Alcohol does not increase in-hospital mortality due to severe blunt trauma: an analysis of propensity score matching using the Japan Trauma Data Bank

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Aim: Alcohol-related problems, including trauma, are a great burden on global health. Alcohol metabolism in the Japanese population is genetically inferior to other races. This study aimed to evaluate the effects of alcohol use among a Japanese severe blunt trauma cohort.

Methods: This retrospective observational study analyzed the data of trauma patients registered in the Japan Trauma Data Bank between 2004 and 2019. The primary outcome of this study was in-hospital mortality. The lengths of hospital and intensive care unit stay were the secondary outcomes. Propensity score matching was used to adjust the anatomical severity and patient background to reduce the potential alcohol use bias.

Results: We analyzed 46,361 patients categorized into nondrinking (n = 37,818) and drinking (n = 8,543) groups. After a 1:1 propensity score matching (n = 8,428, respectively), despite the Glasgow Coma Scale and Revised Trauma Score scores being significantly lower in the drinking group (14 vs. 13 and 7.84 vs. 7.55, P < 0.001, respectively) and intensive care unit length of stay being significantly longer in the drinking group (6 vs. 7 days, P = 0.002), in-hospital mortality was significantly lower in the alcohol group (11.8% vs. 9.0%, P < 0.001) and there were no differences in the duration of hospital stay (19 vs. 19 days, P = 0.848).

Conclusion: Despite increasing physiological severity on admission, after adjusting for anatomical severity, alcohol consumption could be beneficial in severe blunt trauma patients as regards in-hospital mortality.

Key words: Alcohol, in-hospital mortality, intensive care, propensity score matching, trauma

INTRODUCTION

Alcohol-related problems are a great burden on global health.1 Alcohol increases various endogenous diseases, including cardiovascular diseases, neuropsychiatric disorders, malignant neoplasms, and gastrointestinal diseases.1,2 Alcohol also increases trauma risk by increasing the propensity for aggressive behavior and reducing reaction time.2–4 Approximately 30% of all trauma deaths are alcohol-related; moreover, the number of deaths due to alcohol-attributable injury is on the increase globally.3 In Japan, regulations on drunk driving became stricter in 2007, and in 2019, the number of drunk driving-related accidents decreased to 3,047 cases, which is 14% of the peak value in 2000. However, apart from drunk driving, alcohol-related trauma, including falls from heights, stumbling, and traffic accidents, is still an important issue.

There is a racial difference in ethanol metabolism. In particular, some Japanese individuals experience flushing with a small amount of alcohol, which Caucasians or Blacks never experience. This phenomenon can be explained by the genetic variance involved in alcohol metabolism. Alcohol is metabolized to acetaldehyde by antidiuretic hormone (ADH) and acetic acid by aldehyde dehydrogenase (ALDH). Genetic variation has been reported in ADH and ALDH, and Japanese individuals tend to be genetically inferior in alcohol metabolism.5,6

There are numerous studies on alcohol-associated trauma, with results ranging from worsening prognosis to
improvement. However, all these studies were undertaken on European or American populations, who genetically possess superior alcohol metabolism to Japanese individuals. Accordingly, these results would be inapplicable in Japan, and no studies on the impact of alcohol on Japanese trauma patients have been carried out. This study aimed to evaluate the effects of alcohol on Japanese severe blunt trauma patients using a Japanese nationwide trauma database, the Japan Trauma Data Bank (JTDB).

METHODS

THIS RETROSPECTIVE OBSERVATIONAL study was approved by the Institutional Review Board of Nippon Medical School (approval no. B-2020-318) and undertaken in accordance with the ethical standards established in the 1964 Declaration of Helsinki and its later amendments. The requirement for individual informed consent was waived due to the retrospective, observational study design.

