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ORIGINAL ARTICLE

Patient mortality following alcohol use and trauma: a propensity-matched analysis

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Abstract
Objective To examine the outcomes of trauma patients who tested positive for alcohol at the time of hospital arrival versus those who tested negative.
Methods Data were pulled from the National Trauma Data Bank (2007–2010). All injured patients who were ≥14 years of age, sustained a "blunt" or "penetrating" injury, had complete systolic blood pressure (SBP) and heart rate (HR) records, were taken to a level 1 or 2 trauma center, and who received a confirmed blood alcohol test were included in the study. Any blood alcohol concentration (BAC) above the legal limit (≥0.08 g/dL) was considered "positive" for alcohol, and if no alcohol was identified it was considered "negative". Patients' demography and clinical information were compared across groups using Chi-square and Wilcoxon rank sum tests. Logistic regression, propensity score matching, and a follow-up paired analysis were also performed.
Results Of 279,460 total patients, around one-third of the patients (92,960) tested positive for BAC. There were clear demographic differences found between the two groups regarding age, gender, race, and injury type. There was also a significantly higher mortality rate (4.3 vs. 3.1%, $P < 0.001$) and a longer hospital length of stay (4 vs. 3 days, $P < 0.001$) found in the alcohol-negative group. Propensity score matching was also performed resulting in 92,959 patients per group. Using the paired data, the overall mortality observed was 3.1 vs. 3.3% ($P = 0.035$) between the alcohol-positive and alcohol-negative groups, respectively. There was no significant difference noted in the total hospital length of stay (median: 3 vs. 4 days, $P = 0.84$).
Conclusion Patients who tested positive for alcohol following a traumatic injury showed no clinically significant reduction in mortality and no significant difference in total hospital length of stay.

Keywords Injury · Blood alcohol level · Mortality

Introduction

In 2014, the Center for Disease Control (CDC) reported that trauma alone accounts for around 41 million emergency department (ED) visits and 2.3 million hospital admissions across the Unites States each year [1]. In the same year, the World Health Organization (WHO) put out a report which stated that approximately 3.3 million people died in 2012 worldwide solely due to alcohol-related diseases and injuries, and around 25% of those deaths were attributed specifically to traumatic injuries [2]. The National Highway Traffic Safety administration also reported that more than 10,000 deaths in 2013 were due to alcohol intoxication while driving a motor vehicle; this accounted for around 30% of all driving-related fatalities in the United States that year [3]. A recent study from Australia also examined the number of alcohol-related injuries in an urban entertainment zone and found that a significant reduction of alcohol-related serious injuries occurred after implementing more restrictive liquor licensing laws [4]. These studies, among others, provide evidence for the direct connection between alcohol consumption and resulting injury; however, there is little solid evidence for a direct link between alcohol consumption and mortality outcomes.

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Some prior studies done in animal models have attempted to address the connection between blood alcohol concentration (BAC) at the time of injury and associated mortality outcomes, specifically looking at head injury cases. These studies showed that a low-to-moderate BAC at the time of injury may have some neurologically protective effect, whereas high BAC leads to increased mortality and morbidity following head injury [5–7]. However, the clinical studies that have been done looking at BAC in patients with traumatic brain injury (TBI) showed variable outcomes in terms of mortality and morbidity including either no effect, an adverse effect, or a favorable effect on patient mortality [8–11]. These clinical studies used logistic regression models to explore the connection while also attempting to balance the confounders. And although most of these studies found a survival benefit in TBI patients who were alcohol positive, Hadjizacharia and colleagues used 1:1 matched data for alcohol-positive versus alcohol-negative patients and found increased mortality in the alcohol-positive patients. Additionally, Zeckey and colleagues published a study evaluating major trauma patients who were under the influence of acute alcohol intoxication (BAC $\geq$ 0.1%) at the time of injury and found no significant differences either in mortality or hospital length of stay [12].

As previously stated, only a few studies have examined the direct relationship between the presence of alcohol and mortality and morbidity outcomes. The results found have also been inconsistent across these studies, perhaps due to the small sample sizes and use of only standard methodological approaches, and were certainly far from conclusive. Therefore, we designed this study to evaluate the presence of BAC on the mortality outcomes of multiple trauma patients from the largest trauma database in the US using not only logistic regression, but also propensity score matching to compare the mortality outcomes for each of the proposed BAC groups. We hypothesized that the presence of alcohol in the blood at the time of traumatic injury would have no effect on the patient outcomes.

