Critical Care

RESEARCH

Open Access

Influence of alcohol on in-hospital survival rate among patients with traumatic brain injury: a nationwide cohort study

Kazuma Sasaki[1], Takashi Tagami[1,2,4*], Hirofumi Obinata[1], Chie Tanaka[1,3], Kosuke Otake[1,2], Yudai Yoshino[1,2], Akihiro Watanabe[1,2], Ami Shibata[1,2], Kentaro Kuwamoto[1,2], Junichi Inoue[1,2] and Shoji Yokobori[1]

Abstract

Background The impact of alcohol on the prognosis of patients with traumatic brain injury (TBI) remains unclear. While some reports suggest that alcohol may exert neuroprotective effects, others indicate that it can worsen neurological outcomes. This study aimed to evaluate the influence of alcohol consumption on TBI outcomes using a nationwide database in Japan.

Methods We analyzed data from approximately 290 hospitals contributing to the Japan Trauma Data Bank between 2004 and 2018. Patients with head injuries and documented pre-injury alcohol consumption were included. To adjust for potential confounders and institutional clustering, we employed propensity score methods—specifically inverse probability weighting (IPTW) and overlap weighting—and conducted multiple logistic regression with a generalized estimating equation. Covariates in the propensity score model included age, sex, day of the week, time of injury, period of injury, and past medical history. The primary outcome was in-hospital survival. Additionally, we fitted a multivariate logistic regression model (with survival as the outcome) to identify potential interactions and confounders. This model included type of trauma (blunt or penetrating), cause and setting of trauma, head Abbreviated Injury Scale score, multiple trauma status, the Injury Severity Score, and the propensity score.

Results Of the 83,789 patients who met the inclusion criteria, 15,752 had reported alcohol consumption prior to injury (alcohol group) and 68,037 did not (non-alcohol group). In-hospital survival was 91.5% in the alcohol group and 86.4% in the non-alcohol group (risk difference: 5.2%; 95% CI: 4.7–5.7). After adjustment, the alcohol group maintained a higher in-hospital survival rate (IPTW: 92.0% vs. 86.1%, risk difference: 6.2%; 95% CI: 5.9–6.2; overlap weighting: 91.7% vs. 85.4%, risk difference: 7.0%; 95% CI: 6.1–7.8). In the multivariate logistic regression, preinjury alcohol consumption was associated with higher survival (odds ratio: 1.58, 95% CI: 1.47–1.70, $p < 0.001$).

Conclusions In this nationwide study, preinjury alcohol consumption was associated with higher in-hospital survival among patients with TBI. Further research is warranted to elucidate the underlying mechanisms and confirm these findings in more diverse populations.

Keywords Alcohols, Epidemiology, Survival rate, Traumatic brain injuries

*Correspondence:
Takashi Tagami
t-tagami@nms.ac.jp
Full list of author information is available at the end of the article

Introduction

Alcohol consumption is associated with a wide range of adverse health outcomes and poses a considerable burden on healthcare systems worldwide, particularly in the context of trauma [1–4]. Alcohol impairs cognitive function, diminishes motor coordination, and increases the risk of falls by inducing muscle relaxation [5]. The effects of alcohol on trauma outcomes, particularly in patients with traumatic brain injury (TBI), have shown contradictory findings. Although some studies have suggested that alcohol consumption may reduce in-hospital mortality rates in patients with severe blunt trauma [6–13], others have reported no protective effects or even potential harm [14–17]. In addition, the influence of alcohol on the severity of head injuries and subsequent outcomes remains poorly understood.

In emergency situations, predicting the prognosis of TBI in patients who have consumed alcohol can be especially challenging [18]. Altered consciousness and an unreliable patient history may inflate the apparent severity of the injury, potentially leading to over-triage or diagnostic ambiguity. Given these conflicting findings and the clinical complexity of assessing TBI in patients who consume alcohol, a study conducted under more uniform clinical and demographic conditions may help clarify the role of alcohol in TBI outcomes.

Despite a handful of reports indicating a possible protective effect in certain trauma patients, it is unclear whether these findings are generalizable across different patient populations and healthcare systems, especially in light of variations in alcohol metabolism and treatment access [19, 20]. To address this gap, we focused on a single ethnic group within a universal health insurance system, where every individual has access to essential healthcare services [21]. Therefore, we used a Japanese nationwide trauma database to examine the relationship between alcohol consumption and TBI outcomes in this relatively homogenous setting.

Methods

Study design

This retrospective cohort study analyzed data collected between 2004 and 2018 from the Japan Trauma Data Bank (JTDB). Established in 2003 by the Japanese Association for Trauma Surgery and the Japanese Association for Acute Medicine, the JTDB is a comprehensive database that compiles trauma cases from approximately 290 hospitals nationwide.

The JTDB provides a comprehensive set of variables for this study, including patient demographics, such as age, sex, and previous medical history. The clinical data collected included pre-injury alcohol consumption, initial screening results, pathogenesis of brain injury, mechanisms, situation and cause of the injury, and vital signs at the time of prehospital and arrival, including the Glasgow Coma Scale score, systolic blood pressures (SBP), heart rate (HR). Pre-injury alcohol consumption was assessed based on the attending physician's clinical judgment, with or without reference to blood alcohol concentration. Injury severity was assessed using the Abbreviated Injury Scale (AIS) and maximum AIS from the 1998 update for various body sites, including the head, face, neck, chest, abdomen, pelvis, spine, upper and lower extremities, and skin. The AIS is a coding system that categorizes the type and anatomical severity of trauma, evaluating injury severity on a six-point scale. It is objectively assessed by the attending physician after hospital admission. Additional scoring systems included the injury severity score (ISS) and revised trauma score (RTS). Outcome data, including in-hospital survival rate, overall hospital stay, and length of stay in the intensive care unit (ICU) were also collected.

