms. Allareddy et al[13] showed that among 22,932,948 hospitalizations for major surgical procedures, larger hospitals conferred a protective effect against the development of methicillin-resistant *Staphylococcus aureus* infections. Brown et al[14] demonstrated that among 118,611 Medicare beneficiaries hospitalized for acute myocardial infarction, larger hospitals had a significantly reduced 30-day hospital readmission rate, compared to smaller hospitals. The mechanism of this effect is unclear in the TBI population, although adherence to guidelines that emphasize the prevention of secondary brain injury[15-17] may be better implemented at larger hospitals that take

care of a higher volume of severe TBI patients. Furthermore, it has been demonstrated that hospitals with more resources may have a higher spread of patient safety and infection control activities, with small hospitals carrying disproportionately large economic burden for having patient safety programs in place[18].

While several studies have examined the incidence of hospital-acquired pneumonia in TBI patients with multiple injures, our study is the first large epidemiologic investigation of hospital-acquired pneumonia in purely isolated TBI patients. Even in studies with non-isolated TBI in the setting of polytrauma, the incidence of pneumonia varies widely, due to differences in the definition, small sample sizes, and heterogeneity of study design. Two smaller studies examining infectious complications after TBI in the setting of polytrauma have been published, with heterogeneity in their results. Corral et al[19] studied 224 patients retrospectively with severe TBI (the majority in the setting of polytrauma) and found a very high incidence of sepsis (75%) and pneumonia (68%), while Mascia et al[4] found an incidence of pneumonia of 30% in a retrospective study of 373 patients with sever neurologic disorders, only 175 of whom had a TBI. In an analysis of 734 patients with TBI in the setting polytrauma from the National Traumatic Coma Databank, Piek et al[3] documented an incidence of pulmonary infections of 41%. In a study of 109 patients with TBI (the majority of whom had polytrauma), Bronchard et al[20] documented an incidence of early-onset pneumonia of 41.3%. In a prospective study of 134 patients (of which only 38% had an isolated TBI), Zygun et al[21] documented an incidence of ventilator-associated pneumonia of 45%. Lastly, in the placebo arm of a randomized controlled trial of low dose steroids for the prevention of hospital-acquired pneumonia among patients with severe TBI (168 patients, of which only 2.3% had isolated TBI), Asehnoune et al[22] documented an incidence

of hospital-acquired pneumonia of 53%. Thus, our results suggest that the incidence of hospital-acquired pneumonia is lower in isolated severe TBI patients, as compared to the above studies of pneumonia with TBI in the setting of multiple injuries.

While the burden of pneumonia among patients with severe TBI is high, the causal impact of pneumonia on mortality is less clear[23], although several lines of observational evidence suggest a relationship between non-neurologic extracranial complications and worsened mortality in severe TBI patients[3,4,19,24,25]. Furthermore, pneumonia in severe TBI patients increases the duration of mechanical ventilation and length of stay[21], increases medical costs[5], as well as increases secondary brain injures such as fever and hypoxemia[20]. We report a cumulative mortality of 18.2% in patients with isolated severe TBI and hospital-acquired pneumonia, although we chose not to do a multivariable analysis because of our concerns of immortal time bias[26], as the exact time of pneumonia diagnosis was not captured in the NTDB dataset. Nevertheless, despite a proven association with mortality, reducing the burden of hospital-acquired pneumonia may have a positive impact on reducing secondary brain injures, improving neurologic outcomes, and reducing healthcare costs.

Patients with severe TBI may be at a particularly high risk of developing hospital-acquired pneumonia due to impaired airway protective reflexes, dysphagia, and the subsequent risk of aspiration[27]. Several preventative measures aimed at reducing the burden of hospital-acquired pneumonia in all critically ill patients have been studied including early enteral nutrition, selective digestive decontamination, closed suctioning, upright patient positioning, special endotracheal tubes, and subglottic suctioning[28]. Despite multiple suggested preventive

strategies against hospital-acquired pneumonia, a recent meta-analysis by Roquilly et al[5] suggests that only selective digestive decontamination provides a mortality benefit among critically ill patients. While studies have suggested safety and efficacy of this practice[29,30], it is still controversial due to a raised concern for selecting resistant bacterial species. TBI patients, given their high burden of pneumonia and likely deleterious impact on outcomes, may be a subgroup for which more aggressive pneumonia prevention measures, such as selective digestive decontamination, may be appropriate, although this would require further study.