Methods

Data source

The patient data used for this study was retrieved from the 2007–2010 edition of the US National Trauma Data Bank (NTDB) which is maintained by the American College of Surgeons (ACS). The NTBD is currently the largest trauma data repository worldwide, providing its users access to millions of de-identified patient records that are voluntarily contributed from more than 800 facilities located all over the United States. The voluntarily participating medical facilities include rural, suburban, and urban level 1–5 trauma centers that may be university affiliated, community based, or non-teaching. The information collected from injured patients presenting to these facilities is only included in the NTDB repository if the injury diagnosis codes meet the following ICD code criteria, as defined by the International Classification of Diseases, Ninth Revision, Clinical Modifier (ICD-9-CM): 800–959.9 excluding the (ICD-9-CM): 905–909.9, 910–924.9 and 930–939.9.

Patient characteristics and inclusion criteria

All injured patients who were $\geq$14 years of age, who sustained an injury defined as either a "blunt" or "penetrating" type, who had complete systolic blood pressure (SBP) and heart rate (HR) records, were taken to a level 1 or 2 trauma center, and who received a confirmed blood alcohol test at the time of hospital arrival were included in the study. Patients who did not meet all five criteria were excluded from the analytic data set. Other key patient variables also collected for this study included: sex, race, drug test results (prescription and illegal drugs), intent of injury, mechanism of injury, injury severity score (ISS), and initial Glasgow Coma Scale (GCS).

All patients in the data set were divided into two groups based on their BAC assessment at the time of trauma center arrival. The NTDB characterizes lab alcohol testing results as a categorical outcome in which there are four possible outcomes; however, only two of these outcomes were of interest for this study. Patients with the outcome, "No—confirmed by test" comprised the "alcohol negative" group and patients with the outcome, "Yes—confirmed by test [at/beyond legal limit]" comprised the "alcohol positive" group for this study.

Outcomes of interest

The primary outcomes of interest for this study were overall patient mortality and hospital length of stay for patients who were confirmed to have a positive BAC at or above the legal limit versus those who tested negative.

Statistical methods

Trauma patient characteristics including age, gender, race, drug test results, injury intent and mechanism, SBP (continuous and categorical [<90 vs. $\geq$90]), HR, ISS, GCS, ACS trauma center level, and mortality outcomes were first summarized using mean and standard deviation (SD), median with interquartile range (IQR), or frequencies with percentages where appropriate. Chi-square and Wilcoxon rank sum tests were then used to formally compare patients who tested positive for blood alcohol versus those who

tested negative following injury. Patient length of stay was also assessed using Kaplan–Meier methods and the difference between the two groups was tested using a log-rank test. A multivariate logistic regression model with mortality as the outcome was also fit in an attempt to identify any possible interactions or underlying confounders that may not have stood out in the initial univariate analyses. The model included all of the same covariates that were initially examined. Due to the size of the data set, the Hosmer–Lemeshow, Osius–Rojek, and Stukel tests [13] were all performed to help diagnose model fit, while the area under the receiver operating characteristic curve (AUC) [14] was used to examine the predictive accuracy of the fitted model.

After realizing that the two patient populations were simply not well balanced in their baseline demographics, and knowing that any form of prospective study for this case would be unethical, it became clear that different methodology would be needed for this study. As first described by Rosenbaum in 1983, propensity score matching calculates the probability of "treatment" assignment based on baseline characteristics being the same in both the treatment and control groups, and pairs the patients from both groups based on their propensity values [15]. In randomized trials, the subjects are included in the study groups based on random selection; however, in retrospective observational studies, the event of interest has already happened. Therefore, active subject selection can only be based on inclusion criteria and an estimated propensity score. In this study, one-to-one matching was performed using "nearest neighbor" matching by selecting out the patients who had a positive alcohol test result and matching them to patients with a negative alcohol test result using the R package, "MatchIt" [16]. Because the patients' alcohol consumption would have occurred prior to the patient being brought to the trauma center, the only factors that could be considered for the matching criteria were those factors that were also "present" prior to the patient's arrival: age, race, and gender. After the matching was performed, numerical and graphical diagnostics were run to examine the level of improvement that using this matching method provided for patient group comparability.

