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Mortality Following Combined Burn and Traumatic Brain Injuries: An Analysis of the National Trauma Data Bank of the American College of Surgeons

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Abstract

Background—Severe burn and traumatic brain injuries (TBI) lead to significant mortality, and combined burn-TBI injuries may predispose towards even worse outcomes. The purpose of this study was to investigate the mortality of patients with burn, burn with non-TBI trauma, and combined burn/TBI to determine if combined injury portends a worse outcome.

Methods—We obtained the National Trauma Data Bank from 2007–2012, identifying 32,334 patients with burn related injuries, dividing this cohort into three injury types: BURN ONLY, BURN with TRAUMA/NO TBI, and BURN with TBI. For each patient, demographic data was obtained, including age, gender, presence of trauma, TBI, or inhalation injury, burn total body surface area (TBSA), Glasgow Coma Scale, Injury Severity Score, and mortality. Multivariable logistic regression was performed.

Results—Age, gender, and TBSA were similar across the three injury groups, but the incidence of inhalation injury was doubled in the BURN with TRAUMA/NO TBI (15.4%) and BURN with TBI (15.3%) groups when compared to the BURN ONLY (7.2%) group. Mortality differed across injury categories after adjusting for age, TBSA, and inhalation injury. Increased mortality was seen in BURN with TRAUMA/NO TBI versus BURN ONLY (OR = 1.27 [1.06, 1.53]) and was higher when comparing BURN with TBI versus BURN ONLY (OR = 4.22 [2.85, 6.18]). BURN with TBI also had higher mortality when compared to BURN with TRAUMA/NO TBI (OR = 3.33

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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[2.30, 4.82]). The logs odds of mortality also increased with increasing age, TBSA and presence of inhalation injury.

Discussion—This analysis of the NTDB suggests that mortality following burn-related injuries may be higher when burn injury is combined with TBI when compared to burns with other trauma, even after correcting for age, TBSA, and inhalation injury. Further clinical and laboratory research is needed to validate these findings and better understand how to optimize combined TBI and burn injury treatment.

Keywords

Traumatic brain injury; burn; mortality

INTRODUCTION

Severe thermal injuries and traumatic brain injuries (TBI) both have significant patient mortality, and when combined, can be a particularly challenging to the medical team. Little is known about the outcomes of combined burn and TBI injuries. However, combined burn and TBI injury is of particular importance in the military due to explosive devices. In an analysis of 950 US service members treated at the US Institute of Surgical Research burn center from injuries sustained in combat operations in Iraq and Afghanistan between 2003 and 2013, combined injury was associated with increased risk of intensive care unit stay, hospital stay, ventilator days, episodes of shock, concomitant extremity or torso injury, amputation, bacteremia, urinary tract infection, wound infection and thromboembolism, but not mortality [1]. Other studies have shown that combined burn and trauma injuries (without reported TBI) have worse outcomes, even when the individual combined injuries are minor [2–4].

Mortality after any single form of injury is based on injury severity as well as efficacy of treatment. Guidelines for TBI, trauma, and burn resuscitation were created to optimize the treatment of each of these groups. However, aspects of the guideline recommendations may conflict. For example, the two most commonly used burn resuscitation formulas (Parkland and Brooke) emphasize administration of lactated ringers solution at between 2–4 ml/kg/ total body surface area burn in the first 24 hours post-burn [5]. Fluids are titrated based on urine output. albumin or plasma administration in the first 24 hours of burn care have been advocated to decrease fluid resuscitation requirements [6]. Sodium levels are not tightly regulated in burn resuscitation guidelines to the extent they are in TBI. Unlike TBI, hypernatremia in burns has been associated with decreased survival in several studies [7, 8]. TBI guidelines, however, emphasize a fluid conservative approach to avoid cerebral edema, including avoidance of hyponatremia, frequent use of hypernatremia, strict control of blood pressure, and avoidance of albumin administration [9, 10]. This inherent conflict could potentially adversely impact patient outcomes. We hypothesize that patients with combined burn and TBI injuries will have worse outcomes than burn injury combined with other forms of trauma due in part to this discordance.