Data collection

We examined all patients registered in the JTDB from 2004 to 2019. The JTDB is a nationwide, observational multicenter registry of trauma patients in Japan. Patients with an abbreviated injury scale (AIS) score $\geq 3$ were registered in the JTDB. The JTDB was established in 2003 and has been maintained by the Japanese Association for the Surgery of Trauma (Trauma Surgery Committee). Overall, 280 major trauma centers in Japan participate in the JTDB. The following variables were collected from the JTDB: patient demographics (age, sex, and history), clinical data (alcohol screening, mechanism of injury, and vital signs on arrival [Glasgow Coma Scale (GCS) score, systolic blood pressure, diastolic blood pressure, heart rate, and respiration rate]), the maximum AIS90 Update 98 for each region (head, face, neck, thorax, abdomen/pelvis, spine, upper extremity, lower extremity, and skin), Injury Severity Score (ISS), Revised Trauma Score (RTS), and outcome data (length of intensive care unit [ICU] stay, length of hospital stay, and in-hospital mortality). As we intended to analyze the effect of alcohol on severe blunt trauma, the exclusion criteria were as follows: patients without alcohol screening, age $<18$ years, pregnancy, ISS $<15$, death in the emergency or operating room, nonblunt trauma cases, and non-ICU stay.

Alcohol screening

Alcohol screening value was determined based on the criteria set by each participating institution, such as serum detectability or obvious pre-injury drinking episodes. Alcohol screening was carried out by the attending physician. Serum concentrations are not collected in the JTDB. We assigned patients to the drinking and nondrinking groups based on this value.

Outcomes

The primary and secondary study outcomes were in-hospital mortality and lengths of hospital and ICU stay, respectively.

Statistical analysis

Patient data are expressed as medians and interquartile ranges. For nonparametric data, the Mann–Whitney $U$-test was used for continuous variables and the $\chi^2$-test for categorical variables. We used propensity score matching to adjust for anatomical and physical severity and patient background to reduce potential alcohol use bias. A multivariate logistic regression model was used to estimate propensity scores. The primary and secondary outcomes were adjusted for age, sex, comorbidities (cardiac diseases, pulmonary diseases, metabolic diseases, psychiatric diseases, and immunologic diseases/cancers), mechanism of injury, ISS, and maximum AIS score of each region (head, face, neck, thorax, abdomen/pelvis, spine, upper extremity, lower extremity, and skin). Although alcohol directly affects vital signs, especially cognitive function, we did not include vital signs on arrival (systolic blood pressure, diastolic blood pressure, heart rate, respiration rate, and GCS) in the matching values. A 1:1 propensity score matching of the drinking with the nondrinking group was carried out by utilizing nearest-neighbor matching without substitutes. An allowable-caliper width equivalent to 0.1 of the pooled standard deviation of the propensity score logit resulted in pair formation. To estimate the matching balance between the two groups, we used the standardized mean difference of the propensity score estimation variables. After comparing in-hospital mortality values and matching propensity scores in each group, we calculated the absolute difference in mortality with a 95% confidence interval. Using the Kaplan–Meier method, each event–time distribution in each group was estimated. To compute the differences in cumulative 30-day survival, the log–rank test was applied. All statistical analyses were carried out using RStudio 1.3 (RStudio), which is a user interface for R 4.0.3 (The R Foundation for Statistical Computing) with the “Matching” add-on package for propensity score matching. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Between 2004 and 2019, 372,314 patients were included in the JTDB registry; among these, 133,254
patients had missing information on alcohol consumption. Finally, 46,361 patients (nondrinking group, n = 37,818; drinking group, n = 8,543) met the inclusion criteria (Fig. 1).

Patient baseline characteristics are shown in Table 1. There were numerous differences in demographic background between the nondrinking and drinking groups, including female sex (32.5% vs. 12.7%, P < 0.001), age (65 years vs. 57 years, P < 0.001), and comorbidities, such as respiratory disease (4.0% vs. 3.8%, P = 0.23), cardiac diseases (29.1% vs. 22.7%, P < 0.001), metabolic diseases (13.7% vs. 11.1%, P < 0.001), digestive diseases (7.7% vs. 10.1%, P < 0.001), physiatric diseases (16.1% vs. 11.1%, P < 0.001), and immunologic diseases/cancers (10.0% vs. 7.2%, P < 0.001). In the drinking group, the major mechanisms of injury were falls from heights (26.3%), stumbling (23.0%), and pedestrian traffic accidents (12.1%). Although ISS was significantly lower, the maximum AIS score in the head region was significantly higher in the drinking group (22 vs. 21 and 3 vs. 4, respectively, P < 0.001). The GCS score (among other vital signs on arrival), RTS score, and in-hospital mortality were significantly lower in the drinking group (14 vs. 13, P < 0.001; 7.84 vs. 7.55, P < 0.001; and 13.1% vs. 8.9%, P < 0.001, respectively). There was no difference in ICU length of stay (7.0 vs. 7.0 days, P = 0.015); however, hospital length of stay was significantly shorter in the drinking group (20.1% vs. 19.0%, P < 0.001) (Table 2).