Matched patient characteristics were then summarized again using mean and standard deviation (SD), median with interquartile range (IQR), or frequency and percentage as appropriate. The continuous variables were compared using the paired version of the Wilcoxon rank sum test and the categorical variables were compared using either a McNemar test (for unordered binary measures) or a Stuart–Maxwell test (for unordered variables with more than 2 possible outcomes) [17]. The Kaplan–Meier procedure from the "survival" package in R [18, 19] was again used to estimate the median time for the hospital length of stay along with its 95% confidence interval, and a log-rank test was used for the statistical comparison between groups. All p values reported were 2-sided and a P value < 0.05 was considered statistically significant. Clinically significant differences were considered to have occurred if the ISS, GCS, and proportion of patients with SBP $\leq$ 90 mmHg had more than at least 1 unit change between the groups.

Statistical summaries and analyses were performed using both "R: A language and environment for statistical computing" [20] and STATA13 [21].

Results

Unmatched data—univariate analyses

Two hundred seventy-nine thousand, four hundred and six patients qualified for the study. Around one-third of these patients (92,960) tested positive for alcohol with a BAC at or above the legal limit ($\geq$0.08 g/dL), while the remaining two-thirds tested negative for BAC at the time of hospital arrival. There were clear demographic differences found between the two initial groups regarding age (mean $\pm$ SD: 43.9 $\pm$ 20.7 vs. 37.9 $\pm$ 14.5), gender (67.3% male vs. 81.2% male), race (71.9% white vs. 64.0% white), and injury type. A higher number of blunt injuries were found in the alcohol-negative group compared to the alcohol-positive group (89.2% vs. 84.5%, respectively). Other patient injury characteristics including injury severity score (ISS), Glasgow coma score (GCS), initial systolic blood pressure (SBP), and heart rate (HR) were also noticeably different between the two BAC groups. In addition, there was a significantly higher mortality rate (4.3% vs. 3.1%, $P < 0.001$) and a longer median hospital length of stay (4 vs. 3 days, $P < 0.001$) in the alcohol-negative group. See Table 1 for a more complete summary of the unmatched patients' demographics.

Unmatched data—multivariate logistic regression analysis

In order to further examine the relationship between alcohol use and mortality, a multivariate logistic regression model was fit using alcohol test result, age, race, gender, drug use, injury type, injury mechanism, injury intent, ISS, GCS, SBP (<90 vs. $\geq$90), HR, and ACS trauma level as predictors of mortality. After fitting this model, the odds ratio for mortality based on BAC changed very little from 0.70 (95% CI 0.67, 0.73) in the unadjusted analysis to 0.72 (95% CI 0.68, 0.76) in the effects adjusted model. The results of the Hosmer–Lemeshow, Osius–Rojek, and Stukel tests all showed P values < 0.001, which is often to be expected with a data set this large, so more focus was put on the AUC which had a value of 0.946 for the adjusted model, indicating good predicative accuracy.

Table 1 Characteristics of unmatched patients by alcohol test results

	Patients by alcohol test results, frequency (%)	
	Alcohol negative $n = 186,446$	Alcohol positive $n = 92,959$
Male	125,529 (67.3)	75,466 (81.2)
White	134,121 (71.9)	59,486 (64.0)
Injury type		
Blunt	166,303 (89.2)	78,572 (84.5)
Penetrating	20,143 (10.8)	14,388 (15.5)
Intent		
Assault	21,079 (11.3)	22,736 (24.5)
Other	335 (0.2)	277 (0.3)
Self-inflicted	3852 (2.1)	2232 (2.4)
Undetermined	444 (0.2)	358 (0.4)
Unintentional	160,736 (86.2)	67,357 (72.4)
Mechanism		
Cut/pierce	7965 (4.3)	9164 (9.9)
Fall	46,698 (25.0)	19,130 (20.6)
Firearm	12,177 (6.5)	5224 (5.6)
Machinery	1856 (0.1)	101 (0.1)
Other	11,322 (6.1)	12,124 (13.0)
Transport	106,428 (57.1)	47,217 (50.8)
Drug positive	51,133 (27.4)	30,496 (32.8)
Systolic BP		
≥90	180,765 (97.0)	89,271 (96.0)
<90	5681 (3.0)	3689 (4.0)
ACS trauma level		
I	129,358 (69.4)	63,975 (68.8)
II	57,088 (30.6)	28,985 (31.2)
Mean ± SD		
Age	43.9 ± 20.7	37.9 ± 14.5
ISS	12.4 ± 10.0	11.6 ± 9.9
GCS	13.7 ± 3.3	13.0 ± 3.9
Pulse rate	90.6 ± 20.7	96.1 ± 19.8

