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Acute Alcohol Intoxication in Patients with Mild Traumatic Brain Injury: Characteristics, Recovery, and Outcome

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Abstract

A substantial number of patients (30% to 50%) sustains a mild traumatic brain injury (mTBI) while they are under the influence of alcohol. An acute alcohol intoxication (AAI) at the time of injury has been subject of research in severe TBI, but little is known about the relation between AAI and mTBI. This study aimed to describe the characteristics of this intoxicated subgroup and evaluate recovery and outcome in comparison to sober mTBI patients. We included 528 mTBI patients (Glasgow Coma Scale [GCS] score 13–15) admitted to two Level 1 trauma centers as part of a prospective follow-up study. We compared clinical characteristics, demographics, and injury mechanism between groups. Post-concussive complaints, mood disorders, and post-traumatic stress-related complaints were assessed at 2 weeks post-injury, and outcome at 6 months with the Glasgow Outcome Scale Extended (GOSE). Thirty-three percent of the mTBI patients were intoxicated. Results showed that the intoxicated group was younger (36 vs. 40 years; $p=0.001$) and were more frequently of male gender (78% vs. 60%; $p<.001$). The groups also differed in injury related characteristics, with intoxicated patients more frequently sustaining falls or violence-related injuries. The intoxicated group was assessed with a lower GCS score and had a higher hospital admission rate. However, at 2 weeks post-injury, intoxicated patients reported less complaints than the non-alcohol group and showed a better recovery at 6 months (average GOSE scores 7 vs. 7.3; $p=0.030$). We conclude that AAI in mTBI represents a characteristically different group, which has implications for prevention measures, as well as the course of recovery.

Key words: alcohol; complaints; mild traumatic brain injury; outcome; recovery

Introduction

TRAUMATIC BRAIN INJURY is one of the most common neurological disorders, with mild traumatic brain injury (mTBI) accounting for approximately 80% to 90% of all cases.¹ Incidence rates of mTBI are estimated at 100–300/100,000 population, most frequently affecting males younger than 50 years of age.^{2–4} Excessive alcohol consumption leading to acute alcohol intoxication (AAI) is associated with a higher risk of mTBI; up to 30% to 50% of all mTBIs are incurred when individuals are under the influence of alcohol.^{5,6} These rates are not surprising, considering that AAI results in impaired decision making, impaired motor control, a lack of inhibitory control, and an increased tendency for risk-taking that can lead to violent behavior or a vulnerability for victimization.^{5,7} Whereas the majority of patients with mTBI shows a full recovery, 15% to 25% of all cases continue to experience ongoing symptoms 3 months post-injury, causing considerable disability in daily life.⁸

Considering the large proportion of patients with mTBI who are intoxicated at the time of injury, it is important to study the characteristics of this subgroup and the influence of this pre-injury alcohol exposure on functional outcome.

Although there is a substantial body of research on the influence of alcohol on outcome in TBI and the potential underlying pathophysiological mechanisms, this literature mostly concerns patients with severe TBI or groups with varying severity. The results of these studies are inconsistent, with both advantageous and disadvantageous effects of AAI on post-traumatic neural damage being reported with regard to mortality,^{9,10} cognitive recovery,^{11,12} and functional outcome.¹³ This contradiction is also present in studies investigating the pathophysiological mechanism in severe TBI. Studies report both protective and harmful effects through either attenuation^{14,15} or exacerbation¹⁶ of the inflammatory responses.^{14,15}

However, few patient studies have focused on the influence of alcohol on outcome in mild TBI specifically. In their paper on

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outcome prediction in mTBI, Jacobs and colleagues¹⁷ found that besides age and extracranial injuries, a day-of-injury alcohol intoxication was the strongest indicator of a more favorable functional outcome 6 months post-injury. This unexpected finding might be a result of an erroneous assessment of higher injury severity due to the intoxication than actually is the case.^{18,19} However, evidence that AAI affects the initial severity assessment is inconclusive, as several studies report that AAI does not cause clinically significant changes in the Glasgow Coma Scale (GCS) scores, compared with sober TBI patients.^{9,20,21} In animal studies, the neuroprotective effect of alcohol through attenuation of the inflammatory process for mTBI was studied, but results were inconclusive.¹⁵