Patient selection and outcomes

This study analyzed patients who sustained TBI and were registered with the JTDB between 2004 and 2018. This timeframe was selected to ensure that the dataset was contemporary but unaffected by the COVID-19 pandemic. Patients with either isolated or combined head injuries, all of whom had documented AIS scores, were included. We defined head trauma as a head AIS score of 1 or more. Patients were excluded if they lacked information on the head AIS grade or alcohol consumption status.

We assessed the in-hospital survival rate as the primary outcome. The secondary outcomes were the lengths of hospital stay and ICU stay.

Statistical analyses

Data were expressed as numbers (%) or means (standard deviations), as appropriate. Continuous variables were compared using t-tests or the Mann–Whitney U test, and categorical variables were compared using the chi-square test or Fisher's exact test. Patients were categorized into two groups: those who consumed alcohol before injury (alcohol group) and those who did not (non-alcohol group). Missing data were handled via multiple imputation. To address potential confounding, we employed propensity score methods and logistic regression. The propensity score for pre-injury alcohol consumption was estimated using multiple logistic regression, incorporating a priori selected patient demographics and controlling for institutional clustering via a generalized estimating equation. Covariates in the model included age, sex, day of the week, time of injury, period of injury, and past medical history.

Time of injury was classified as daytime (07:00–18:00) or nighttime (18:00–07:00), while the study period was divided into three phases—early (2004–2009), middle (2010–2014), and late (2015–2018)—reflecting changes in the Road Traffic Act. Days of the week were grouped as weekdays (Monday–Thursday), weekends (Friday), or holidays (Saturday, Sunday, and public holidays). The C-statistic was calculated to evaluate the goodness of fit for the propensity score model.

We then performed inverse probability weighting (IPTW) and overlap weighting (OW) to compare outcomes between the alcohol and non-alcohol groups [22–25]. These methods minimize bias by weighing patients according to their propensity scores, thereby achieving balanced comparisons. In IPTW, weights were defined as: $Wi = Zi/ei + (1\text{-}Zi)/1\text{-}ei$, where Zi was an indicator variable denoting whether or not the i th subject was treated, and ei denoted the propensity score for the i th subject [24–26]. Overlap weighting emphasizes patients whose characteristics overlap between groups and achieves exact balance on the means of measured covariates. Overlap weights were defined as: $Wi = Zi \cdot (1\text{-}ei) + (1\text{-}Zi)ei$ [22, 23].

We additionally fitted a multivariate logistic regression model—with survival as the outcome—to identify potential interactions and confounders. This model included type of trauma (blunt or penetrating), cause and setting of trauma, type and Abbreviated Injury Scale (AIS) score of head injury, multiple trauma status, the Injury Severity Score (ISS) and the propensity score.

As an further sensitivity analysis, we performed additional sub-analyses focusing on patients with an AIS score of ≥ 3 and, separately, ≥ 4. For these subsets, we repeated our primary outcome assessments, including unadjusted comparisons, inverse probability weighting (IPTW), overlap weighting (OW), and multivariable logistic regression.

We also conducted a causal mediation analysis to examine whether alcohol consumption (exposure) affects survival (outcome) directly or indirectly through head injury severity (mediator) [27]. The assumed causal structure illustrating how alcohol may influence injury severity, which in turn impacts survival (indirect effect), and how alcohol may also exert a direct effect on survival independent of injury severity. We estimated the natural direct and indirect effects using a counterfactual framework and a nonparametric structural equation model, as recommended by Hayes [27].

All analyses were performed using SPSS version 28.0.1.1 for Windows (IBM Corp., Armonk, NY, USA) and STATA version 17 (StataCorp, College Station, TX, USA).

Results

Among the 361,706 patients registered in the JTDB, 83,789 had documented head injuries and drinking status. These individuals were categorized into two groups: the alcohol group (n = 15,752) and the non-alcohol group (n = 68,037) (Fig. 1).

Table 1 presents patient characteristics before and after IPTW and OW. Prior to weighing, the alcohol