Propensity-matched data analyses

Propensity score matching was then performed using a 1:1 ratio between the alcohol-positive and alcohol-negative groups. After the matching, each group contained 92,959 patients. There was almost 90% improvement in all the standardized mean differences in the patients' demography (age, race, and sex) after matching (Fig. 1). While there was also marked improvement within several of the other previously problematic baseline patient characteristics after matching, there were still some statistically significant differences seen which were not deemed clinically significant between the two BAC groups. For the alcohol-positive group versus the alcohol-negative group these included:

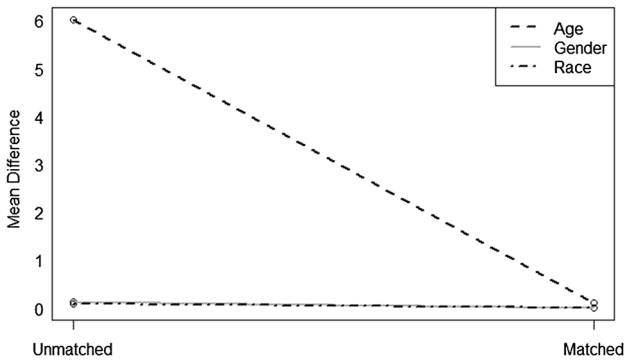

Fig. 1 Change in demographic mean differences after propensity score matching

SBP ≤ 90 (4.0 vs. 3.0%), ISS (mean ± SD: 11.6 ± 9.9 vs. 12.2 ± 10.1), and GCS (mean ± SD: 13.0 ± 3.9 vs. 13.7 ± 3.3). See Table 2 for a full demographic summary of the matched patient groups. We largely attribute these statistically significant differences to the size of the data set.

Using the paired data, the overall mortality observed was 3.1 vs. 3.3% ($P = 0.035$) between the alcohol-positive and alcohol-negative groups, respectively, as shown in Table 3. No significant difference was noted in the median hospital length of stay (3 vs. 4 days, $P = 0.84$) (Fig. 2). The absolute risk reduction (ARR) in mortality between the two groups was 0.002 (CI 0.000, 0.003) with an odds ratio of 0.95 (95% CI 0.897, 0.996).

Discussion

The results of this large-scale retrospective study showed an overall significant survival benefit and decreased hospital length of stay in patients who tested positive for alcohol following injury in the original unmatched NTDB patient sample. After performing propensity score matching to select pairs of patients into the study, the reanalysis still showed a statistically significant survival benefit, but no clinically significant difference with only a 0.2% difference in mortality between the BAC-positive vs. BAC-negative groups. There was also no clinically or statistically significant difference found in hospital length of stay, which echoes the findings of Zeckey and colleagues [12].

The majority of historical studies looking at the relationship between alcohol, injury, and mortality examined these results only in head injury and TBI cases. A seemingly "neuroprotective" effect of alcohol after head injury was well documented in prior animal study models [5, 22]. However, across multiple clinical studies, the injury and mortality results were rather variable. Some studies showed better outcomes for those with alcohol present in the bloodstream,

Table 2 Characteristics of matched patients by alcohol test results

	Patients by alcohol test results, frequency (%)	
	Alcohol negative $n = 92{,}959$	Alcohol positive $n = 92{,}959$
Male[a]	75,465 (81.2)	75,465 (81.2)
White[a]	60,279 (64.8)	59,485 (64.0)
Injury type		
Blunt	79,607 (85.6)	78,572 (84.5)
Penetrating	13,353 (14.4)	14,388 (15.5)
Intent		
Assault	14,388 (15.5)	22,736 (24.5)
Other	252 (0.3)	277 (0.3)
Self-inflicted	2233 (2.4)	2232 (2.4)
Undetermined	280 (0.3)	358 (0.4)
Unintentional	75,806 (81.5)	67357 (72.4)
Mechanism		
Cut/pierce	5248 (5.6)	9164 (9.9)
Fall	17,694 (19.0)	19,130 (20.6)
Firearm	8103 (8.7)	5224 (5.6)
Machinery	1156 (1.2)	101 (0.1)
Other	7187 (7.7)	12,124 (13.0)
Transport	53571 (57.6)	47,216 (50.8)
Drug positive	29,188 (31.4)	30,495 (32.8)
Systolic BP		
≥90	90,209 (97.0)	89,270 (96.0)
< 90	2750 (3.0)	3689 (4.0)
ACS trauma level		
I	65,903 (70.9)	63,974 (68.8)
II	27056 (29.1)	28,985 (31.2)
Mean ± SD		
Age[a]	37.8 ± 14.6	37.9 ± 14.5
ISS	12.2 ± 10.1	11.6 ± 9.9
GCS	13.7 ± 3.3	13.0 ± 3.9
Pulse rate	91.4 ± 20.9	96.1 ± 19.8