Even though the direction of the effect is unclear, it can be hypothesized that intoxication at the time of injury could have a substantial influence on the outcome following TBI. Research on AAI in mTBI is scarce, and so far no attempt has been made to describe the characteristics of this subpopulation in mTBI. Currently, effects of AAI on outcome have mainly been demonstrated in experimental animal studies, which are not likely to match the mechanisms and outcomes of clinical mTBI.²² It has been recognized that outcome in mTBI is strongly related to psychological factors, such as emotional distress in the form of mood- or post-traumatic stress (PTSD)-related complaints.²³ With regard to the latter, AAI could play a role in the severity of these trauma induced complaints by dampening the stress response.²⁴

Therefore, the goal of this study was to compare mTBI patients with acute alcohol intoxication with sober mTBI patients on clinical characteristics, demographics, and injury mechanism. In addition, we investigated the influence of AAI on complaints, depression, anxiety, and impact of events at 2 weeks post-injury and functional outcome at 6 months post-injury. Based on the findings of Jacobs and colleagues¹⁷ we expected patients who were intoxicated to have a better outcome. Further, we hypothesized that the protective effect of alcohol also influences the development of mood- and PTSD-related complaints.

Methods

Design and setting

A prospective follow-up study on outcome in mTBI was conducted in two Level I trauma centers: University Medical Center Groningen (UMCG) and St. Elisabeth Hospital Tilburg (EZH). Patients included received questionnaires 2 weeks and 6 months after injury. Demographic variables and injury characteristics were obtained from the hospital records. On admission, GCS scores were determined as part of the neurological examination. On the basis of these records, the Injury Severity Score (ISS) was determined.²⁵ On admission, GCS scores were determined as part of the neurological examination. A computed tomography (CT) scan of the brain was performed on admission and CT abnormalities were defined by the Marshall score (category 1 = no abnormalities, categories 2–6 = abnormalities).²⁶

Participants

Patients with mTBI between 16 and 65 years of age admitted to the emergency departments (ED's) of the UMCG and EZH between February 2013 and October 2014 were included in this study. MTBI was defined as an injury to the head caused by external physical force resulting in a GCS score of 13–15, loss of consciousness of ≤ 15 min (documented, reported or self-reported), and/or post-traumatic amnesia of ≤ 24 h. These criteria are in accordance with the recommended guidelines of the World Health Organization Collaborating Center Task Force.²⁷ Patients suffering from a severe multi-trauma, chronic alcohol and/or drug abuse, and

major psychiatric or neurological disorders were excluded. Patients without a permanent home address were excluded due to anticipated follow-up difficulties.

The presence of an alcohol intoxication was assessed by emergency physicians according to the following criteria: recent ingestion of alcohol (by self-report or as reported by an observer), a physical exhibition of intoxication of the patient (e.g., slurred speech, alcohol odor) and if available, blood alcohol levels (BAL). Based on these criteria, patients were divided into four subgroups: 1) no alcohol consumption on the day of injury; 2) clear alcohol intoxication; 3) alcohol consumption on the day of injury but no clear intoxication; and 4) unknown. For comparative analyses, only the first two groups were used.

Measures

All measures were taken at 2 weeks post-injury, except for the Glasgow Outcome Scale Extended (GOSE), which was determined 6 months post-injury.

Post-concussive complaints

The Head Injury Symptom Checklist contains the 21 most commonly described post-concussive symptoms. It is derived from the Rivermead Post-concussion Symptoms Questionnaire,²⁸ which is the most common measure for post-concussive complaints. For all 21 complaints, a pre-injury and a current symptom level were indicated by the patient. Values range from 0 to 2 (0 = never, 1 = sometimes, 2 = often). The total amount of complaints (from 0 to 21) and the severity of complaints (0 to 42) can be determined.