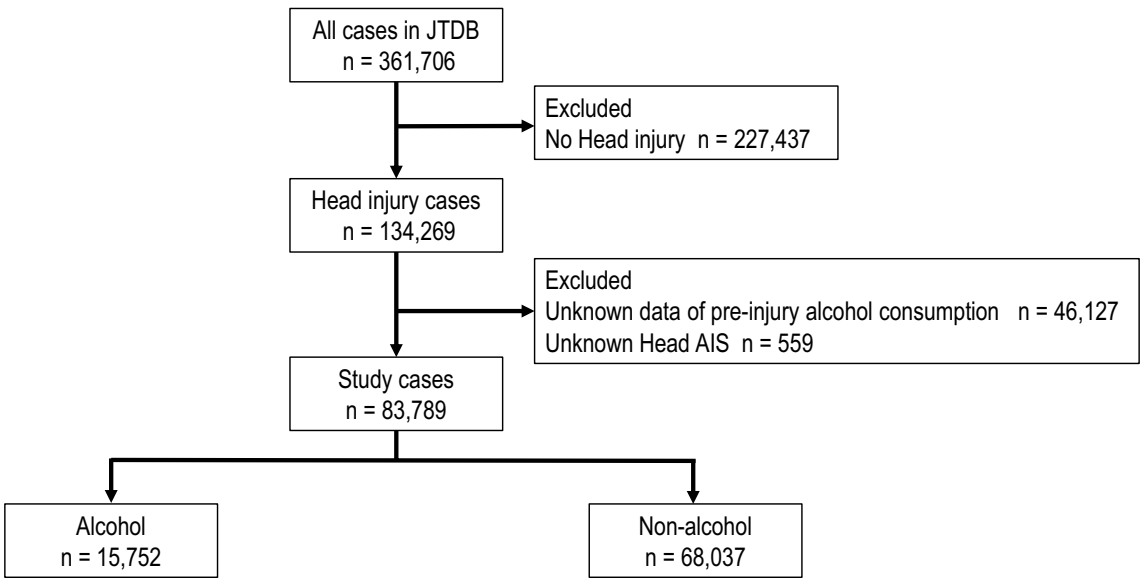

Fig. 1 Patient selection. AIS, Abbreviated Injury Scale, JTDB, Japan Trauma Databank

Table 1 Characteristics of patients before and after adjustment by IPTW and Overlap weighting

	Unadjusted groups					IPTW groups					Overlap weighting groups				
	Non-alcohol (n = 68,037)		Alcohol (n = 15,752)		Standardized difference (%)	Non-alcohol (n = 83,708)		Alcohol (n = 85,019)		Standardized difference (%)	Non-alcohol (n = 10,951)		Alcohol (n = 11,009)		Standardized difference (%)
Age, year (SD)	54.8	(26.9)	54.3	(17.6)	3.4	54.8	(26.7)	54.3	(18.2)	2.8	54.0	(26.3)	54.0	(17.7)	−0.5
Gender, male (n, %)	43,426	(63.8)	13,642	(86.6)	−54.3	(68.1)		(67.3)		1.6	(82.9)		(83.1)		0.0
Period (n, %)															
2001–2009	13,808	(20.5)	3691	(23.6)	−7.4	(20.6)		(23.5)		−7.2	(20.9)		(23.7)		−6.7
2010–2014	32,278	(47.9)	7657	(48.9)	−2.0	(47.9)		(48.7)		−1.5	(47.9)		(48.8)		−1.8
2015–2019	21,303	(31.6)	4310	(27.5)	9.0	(31.5)		(27.8)		8.1	(31.2)		(27.5)		8.1
Day of week (n, %)															
Weekday	35,949	(52.8)	6666	(42.3)	21.2	(50.9)		(52.0)		−2.3	(45.4)		(45.3)		0.1
Weekend	10,537	(15.5)	2298	(14.6)	2.5	(15.3)		(14.6)		1.9	(15.0)		(14.9)		0.2
Holiday	21,551	(31.7)	6788	(43.1)	−23.8	(33.8)		(33.3)		1.0	(39.6)		(39.8)		−0.3
Time zone (18:00–7:00) (n, %)	31,710	(46.6)	12,931	(82.1)	−79.8	(53.3)		(52.9)		0.8	(76.9)		(76.9)		0.0
Previous history (n, %)															
Diabetes mellitus	13,402	(19.7)	2662	(16.9)	7.2	(19.3)		(20.0)		−1.8	(17.5)		(17.4)		0.1
Hypertension	18,881	(27.8)	3640	(23.1)	10.7	(27.0)		(26.9)		0.2	(24.1)		(23.8)		0.5
Chronic heart failure	6834	(10.0)	1441	(9.1)	3.0	(10.0)		(11.8)		−5.8	(9.7)		(9.6)		0.5
Cerebral vessel disease	3825	(5.6)	556	(3.5)	10.0	(5.2)		(5.6)		−1.7	(4.0)		(4.0)		0.1
Dialysis	1148	(1.7)	62	(0.4)	12.8	(1.4)		(1.6)		−1.2	(0.5)		(0.5)		0.3
Liver cirrhosis	422	(0.6)	252	(1.6)	−9.4	(0.9)		(1.0)		−1.2	(1.3)		(1.3)		0.1
Blood disease	219	(0.3)	24	(0.2)	3.5	(0.3)		(0.4)		−2.0	(0.2)		(0.2)		0.0
anti-coagulation therapy	1736	(2.6)	224	(1.4)	8.1	(2.3)		(2.5)		−1.1	(1.6)		(1.6)		−0.3

IPTW; inverse probability of treatment weighting, S; standard deviations

group comprised predominantly male patients (86.1%) and those who were more likely to sustain injuries on holidays (43.1%) and at night (82.1%). In addition, this group showed a higher prevalence of liver cirrhosis (1.6%). After applying IPTW and OW, all of these baseline differences were well balanced between the two groups (i.e. standardized differences < 10%).

Table 2 summarizes the types of traumatic brain injuries, head injury severity (head AIS scores), trauma type, mechanism, cause, and situation of injury. Notably, the alcohol group showed higher incidences of traumatic subarachnoid hemorrhage and contusions. In terms of injury context, falls occurred more frequently in the alcohol group (58.6% vs. 46.1%), whereas traffic accidents were less common (30.8% vs. 45.5%).

