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Authors

Taylor, Sandra L
Sen, Soman
Greenhalgh, David G
et al.

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A Competing Risk Analysis for Hospital Length of Stay in Patients With Burns

Sandra L. Taylor, PhD, Soman Sen, MD, David G. Greenhalgh, MD, MaryBeth Lawless, RN, Terese Curri, MS, and Tina L. Palmieri, MD

Department of Public Health Sciences, University of California Davis Medical Center, Sacramento (Taylor, Palmieri); Department of Surgery, Shriners Hospitals for Children—Northern California, Sacramento (Sen, Greenhalgh, Lawless, Curri, Palmieri); Burn Department, Shriners Hospitals for Children—Northern California, Sacramento (Sen, Greenhalgh, Palmieri)

Abstract

IMPORTANCE—Current outcome predictors for illness and injury are measured at a single time point—admission. However, patient prognosis often changes during hospitalization, limiting the usefulness of those predictions. Accurate depiction of the dynamic interaction between competing events during hospitalization may enable real-time outcome assessment.

OBJECTIVE—To determine how the effects of burn outcome predictors (ie, age, total body surface area burn, and inhalation injury) and the outcomes of interest (ie, mortality and length of stay) vary as a function of time throughout hospitalization.

DESIGN, SETTING, AND PARTICIPANTS—In this retrospective study, we used the American Burn Association’s National Burn Repository, containing outcomes and patient and injury characteristics, to identify 95 579 patients admitted with an acute burn injury to 80 tertiary American Burn Association burn centers from 2000 through 2009. We applied competing risk statistical methods to analyze patient outcomes.

MAIN OUTCOMES AND MEASURES—We estimated the cause-specific hazard rates for death and discharge to assess how the instantaneous risk of these events changed across time. We

Corresponding Author: Tina L. Palmieri, MD, Burn Department, Shriners Hospitals for Children—Northern California, 2425 Stockton Blvd, Ste 718, Sacramento, CA 95817 (tina.palmieri@ucdmc.ucdavis.edu).

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Study concept and design: Taylor, Greenhalgh, Palmieri.

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Drafting of the manuscript: Taylor, Sen, Lawless, Curri, Palmieri.

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further evaluated the varying effects of patient age, total body surface area burn, and inhalation injury on the probability of discharge and death across time.

RESULTS—Maximum length of stay among patients who died was 270 days and 731 days among those discharged. Total body surface area, age, and inhalation injury had significant effects on the subdistribution hazard for discharge ($P < .001$); these effects varied across time ($P < .002$). Burn size (coefficient -0.046) determined early outcomes, while age (coefficient -0.034) determined outcomes later in the hospitalization. Inhalation injury (coefficient -0.622) played a variable role in survival and hospital length of stay.

CONCLUSIONS AND RELEVANCE—Real-time measurement of dynamic interrelationships among burn outcome predictors using competing risk analysis demonstrated that the key factors influencing outcomes differed throughout hospitalization. Further application of this analytic technique to other injury or illness types may improve assessment of outcomes.

Identification of factors predicting length of stay (LOS) and mortality has been a core component of outcome studies and quality-of-care analyses in illness and injury. Predictors allow for design and evaluation of therapies and provide physicians as well as patients with estimates of survival and LOS. The vast majority of predictors are gathered at admission, and their effects are assumed to remain unchanged across time.¹⁻³ In patients with burn injuries, age, total body surface area (TBSA) burn, and inhalation injury form the burn outcomes triad.³⁻⁸ Data on all these factors are gathered at admission and used to estimate outcomes. However, these parameters may or may not retain their initial predictive value in the weeks and months after hospitalization. As the medical field strives to improve quality of care, accurate depiction of factors throughout the spectrum of care, not just at the time of admission, becomes imperative.

