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Hypertension after injury among burned combat veterans: A retrospective cohort study

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ABSTRACT

Background: The long-term health effects of burn are poorly understood. We sought to evaluate the relationship between burn and the subsequent development of hypertension.
Methods: Retrospective cohort study of patients admitted to our burn center from 2003 to 2010. Data collected included demographic variables, burn size, injury severity score, presence of inhalation injury, serum creatinine, need for renal replacement therapy, as well as days spent in the hospital, in the intensive care unit and on mechanical ventilation. Data for the subsequent diagnosis of hypertension was obtained from medical records. Cox proportional hazard regression models were performed to determine what factors were associated with hypertension.
Results: Of the 711 patients identified, 670 were included for analysis after exclusions. After adjustment, only age (HR 1.06 per one year increase, 95% confidence interval 1.03–1.08; $p<0.001$), percentage of total body surface area burned (HR 1.11 per 5% increase, 95% confidence interval 1.04–1.19; $p=0.002$) and acute kidney injury (HR 1.68, 95% confidence interval 1.05–2.69; $p=0.03$) were associated with hypertension.
Conclusion: Burn size is independently associated with the subsequent risk of hypertension in combat casualties. Clinical support for primary prevention techniques to reduce the incidence of hypertension specific to burn patients may be warranted.
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1. Introduction

The American Burn Association estimates that approximately 486,000 individuals are admitted for treatment to hospitals or emergency departments for burns each year in the United States [1]. Burn has been associated with adverse outcomes to include acute kidney injury (AKI) [2] and acute respiratory distress syndrome [3], as well as long-term consequences to include decreased health related quality of life [4], lingering physical disabilities [5,6], and adverse mental health outcomes [7,8]. However, there remains a paucity of evidence regarding chronic medical conditions in patients with burn.

Emerging evidence from other populations suggests that an acute illness or injury can impact the long term risk of a variety of chronic medical conditions. One study of 43,611 hospitalized patients from Kaiser Permanente in Northern California found that AKI increased the risk of hypertension (HTN) [9]. This increased risk lasted for 2 years after the index hospitalization and persisted after adjustment. Work done in combat casualties demonstrated that more severe injuries increased the long-term risk of HTN, coronary artery disease, diabetes and chronic kidney disease [10]. Another study examined patients that were hospitalized for pneumonia and found that these patients had an increased risk of subsequent cardiovascular disease compared to matched controls [11]. This work from diverse populations implies that a severe insult such as burn could have similar effects on long-term medical outcomes. Considering the number of burns that occur each year, such an association between burns and long-term development of chronic diseases may represent a previously unrecognized public health burden.

When considering the long-term effects of an acute insult, military personnel provide a unique opportunity to study otherwise healthy young adults who sustain an injury at a discrete point in time. One common injury among combat casualties is burn [12]. While coronary artery disease, diabetes and chronic kidney disease are rare in injured cohorts, HTN occurs more frequently [10] and is therefore more amenable to study. We sought to investigate the relationship between the severity of burn, health and demographic factors and the development of hypertension. We hypothesized that the severity of burn (i.e. primary exposure) would be associated with the subsequent development of HTN (i.e. primary outcome). To examine this hypothesis, we performed a retrospective cohort study of combat casualties with burns suffered in support of combat operations in Iraq and Afghanistan.

2. Material and methods

2.1. Study design and patient population

Our retrospective cohort study included patients admitted to the United States Army Institute of Surgical Research (USAISR) burn center from 1 January 2003 to 31 May 2010. These patients were then followed using administrative databases until 31 December 2011. The US Army Medical Research and Materiel Command Institutional Review Board (IRB) and the University of Texas Health Science Center San Antonio IRB reviewed and approved the study protocol. Given the minimal risk nature of the study, the requirement for informed consent was waived. Patients were included for analysis if they were injured in Iraq or Afghanistan and survived their initial hospitalization. Patients were excluded if they had pre-existing HTN or had data missing for a variable of interest. Pre-existing HTN was defined as a diagnosis of HTN by the International Classification of Disease, 9th edition (ICD-9) or prescription for an anti-hypertensive medication (see Supplemental material).

2.2. Measures

We defined HTN as either an ICD-9 code diagnoses or a prescription for an anti-hypertensive medication. The specific ICD-9 diagnostic codes and medication prescriptions used to define HTN are listed in the Supplemental material. Variables reflecting the patients' initial hospitalization were obtained from COLLECTOR (a prospectively collected database of admissions to the USAISR burn center that is updated and validated daily) for subjects admitted from 1 January 2003 to 31 May 2010. These variables included: age, serum creatinine, need for renal replacement therapy (RRT), gender, race, days in the hospital, days in the intensive care unit (ICU), days on mechanical ventilation, injury severity score (ISS [13]), presence of inhalation injury (IH), percentage of total body surface area burned (TBSA) and percentage of full thickness burn (FT TBSA). For the purposes of analysis, only a subject's first admission was considered for analysis. Data on ICD-9 diagnostic codes and prescribed anti-hypertensive medications were obtained from the Military Health System Data Repository (MDR) [14] from January 1, 2003 to December 31, 2011. MDR collects data on ICD-9 diagnostics codes and prescriptions from both the inpatient and outpatient environments. These data were then merged with ICD-9 diagnostic codes from the Veterans Health Administration Medical SAS outpatient dataset using a unique patient identifier to get patient level data. The date of this query extended over a 9 year period from 1 January 2003 through 31 December 2011.

AKI was determined using the Kidney Disease: Improving Global Outcomes (KDIGO) creatinine based diagnostic criteria [15] at any point during hospitalization. To meet this definition of AKI, a subject must have had either a 50% increase in the baseline serum creatinine or an acute rise of 0.3 mg/dl over a 48 h period. We did not have access to measured baseline creatinines for study subjects. Therefore, one was calculated using the Modification of Diet in Renal Disease (MDRD) study equation assuming an estimated glomerular filtration rate of 75 ml/min/1.73 m^2. The KDIGO guidelines also give diagnostic criteria for AKI based on decreases in urine output. However, this was not available for the study subjects. For the purposes of this analysis, mechanical ventilation and ICU stay were considered as dichotomous variables, i.e. days in the ICU or on mechanical ventilation $\geq$1 compared with 0. Hospital days was analyzed as a categorical variable based on quartiles for the entire cohort.

2.3. Statistics

Standard descriptive statistics were used to compare the groups that developed HTN by our definition with those that

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