Depression and anxiety

The presence or absence of depression and/or anxiety was assessed by means of the Hospital Anxiety and Depression Scale (HADS).²⁹ The HADS is a 14-item questionnaire, containing two subscales (depression and anxiety) of seven items each. Items are rated on a scale from 0–3. A cut-off score of ≥ 8 was recommended for establishing the presence of both depression and anxiety.³⁴ At this cut-off, an optimal balance between sensitivity and specificity (approximately 0.80) was established.³⁰

Post-traumatic stress

The Impact of Event Scale (IES) is a self-report measure of post-traumatic stress.³¹ The IES consisted of 15 statements, with scores ranging from 0 to 5. Seven items on the scale concerned “intrusion,” which is described as strong waves of emotion towards the event. The other eight items were directed at symptoms of “avoidance”—staying away from reminders of the event. In a study by van der Ploeg and colleagues, support was found for the construct validity and an adequate reliability.³²

Secondary outcome measures

The GOSE³⁷ provides eight categories of outcome ranging from 1 (death) to 8 (full recovery). A score of 7 or 8 is generally regarded as a good recovery. A structured questionnaire is used to determine the GOSE, which patients may either fill out at the outpatient clinic or at home. The GOSE has been found to be practical in use and to have a “very good” inter-rater reliability (0.85).³⁷

Statistical analysis

The data were analyzed with SPSS 22.0 (IBM, Inc., Armonk, NY).³⁸ Differences in patient demographics and clinical characteristics between the intoxicated and the non-alcohol group were tested using the χ^2 test (two-tailed) for categorical data, two sample Student's *t*-test for parametric data, and the Mann-Whitney *U* test for

FIG. 1. Flowchart of inclusion procedures.

non-parametric data. Since there was a significant difference between the groups regarding gender and age, we included these variables as covariates in the 2-week and 6-month analyses. A one-way analysis of covariance (ANCOVA) was used to compare groups. *Post hoc* mean comparisons were performed using univariate tests under the Bonferroni criterion. Alpha was set at 0.05, two-sided.

Results

Inclusion procedure and population

Figure 1 shows the flowchart of included mTBI patients. Of the 586 mTBI patients fulfilling inclusion criteria, 18 patients falling under group 3 (alcohol consumed, no clear intoxication) and 40 patients falling under group 4 (intoxication unknown) were excluded from further analysis. Five hundred and twenty-eight patients filled out the baseline questionnaire and were included in the 2-week post-injury analysis.

Six-month outcome scores were available for a subgroup of 303 patients of the final study population that filled out the 2-week questionnaire. In this subgroup, 29% of the patients were intoxicated at time of injury, which was comparable to the 2-week

group (33% intoxicated). The non-alcohol patient group used in the outcome analysis did not differ significantly from the non-alcohol patient group included in the 2-week analysis with regard to age, gender, educational level, GCS score, hospital admission, ISS and the presence of CT abnormalities. Likewise, the intoxicated patients in the outcome analysis did not differ from the intoxicated group from the 2-week analysis on the same criteria. The intoxicated subgroup used in the outcome analysis was only slightly older than the group used in the 2-week analysis (36.5 vs. 41.8 years; $p < 0.001$). With regard to the two participating trauma centers, no differences between these patients groups were found on percentage of intoxicated patients ($\chi^2 = 3.61$ [1]; $p = 0.058$), hospital admittance rate ($\chi^2 = 0.71$ [1]; $p = 0.399$), and all of the 2-week measures and 6-month outcome score.

