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Burn injury outcomes in patients with pre-existing diabetic mellitus: Risk of hospital-acquired infections and inpatient mortality☆

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ABSTRACT

Background: Diabetes mellitus (DM) is a major cause of illness and death in the United States, and diabetic patients are at increased risk for burn injury. We therefore sought to examine the impact of pre-existing DM on the risk of inpatient mortality and hospital acquired infections (HAI) among burn patients.

Methods: Adult patients ($\geq$18 years old) admitted from 2004 to 2013 were analyzed. Weighted Kaplan–Meier survival curves – adjusting for patient demographics, burn mechanism, presence of inhalation injury, total body surface area, additional comorbidities, and differential lengths of stay– were used to estimate the 30-day and 60-day risk of mortality and HAIs.

Results: A total of 5539 adult patients were admitted and included in this study during the study period. 655 (11.8%) had a pre-existing DM. The crude incidence of HAIs and in-hospital mortality for the whole burn cohort was 8.5% (n = 378) and 4.4% (n = 243), respectively. Diabetic patients were more likely to be older, female, have additional comorbidities, inhalational injury, and contact burns. After adjusting for patient and burn characteristics, the 60-day risk of HAI among patients with DM was significantly higher, compared to non-diabetic patients (RR 2.07, 95% CI 1.28, 6.79). However, no significant difference was seen in the 60-day risk of mortality (RR 1.34, 95% CI 0.44, 3.10).

Conclusions: Pre-existing DM significantly increases the risk of developing an HAI in patients following burn injury, but does not significantly impact the risk of inpatient mortality. Further understanding of the immune modulatory mechanism of burn injury and DM is imperative to better attenuate the acquisition of HAIs.

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1. Introduction

Diabetes mellitus (DM) affects roughly 12% of adults in the United States, or 29.1 million people, and represents a major burden to the healthcare system. The cost of DM care due to increased health care utilization and lost productivity was approximately $245 billion in 2012 [1]. Over the past 3 decades, the prevalence of adults diagnosed with DM in the US has increased substantially [2]. Diabetics are at increased risk for burn injury due to peripheral neuropathy, which is associated with decreased sensory and motor function and leads to the inability to quickly withdraw extremities from heat source [3–5]. Subsequently, a substantial proportion of patients admitted to burn centers are diabetic [6].

Burn injuries are often associated with complications, even in otherwise healthy individuals. Diabetics may be at increased risk for complications and mortality. For example, diabetics have a predilection for atherosclerotic occlusion in small and large vessels thus facilitating development of ischemic extremities. Diabetics also exhibit wound repair failures and infections [5,7,8]. This is commonly attributable to microangiopathy and altered neutrophil migration [9] with reduced bacteriocidal activity and impaired phagocytosis [10,11]. With increased longevity of the US population and the concomitant rise in the number of diagnosed diabetics, it is likely that the number of diabetics admitted to the hospital following burn that may indicate intensive medical or surgical care will also increase. While existing data suggests that tight glycemic control following burn injury improves complication and mortality rates, it is unclear whether pre-existing DM impacts patient outcomes after burn injury [12,13].

Thus, the primary objective of this study is to estimate the impact of diabetes on the risk of hospital acquired infections (HAIs) and inpatient mortality after being hospitalized for burn injury.

2. Methods

Patients were identified using the North Carolina Jaycee Burn Center registry, which consists of data collected on all admitted patients in real-time for reporting to the National Burn Repository. Adult (≥18 years old) patients admitted with burn injury including inhalation injury only between January 1, 2004 and December 31, 2013, were eligible for inclusion. Only a patient's first hospitalization, for their first burn, within the time period was included for analysis.

Registry data was then linked to the Carolina Data Warehouse for Health (CDW-H), which is a central repository for clinical and administrative data from the entire UNC Healthcare System, which includes the Jaycee Burn Center [14]. Registry data were validated using CDW-H data and manual chart review. Missing and illogical registry data were abstracted using similar methods. Patients were excluded if discharge date could not be determined (n = 37).

Diabetes mellitus was identified using both the comorbidities recorded in the burn registry and International Statistical Classification of Diseases and Related Health Problems (ICD-9) diagnostic codes attached to the inpatient billing records (ICD-9-CM 250). Mortality during the inpatient hospitalization was also captured using both the registry and CDW-H records. Hospital-acquired infections (HAIs) were identified using the UNC Hospital Epidemiology database, which documents HAIs identified through real-time, hospital-wide surveillance. Surveillance is performed in accordance with the Centers of Disease Control and Prevention (CDC) criteria and definitions [15]. Only a patient's first HAI was included in analyses.

Bivariate analyses comparing demographics, comorbidities, burn characteristics, and patient outcomes (inpatient mortality, HAIs, length of stay) between diabetic and non-diabetic patients were performed using Chi-square and Wilcoxon–Mann–Whitney tests, where appropriate. Comorbidities were identified using inpatient ICD-9-CM diagnostic codes and included prior myocardial infarction (412–412.9), congestive heart failure (428–428.9), peripheral vascular disease (441–441.9, 443.9, 785.4, and V43.4), cerebrovascular disease (438–438.9), pulmonary disease (490.0–496.9, 500–505.9, and 506.4), and renal disease (582–582.9, 583–583.7, 585–586.9, and 588–588.9). Yearly admit rates of diabetic patients were calculated using Poisson regression. A p-value < 0.05 was considered statistically significant. Revised Baux scores were calculated as described by Osler et al. [16]. Multivariable linear regression, adjusting for demographics, comorbidities, and burn characteristics, was used to estimate the average effect diabetes had on length of stay.

Kaplan–Meier survival curves were used to estimate the cumulative 30-day and 60-day risks of mortality among patients with and without DM. An Aalen-Johansen estimator was used to estimate the 30-day and 60-day cumulative incidence of HAIs in order to account for mortality as a competing risk [17]. Both risk differences (RDs) and risk ratios (RRs) were calculated. Only patients admitted for at least 2 days (i.e. at risk for an HAI as per CDC criteria) were included in HAI analyses. Weighted survival curves were used to estimate the standardized, cumulative 30-day and 60-day risk for both mortality and HAIs [18,19]. Standardized estimates were adjusted using inverse-probability of treatment weights (IPTW) to account for confounding and inverse-probability of censoring weights to account for potentially informative censoring.

Briefly, the IPTW for each patient was estimated using logistic regression which modeling the probability of DM using admit year (categorized into tertiles, 2004–2007, 2008–2010, and 2011–2013), patient age (modeled as a linear spline with knots at 30, 45, 60, and 75 years old), gender, race/ethnicity, comorbidities, burn mechanism, total burn surface area (modeled as a linear spline with knots at 20, 35, 50 and 65), and inhalational injury. Weights were stabilized using the marginal (i.e. overall) probability of having diabetes in the cohort. The inverse-probability of censoring weights was also estimated using logistic regression. The probability of censoring (i.e. being discharged alive) was estimated using DM status and all covariates included in the IPTW model. These weights were also stabilized using the marginal probability of being censored. Weights were then multiplied together to obtain a final weight for each patient and truncated at 5% and 95%.

Confidence intervals for both the crude and standardized cumulative incidence measures were calculated using a nonparametric bootstrap. Specifically, 500 resamples with