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Association between blood alcohol concentration and mortality in critical illness☆,☆☆

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ABSTRACT

Objective: In animal models of renal, intestinal, liver, cardiac, and cerebral ischemia, alcohol exposure is shown to reduce ischemia-reperfusion injury. Inpatient mortality of trauma patients is shown to be decreased in a dose-dependent fashion relative to blood alcohol concentration (BAC) at hospital admission. In this study, we examined the association between BAC at hospital admission and risk of 30-day mortality in critically ill patients.
Design: We performed a 2-center observational study of patients treated in medical and surgical intensive care units in Boston, Massachusetts.
Setting: Medical and surgical intensive care units in 2 teaching hospitals in Boston, Massachusetts.
Patients: We studied 11 850 patients, 18 years or older, who received critical care between 1997 and 2007. The exposure of interest was the BAC determined in the first 24 hours of hospital admission and categorized a priori as BAC less than 10 mg/dL (below level of detection), 10 to 80 mg/dL, 80 to 160 mg/dL, and greater than 160 mg/dL. The primary outcome was all-cause mortality in the 30 days after critical care initiation. Secondary outcomes included 90- and 365-day mortality after critical care initiation. Mortality was determined using the US Social Security Administration Death Master File, and 365-day follow-up was present in all cohort patients. Adjusted odds ratios (ORs) were estimated by multivariable logistic regression models with inclusion of covariate terms thought to plausibly interact with both BAC and mortality. Adjustment included age, sex, race (white or nonwhite), type (surgical vs medical), Deyo-Charlson index, sepsis, acute organ failure, trauma, and chronic liver disease.
Results: Thirty-day mortality of the cohort was 13.7%. Compared to patients with BAC levels less than 10 mg/dL, patients with levels greater than or equal to 10 mg/dL had lower odds of 30-day mortality; for BAC levels 10 to 79.9 mg/dL, the OR was 0.53 (95% confidence interval [CI], 0.40-0.70); for BAC levels 80 to 159.9 mg/dL, it was 0.36 (95% CI, 0.26-0.49); and for BAC levels greater than or equal to 160 mg/dL, it was 0.35 (95% CI, 0.27-0.44). After multivariable adjustment, the OR of 30-day mortality was 0.97 (0.72-1.31), 0.79 (0.57-1.10), and 0.69 (0.54-0.90), respectively. When the cohort was analyzed with sepsis as the outcome of interest, the multivariable adjusted odds of sepsis in patients with BAC 80 to 160 mg/dL or greater than 160 mg/dL were 0.72 (0.50-1.04) or 0.68 (0.51-0.90), respectively, compared to those with BAC less than 10 mg/dL. In a subset of patients with blood cultures drawn (n = 4065), the multivariable adjusted odds of bloodstream infection in patients with BAC 80 to 160 mg/dL or greater than 160 mg/dL were 0.53 (0.27-1.01) or 0.49 (0.29-0.83), respectively, compared to those with BAC less than 10 mg/dL.
Conclusions: Analysis of 11 850 adult patients showed that having a detectable BAC at hospitalization was associated with significantly decreased odds of 30-day mortality after critical care. Furthermore, BAC greater than 160 mg/dL is associated with significantly decreased odds of developing sepsis and bloodstream infection.

1. Introduction

Alcohol abuse and dependence is highly prevalent in the population [1]. It is estimated that between 10% and 30% of critically ill patients have an alcohol use disorder (AUD) defined as alcohol dependence or harmful use of alcohol [2-8]. The alcohol-attributable disease burden is generally seen in younger patients and is primarily related to cirrhosis

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of the liver, neuropsychiatric disorders, and unintentional or intentional injury [9]. Epidemiologic studies support that the risk of coronary heart disease, cardiomyopathy, diabetes, and stroke is reduced with light to moderate alcohol intake [10-13].

The relationship between blood alcohol concentration (BAC) and inhospital mortality has been explored outside the intensive care unit (ICU) with some studies indicating an increase in mortality [14-16], others showing a decrease in mortality [17-23], and others indeterminate [24-29]. A recent large observational study of all level 1 and 2 trauma units in the State of Illinois demonstrated that inpatient mortality was decreased in a BAC dose-dependent fashion and showed slightly lower proportion of infections in patients with blood alcohol present [30]. Biological data show that acute alcohol administration improves experimental ischemia-reperfusion injury and subsequent organ dysfunction [31-43].

Given that alcohol use is likely to be highly prevalent in patients admitted to the ICU, and the possible alteration of inflammation related to acute alcohol use [40,42,43], and the importance of inflammation in critical care outcomes, we sought to elucidate the effect of alcohol on critical illness mortality. We performed a multiyear 2-center observational cohort study of critically ill patients among whom BAC was measured within 24 hours of hospitalization. The objective of this study was to test our hypothesis that alcohol intoxication at hospital presentation is associated with a decreased odds of 30-day all-cause mortality after critical care.

2. Materials and methods

2.1. Source population

We extracted administrative and laboratory data from individuals admitted to 2 teaching hospitals in Boston, Massachusetts: Brigham and Women's Hospital (BWH), with 793 beds, and Massachusetts General Hospital (MGH), with 902 beds. The 2 hospitals provide primary as well as tertiary care to an ethnically and socioeconomically diverse population within eastern Massachusetts and the surrounding region.