Table 3 reports the primary and secondary outcomes. In-hospital survival was 91.5% in the alcohol group and 86.4% in the non-alcohol group (risk difference: 5.2%; 95% CI: 4.7–5.7). After adjustment, the alcohol group maintained a higher in-hospital survival rate (IPTW: 92.0% vs. 86.1%, risk difference: 6.2%; 95% CI: 5.9–6.2; overlap weighting: 91.7% vs. 85.4%, risk difference: 7.0%; 95% CI: 6.1–7.8). Moreover, the alcohol group experienced a shorter average hospital stay (IPTW: 18.8 vs. 16.5 days, mean difference 2.2, 95% CI 1.7–2.7; OW: 18.9 vs. 16.4 days, mean difference 2.5, 95% CI 1.2–3.7). In IPTW analysis, ICU length of stay was shorter in the alcohol group compared to the non-alcohol group (mean difference: 0.65 days, 95% CI: 0.18–1.12). However, in OW analysis, no clear difference was detected (mean difference: 0.90 days, 95% CI: − 0.27–2.13).

The multivariate logistic regression, adjusted for all variables listed in Tables 1 and 2, confirmed that alcohol consumption was associated with higher survival rates (odds ratio: 1.58, 95% CI: 1.47–1.70). Table 4 presents the primary outcomes for cases with AIS ≥ 3 and ≥ 4, along with the results of the multivariate logistic regression analysis, demonstrating that the alcohol group consistently exhibited higher survival rates across all methods.

A causal mediation analysis was performed to assess whether the relationship between alcohol consumption and survival was mediated by injury severity, as measured by the AIS score. Alcohol consumption was associated with a decrease in AIS score (HR: − 0.103; 95% CI: − 0.109 to − 0.096). AIS score was positively associated with survival (HR: 0.041; 95% CI: 0.039–0.044). Additionally, alcohol consumption was directly associated with survival independent of injury severity (HR: 1.71; 95% CI: 1.67–1.75). Detailed mediation results are presented in Fig. 2.

Discussion

In this nationwide trauma database study, we analyzed 83,789 patients with head injuries to assess the association of pre-injury alcohol intake on outcomes. Our findings suggested that, even after adjusting for confounding factors, the alcohol group had a higher in-hospital survival rate than the non-alcohol group.

The survival advantage observed in the alcohol group may be influenced by multiple factors. We employed a propensity score approach that accounted for patient demographics, institutional differences, and variations in injury timing, such as nighttime, holidays, and weekends, when resource and staff availability might be reduced. After applying IPTW and OW, all of these baseline differences were well balanced between the two groups. Despite these adjustments, the alcohol group demonstrated a survival advantage. One plausible explanation lies in the differences in trauma mechanisms and injury patterns between the alcohol and non-alcohol groups. The alcohol group had a significantly higher proportion of falls, whereas the non-alcohol group had more traffic-related injuries. Falls typically result in different injury biomechanics compared to high-energy mechanisms such as motor vehicle collisions. Additionally, specific TBI types, including subarachnoid hemorrhage and contusions, were more frequently observed in the alcohol group. These variations in trauma mechanism and injury pattern may inherently influence survival outcomes, independent of alcohol consumption. Although residual confounding related to injury biomechanics might not be fully excluded, our multivariable logistic regression model adjusted for these factors.

Alcohol's sedative effects may have influenced initial clinical assessment and triage decisions (i.e. leading to over-triage), contributing to disparities in medical intervention. Patients with alcohol-related TBI often present with lower GCS scores, which can lead to increased vigilance, early neuroimaging, and closer monitoring in the emergency setting. This could result in more aggressive supportive care, thereby reducing the likelihood of delayed diagnoses or secondary brain injury progression. While our sensitivity analyses (subgroup analyses of AIS ≥ 3, AIS ≥ 4) suggest that over-triage does not entirely explain the survival advantage, triage biases remain a potential contributing factor.

Our mediation analysis suggests that the association between alcohol consumption and improved survival in TBI patients may be explained by two distinct pathways: an indirect effect mediated by injury severity and a direct effect independent of injury severity. The indirect pathway aligns with the hypothesis that alcohol consumption is associated with less severe head injuries, as reflected in lower AIS scores, which in turn contributes to improved