The purpose of this study was to investigate the mortality of patients with burn, burn/non-TBI trauma, and combined burn/TBI to determine if the combination of combined TBI and burn injury portends a worse outcome.

METHODS

We obtained the National Trauma Data Bank (NTDB) of the American College of Surgeons over a six-year period (2007–2012) to describe the mortality risk across three patient groups: patients with burn injuries only, burn injuries combined with non-TBI trauma, and burn injuries combined with trauma and TBI. We initially identified 61,245 records for patients with a burn-related injury based on ICD-9 codes. We included patients with a 948 ICD-9 code (provides a measure of burn size) as well as patients with inhalation injury (codes 986 or 987.9). Subsequently, we removed 25 patients with no age information, 6,141 patients without information on Glasgow Coma Scores (GCS) or Injury Severity Scores (ISS), 5,661 patients that were transferred to another hospital, 337 patients that left against medical advice, and 1,966 patients with an uncertain survival status. After further restricting our search for patients 18 years and older, we identified 32,334 subjects for this analysis (Figure 1).

For each patient, demographic data was obtained, including age, gender, presence of trauma, presence of TBI, presence of inhalation injury, burn total body surface area (TBSA), GCS, ISS, and mortality. TBSA was derived from the first decimal portion of 948 ICD-9 codes and converted to an integer of 1 through 10 representing 10% increments of TBSA. Patients experiencing trauma in addition to burns were identified based on the following ICD-9 codes:

1. Fractures (800–829)
2. Dislocation (830–839)
3. Sprains/Strains (840–848)
4. Intracranial Injury (850–854)
5. Internal Injury (860–869)
6. Open Wounds (870–897)-excludes burns
7. Injury to Blood Vessels (900–904)-excludes accidental medical procedure
8. Contusion (920–924)
9. Crushing Injury (925–929)
10. Injury to Nerves and Spinal Cord (950–957)
11. Traumatic Anuria/Crush Syndrome (958.5)
12. Traumatic subcutaneous emphysema (958.7)
13. Toxic Effects of Substances (980–989)

We further identified patients with TBI based on these ICD-9 codes: 800, 801, 803, 804 (.00–.06, .09, .1–.4, .5, .52–.56, .59), 850 (.0–.5., .9), 851, 852, 853, 854.

The NTDB contains three different Injury Severity Scores within its database. The ISSLOC is the ISS value entered locally by the hospital that treated the patient. The ISSAIS is calculated from the Abbreviated Injury Scores (AIS), and the ISSICD is calculated from ICD-9 codes after converting ICD-9 codes to component AIS values. For this analysis, the ISSLOC was used when available. If the ISSLOC was missing, the ISSAIS was used; if both the ISSLOC and the ISSAIS were missing, the ISSICD was used.

For purposes of analysis, our cohort of patients were divided into three injury types. The first group, BURN ONLY, contained patients with burn injury with no reported systemic trauma, including TBI. The second group, BURN with TRAUMA/NO TBI, contained patients with burn injury and concomitant systemic trauma, excluding TBI, while the third group, BURN with TBI, contained patients with burn injury with concomitant systemic trauma, including TBI.