The postmatched patient characteristics (after adjusting for anatomical and physical severity) and patient demographics are shown in Table 1. After propensity score matching, there were no significant differences in age, sex, comorbidities, ISS, maximum AIS score in each region, and mechanism of injury between the two groups. The GCS and RTS scores remained significantly lower in the drinking group (14 vs. 13 and 7.84 vs. 7.55, P < 0.001, respectively). In-hospital mortality was significantly lower in the drinking group (11.8% vs. 9.0%, P < 0.001) (Fig. 2). Intensive care unit length of stay was significantly longer in the drinking group (6 vs. 7 days, P = 0.002); however, hospital length of stay was not different between the two groups (19.0% vs. 19.0%, P = 0.85) (Table 2).

**DISCUSSION**

This is the first study in Japan to investigate the effect of alcohol on in-hospital mortality among patients with severe blunt trauma. The results showed that alcohol consumption before trauma decreased in-hospital mortality and did not increase the length of hospital stay; however, it increased ICU length of stay, after adjusting for anatomical severity. In Europe and the United States, where Caucasians or Blacks are dominant, some similar studies have reported that alcohol did not increase in-hospital mortality due to severe trauma. Although weak alcohol metabolism is dominant in Japan (sometimes described as an ethnically homogeneous nation-state), this study presented similar results.

Our study showed that alcohol consumption did not increase in-hospital mortality; instead, it reduced mortality in Japanese patients with severe blunt trauma. In particular, Asians possess the $ALDH2^*2$ allele, which provides poor alcohol metabolic ability and leads to excessive acetaldehyde build-up, with prevalence varying by ethnicity. Approximately 40% of Japanese individuals reportedly possess at least one $ALDH2^*2$ allele, including approximately

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**Fig. 1.** Study inclusion flowchart. AIS, Abbreviated Injury Scale; ICU, intensive care unit; ISS, Injury Severity Score.
5% who are homozygous for ALDH2*2. Contrastingly, Caucasians or Blacks possess ALDH2*1 at a 100% rate. These genetic mutations lead to excessive accumulation of the alcoholic metabolite, acetaldehyde. Excess acetaldehyde concentrations contribute not only to heightened responses with alcohol but also reduced heavy alcohol use, alcohol-associated problems, and alcohol-use disorders.5,6 Previous reports have shown that alcoholism increases in-hospital mortality.17 The JTDB lacks information on alcohol abuse; hence, the number of patients abusing alcohol in both groups, especially the drinking group, is unclear. However, for the above reasons, Japanese populations consume less