Table 2 Distribution of trauma-related variables

	Non-alcohol (n = 68,037)		Alcohol (n = 15,752)		Standardized difference (%)
Type of trauma (n, %)					
Blunt	66,515	(97.8)	15,312	(97.2)	3.6
Penetrate	479	(0.7)	129	(0.8)	−1.3
Cause of trauma (n, %)					
Accident	59,325	(87.2)	13,882	(88.1)	−2.8
Suicide	2129	(3.1)	396	(2.5)	3.7
Assault	666	(1.0)	573	(3.6)	−17.8
Situation (n, %)					
Traffic accident	30,903	(45.5)	4851	(30.8)	30.5
Fall	31,360	(46.1)	9235	(58.6)	−25.3
Machinery	152	(0.2)	1	(0.0)	6.4
Train accident	291	(0.4)	177	(1.1)	−7.9
Type of head injury (n, %)					
AEDH	6125	(9.0)	1881	(11.9)	−9.6
ASDH	22,261	(32.7)	4929	(31.3)	3.1
Traumatic SAH	24,902	(36.6)	6680	(42.4)	−11.9
Contusion	16,717	(24.6)	4789	(30.4)	−13.1
ICH	57	(0.1)	12	(0.1)	0.3
DBI	3024	(4.4)	497	(3.2)	6.7
Others	40,189	(59.1)	10,071	(63.9)	−10.0
Head AIS (n, %)					
1	3581	(5.3)	1057	(6.7)	−6.1
2	22,207	(32.6)	5250	(33.3)	−1.5
3	27,967	(41.1)	6924	(44.0)	−5.8
4	9898	(14.5)	1737	(11.0)	10.6
5	4147	(6.1)	760	(4.8)	5.6
6	228	(0.3)	23	(0.1)	3.9
Multiple trauma (n, %)	39,297	(57.8)	8489	(53.9)	7.8
Other trauma (n, %)					
Face	14,744	(21.7)	4129	(26.2)	−10.7
Neck	486	(0.7)	101	(0.6)	0.9
Chest	18,498	(27.2)	3179	(20.2)	16.5
Abdominal	5182	(7.6)	908	(5.8)	7.4
Pelvic	11,143	(16.4)	2135	(13.6)	7.9
Upper extremities	15,495	(22.8)	2939	(18.7)	10.2
Lower extremities	17,279	(25.4)	2790	(17.7)	18.8
External	2875	(4.2)	613	(3.9)	1.7
Vital signs (mean, SD)					
Prehospital SBP	141.7	(33.9)	131.7	(30.2)	31.1
Prehospital HR	86.5	(23.7)	86.1	(20.5)	1.8
SBP on Arrival	135.6	(42.1)	131.3	(34.6)	11.1
HR on Arrival	85.0	(26.9)	86.0	(21.6)	−4.0
GCS Eye on Arrival	3.18	(1.16)	2.97	(1.20)	17.8
GCS Verbal on Arrival	3.84	(1.5)	3.60	(1.48)	16.1
GCS Motor on Arrival	5.18	(1.6)	5.11	(1.59)	4.4
Total GCS on Arrival	12.14	(4.0)	11.65	(3.95)	12.3
ISS	19.5	(17.4)	12.6	(10.8)	47.5
RTS	6.93	(1.79)	6.93	(1.52)	0.00

AIS; abbreviated injury scale, ASDH; acute subdural hematoma, AEDH; acute epidural hematoma, DBI; diffuse brain injury, GCS; glasgow coma scale, HR; heart rate, ICH; intracranial hemorrhage, IPTW; inverse probability of treatment weighting, ISS; injury severity scale, SBP; systolic blood pressure, RTS; revised trauma score, tSAH; traumatic subarachnoid hematoma

Table 3 Comparison of in-hospital outcomes between non-alcohol and alcohol group

	Unadjusted groups			IPTW Groups			Overlap weighting Groups		
	Non-alcohol (n = 68,037)	Alcohol (n = 15,752)	Risk difference, % (95%CI)	Non-alcohol (n = 83,708)	Alcohol (n = 85,019)	Risk difference, % (95%CI)	Non-alcohol (n = 10,951)	Alcohol (n = 11,009)	Risk difference, % (95%CI)
In-hospital survival rate (n, %)	58,760 (86.4)	14,417 (91.5)	5.2 (4.7–5.7)	72,078 (86.1)	78,193 (92.0)	6.2 (5.9 – 6.2)	9352 (85.4)	10,093 (91.7)	7.0 (6.1- 7.8)
	Unadjusted groups			**IPTW groups**			**Overlap weighting groups**		
	Non-alcohol (n = 68,037)	**Alcohol (n = 15,752)**	**Mean difference (95%CI)**	**Non-alcohol (n = 83,708)**	**Alcohol (n = 85,019)**	**Mean difference (95%CI)**	**Non-alcohol (n = 10,951)**	**Alcohol (n = 11,009)**	**Mean difference (95%CI)**
In hospital days (days, SD)	18.7 (42.7)	16.5 (54.1)	2.2 (1.4–3.0)	18.8 (42.4)	16.5 (53.2)	2.2 (1.7–2.7)	18.9 (14.4)	16.4 (53.8)	2.5 (1.2–3.7)
ICU days (days, SD)	8.1 (33.2)	7.8 (49.7)	0.4 (−0.3–1.1)	8.2 (32.0)	7.5 (53.2)	0.7 (0.2–1.1)	8.5 (26.3)	7.6 (53.0)	0.9 (– 03.–2.1)

CI; confidence interval, ICU; intensive care unit, IPTW; inverse probability of treatment weighting, SD; standard difference

Table 4 Subgroup analysis of in-hospital survival rates in patients with severe traumatic brain injury (AIS ≥ 3 and AIS ≥ 4)

	Unadjusted groups analysis			IPTW analysis			Overlap weighting analysis		
	Non-alcohol (n = 42,249)	Alcohol (n = 9445)	Risk Difference % (95%CI)	Non-alcohol (n = 51,918)	Alcohol (n = 52,171)	Risk Difference % (95%CI)	Non-alcohol (n = 6734)	Alcohol (n = 6615)	Risk Difference % (95%CI)
AIS **≥** ***3*** **cohorts**									
In-hospital survival rate (n, %)	35,660 (84.4)	8575 (90.8)	6.3 (5.7–7.1)	43,633 (84.0)	47,595 (91.2)	7.2 (6.8–7.6)	5588 (83.0)	6015 (90.9)	7.9 (6.8–9.1)
	Unadjusted groups analysis			**IPTW analysis**			**Overlap weighting analysis**		
	Non-alcohol (n = 2253)	**Alcohol (n = 1781)**	**Risk Difference % (95%CI)**	**Non-alcohol (n = 17,523)**	**Alcohol (n = 14,857)**	**Risk Difference % (95%CI)**	**Non-alcohol (n = 2253)**	**Alcohol (n = 1781)**	**Risk Difference % (95%CI)**
AIS **≥** ***4*** **cohorts**									
In-hospital survival rate (n, %)	1797 (79.8)	1529 (85.9)	6.1 (3.8–8.4)	14,194 (81.0)	12,724 (85.6)	4.6 (3.8–5.5)	1797 (7.98)	1529 (8.59)	6.1 (3.8–8.4)