Statistical Methods

Categorical variables were summarized by proportions and quantitative variables with means and standard deviations or as medians [25th and 75th quantiles]. We used logistic regression to evaluate the effect of TBI on mortality in patients with burns with and without non-TBI trauma. Model parameters were estimated with generalized estimating equations and a robust covariance estimate assuming an exchangeable working correlation structure was used to account for possible correlation of outcomes among patients treated at the same facility. We first conducted univariate logistic regression analyses comparing mortality across injury types, GCS and ISS categories. Glasgow Coma Scores were categorized as mild (GCS 13–15), moderate (GCS 9–12) and severe (GCS 3–8), while the ISS was categorized as mild (1–15), moderate (16–25) and severe (>= 26). Next, mortality was modeled as a function of TBSA, age, inhalation injury (present/absent), and trauma injury type (Burn only, non-TBI trauma, TBI). Age was included as a continuous variable centered at 40 years. Burn TBSA was categorized into quintiles, specifically [0–20], (20–40], (40–60], (60–80], (80–100]. Only main effects were included in the model due to small numbers of observations in some combinations of age, injury, inhalation injury, and burn size. All statistical tests were two-sided and evaluated at a significance level of 0.05. Statistical analyses were conducted using SAS Software Version 9.4.

RESULTS

Baseline characteristics of the 32,334 patients included in this analysis can be found in Table 1. Eighty-eight percent of the patients fell into the BURN ONLY group, while 9% and 3% fell into the BURN with TRAUMA/NO TBI and BURN with TBI groups, respectively. Age, gender, and TBSA were similar across the three groups, but the incidence of inhalation injury was doubled in the BURN with TRAUMA/NO TBI (15.4%) and BURN with TBI (15.3%) groups when compared to the BURN ONLY (7.2%) group. The BURN with TBI group generally had a lower GCS and higher ISS on admission when compared to the two other groups (Figure 2). Patients in the BURN with TRAUMA/NO TBI group tended to have GCS and ISS intermediate to the BURN ONLY and BURN with TBI groups. Notably, the BURN with TBI group had the largest proportion of patients with GCS 3.

Mortality differed significantly across GCS severity groups ($p < 0.001$) with the odds of mortality higher for severe (OR = 16.25 [13.59, 19.43]) and moderate (OR = 6.66 [5.00, 8.87]) GCS categories relative to the mild. Severe GCS had higher odds of mortality than moderate GCS patients as well (OR = 2.44 [1.83, 3.25]). Considering injury types, observed mortality was higher for patients with a severe GCS and BURN with TBI patients than for BURN ONLY and BURN with TRAUMA/NO TBI patients with severe GCS. Observed mortality by injury type across GCS severity is shown in Table 1.

Mortality differed significantly across ISS groups as well ($p < 0.001$). The odds of mortality were higher for severe (OR = 49.99 [40.63, 61.51]) and moderate (OR = 13.82 [11.54, 15.54]) ISS groups relative to the mild group and for severe versus moderate (OR = 3.62 [3.16, 4.14]). Observed mortality by injury type across ISS severity is shown in Table 1. There is a clear trend towards increased mortality in the BURN ONLY group with a moderate to severe ISS. This appears to be driven by the presence of inhalation injury and possibly age. Of those patients with a severe ISS, 42.8%, 23.4% and 17.9% in the BURN ONLY, BURN with TRAUMA/NO-TBI, and BURN with TBI groups had inhalation injury, respectively. BURN ONLY patients with severe ISS scores were also older, with a median age of 47 years, compared to 40 years in the BURN with TRAUMA/NO TBI group and 38 years in the BURN with TBI group.

Mortality differed significantly across injury categories ($p < 0.001$). Mortality was highest for BURN with TBI, followed by BURN with TRAUMA/NO TBI and BURN ONLY (Table 1). The odds ratios for BURN with TBI vs. BURN ONLY was 2.43 [1.95, 3.03], BURN with TRAUMA/NO TBI versus BURN ONLY was 1.20 [1.01, 1.43], and BURN with TBI versus BURN with TRAUMA/NO TBI was 2.03 [1.65, 2.48]. Mortality continued to differ across injury categories after adjusting for age, TBSA, and inhalation injury (Table 2). The adjusted odds ratio for BURN with TRAUMA/NO TBI versus BURN ONLY remained similar to the unadjusted odds ratio (OR = 1.27 [1.06, 1.53]) but increased for BURN with TBI versus BURN with TRAUMA/NO TBI (OR = 3.33 [2.30, 4.82]) and for BURN with TBI versus BURN ONLY (OR = 4.22 [2.85, 6.18]). The logs odds of mortality also increased with increasing age, TBSA and presence of inhalation injury. Using this logistic regression model, we estimated mortality across TBSA quintiles and injury types at age 45 and 65 years old (Figure 3); predicted mortality shows a stepwise increase with an increase in TBSA and in the presence of TBI and inhalation injury.