Mechanism of injury and clinical presentation

Table 1 represents demographic and clinical characteristics for the total mTBI group and for the two subgroups (non-alcohol vs. intoxicated). Of the 528 patients, 172 patients (33%) were intoxicated at the time of injury. A comparison of the intoxicated

TABLE 1. PATIENT DEMOGRAPHIC, CLINICAL, AND PREMORBID CHARACTERISTICS

Variable	mTBI total (n = 528)	1) No alcohol (n = 356)	2) Intoxication (n = 172)	Difference 1–2	
				Statistic (df)	p
Male gender	347 (65.7%)	213 (59.8%)	134 (77.9%)	$\chi^2 = 16.82$ (1)	<0.001
Age	38.8 (15.7), 16–65	40.28 (15.9), 16–65	35.73 (14.8), 16–65	t = 3.15 (526)	0.002
Education	5.17 (2.3) 1–9	5.16 (2.3), 1–9	4.88 (2.2), 1–9		NS
GCS score	14.5 (0.6) 13–15	14.65 (0.6), 13–15	14.30 (0.7), 13–15	z = -5.94(528)	<0.001
Hospital admission (yes)	306 (58%)	195 (54.8%)	111 (64.5%)	$\chi^2 = 4.39$ (1)	0.039
-If yes, more than 1 day	160 (53%)	119 (61%)	41 (38.5%)	$\chi^2 = 14.83$ (1)	<0.001
ISS	7.5 (4.9), 4–39	7.7 (5.0), 4–39	7.2 (4.8), 4–30		NS
CT abnormalities	57 (11.9%)	37 (11.3%)	20 (12.1%)		NS
-Contusion	22 (42.3%)	13 (36.1%)	9 (45%)		NS
-Hemorrhage	46 (80.7%)	29 (78.4%)	17 (85%)		NS
-Epidural	8 (14%)	3 (8.1%)	5 (25%)		NS
-Subdural	11 (19.3%)	10 (27%)	1 (5%)		NS
-Subarachnoid	27 (47.4%)	16 (43.2%)	11 (55%)		NS

Mean ($\pm$ SD), range; all others = number (%).

mTBI, mild traumatic brain injury; NS, nonsignificant; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; CT, computed tomography.

TABLE 2. MECHANISM OF INJURY

Variable	mTBI total (n = 528)	1) Non- alcohol (n = 356)	2) Intoxication (n = 172)	Difference 1–2	
				χ^2 (df)	p
Mechanism of injury				56.68 (4)	<0.001
-Falls	328 (62.1%)	196 (55.1%)	132 (76.7%)	24.09 (1)	<0.001
-Collision	131 (24.8%)	115 (32.2%)	16 (9.3%)	32.56 (1)	<0.001
-Violence	35 (6.6%)	14 (3.9%)	21 (12.2%)	12.89 (1)	<0.001
-Sports	16 (3%)	16 (4.5%)	-	7.93 (1)	0.005
-Other	17 (3.2%)	15 (4.2%)	2 (1.2%)	3.43 (1)	0.064

Number (%)

mTBI, mild traumatic brain injury.

group with the non-alcohol group shows significantly more males in the intoxicated group, with a significantly lower age and GCS score. Of the total mTBI group, 306 patients were admitted to the hospital with an average of 3 days (range 1–60; SD = 4.87). The group that was admitted to the hospital consisted of significantly more intoxicated patients, although a significantly larger part of the intoxicated group was discharged after just one day (62% vs. 39%). No significant differences were found with regard to the ISS and the presence of CT scan abnormalities.

Table 2 shows the injury mechanisms for the total mTBI group and for the two subgroups (intoxicated vs. non-alcohol). Significant differences in all trauma mechanisms were present. Compared with the non-alcohol group, a higher percentage of injuries in the intoxicated group was caused by falls (77% vs. 55%) and violence (12% vs. 4%). Less traffic-related causes, like (car) collisions (9% vs. 32%), and less sports accidents (0% vs. 5%) were present in the intoxicated group, compared with the non-alcohol group.