There are some limitations to our study. First, given our large retrospective data analysis, especially from a registry that was not collected for the purpose of research, certain variables may be prone to inaccuracies and coding errors. Furthermore, some variables (especially admission GCS, hypotension, and heart rate) were prone to missing data approaching 25%, although upon our investigation of the data, the missingness appeared to be non-differential when stratified by exposure categories. Second, while a great deal of diagnostic data is captured in the NTDB dataset, granular data, especially regarding physiologic variables, is not captured, thus we are unable to capture the influence of ICU physiology on outcomes. Third, ascertainment of hospital-acquired pneumonia may have been incomplete, given the variability to reporting of complications by facilities in the NTDB; to mitigate this, we excluded all patients at facilities that did not report at least one pneumonia complication. Lastly, the necessary time for a facility characteristic to have a meaningful impact on infectious complications has not been well described in the literature and the time period of one week seemed reasonable to us; despite this assumption, multiple sensitivity analyses using other time points revealed no significant changes to our risk estimates.

In conclusion, there is a high burden of hospital-acquired pneumonia in isolated severe TBI patients, and larger hospitals conferred a reduced risk for the development of hospital-acquired pneumonia than smaller hospitals. Future research should aim to explore the mechanism of the impact of facility characteristics and infectious complications in TBI patients, examine the impact of pneumonia prevention measures in the TBI population, and better clarify the impact of in-hospital infectious complications on patient-level outcomes in isolated severe TBI.

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TABLE 1 CLINCAL AND DEMOGRAPHIC CHARACTERISTICS STRATIFIED BY FACILITY TYPE

	Teaching Status		Hospital Beds			Trauma Hospital Designation*****	
	Community/Non-Teaching (n=8,895)	**University/Teaching (n=11,709)**	**≤ 200 (n=476)**	**201-400 (n=4,225)**	**>400 (n=15,903)**	**Non-trauma (n=6,831)**	**Trauma (n=13,597)**
Age (mean ± SD)	62.7 ± 19.5	64.2 ± 19.1	61.2 ± 19.6	62.6 ± 19.9	63.6 ± 19.2	64.1 ± 19.4	62.9 ± 19.3
Male [n(%)]	5,863 (65.9)	7,909 (67.6)	318 (66.8)	2,941 (69.6)	10,513 (66.1)	4,497 (65.8)	9,146 (67.3)
Hypotension at admission [n(%)]*	107 (1.2)	126 (1.1)	4 (0.84)	53 (1.3)	176 (1.1)	68 (1.0)	164 (1.2)
ISS (mean ± SD)**	16.9 ± 2.8	17.1 ± 2.9	16.7 ± 2.4	17.2 ± 3.0	17.0 ± 2.8	16.9 ± 2.7	17.1 ± 3.0
Admission GCS (mean ± SD)*** #	11.8 ± 4.3	11.4 ± 4.5	11.7 ± 4.2	11.5 ± 4.4	11.6 ± 4.4	11.7 ± 4.3	11.5 ± 4.5
Admission HR (mean ± SD)****	85.4 ± 21.9	85.7 ± 20.8	87.0 ± 22.5	85.6 ± 22.2	85.5 ± 21.0	85.7 ± 21.3	85.5 ± 21.3
Need for a ventilator [n(%)]	3,917 (44.0)	5,190 (44.3)	178 (37.4)	1,980 (46.9)	6,949 (43.7)	2,967 (43.4)	6,083 (44.7)
Race [n(%)]							
White	3,898 (43.8)	4,973 (42.5)	177 (37.2)	1,905 (45.1)	6,789 (42.7)	2,862 (41.9)	5,985 (44.0)
African-American	385 (4.3)	896 (7.7)	43 (9.0)	167 (4.0)	1,071 (6.7)	472 (6.9)	809 (6.0)
Asian/PI	94 (1.1)	189 (1.6)	5 (1.1)	62 (1.5)	216 (1.4)	99 (1.5)	184 (1.4)
Other	466 (5.2)	806 (6.9)	24 (5.0)	296 (7.0)	952 (6.)	372 (5.5)	899 (6.6)
Missing	4,052 (45.6)	4,845 (41.4)	227 (47.7)	1,795 (42.5)	6,875 (43.2)	3,026 (44.3)	5,720 (42.1)