DISCUSSION

It is well established that certain risk factors are associated with worse outcome in isolated burn and traumatic brain injuries. For burn patients, mortality is associated with age, TBSA and the presence of inhalation injury [11–14]. For TBI, mortality risk factors include GCS, pupillary reactivity, midline shift on computed tomography imaging, intracranial hypertension, hypoxemia, hypotension, and age [15, 16]. Unfortunately, little is known about concomitant burn injuries and TBI. In the only previously published work (in abstract version only) describing combined burn-TBI, only 10% of patients treated for burn injury at single military hospital had a documented TBI [1]. In addition, studies looking at combined burn and non-TBI trauma injuries, 0.38–43% of burn patients had concomitant trauma [2–4].

In the combat theater, blast injuries are common, particularly from improvised explosive devices, and will likely increase the incidence of combined injury [17–19]. Our current analysis of the NTDB, which analyzed thousands of patients, showed similar results, with non-TBI traumatic injuries documented in 9% of burn patients, while TBI was documented in only 3% of burn patients. The true incidence of combined burn-TBI is unclear, as it has not been the focus of a prospective study. Brain imaging guidelines specific to the burn-injured patient have not been developed, and no prospective observational study has assessed the incidence of TBI on admission in the burn patient. Vigilance in identifying TBI in burn injured patients could influence treatment paradigms that may mitigate some of the inherent risk associated with the combined injury.

As with previous studies, our analysis of adult burn patients showed that mortality is most strongly associated with age, TBSA and inhalation injury. We also showed that the presence of concomitant burn injury and TBI increases mortality, and this has a synergistic effect with TBSA and inhalation injury (Figure 3). There are a number of reasons this may be the case. There is emerging literature supporting the hypothesis that disruption of the blood-brain barrier and increased neuro-inflammation in the setting of burn injury [20, 21]. A recent study in sheep with burn and inhalation injury reported basement membrane disruption and blood vessel dilation throughout the brain as well as microvascular bleeding with no changes in vital signs, suggesting that the blood brain barrier may indeed be disrupted in isolated burn injury [22]. A single study of brain imaging in burns throughout the hospital course reported that significant cerebral issues exist, particularly in the white matter [23]. Identification of imaging criteria for burn injury, particularly with accompanying inhalation injury, will require a prospective multicenter observational study.

Secondly, management of burn injuries requires significant volume resuscitation with albumin and crystalloid given significant insensible losses that occur through injured skin. This contrasts with the general management of TBI, in which resuscitation is somewhat fluid restrictive with a target of euvolemia. The rationale for this relatively restrictive fluid management practice is that the disruption of the blood-brain barrier that occurs after TBI promotes third-spacing of water into the brain and worsening cerebral edema. This is indirectly seen in TBI patients who have higher mortality with a high-volume resuscitation [24–27]. In addition, resuscitation with albumin has been shown to increase mortality in TBI patients [10], the most likely mechanism of action being increased ICP secondary to worsening cerebral edema [28]. Accordingly, albumin is typically avoided for at least the first week following TBI. Thirdly, burn patients often require many trips to the OR for surgical debridement within the first couple of weeks after injury, which can be associated with significant volume losses and hypotension. This occurs during a period of time when patients with TBI are most vulnerable to episodes of hypotension, an important independent risk factor of mortality following TBI [16].