Hospital LOS is among the most commonly analyzed outcome measures and can be viewed as a benchmark for measuring changes during hospitalization. Studies that deal with LOS address 2 basic issues: length of hospitalization and which factors influence duration of hospitalization. Multiple linear regression has been used to analyze LOS data in patients with burns, but violations of model assumptions (namely, that residuals are normally distributed and variance is independent of the mean) and outlier effects call into question the validity of LOS findings.⁹ Furthermore, how the analytical dataset is defined can have profound effects on the results. For example, in LOS studies on patients with burns, results differ if one analyzes survivors alone, nonsurvivors alone, or the combination of survivors and nonsurvivors.¹⁰⁻¹⁸ While age is a predictor of LOS in survivors, age is not predictive in nonsurvivors.¹⁰ Nonsurvivors have a shorter LOS and lower overall costs than survivors. Finally, TBSA burn has opposing effects on LOS for survivors vs nonsurvivors (ie, TBSA burn increases LOS in survivors but decreases it in nonsurvivors). Evaluating these factors in the combined group of survivors and nonsurvivors is subject to population bias, as survivors far outnumber nonsurvivors. Hence, conclusions may hold true for generalized populations but obscure important subpopulation dynamics. Conversely, analysis by survival groups restricts the interpretation to only what would occur if the competing risk were not a possibility. Neither analysis reflects the reality or interrelation between the outcomes.

Survival analysis methods are designed to evaluate time to event data. Classically, the event of interest is death, but time to any event can be modeled with this method. Competing risk analyses extend survival analysis methods to situations with multiple possible events, where the occurrence of one either precludes the others or substantially alters the probability of other events. Length of stay for patients with burns is time to event data with 2 possible but mutually exclusive events: death and discharge. Meaningful interpretation and understanding of hospital LOS for patients with burns necessitates a competing risk approach that analyzes cumulative incidence of the possible outcomes across time, thus providing insight into the risk of each event individually and in relation to each other.

In this study, we applied competing risk statistical methods to analyze hospital LOS for patients with burns reported in the American Burn Association's National Burn Repository, a national database. We first estimated the cumulative incidence of death and discharge to understand the overall pattern of hospital LOS for these 2 outcomes and subsequently estimated the cause-specific hazard rates to understand how the instantaneous risk of these events changed across time. We then investigated the effects of patient age, TBSA of the burn, and the presence of inhalation injury on the cumulative incidence of death and discharge. We hypothesized that the effects of traditional burn outcome predictors on LOS and mortality vary during hospitalization, a concept not addressed by current modeling techniques.

Methods

The National Burn Repository contains outcomes and patient and injury characteristics for patients admitted to burn centers for treatment of burns. We obtained the American Burn Association's 2009 release of the National Burn Repository consisting of 286 293 admission records. To focus on recent burn care and outcomes, we restricted our analysis to admissions in 2000 or later ($n = 210\ 683$). We excluded records missing information on survival to discharge ($n = 12\ 226$), age ($n = 5441$), burn size ($n = 42\ 545$), inhalation injury ($n = 12\ 861$), or hospital LOS ($n = 4471$).¹⁹ We also removed 6530 records with unreliable information (eg, TBSA that is affected by a burn $>100\%$, records from facilities with questionable patient ages or mortality rates), 23 084 records associated with readmissions, 3690 records of patients with nonburn injuries, and 3218 records identified as probable duplicates. This screening left 95 579 records of initial hospital visits with the minimum information for necessary analysis (ie, patient age, burn or inhalation injury, hospital discharge status, and LOS). This study was approved by the University of California Davis Human Subjects Review Board. No patient consent for participation was required by the University of California Davis Institutional Review Board.

For the competing risks of death and discharge, we calculated cumulative incidence function (CIF) for each event. The CIF is the probability that an event of type j occurs by time t . We then estimated the cause-specific hazard rates for each event type using an Epanechnikov kernel-based smoothing algorithm with a locally determined bandwidth. The cause-specific hazard rate is the instantaneous risk of experiencing a specified event of interest (eg, discharge) at time t given that the patient is alive at time t and has not yet experienced the event.

To evaluate the effect of burn size, age, and inhalation injury on the CIFs of death and discharge, we first applied Fine and Gray's²⁰ proportional hazard regression approach. This approach extends the Cox proportional hazard model to account for the presence of competing events by modeling the effect of the covariates on the subdistribution hazard. Robust estimators were used for the variance to account for potential correlation of outcomes of patients treated at the same facility. A key assumption of the Fine and Gray model is that the effects of the covariates are proportional to the baseline hazard and are constant across time. We used Scheike and Zhang's²¹ Cramer-von Mises type goodness-of-fit test to determine the proportionality assumption for each factor and fit time-varying coefficients where this test indicated significant ($P < .05$) departure from proportionality. Statistical analyses were conducted in R programming language, version 2.15.2.²² The R package `cmprsk`²³ was used to estimate the CIFs for each event type. Cause-specific hazard rates were estimated with `muhaz` and regression analyses were conducted with the `time reg` package.^{24,25}