Complaints at 2 weeks post-injury

ANCOVAs were conducted with the data on presence of AAI at the time of injury as the independent variable and self-reports of complaints, mood, and impact of events at 2 weeks after the injury as dependent variables. Age, gender, and GCS score were added as covariates (Table 3). The covariate gender was significantly related to patients' self-report of total number and severity of complaints, the level of experienced anxiety and depression and impact of event. Females reported more complaints and more severe complaints, a higher level of experienced anxiety and depression, and a greater impact of event. The covariate GCS score was significantly related to patient's self-report of the total number and severity of complaints. Patients with a lower GCS score reported more and more severe complaints.

After adjustment for age, gender, and GCS score, a statistically significant difference in the number and severity of complaints 2 weeks post-injury was found between the non-alcohol and intoxicated group. *Post hoc* analysis (Bonferroni adjusted) showed that the number (6.4 vs. 5.1) and severity (6.3 vs. 8.1) of reported complaints 2 weeks post-injury was significantly higher in the non-alcohol group, compared with the intoxicated group ($p = 0.007$ and $p = 0.005$, respectively). With regard to mood, we found a significant difference on the depression scale of the HADS, with intoxicated patients having a lower depression score than sober patients (2.9 vs. 4; $p = 0.035$). No significant differences were found between the non-alcohol group and the intoxicated group with regard to anxiety (3.8 vs. 4.6) and impact of events (15.7 vs. 15.6) 2 weeks post-injury.

Table 4 represents the presence of the different complaints for the total mTBI group and the two subgroups (non-alcohol vs. in-

toxicated). Significant differences in different domains of complaints were present. Compared with the non-alcohol group, a lower percentage of the intoxicated patients reported experiencing fatigue (56% vs. 37%), poor concentration (42% vs. 20%), slowness (38% vs. 17%), and forgetfulness/memory problems (33% vs. 23%). The intoxicated group also reported having less problems sleeping through the night (21% vs. 10%) and had less complaints of pain in the neck (31% vs. 19%) and arms (24% vs. 11%), compared with the non-alcohol group.

Six-month outcome

A GOSE score at 6 months was available for 305 patients. The scores ranged from 4 to 8. The majority of the patients reported a good recovery (score 7 and 8, 71%), 24% of patients a moderate disability, and a minority a relatively severe disability (score 4, 5%) 6 months post-injury. To determine differences in outcome between groups, an ANCOVA was conducted with the presence of AAI at the time of injury as the independent variable and the score on the GOSE

TABLE 3. ANCOVA FOR AAI ON COMPLAINTS, MOOD, AND IMPACT OF EVENTS AT 2 WEEKS WITH COVARIATES AGE, GENDER, AND GCS SCORE

Variable	Df	F	p	Significance of covariates		
				Age	Gender	GCS score
Complaints (total)						
Intoxication (AAI)	1	7.28	0.007	0.200	<0.001	0.003
Error	369					
Total	374					
Complaints (severity)						
Intoxication (AAI)	1	7.53	0.006	0.310	<0.001	0.003
Error	369					
Total	374					
HADS Anxiety						
Intoxication (AAI)	1	1.61	0.206	0.276	<0.001	0.819
Error	369					
Total	374					
HADS Depression						
Intoxication (AAI)	1	4.49	0.035	0.371	0.002	0.147
Error	369					
Total	374					
Impact of events						
Intoxication (AAI)	1	0.38	0.537	0.108	0.011	0.972
Error	369					
Total	374					

ANCOVA, analysis of covariance; AAI, acute alcohol intoxication; GCS, Glasgow Coma Scale; HADS, Hospital Anxiety and Depression Scale.