In addition to GCS, ISS was also was found to be a risk factor for mortality, a finding consistent with the only other study looking at combined burn-TBI injuries [1]. We also found that BURN ONLY patients had worse outcomes with moderate and severe ISS when compared to the other two groups. This is consistent with Hawkins et al. [3], who in their analysis of the NTDB from 1994–2002, showed that burn only patients had a higher mortality than patients with combined burn and non-TBI trauma at any given ISS. We suspect this is driven by the presence of inhalation injury, as in our analysis, patients with a severe ISS and BURN ONLY had more than double the frequency of inhalation injury in the BURN with TBI group with a severe ISS. However, this data should be interpretably cautiously given the variable ways the ISS is recorded in the NTDB. In addition, it is not clear how accurate ISS reflects burn injury in the setting of other traumatic injuries and the ISS may actually obscure the relationship between burn and mortality [29].

Strengths of this study include the large sample size available through the NTDB. However, such an analysis is limited by its retrospective nature and reporting bias. The NTDB has the same limitations as any national database: variable data quality, data entry errors, data omission, and chart abstraction errors. For example, stratifying injury severity and response to resuscitation using vital signs was limited by the large number of missing data fields. Data collection from burn and non-burn facilities may differ, leading to bias and misrepresentation of the data, including how TBSA is calculated and the presence of inhalation injury determined. In addition, the ISS is reported using thee different calculations. We tried to mitigate this bias to the extent we could by ranking the ISS scores in order of preference (ISSLOC > ISSAIS > ISSICD) and only analyzing the most favorable ISS available per patient. Perhaps one of the most significant disadvantages in using the NTDB for burn analysis is that the NTDB is not the sole registry for burn patients, and as such, may not include those cases reported only to the National Burn Repository. This is evident in one analysis in which the prevalence of combined burn and non-TBI trauma was 0.44% in the NTDB and 5.8% in the National Burn Repository (NBR) [4]. Hence, this study should not be used to determine the incidence of combined burn and TBI. A common data set for burn injury parameters between the NTDB and the NBR would enable database linkage and more robust interpretation. Specifically, elements that should be common to BOTH the NBR and NTDB should span burn injury severity (TBSA burn size, inhalation injury, Baux score), traumatic injury severity (TBI type, GCS, ISS, etc) and comorbidity descriptions. Finally, there may be further un-identified cofounders that may influence the results of our analysis.

Despite these limitations, our study raises important questions regarding the treatment of populations with combined injuries that have potentially differing treatment priorities. Our findings suggest that such complex injuries may have worse outcomes and that standardized protocols should be applied thoughtfully, taking all injuries and physiologic aberrancies into consideration. Precision in identification of injuries will need to be matched by precision in injury treatment. Unraveling the complexities accompanying combined burn injury and TBI will require a stepwise approach beginning with identifying the true incidence of the event, progression of both TBI and burn injury during treatment, outcomes, and identification of injury severity biomarkers to identify populations at risk. Ours is but the first step in the chain.

CONCLUSIONS

In conclusion, the incidence of combined burn and TBI in the NTDB is low but the mortality risk higher when compared to burn injury alone. In the combined injury group, age, TBSA, and the presence of inhalation injury continue to have the greatest influence on mortality. Prospective research is necessary to better understand the pathophysiological mechanisms driving this increased mortality and identifying individualized treatment options to mitigate risk.