The multivariate logistic regression, adjusted for all variables listed in Tables 1 and 2, confirmed that alcohol consumption was associated with higher survival rates 1.62 (1.48–1.70)The multivariate logistic regression, adjusted for all variables listed in Tables 1 and 2, confirmed that alcohol consumption was associated with higher survival rates 1.38 (1.20–1.59).

CI; confidence interval, ICU; intensive care unit, IPTW; inverse probability of treatment weighting, SD; standard difference

survival. This may be partially attributable to over-triage, where alcohol-related altered consciousness leads to a higher likelihood of hospital admission and intensive monitoring for milder injuries. However, the persistence of a direct effect even after adjusting for injury severity suggests that other mechanisms may be involved. While speculative, potential explanations include the neuroprotective and anti-inflammatory properties of alcohol, which have been proposed in preclinical studies [28–30].

Emerging evidence suggests that alcohol may have biological effects that influence TBI outcomes, with preclinical studies indicating its potential role in modulating inflammatory pathways and reducing secondary brain injury [28–30]. While our mediation analysis demonstrated that injury severity only partially mediated the relationship between alcohol consumption and survival, this suggests that additional, yet unexplored, factors may contribute to the observed survival differences. However,

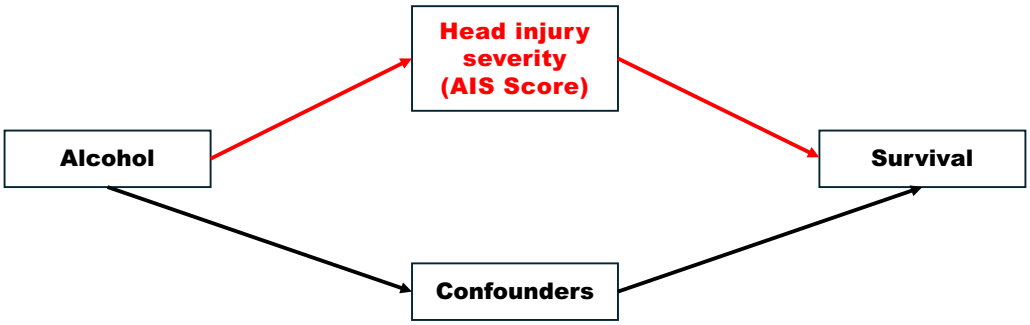

Fig. 2 Directed acyclic graph (DAG) depicting the assumed causal structure. We modeled head injury severity (AIS score) as a mediator (M) between Drinking (X) and Survival (Y). Our analysis yielded the following key findings: Effect of Drinking on AIS Score: Drinking was associated with a statistically significant reduction in the AIS score (HR: –0.103; 95% CI: –0.109 to –0.096), indicating that, on average, the alcohol group had lower injury severity. Indirect Effect via AIS: AIS score was associated with survival (HR: 0.042; 95% CI: 0.039–0.044), indicating that a lower AIS score confers a higher likelihood of survival. Direct Effect of Drinking: Even after adjusting for AIS, alcohol consumption remained associated with improved survival outcomes (HR: 1.71; 95% CI: 1.67–1.75)

clinical validation of these mechanisms remains limited, and caution is warranted in interpreting these findings.

It is essential to emphasize that these results should not be misinterpreted as endorsing alcohol consumption. Alcohol is associated with numerous well-documented health risks, including increased trauma susceptibility, long-term neurotoxicity, and systemic health consequences. Any potential survival advantage observed in TBI patients must be considered within the broader context of its detrimental effects. Nonetheless, our findings serve as hypothesis-generating evidence, highlighting the need for future research to investigate potential biological mechanisms underlying alcohol-related TBI outcomes in both preclinical and clinical settings.

One strength of this study is its focus on the Japanese population, which has relatively homogeneous genetic factors affecting alcohol metabolism. Many prior investigations encompassed mixed ethnic cohorts, potentially obscuring the effects of metabolic variations in alcohol dehydrogenase and aldehyde dehydrogenase [19, 20, 31–33]. In contrast, our homogeneous sample minimized the confounding from such differences, thereby enhancing confidence in the observed association. Furthermore, conducting this investigation within a universal health insurance system likely reduced disparities in treatment access and quality of care, supporting the idea that the observed survival benefit is not merely a byproduct of unequal healthcare resources [21].

From a clinical standpoint, recognizing that some patients with head injuries who consume alcohol may retain relatively favorable prognoses highlights the importance of careful triage and management. Although we do not advocate alcohol consumption—given its well-documented harms—our results remind clinicians that the initial severity of consciousness impairment might not always translate into poor outcomes. More detailed assessment tools, including blood alcohol concentration measurements, could improve the prognostic accuracy and resource allocation in emergency settings. Our findings may serve as a foundation for developing more accurate triage and prognostic assessment strategies for TBI patients with a history of alcohol consumption.