| Table 1. Pre- and postmatching characteristics of patients with severe blunt trauma |
|-----------------------------------|----------------|----------------|----------------|----------------|----------------|
|                                   | Prematching    | Postmatching   |                 |                 |                 |
|                                   | Nondrinking    | Drinking       | P-value         | Nondrinking    | Drinking       | P-value         |
|                                   | n = 37,818     | n = 8,543      |                 | n = 8,428      | n = 8,428      |                 |
| Age, years                        | 65.00 (45.00, 77.00) | 57.00 (42.00, 68.00) | <0.001 | 57.00 (36.00, 71.00) | 57.00 (42.00, 68.00) | 0.455 |
| Men                               | 25,545 (67.5)  | 7,454 (87.3)   | <0.001          | 7,348 (87.2)   | 7,339 (87.1)   | 0.854 |
| Comorbidities                     |                |                |                 |                |                |                 |
| Cardiovascular diseases           | 10,990 (29.1)  | 1,939 (22.7)   | <0.001          | 1,886 (22.4)   | 1,938 (23.0)   | 0.348 |
| Psychiatric diseases              | 6,094 (16.1)   | 949 (11.1)     | <0.001          | 955 (11.3)     | 942 (11.2)     | 0.770 |
| Metabolic diseases                | 5,167 (13.7)   | 1,009 (11.8)   | <0.001          | 965 (11.4)     | 1,005 (11.9)   | 0.350 |
| Immunologic diseases or cancer    | 3,769 (10.0)   | 616 (7.2)      | <0.001          | 617 (7.3)      | 615 (7.3)      | 0.976 |
| Respiratory diseases              | 1,531 (4.0)    | 321 (3.8)      | 0.227           | 325 (3.9)      | 316 (3.7)      | 0.747 |
| Digestive diseases                | 2,923 (7.7)    | 863 (10.1)     | <0.001          | 843 (10.0)     | 850 (10.1)     | 0.878 |
| Vital signs on arrival            |                |                |                 |                |                |                 |
| Systolic blood pressure, mmHg     | 135.00 (112.00, 158.00) | 128.00 (108.00, 149.00) | <0.001 | 137.00 (118.00, 159.00) | 128.00 (108.00, 149.00) | <0.001 |
| Heart rate, b.p.m.                | 84.00 (71.00, 99.00) | 85.00 (74.00, 100.00) | <0.001 | 83.00 (70.00, 97.00) | 86.00 (74.00, 100.00) | <0.001 |
| Respiratory rate, breaths/min     | 20.00 (18.00, 25.00) | 20.00 (17.00, 24.00) | <0.001          | 20.00 (17.00, 24.00) | 20.00 (17.00, 24.00) | 0.490 |
| Glasgow Coma Scale                | 14.00 (11.00, 15.00) | 13.00 (9.00, 15.00) | <0.001          | 14.00 (11.00, 15.00) | 13.00 (9.00, 15.00) | <0.001 |
| ISS                               | 22.00 (17.00, 29.00) | 21.00 (17.00, 26.00) | <0.001          | 21.00 (17.00, 26.00) | 21.00 (17.00, 26.00) | 0.184 |
| RTS                               | 7.84 (6.90, 7.84) | 7.55 (5.97, 7.84) | <0.001          | 7.84 (6.90, 7.84) | 7.55 (5.97, 7.84) | <0.001 |
| Mechanism of injury               |                |                |                 |                |                |                 |
| Traffic accident                  |                |                |                 |                |                |                 |
| (1) Car                           | 5,518 (14.6)   | 746 (8.7)      | <0.001          | 790 (9.4)      | 746 (8.9)      | 0.251 |
| (2) Motor cycle                   | 5,276 (14.0)   | 586 (6.9)      | 567 (6.7)       | 586 (7.0)      |                   |                 |
| (3) Bicycle                       | 3,256 (8.6)    | 710 (8.3)      | 745 (8.8)       | 710 (8.4)      |                   |                 |
| (4) Pedestrian                    | 4,118 (10.9)   | 1,030 (12.1)   | 987 (11.7)      | 1,016 (12.1)   |                   |                 |
| Train                             | 160 (0.4)      | 111 (1.3)      | 79 (0.9)        | 102 (1.2)      |                   |                 |
| Fall                              | 10,923 (28.9)  | 3,021 (35.3)   | 3,078 (36.5)    | 2,976 (35.3)   |                   |                 |
| Stumble                           | 6,006 (15.9)   | 1,965 (23.0)   | 1,836 (21.8)    | 1,931 (22.9)   |                   |                 |
| Sports                            | 393 (1.0)      | 17 (0.2)       | 19 (0.2)        | 17 (0.2)       |                   |                 |
| Others                            | 2,168 (5.7)    | 357 (4.2)      | 327 (3.9)       | 344 (4.1)      |                   |                 |
| Head_AIS score                    | 3.00 (0.00, 4.00) | 4.00 (0.00, 4.00) | <0.001          | 4.00 (0.00, 4.00) | 4.00 (0.00, 4.00) |                 |
| AIS ≥3                            | 16,514 (43.7)  | 4,516 (52.9)   | <0.001          | 4,323 (51.3)   | 4,430 (52.6)     | 0.102 |

Data are expressed as median (interquartile range) or number (%). AIS, Abbreviated Injury Scale; ISS, Injury Severity Score; RTS, Revised Trauma Score.
alcohol than other races, and the number of alcoholics in Japan is lower than in other countries.\(^5\)\(^6\) Furthermore, Japanese individuals need not consume a large amount of alcohol to get heavily drunk.\(^18\) These facts regarding the Japanese drinking style may help explain our results.