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HIGHLIGHTS

Our analysis of the National Trauma Data Bank suggests that:

- Traumatic brain injury (TBI), when combined with burn injury, may contribute to increased burn patient mortality
- Both TBI and other systemic trauma in combination with burn injury increase mortality; however, TBI combined with burn injury may have greater impact on survival.
- Mortality after burn injury and burn injury combined with either trauma or TBI increases with age, burn total body surface area (TBSA) and inhalation injury
- Inhalation injury is more common in burn patients with traumatic injuries

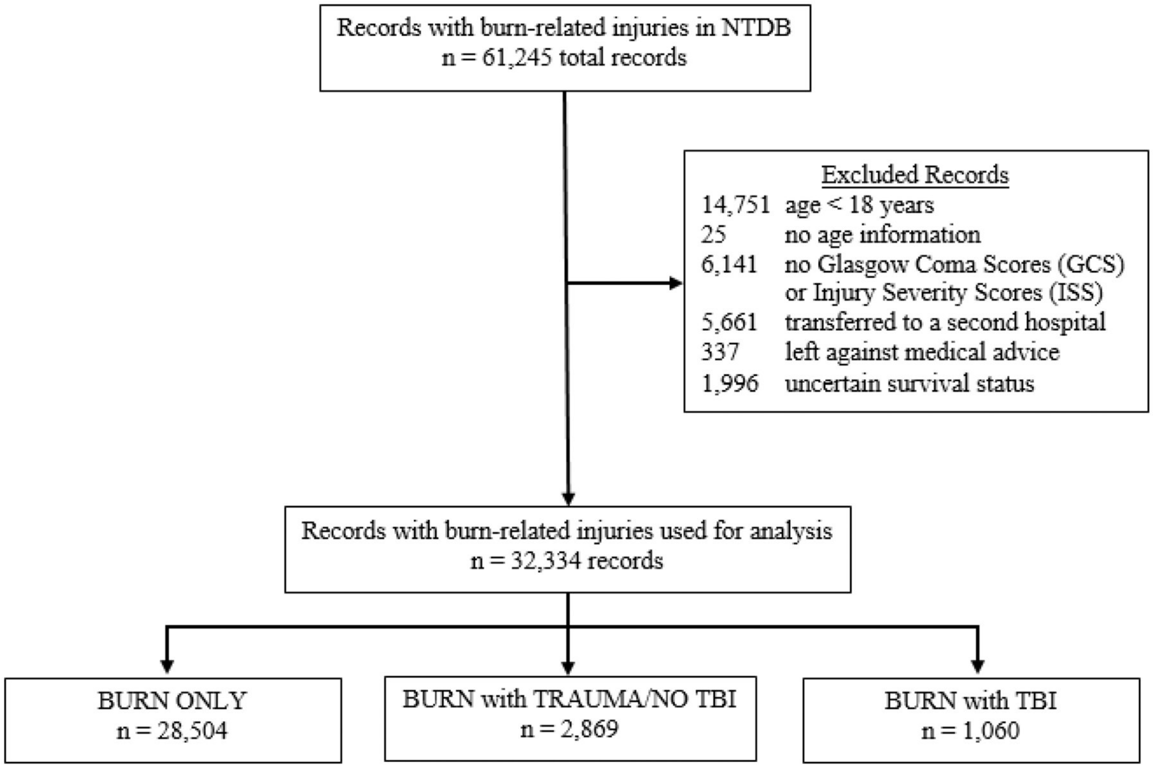
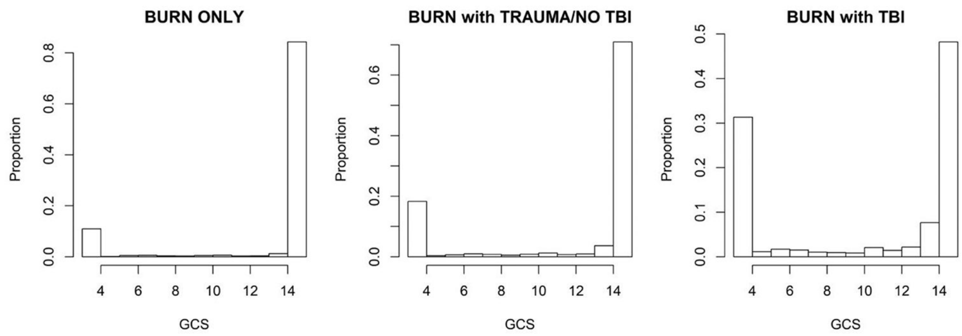


Figure 1.