This study has several limitations. We relied on reported alcohol consumption rather than objective blood alcohol concentration (BAC) measurements, making it unclear whether attending physicians referenced BAC in their assessments. The lack of BAC data also precluded an evaluation of potential dose–response effects, which could have provided further insight into alcohol's impact on TBI outcomes. Future studies incorporating precise BAC measurements are needed to address this limitation. Additionally, while we adjusted for multiple confounding factors—including trauma type, cause and setting of trauma, and severity measures such as AIS and ISS—inherent differences between the alcohol and non-alcohol groups may persist. Although our subgroup analyses restricted to AIS ≥ 3 and AIS ≥ 4 confirmed similar trends in survival outcomes, residual confounding due to unmeasured factors cannot be fully excluded. Our retrospective cohort design inherently limits causal inferences and cannot fully account for all potential biases, including over-triage in the alcohol group and potential misclassification of injury severity due to alcohol's physiological effects. Because the analysis relied on a single national database, it may not capture regional variations in trauma care, limiting the generalizability of our findings. Moreover, patients were not stratified by the frequency or chronicity of alcohol use, which can affect physiological tolerance and clinical outcomes. Finally, we did not account for the impact of co-occurring

substances, nor did we address alcohol's sedative properties, both of which may influence consciousness level and injury severity, complicating the interpretation of our results.

Conclusion

In conclusion, our findings suggest that alcohol consumption prior to traumatic brain injury may be associated with higher in-hospital survival rates and shorter hospital stays. Our findings may provide a basis for improving triage accuracy and prognostic evaluation methods for TBI patients with a history of alcohol consumption. Further investigations are warranted to elucidate the biological mechanisms underlying these observations and to confirm their applicability in more diverse populations.

Abbreviations

AHD	Alcohol dehydrogenase
AIS	Abbreviated injury scale
ALDH	Aldehyde dehydrogenase
BAC	Blood alcohol concentration
CI	Confidence interval
ICU	Intensive care unit
IPTW	Inverse probability of treatment weighting
ISS	Injury severity score
JTDB	Japan Trauma Data Bank
OW	Overlap weighting
RTS	Revised trauma score
TBI	Traumatic brain injury

Acknowledgements

Not applicable.

Author contributions

Kazuma Sasaki and Takashi Tagami contributed to the study conception, design, acquisition and analysis of the data. All the authors contributed to drafting of the manuscript, figures, and tables. All the authors read and approved the final manuscript.

Funding

This study was not supported by any sponsor or funder.

Availability of data and materials

The dataset generated and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee at the Nippon Medical School Hospital (B-2020-318) and adhered to the principles of the Declaration of Helsinki. Because this study analyzed anonymized information, the requirement for informed consent was waived.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Emergency and Critical Care Medicine, Nippon Medical School Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan. [2]Department of Emergency and Critical Care Medicine, Nippon Medical School Musashikosugi Hospital, 1-396 Kosugi-cho, Nakahara-ku, Kawasaki city, Kanagawa 211-8533, Japan. [3]Department of Emergency and Critical Care Medicine, Nippon Medical School Tamanagayama Hospital, 1-7-1 Nagayama, Tama city, Tokyo 206-8512, Japan. [4]Department of Emergency and Disaster Medicine, The Jikei University School of Medicine, 3-25-8 Nishi-Shinbashi, Minato-ku, Tokyo, 105-0003, Japan.

Received: 21 December 2024 Accepted: 9 March 2025
Published online: 24 March 2025