[a] Indicates that the variable was used for propensity score matching

while other studies showed either no significant difference in mortality or even higher mortality in patients who tested positive for BAC following head injury [23–25]. One potential reason for this may be that post-traumatic inflammatory reactions could contribute to an increase in morbidity and mortality, masking the effects of the inflammatory cascade (including IL 6) which could impact the outcome not only in TBI, but also in multi-system trauma victims [26, 27].

Only a few larger scale studies have looked deeper at the relationship of alcohol and mortality among a sample patient population with multiple types of trauma. One current example comes from Rootman and colleagues who analyzed their study data using patients with multiple types of trauma [28]. Their study included more than 2000 patients and demonstrated that alcohol- and drug-positive patients do not seem to differ in terms of major clinical outcomes such as hospital length of stay, intensive care unit (ICU) days, or mortality from non-intoxicated individuals Whereas, Plurad et al. used a data sample of more than 3000 patients who were classified as an "occupant" involved in a motor vehicle crash, who were also tested for alcohol as a part of initial assessment, to evaluate the association of blood alcohol presence to mortality [29]. Their study showed a lower mortality rate in the patients who tested positive for alcohol with a BAC ≥ 0.08 g/dL, [OR: 0.41 (95% CI 0.16, 0.94), $P = 0.0469$]. Stöbig and colleagues also analyzed more than 10 years of accident data from the German in-Depth Accident Study (GIDAS) data set, where 1769/20,741 (8.5%) injured patients were tested for BAC. More than 46% of patients tested positive (BAC ≥ 0.1%) for alcohol. They also looked at the all-cause mortality from the motor vehicle crashes and found that the mortality rate was more than double in BAC-positive cases compared to BAC-negative cases, respectively (4.6 vs. 2.2%) [30]. The majority of the studies described above had either a smaller sample size or used only standard analysis methods to control for the assumed baseline characteristic differences. Even fewer studies focusing on the association between alcohol and mortality have utilized any sort of matching methodology for a more balanced comparison. For example, Chen and colleagues utilized the NTDB to examine around 100,000 traumatic brain injured (TBI) patients [31]. They used the patients' age for the basis of an exact matching methodology implemented to help balance their two groups (alcohol-positive and alcohol-negative patients), and found no significant difference in patient mortality. In comparison, our study

Table 3 Association between alcohol test result and patient mortality

Unmatched sample ($n = 279{,}405$)		OR (95% CI)	*P* value	ARR % (95% CI)
Mortality: 8095 (4.3%) vs. 2871 (3.1%)	Raw data result	0.70 [0.67, 0.73]	<0.001	1.3% [1.1%, 1.4%]
	Logistic regression result	0.72 [0.68, 0.76]	<0.001	1.3% [0.9%, 1.6%]
Propensity-matched sample ($n = 185{,}918$)				
Mortality: 3031 (3.3%) vs. 2871 (3.1%)	Paired McNemar result	0.95 [0.90, 1.00]	0.04	0.2% [0.0%, 0.3%]

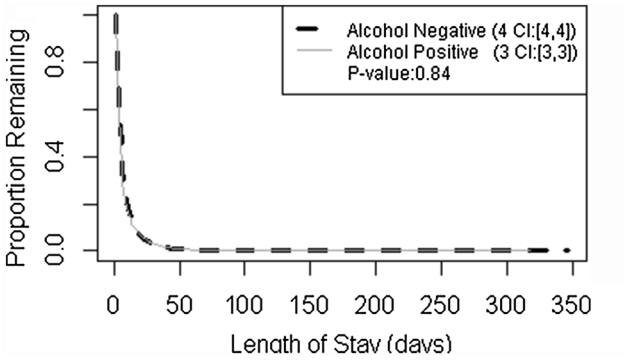

Fig. 2 Proportion of matched trauma patients remaining in hospital care over time by alcohol test result (positive vs. negative)

showed that one-third of the patients who sustained traumatic injury and were brought to either a level 1 or level 2 ACS trauma center tested positive for blood alcohol above the legal limit of ≥0.08 g/dL in the unmatched sample. We then used propensity score matching as first suggested by Rubin [32] to balance the baseline patient age, gender, and race characteristics.