Results

The 95 579 records were from 80 burn care facilities and included admissions from 2000 through 2009. A total of 4112 patients (4.3%) died. The maximum LOS among patients who died was 270 days and was 731 days among those discharged. Consistent with results of previous mortality investigations,^{26–28} patients who died in the hospital were older and had larger burns than did discharged patients (Table 1). Approximately half the patients who died sustained an inhalation injury vs 7.2% of the discharged patients. Most patients treated in a burn center had short LOS: 30% were discharged after 1 day, 62% within 1 week, and 90% within 30 days (Figure 1A and B). Patients who died generally died early in their hospital stay: 27% of those who died did so within 1 day of admission and 50% of the deaths occurred within 6 days (Figure 1B).

We further investigated the characteristics of patients who died within 1 day of admission. These patients tended to have much larger burns than did patients who died later. Median TBSA of the burn (25th, 75th quantile) for patients who died within 1 day was 63.5% (32.0%, 88.0%) compared with 36.9% (15.0%, 56%) for patients who died later during their hospital stay. The age distribution was similar, with a median age of those who died within 1 day of 56.9 years (38.0 years, 76.9 years) vs 57.8 years (41.8 years, 75.0 years) for those who died after 1 day. Inhalation injury was more prevalent among patients who died within 1 day (61%) vs those who died later (47%).

Estimates of the cause-specific hazard rate for discharge showed a high likelihood of discharge initially on admission with a rapid decline across time. At longer LOS (eg, >50 days), the likelihood of patient discharge on any particular day was relatively low. Consistent with the low mortality among patients with burns (<5%), the hazard rate of death was much lower (Figure 1D) than for discharge (Figure 1C). The risk of death likewise declined initially but subsequently increased after about 100 days.

Burn size, age, and inhalation injury had significant effects on the discharge subdistribution hazard ($P < .001$ for all factors) (Table 2). Increases in TBSA of the burn, age, and the

presence of inhalation injury decreased the hazard ratio of discharge (Table 1). The goodness-of-fit test indicated that the effects of all 3 factors varied significantly across time ($P < .002$ for all factors). We fit the proportional hazard model allowing the coefficient of each factor to vary across time. All 3 factors remained highly significant predictors of the subdistribution hazard for discharge ($P < .001$ for all factors). With only 2 events of interest (death and discharge), modeling results for the sub-distribution hazard of death are complementary to those of discharge and are not shown.

The effects of burn size and age varied substantially across time. Burn size had a large initial influence on the probability of discharge early in the course of a hospital stay, with TBSA of larger burns reducing the likelihood of discharge (Figure 2A). Across time, however, the influence of TBSA of the burn on the likelihood of discharge declined. Age showed an opposite pattern to burn size. The estimated effect of age on the likelihood of discharge was initially small but increased across time, with older patients less likely to be discharged than younger patients (Figure 2B). Notably, the time-invariant model underestimated the effect of burn size and overestimated the effect of age on discharge for LOS less than 100 days (Figure 2A). Failing to account for the temporal changes in the effects of these factors could lead to inaccurate estimation of LOS. Finally, while inhalation injury significantly decreased the likelihood of discharge, there was no discernible temporal pattern to the effect size (Figure 2C). This finding contrasts with several previous studies in which inhalation injury had no significant effect on LOS.^{10,12,16}

Using the time-varying coefficients, we predicted the CIFs for discharge and death at varying burn sizes and ages, with and without inhalation injury. Both increasing burn size and increasing age reduced the probability of discharge and extended the LOS (eFigure in the Supplement). The predicted probability of mortality was much less than the probability of discharge for small burns and young patients. With older patients and larger burns, however, the probability of mortality became sizable and exceeded the probability of discharge. The presence of inhalation injury further reduced the probability of discharge and extended hospital LOS (eFigure in the Supplement). The effect of inhalation injury was most apparent in patients with moderate burn sizes and of middle age. For example, for a 50-year-old patient with 50% TBSA burn injury, the probability of discharge exceeded the probability of death after 50 days. However, with the addition of inhalation injury, the probability of death was always greater than the probability of discharge.