Flowchart of our analysis of the National Trauma Data Bank (NTDB) of patients with burn injuries from 2007–2012

A.



B.

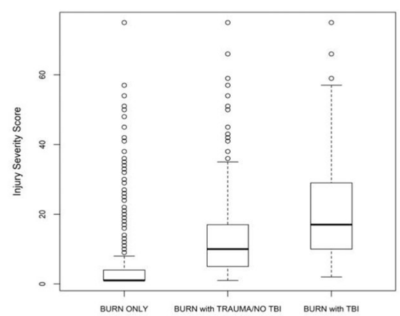


Figure 2.

Distribution of (A) Glasgow Coma Scores (GCS) and (B) Injury Severity Scores Across Injury Type.

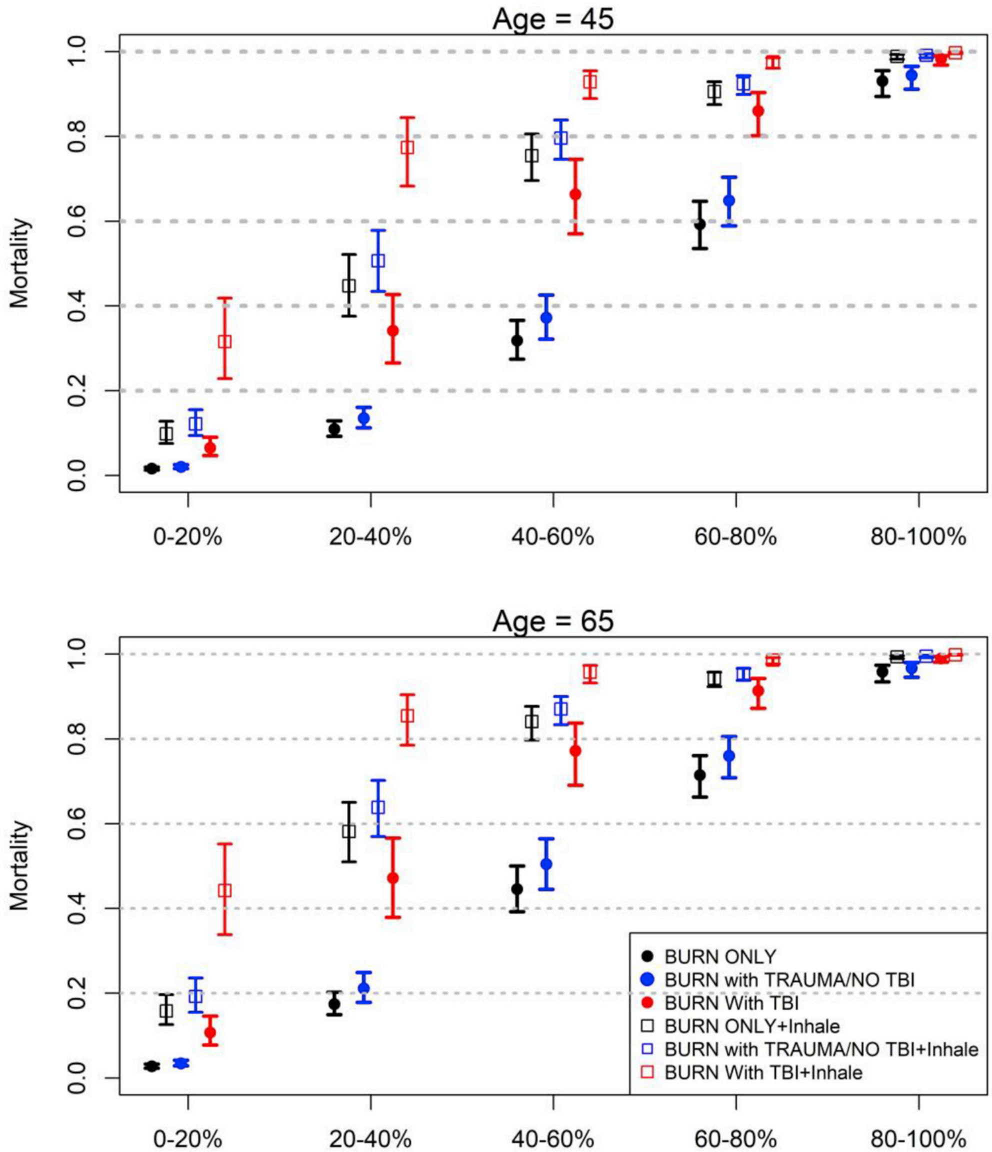


Figure 3.

Estimated mortality using logistic regression models across Burn Total Body Service Area (TBSA) quintiles, injury type and presence of inhalation injury in patients aged 45 and 65 years. Predicted mortality shows a stepwise increase with an increase in TBSA and in the presence of TBI and inhalation injury.

Table 1.

Summary statistics for patients with burn-related injuries in the National Trauma Data Bank

	Burn Only (n=28,405)	Burn with Trauma/No TBI (n=2,869)	Burn with TBI (n=1,060)
Age	43.9 ± 17.2	42.8 ± 16.9	41.0 ± 16.9
Gender (% Male)	20,519 (72.3%)	2,186 (76.2%)	801 (75.6%)
TBSA Category			
0–20%	24,939 (87.8%)	2,430 (84.7%)	897 (84.6%)
20–40%	2,175 (7.7%)	255 (8.9%)	98 (9.2%)
40–60%	631 (2.2%)	106 (3.7%)	30 (2.8%)
60–80%	346 (1.2%)	38 (1.3%)	17 (1.6%)
80–100%	314 (1.1%)	40 (1.4%)	18 (1.7%)
Inhalation Injury (%)	2,033 (7.2%)	443 (15.4%)	162 (15.3%)