In order to verify the patient-matching quality, the baseline covariate balance was checked using standardized mean differences between the groups on observed covariates (age, sex, and race). We found < 10% difference in the mean standardized differences between the matched groups for each covariate checked, indicating that the matching procedure was successful. We had also planned to use "XBalance" from the R package "RItools" [33, 34] to provide further insight on the matching outcomes; however, our large sample size made using it problematic. Absolute risk reduction was also used to further assess the effect of alcohol on mortality in the matched pair sample as previously suggested by Dr. Peter Austin [35]. In prior studies, he and his colleagues demonstrated that after propensity score matching, using the odds ratio from logistic regression analyses for a binomial outcome can introduce bias in determining the treatment effect on patient outcomes [14, 35, 36].

Overall, this study showed that the beneficial effect of alcohol on mortality seen in the initial unmatched sample (3.1 vs. 4.3% $P < 0.001$) has nearly disappeared after reanalysis in the matched pair sample (3.1 vs. 3.3%, $P = 0.035$). While the difference is still statistically significant, which can certainly be attributed to the larger sample size, the potential clinically significant difference is gone. The impact of alcohol on patient ISS, GCS, and vital signs [heart rate, SBP ≤ 90] was also not clinically significant. Similarly, no significant difference was found between the two BAC groups in the matched sample for median hospital length of stay (3 vs. 4 days, $P = 0.84$) and the absolute risk reduction in mortality for the matched sample was 0.002 (95% CI 0.000, 0.003) indicating very little risk difference.

Limitations

As with any study, there were some limitations that simply could not have been addressed. The study was performed using a sample of patients from a large existing data set and the retrospective design of the study carries inherent risks that any retrospective study from a large data repository would have. A large number of patients had missing observations for certain baseline covariates, vital signs, and patient outcomes which required list-wise deletion. There was also a lack of detailed information about the exact blood alcohol level due to the categorical, rather than exact continuous, format that the NTDB requires from submitting institutions. Furthermore, not all patients listed in the database were tested or were confirmed as being tested for alcohol at the time of hospital arrival. Any information from patients who died at the scene was also missing because it is not available from the database given that they only capture data from patients who presented to a trauma center; thus creating an incomplete picture of the entire affected patient population. However, with these limitations in mind, we note that performing any sort of prospective randomized trial to compare alcohol consumption and its effect on patient outcomes after injury is highly unethical. Therefore, the best strategy is to utilize the existing data that have been collected and perform the propensity-matched analysis which can help to both randomly select the patients into the study while also removing some of the selection bias based on patient characteristics. However, propensity score matching is only part of the solution for these limitations because it cannot balance any missing or unmeasured variables which may have contributed to the overall patient results, ultimately leading to bias from unmeasured confounding.

Areas for follow-up study

Given that this study could only examine data from patients who actually presented to a trauma center, we feel that further studies could use a similar approach to instead examine trauma patient mortality data records. This would give insight into the most critical trauma injury cases and could help complete the "snapshot" of the full affected population. We also note that since the patients in these records would have already expired, the most important covariates to examine would come from the forensic evidence noted from the scene of the injury or from patient autopsy reports where available. The number of alcohol-positive patients could be limited or difficult to verify based on the information available, but further information

from these cases is necessary for understanding the complete range of potential patient factors that can affect mortality.

Conclusion

This study showed that around one-third of patients who sustained traumatic injuries and were brought to level 1 or level 2 ACS trauma centers tested positive for blood alcohol levels above the United States national legal limit. The follow-up data analysis showed a clinically negligible difference in mortality and no significant difference in hospital length of stay for patients who tested positive at the time of hospital arrival versus those who tested negative. There were also no clinically significant differences seen in the ISS or GCS between the groups.

Compliance with ethical standards

All procedures followed were in accordance with the ethical standards of the Institutional Review Board of Meridian Health and with the Helsinki Declaration of 1975, as revised in 2008. Since the study was done using a de-identified National database from the American College of Surgeons that is available to all researchers, this study was exempted from IRB review as per policy.

Conflict of interest The authors (Nasim Ahmed and Patricia Greenberg) declare that they have no conflicts of interest.

Informed consent Given that this study was done using a de-identified National database from the American College of Surgeons that is available to all researchers, this study was exempted from IRB review as per policy and no informed consent was required.

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