Discussion

This study is unique in burn care investigations in using competing risk methods to investigate predictive factors (ie, age, TBSA of the burn, and inhalation injury) of LOS and allowing factor effects to vary across time. Through this approach, we captured the interaction between hospital LOS and death and elucidated greater complexities in the effects of TBSA of the burn, age, and inhalation injury on LOS than previously recognized. We showed that the likelihood of discharge varied throughout hospitalization. Burn size was the driver of early outcomes, while age became important later in hospitalization. Inhalation injury also influenced the probability of survival and LOS. For some patients, the risk of death was higher than the likelihood of discharge subsequent to admission (ie, patients older

than 75 years with more than 25% TBSA of the burn and inhalation injury), while for other groups, such as young children, the likelihood of death was always lower than the likelihood of discharge across time.

Burn size is likely the main determinant of early outcomes for several reasons. First, the size and depth of a burn determines initial treatment and resource needs. The larger the burn, the greater the physiological burden and the higher the likelihood of death from burn shock. Second, burn size influences how quickly a patient can be discharged. Larger wounds result in increased surgical intervention, dressing changes, and pain; hence, patients with larger burns generally have longer LOS. Across time, the effect of burn size on the likelihood of discharge declines as the influence of other factors (eg, age, co-morbidities, and complications) affect patient wound healing.

Age follows the opposite pattern of burn size. A patient with a burn of a particular size will be admitted regardless of age, and the likelihood of discharge during the first few days will depend more on the injury characteristics than age per se. However, across time, age plays an increasing role in whether a patient is discharged; this pattern could reflect comorbidities, complications, or prolonged healing times, which are more common in older patients.

Our study clarifies some of the inconsistencies in the literature regarding LOS after a burn injury. Previous studies assessing survivors and nonsurvivors have demonstrated a significant positive relationship between LOS and burn size^{10,12,13,15,16} and age.^{10–13,16} However, in studies restricting the analysis to either survivors or nonsurvivors, the results differ.^{14,15,17,18} In nonsurvivors, age was not a significant predictor of LOS; however, age was significant for survivors. Our results show that the majority of deaths after a burn injury occur in the first few days after the burn injury, and that patients die owing to injury severity. Late deaths are likely related to other factors, such as comorbidities and age.¹⁸ Furthermore, burn size had opposite effects on LOS between survivors and nonsurvivors. Consistent with our study, LOS increased with burn size among survivors but decreased for nonsurvivors.¹⁰ Ironically, patients who die have shorter LOS than those who survive.

Another perspective gained from the competing risk analysis is related to the relationship between survival and discharge. Although determinations of burn survival are made at admission based largely on injury severity, our analysis suggests that there is a point later in hospitalization at which the likelihood of death is greater than discharge (or conversely, when discharge is more likely than death). These transitions may provide physicians with a valuable benchmark with which to reassess patient treatment and outcomes. Further study will be required to determine if these transitions are valid for individual patients.

Competing risk analysis may also play a role in the determination of quality-of-care paradigms for injury and illness across time. Current methods use a 2-dimensional linear approach to measure outcomes at a given time. However, this approach provides little insight into the quality of care during hospitalization. For example, the outcome of a 50-year-old man who dies at 2 days vs 30 days from a 70% TBSA burn injury is ultimately assessed as a treatment failure. However, the timing of death may be a reflection of the quality of care for resuscitation in the first 48 hours (ie, one center successfully resuscitated the patient, while

the other was unsuccessful). The patient who survives those 30 days will generate greater hospital costs and longer LOS, both of which may generate a negative impression in terms of cost-effective quality of care in the current system. Ultimately, assessment of competing risks across time should be incorporated into quality-of-care measurement paradigms.

The strength of this study lies in the large data set and the use of competing risk methods with variable predictor effects across time after burn injury to assess burn outcomes. However, the data from large administrative data sets have pitfalls that must be acknowledged. Approximately 60% of the excluded records were omitted to focus on our population of interest (ie, outcomes for initial admissions of patients with burns admitted since 2000) and hence were excluded for reasons unrelated to data quality. The remaining 40% of the excluded records were omitted owing to missing or unreliable information. In restricting the data set in this way, we sought to create a high-quality, reliable data set. Any data set will have concerns regarding data quality, but we exhaustively applied stringent criteria to minimize data irregularities. Second, burn size and inhalation injury are determined by individual centers and their accuracy cannot be confirmed objectively, which could lead to individual center variability in diagnosis. However, the reliability of burn size estimates among different burn care professionals has been evaluated in several studies.^{29,30} There is consistency among burn care surgeons and burn care nurses with respect to burn size estimation, which increases with experience. Hence, the accuracy of burn size estimates is likely to be greatest at burn centers, which have the most experience with burn injuries. Likewise, criteria for inhalation injury identification have been documented in the Advanced Burn Life Support course, completion of which is required for burn center verification. This experience reduces variability in diagnosis among centers, as demonstrated by the consistencies in patient characteristics and outcomes in the National Burn Repository.