GCS [25^{th}, 75^{th}]	15 [15, 15]	15 [13, 15]	14 [3, 15]
ISS [25^{th}, 75^{th}]	1 [1, 4]	10 [5, 17]	17 [10, 29]
Mortality	1,787 (6.3%)	254 (8.9%)	176 (16.6%)
Mortality by GCS			
Mild	620 (2.5%)	54 (2.4%)	14 (2.3%)
Moderate	78 (16.7%)	14 (14.6%)	7 (12.5%)
Severe	1089 (30.7%)	187 (30.9%)	155 (39.8%)
Mortality by ISS			
Mild	510 (2.0%)	57 (2.8%)	10 (2.3%)
Moderate	631 (28.8%)	61 (13.1%)	13 (4.7%)
Severe	646 (63.5%)	136 (35.3%)	153 (43.5%)

GCS = Glasgow Coma Scale; ISS = Injury Severity Score; TBSA = burn total body surface area

Table 2.

Logistic regression model relating mortality to age, injury type, total body service area (TBSA).

Parameter	Level	Estimate	LCL	UCL	p-value
Intercept		−4.37	−4.59	−4.14	<.0001
Age		0.0541	0.0483	0.060	<.0001
Injury Type[a]	Trauma/No TBI	0.238	0.053	0.422	0.011
	TBI	1.44	1.057	1.82	<.0001
TBSA[b]	80–100%	6.69	6.19	7.19	<.0001
	60–80%	4.47	4.21	4.73	<.0001
	40–60%	3.34	3.10	3.570	<.0001
	20–40%	2.00	1.81	2.20	<.0001
Inhalation Injury		1.88	1.65	2.11	<.0001

[a:] Reference group is BURN ONLY

[b:] Reference group is TBSA 0–20%

LCL: lower confidence limits 95%

UCL: upper confidence limits 95%