References

1. Chen CM, Yi HY, Yoon YH, Dong C. Alcohol use at time of injury and survival following traumatic brain injury: results from the National Trauma Data Bank. J Stud Alcohol Drugs. 2012;73(4):531–41.
2. Langlois JA, Rutland-Brown, Wesley, Thomas, Karen E. Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths. In: Edited by National Center for Injury P, Control, Division of Injury R, Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; 2006.
3. Collaborators GBDA. Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2018;392(10152):1015–35.
4. Cherpitel CJ, Ye Y, Poznyak V. Single episode of alcohol use resulting in injury: a cross-sectional study in 21 countries. Bull World Health Organ. 2018;96(5):335–42.
5. Stein DJ, Benjet C, Gureje O, Lund C, Scott KM, Poznyak V, van Ommeren M. Integrating mental health with other non-communicable diseases. BMJ. 2019;364: l295.
6. Sasaki K, Obinata H, Yokobori S, Sakamoto T. Alcohol does not increase in-hospital mortality due to severe blunt trauma: an analysis of propensity score matching using the Japan Trauma Data Bank. Acute Med Surg. 2021;8(1): e671.
7. Berry C, Ley EJ, Margulies DR, Mirocha J, Bukur M, Malinoski D, Salim A. Correlating the blood alcohol concentration with outcome after traumatic brain injury: too much is not a bad thing. Am Surg. 2011;77(10):1416–9.
8. Tien HC, Tremblay LN, Rizoli SB, Gelberg J, Chughtai T, Tikuisis P, Shek P, Brenneman FD. Association between alcohol and mortality in patients with severe traumatic head injury. Arch Surg. 2006;141(12):1185–91.
9. Talving P, Plurad D, Barmparas G, Dubose J, Inaba K, Lam L, Chan L, Demetriades D. Isolated severe traumatic brain injuries: association of blood alcohol levels with the severity of injuries and outcomes. J Trauma. 2010;68(2):357–62.
10. Afshar M, Netzer G, Salisbury-Afshar E, Murthi S, Smith GS. Injured patients with very high blood alcohol concentrations. Injury. 2016;47(1):83–8.
11. Stehman CR, Moromizato T, McKane CK, Mogensen KM, Gibbons FK, Christopher KB. Association between blood alcohol concentration and mortality in critical illness. J Crit Care. 2015;30(6):1382–9.
12. Zeckey C, Dannecker S, Hildebrand F, Mommsen P, Scherer R, Probst C, Krettek C, Frink M. Alcohol and multiple trauma: is there an influence on the outcome? Alcohol. 2011;45(3):245–51.
13. Jung E, Ro YS, Jeong J, Ryu HH, Shin SD. Alcohol intake before injury and functional and survival outcomes after traumatic brain injury: Pan-Asian trauma outcomes study (PATOS). Medicine (Baltimore). 2023;102(34): e34560.
14. Pandit V, Patel N, Rhee P, Kulvatunyou N, Aziz H, Green DJ, O'Keeffe T, Zangbar B, Tang A, Gries L, et al. Effect of alcohol in traumatic brain injury: is it really protective? J Surg Res. 2014;190(2):634–9.
15. Ahmed N, Kuo YH, Sharma J, Kaul S. Elevated blood alcohol impacts hospital mortality following motorcycle injury: a National Trauma Data bank analysis. Injury. 2020;51(1):91–6.
16. Ahmed N, Greenberg P. Patient mortality following alcohol use and trauma: a propensity-matched analysis. Eur J Trauma Emerg Surg. 2019;45(1):151–8.
17. Peng SH, Hsu SY, Kuo PJ, Rau CS, Cheng YA, Hsieh CH. Influence of alcohol use on mortality and expenditure during hospital admission: a cross-sectional study. BMJ Open. 2016;6(11): e013176.
18. Rogan A, Patel V, Birdling J, Lockett J, Simmonds H, McQuade D, Quigley P, Larsen P. Alcohol and acute traumatic brain injury in the emergency department. Emerg Med Australas. 2021;33(4):718–27.

19. Eng MY, Luczak SE, Wall TL. ALDH2, ADH1B, and ADH1C genotypes in Asians: a literature review. Alcohol Res Health. 2007;30(1):22–7.
20. Wall TL, Luczak SE, Hiller-Sturmhöfe S. Biology, genetics, and environment: underlying factors influencing alcohol metabolism. Alcohol Res Curr Rev. 2016;38(1):59.
21. Ikegami N, Anderson GF. In Japan, all-payer rate setting under tight government control has proved to be an effective approach to containing costs. Health Aff (Millwood). 2012;31(5):1049–56.
22. Thomas LE, Li F, Pencina MJ. Overlap weighting: a propensity score method that mimics attributes of a randomized clinical trial. JAMA. 2020;323(23):2417–8.
23. Li F, Thomas LE, Li F. Addressing extreme propensity scores via the overlap weights. Am J Epidemiol. 2018;188(1):250–7.
24. Austin PC. The use of propensity score methods with survival or time-to-event outcomes: reporting measures of effect similar to those used in randomized experiments. Stat Med. 2014;33(7):1242–58.
25. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res. 2011;46(3):399–424.
26. Tagami T, Tosa R, Omura M, Fukushima H, Kaneko T, Endo T, Rinka H, Murai A, Yamaguchi J, Yoshikawa K, et al. Effect of a selective neutrophil elastase inhibitor on mortality and ventilator-free days in patients with increased extravascular lung water: a post hoc analysis of the PiCCO Pulmonary Edema Study. J Intensive Care. 2014;2(1):67.
27. Hayes AF. Introduction to mediation, moderation, and conditional process analysis. 2021.
28. Wang F, Wang Y, Geng X, Asmaro K, Peng C, Sullivan JM, Ding JY, Ji X, Ding Y. Neuroprotective effect of acute ethanol administration in a rat with transient cerebral ischemia. Stroke. 2012;43(1):205–10.
29. Gottesfeld Z, Moore AN, Dash PK. Acute ethanol intake attenuates inflammatory cytokines after brain injury in rats: a possible role for corticosterone. J Neurotrauma. 2002;19(3):317–26.
30. Kelly DF, Kozlowski DA, Haddad E, Echiverri A, Hovda DA, Lee SM. Ethanol reduces metabolic uncoupling following experimental head injury. J Neurotrauma. 2000;17(4):261–72.
31. Wall TL, Luczak SE, Orlowska D, Pandika D. Differential metabolism of alcohol as an intermediate phenotype of risk for alcohol use disorders: Alcohol and aldehyde dehydrogenase variants. Genetic influences on addiction: an intermediate phenotype approach. Cambridge: Boston Review; 2013. p. 41–63.
32. Luczak SE, Glatt SJ, Wall TL. Meta-analyses of ALDH2 and ADH1B with alcohol dependence in Asians. Psychol Bull. 2006;132(4):607–21.
33. Osier MV, Pakstis AJ, Soodyall H, Comas D, Goldman D, Odunsi A, Okonofua F, Parnas J, Schulz LO, Bertranpetit J, et al. A global perspective on genetic variation at the ADH genes reveals unusual patterns of linkage disequilibrium and diversity. Am J Hum Genet. 2002;71(1):84–99.

Publisher's Note