Second, using the model for prognostication in any individual patient is not necessarily appropriate because survival rates and LOS estimates are for populations rather than individuals. Third, other factors (ie, comorbidities) are not accounted for in the model and may influence LOS. Finally, although the data analyzed comprised more than 90 000 individuals, they may not be representative of burn care in other centers. Given the large number of records and the consistency of data, however, it is unlikely that there are significant differences at other centers.

Not all factors and results that are considered apparently obvious have been proven to contribute to patient outcomes. We believe that it is important to question our biases, critically evaluate our assumptions, and test factors that we think make a difference. Our results are important for 2 reasons. First, they emphasize that different phases of care may have different optimal therapies. For example, trials concentrating solely on the early phase of hospitalization are unlikely to be successful for decreasing mortality for events that occur subsequent to hospitalization, such as pneumonia. Second, our results introduce the concept of time- and age-specific care paradigms: older adults with prolonged hospitalization have different morbidity and mortality predictive factors. The next step is to use competing risks to identify critical junctures in care at which to target meaningful interventions.

Age, TBSA of the burn, and inhalation injury have been the foundation for burn injury outcome estimation for many years.^{3–8} The influence of these factors has been assumed to be static; that is, the factors have been assumed to have a non-changing and nonintegrative effect across time. Our study challenges those traditional assumptions by demonstrating that the factors influencing outcomes have variable influence at different times during hospitalization. The variable distribution of death after burn injury, in contrast to the progressive decline in discharge across time, suggests that different factors are driving these outcomes. Assessing the predictive value of outcome determinants via competing risk analysis provides insight into those factors and can help to refocus clinical studies to address issues that are important at a given time in hospitalization. The effects of time on variable interactions should be considered in the development of quality-of-care outcome measures for patients with burns.

Conclusions

Burn injury poses challenges to the physician, patient, and health system. Understanding how factors integrate and influence each other represents an important advancement in optimizing patient outcomes, improving patient care, allocating resources, and informing families. Competing risk methods and allowing for the variable influence of outcome predictors across time provide additional perspective that can assist in optimizing outcomes for patients with burns and other patients requiring intensive treatment across time. Further application of this analytic technique to other injury or illness types may improve assessment of outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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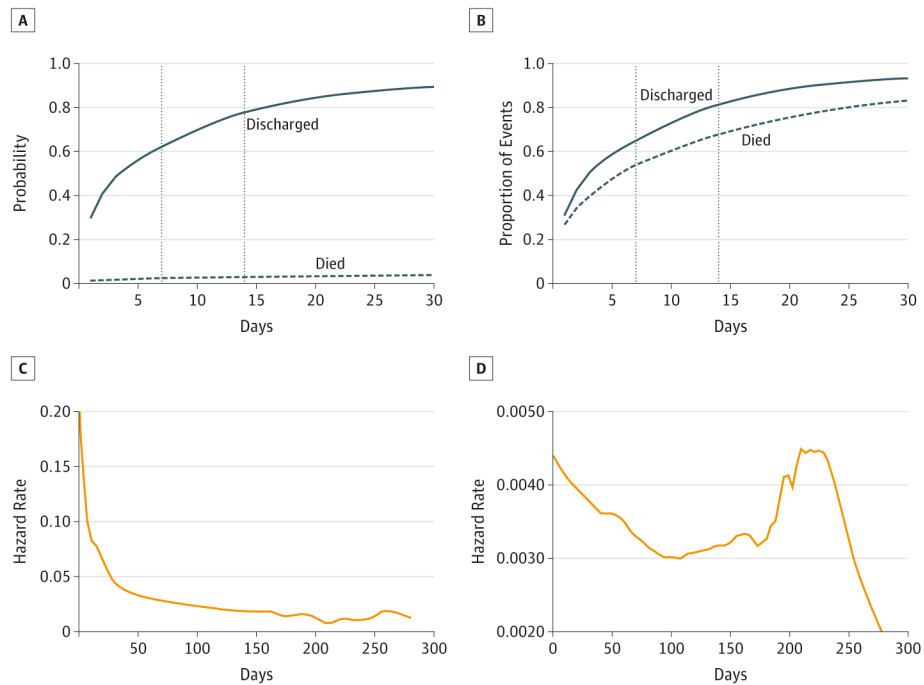