Insurance [n(%)]							
Private	1,680 (18.9)	2,027 (17.3)	127 (26.7)	836 (19.8)	2,744 (17.3)	1,284 (18.8)	2,409 (17.7)
Public	5,113 (57.5)	6,821 (58.3)	240 (50.4)	2,400 (56.8)	9,294 (58.4)	4,277 (62.6)	7,499 (55.2)
Self-Pay	719 (8.1)	1,005 (8.6)	43 (9.0)	376 (8.9)	1,305 (8.2)	541 (7.9)	1,180 (8.7)
Other	446 (5.0)	662 (5.7)	50 (10.5)	222 (5.3)	836 (5.3)	350 (5.1)	757 (5.6)
Missing	937 (10.5)	1,194 (10.2)	16 (3.4)	391 (9.3)	1,724 (10.8)	379 (5.6)	1,752 (12.9)
Transfer from another facility [n(%)]	3,438 (38.7)	6,073 (51.9)	133 (27.9)	1,540 (36.5)	7,838 (49.3)	3,011 (44.1)	6,422 (47.2)

*Missing in 5,201 (25.2%) subjects

**Missing in 1,676 (8.1%) subjects

*** Missing in 5,875 (28.5%) subjects

Severe TBI defined by AIS criteria, rather than GCS (see methods)

****Missing in 5,087 (24.7%) subjects

*****Missing in 176 (0.85%) observations

GCS = Glasgow Coma Scale

ISS = Injury Severity Score

HR = Heart Rate

PI = Pacific Islander

TABLE 2 CLINCAL AND DEMOGRAPHIC CHARACTERISTICS STRATIFIED BY DEVELOPMENT OF HOSPITAL-ACQUIRED PNEUMONIA

	No Hospital-Acquired Pneumonia (n=17,041)	Hospital-Acquired Pneumonia (n=3,563)
Age (mean ± SD)	64.2 ± 19.0	59.2 ± 20.3
Male [n(%)]	11,089 (65.1)	2,683 (75.3)
Hypotension at admission [n(%)]*	176 (1.03)	57 (1.6)
ISS (mean ± SD)**	16.8 ± 2.6	18.1 ± 3.8
Admission GCS (mean ± SD)*** #	12.0 ± 4.2	9.6 ± 4.9
HR at admission (mean ± SD)****	85.3± 21.0	86.6 ± 23.7
Need for a ventilator [n(%)]	6,313 (37.1)	2,794 (78.4)
Race [n(%)]		
White	7,336 (43.1)	1,876 (43.9)
African-American	1,048 (6.2)	280 (6.6)
Asian/PI	225 (1.3)	65 (1.5)
Other	1,031 (6.1)	277 (6.5)
Missing	7,401 (43.4)	1,469 (42.0)
Insurance [n(%)]		
Private	3,024 (17.8)	683 (19.2)
Public	9,984 (58.6)	1,950 (54.7)
Self-Pay	1,400 (8.2)	324 (9.1)

Other	873 (5.1)	235 (6.6)
Missing	1,760 (10.3)	371 (10.4)
Transfer from another facility [n(%)]	8,062 (47.3)	1,449 (40.7)
Mortality [n(%)]***	1,523 (8.9)	647 (18.2)

*Missing in 5,201 (25.2%) subjects

**Missing in 1,676 (8.1%) subjects

*** Missing in 5,875 (28.5%) subjects

Severe TBI defined by AIS criteria, rather than GCS (see methods)

****Missing in 5,087 (24.7%) subjects

*****Missing in 73 (0.35%) subjects

GCS = Glasgow Coma Scale

ISS = Injury Severity Score

HR = Heart Rate

PI = Pacific Islander

TABLE 3 ASSOCIATIONS OF FACILITY LEVEL FACTORS AND THE DEVELOPMENT OF HOSPITAL-ACQUIRED PNEUMONIA

	Crude RR (95% CI)	Adjusted RR (95% CI)*#
Teaching Hospital	0.96 (0.90 - 1.02)	1.00 (0.88 - 1.12)
Hospital Beds		
≤200	ref	ref
201-400	0.93 (0.77 - 1.12)	**0.72 (0.53 - 0.96)**
>400	0.81 (0.68 - 0.97)	**0.66 (0.49 - 0.88)**
Trauma Hospital Designation	1.06 (0.99 - 1.13)	1.04 (0.92 - 1.19)

*Adjusted for age, admission hypotension, admission heart rate, admission Glasgow Coma Scale, Injury Severity Score, and need for a ventilator

#Adjusted for clustering by facility