2.2. Data sources

Data on all patients admitted to BWH or MGH between August 3, 1997, and January 5, 2007, were obtained through the Research Patient Data Registry (RPDR), a computerized registry that serves as a central data warehouse for all inpatient and outpatient records at Partners HealthCare sites, which includes BWH and MGH. The RPDR has been used for other clinical research studies [44,45]. Approval for the study was granted by the Partners Human Research Committee Institutional Review Board.

2.3. Study population

During the study period, there were 54 392 unique patients, 18 years or older, who received critical care [46]. Critical care was determined by *Current Procedural Terminology* (*CPT*) code 99291 (critical care, first 30-74 minutes) assignment during hospital admission and is previously validated in the RPDR database [44]. Exclusions included 2372 patients assigned *CPT* code 99291 who received care only in the emergency department, 205 foreign patients as vital status in this study is determined by the Social Security Administration Death Master File, 166 patients with missing laboratory data, and 39 799 patients without BAC measured. Thus, 11 850 patients constituted the total study population.

2.4. Exposure of interest and comorbidities

The exposure of interest was the BAC determined in the first 24 hours of hospital admission and categorized a priori as BAC below level of detection (<10 mg/dL), 10 to 80 mg/dL, 80 to 160 mg/dL (the legal limit in most countries), and greater than 160 mg/dL [47,48].

Race was either self-determined or designated by a patient representative/health care proxy. Patient admission "type" was defined as "medical" or "surgical" and incorporates the diagnosis-related group methodology [49]. We used the Deyo-Charlson Index to assess the burden of chronic illness [50], which is well studied and validated [51,52]. We used the validated *International Classification of Diseases, Ninth Revision*, coding algorithms developed by Quan et al [51] to derive a comorbidity score for each patient from individual physician billing codes obtained from all outpatient and inpatient encounters at BWH or MGH before hospital discharge. Sepsis is defined by the presence of any of the following *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*), codes: 038.0-038.9, 790.7, 117.9, 112.5, or 112.81, 3 days before critical care initiation to 7 days after critical care initiation [53], an approach that we have validated in our database [54]. *Acute kidney injury* (*AKI*) was defined as RIFLE class Injury or Failure occurring between 3 days before critical care initiation and 7 days after critical care initiation [55]. We classified patients according to the maximum RIFLE class (class Risk, class Injury or class Failure) defined as a fold change in serum creatinine from preadmission serum creatinine [54,55].

Acute organ failure was adapted from Martin et al [53] and defined by a combination of *ICD-9-CM* and *CPT* codes relating to acute organ dysfunction assigned from 3 days before critical care initiation to 30 days after critical care initiation [44,54]. Acute failure is the summation of the number of acute organ failure categories (respiratory, cardiovascular, renal, hepatic, hematologic, metabolic, and/or neurologic) [53] present by *ICD-9-CM* code assignment.

For severity of illness risk adjustment, we used the acute organ failure score, an ICU risk prediction score created from demographics (age and race), patient admission "type" as well as *ICD-9-CM* code–based comorbidity, sepsis, and acute organ failure covariates, which has similar discrimination for 30-day mortality as Acute Physiology and Chronic Health Evaluation II [56]. We determined the traditional ICD-derived Injury Severity Score (ICISS) via the product of all survival risk ratios for an individual patient's traumatic *ICD-9* codes with more severe injuries having lower ICISS scores [57,58].

Alcohol use disorders were determined by *ICD-9-CM* codes at any time before discharge (alcohol abuse: 305.0-305.03; alcohol dependence: 303.0-303.93) [59]. *Neighborhood poverty rate* was defined as the percentage of each neighborhood's residents with incomes below the federal poverty line [44] and determined via submission of patient addresses for geocoding linked to US Census data at the census tract level [60-62]. To determine neighborhood socioeconomic disadvantage, we used geocoded residential address data [63] from electronic health records then linked the zip + 4 data to the Area Deprivation Index developed by Singh et al [64] and linked to the 2000 US census by Kind et al [65].

Chronic liver disease was determined by *ICD-9-CM* codes 571.x, 70.54, and 703.2 at any time before discharge [66]. MELD Score (Model For End-Stage Liver Disease) was calculated with the United Network for Organ Sharing modifications. Diabetes mellitus is defined by *ICD-9-CM* code 250.xx in the 2-years before hospital discharge [67,68]. *Early ICU admission* is defined as ICU admission within 48 hours of hospital admission.

Inotropes or vasopressors were considered to be present if prescribed 3 days before critical care initiation to 7 days after critical care initiation [69,70]. Using electronic pharmacy records, exposure to inotropes and vasopressors was determined in the 7 days after the critical care initiation date for dopamine, dobutamine, epinephrine, norepinephrine, phenylephrine, milrinone, and vasopressin. *Mechanical ventilation* is defined as intubation (*CPT* 31500) or mechanical ventilation management (*CPT* 94656 or 94657) or tracheostomy (*CPT* 31600) performed after critical care initiation [71].

For the presence of malnutrition, data were collected in a subset of cohort patients at the time of initial nutrition consultation by a registered dietitian between 2005 and 2007 performed 10 days before