Figure 1. Thirty-Day Discharge and Death Rates for Patients With Burn Injury

A, Cumulative incidence functions for death after admission. Dashed vertical lines mark 1 and 2 weeks. B, Proportion of deaths and discharges for the first 30 days after admission. C, Smoothed cause-specific hazard rates for discharge. D, Smoothed cause-specific hazard rates for death.

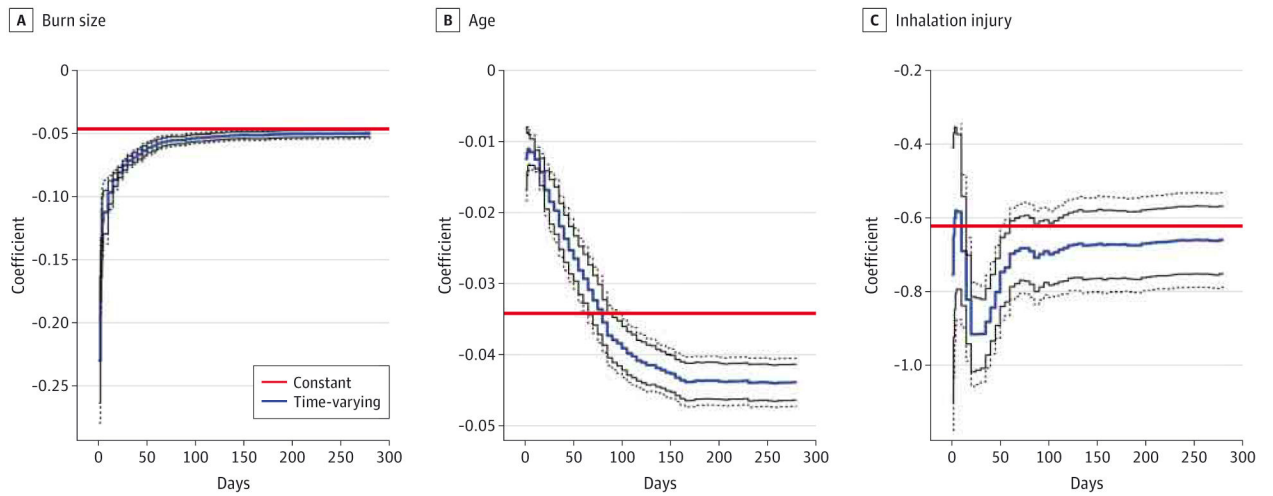


Figure 2. Effects of Burn Size, Age, and Inhalation Injury Across Time

Estimated constant and time-varying coefficients for the effect on the subdistribution hazard of discharge with death as a competing risk. Black solid and dotted lines show pointwise 95% confidence limits and 95% confidence bands, respectively. A, Burn size. B, Age. C, Inhalation injury.

Table 1

Characteristics of Patients Who Were Discharged and Those Who Died in the Hospital

Characteristic	Died in the Hospital (n = 4112)	Discharged (n = 91 467)
Age, y, median (25th, 75th quantiles)	57.6 (41.0, 75.5)	28.0 (8.9, 45.8)
Burn TBSA, %, median (25th, 75th quantiles)	38.0 (17.0, 67.5)	5.0 (2.0, 10.0)
Length of stay, d, median (25th, 75th quantiles)	6.0 (1.0, 20.0)	4.0 (1.0, 11.0)
Presence of inhalation injury, %	50.7	7.2

Abbreviation: TBSA, total body surface area.

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Table 2Estimated Coefficients for Discharge With Death as a Competing Event^a

Characteristic	Coefficient, Mean (SE)	Z Statistic	P Value
Burn size	-0.046 (0.001)	-39.1	<.001
Age	-0.034 (0.001)	-31.8	<.001
Inhalation injury	-0.622 (0.041)	-15.2	<.001

^aFine and Gray²⁰ competing risk regression analysis.

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