Some animal experiments have revealed that alcohol suppresses ischemia–reperfusion injury of major organs, including the brain, heart, and kidney.\(^19\)\(^-\)\(^24\) A clinical study reported that ICU patients with positive blood alcohol levels experienced significantly less bloodstream infection, sepsis, and multiorgan failure than those without alcohol; this does not hold true for patients who abuse alcohol.\(^25\) Alcohol also has sedative and analgesic effects. Our data revealed that the RTS, a physiologic scoring system for trauma patients, was lower in the drinking group due to a poorer GCS score. The physiological severity of patients in the drinking group might be increased due to impaired consciousness caused by the sedative effect; this compounds the anatomical severity at the time of admission, leading to higher frequencies of ventilator management and longer ICU stay durations. However, with appropriate initial treatment and systemic management, the mortality rate might be improved due to the organ protective effects of alcohol.

This study has some limitations. First, this was a retrospective observational study. Approximately half of the cases had missing “drinking” (35%) or AIS/ISS score (18%) data. Moreover, the “drinking” value was determined based on the criteria set by each institution; hence, the possibility that some drinkers were included in the nondrinking group cannot be ruled out. Second, the JTDB does not contain information on ADH and ALDH genotypes, blood alcohol levels, alcohol consumption, duration of drinking, or history of alcohol dependence, which could affect the results of this study. In addition, it should be noted that this study did not target alcoholic patients who are reported to experience high in-hospital mortality.\(^17\) Third, the JTDB does not collect information on the use of other drugs, including opioids or cannabis. However, in Japan, drug abuse is lower than in other countries.\(^26\) Fourth, the JTDB does not have any information on race, therefore our results might include some non-Japanese patients. However, more than 95% of Japanese residents are of Japanese origin; hence, the JTDB data should comprise mostly Japanese data. Fifth, the cause of death could not be analyzed because there was no information in the JTDB. We also excluded patients who died before hospitalization. In addition, obvious social death, such as brain prolapse or trunk dissection, might not have been included in the JTDB. However, in this study, all causes of death related to alcohol were analyzed; therefore, the results

### Table 2. Outcomes before and after matching of patients with severe blunt trauma

|                        | Prematching |                   | Postmatching |                   | P-value | P-value |
|------------------------|-------------|-------------------|--------------|-------------------|---------|---------|
|                        | Nondrinking | Drinking          | P-value      | Nondrinking      | Drinking | 0.001   |
| n=37,818               | n=8,543     |                   |              | n=8,428          | n=8,428 |         |
| Mortality (%)          | 4,936 (13.1)| 762 (8.9)         | <0.001       | 992 (11.8)       | 764 (9.0)| <0.001  |
| Hospital stay, days    | 21.00 (8.00, 41.00) | 19.00 (7.00, 39.00) | <0.001       | 19.00 (8.00, 38.00) | 19.00 (7.00, 39.00) | 0.848   |
| ICU stay, days         | 7.00 (2.00, 19.00) | 7.00 (2.00, 18.00) | 0.015        | 6.00 (2.00, 16.00) | 7.00 (2.00, 18.00) | 0.002   |
| Dead from injury, days | 2.00 (0.00, 8.00) | 2.00 (1.00, 8.00)  | 0.040        | 2.00 (1.00, 8.00)  | 2.00 (1.00, 8.00)  | 0.823   |
| Tracheal intubation (%)| 9,324 (24.7)| 2,089 (24.5)      | 0.706        | 1,922 (22.8)     | 2,054 (24.4)| 0.017   |

Data are expressed as median (interquartile range) or number (%). ICU, intensive care unit.

### Fig. 2. In-hospital mortality rate of patients with severe blunt trauma was significantly lower in the drinking group than in the nondrinking group (11.8% vs. 9.0%, \(P < 0.001\))
CONCLUSION

In this retrospective study, we determined the correlation between alcohol consumption and in-hospital mortality in patients with severe blunt trauma in Japan. After adjusting for anatomical severity and patient demographics, alcohol consumption did not increase in-hospital mortality; instead, it decreased it, despite increased physiological severity on admission. Although there was no difference in hospital length of stay, ICU length of stay was longer, and the probability of mechanical ventilation was also higher in the drinking group.

ACKNOWLEDGMENTS

None.

DISCLOSURE

Approval of the research protocol: This retrospective observational study was approved by the Institutional Review Board of Nippon Medical School and was carried out in accordance with the ethical standards established in the 1964 Declaration of Helsinki and its later amendments. The requirement for individual informed consent was waived due to the retrospective observational study design. Informed consent: N/A. Registry and the registration no. of the study: N/A. Animal studies: N/A. Conflict of interest: None.

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