TABLE 4. COMPLAINTS 2 WEEKS POST-INJURY

Variable complaints	mTBI total (n = 528)	1) Non-alcohol (n = 356)	2) Intoxication (n = 172)	Difference 1–2	
				χ^2	p
<i>Somatic and cognitive</i>					
Headache	227 (43.0%)	162 (45.5%)	65 (37.8%)	2.82 (1)	0.111
Dizziness	239 (45.3%)	170 (47.8%)	69 (40.1%)	2.73 (1)	0.113
Balance disorders	148 (28.0%)	107 (30.1%)	41 (23.8%)	2.22 (1)	0.148
Drowsiness	237 (44.9%)	169 (47.3%)	70 (40.5%)	2.35 (1)	0.136
Fatigue	263 (49.8%)	199 (55.9%)	64 (37.2%)	16.20 (1)	<0.001
Forgetfulness	158 (29.9%)	118 (33.1%)	40 (23.3%)	5.41 (1)	0.020
Poor concentration	184 (34.8%)	149 (41.9%)	35 (20.3%)	23.62 (1)	<0.001
Slowness	165 (31.3%)	135 (37.9%)	30 (17.4%)	22.64 (1)	<0.001
Noise intolerance	170 (32.2%)	122 (34.3%)	48 (27.9%)	2.15 (1)	0.164
<i>Neck somatic</i>					
Neck pain	143 (27.1%)	110 (30.9%)	33 (19.2%)	8.06 (1)	0.005
Neck Stiffness	142 (26.9%)	103 (28.9%)	39 (22.7%)	2.31 (1)	0.129
<i>Auditive</i>					
‘Tinnitus’	79 (15.0%)	60 (16.9%)	19 (11.0%)	3.07 (1)	0.091
Hearing loss	39 (7.4%)	27 (7.6%)	12 (7.0%)	0.063 (1)	0.861
<i>Emotional</i>					
Irritability	95 (18.0%)	71 (19.9%)	24 (14.0%)	2.82 (1)	0.116
Anxiety	60 (11.4%)	39 (11.0%)	21 (12.2%)	0.18	0.670
Trouble falling asleep	74 (14.0%)	53 (14.9%)	21 (12.2%)	0.69 (1)	0.406
Trouble sleeping through	91 (17.2%)	74 (20.8%)	17 (9.9%)	9.66 (1)	0.002
<i>Non–post-traumatic</i>					
Dry mouth	80 (15.2%)	60 (16.9%)	20 (11.6%)	2.46 (1)	0.117
Arm pain	104 (19.7%)	85 (23.9%)	19 (11.0%)	12.07 (1)	0.001
Itchiness	40 (7.6%)	31 (8.7%)	9 (5.2%)	2.00 (1)	0.157

Number (%)

mTBI, mild traumatic brain injury.

6 months post-injury as the dependent variable (Table 5). Age, gender, and GCS score were added as covariates and were significantly related to the GOSE score. A lower age, male gender, and lower GCS score was associated with a better outcome. After adjustment for these variables, a significant difference in mean GOSE scores was present 6 months post-injury between the non-alcohol and intoxicated group (7 vs. 7.3, respectively). Intoxicated patients had a significantly higher outcome score than sober patients ($p=0.03$).

TABLE 5. ANCOVA FOR AAI ON GOSE SCORES AT SIX MONTHS (OUTCOME) WITH COVARIATES AGE, GENDER, AND GCS SCORE

Variable	Df	F	p	Significance of covariates		
				Age	Gender	GCS score
GOSE						
Intoxication (AAI)	1	4.75	0.030	<0.001	0.022	0.023
Error	298					
Total	303					

ANCOVA, analysis of covariance; AAI, acute alcohol intoxication; GOSE, Glasgow Outcome Scale Extended; GCS, Glasgow Coma Scale.

Discussion

Most clinical and laboratory studies investigating the effects of AAI on outcome following traumatic brain injury have focused on severe TBI or groups with varying severity. This consecutive co-

hort study is one of the first to focus on AAI in a mTBI population. We aimed to describe the characteristics of those mTBI patients that were clearly intoxicated with alcohol at the time of injury and compare this group with mTBI patients who had not consumed alcohol. The main findings comprise several differences in injury-related characteristics between these groups. Moreover, we found that although intoxicated patients initially seem to have a more severe injury, they report less complaints at 2 weeks post-injury and have a better outcome 6 months post-injury.

In our study, we found that one-third of mTBI patients were intoxicated with alcohol at the time of injury, consistent with results reported in the literature.^{5,6} Our results reveal important differences regarding injury-related characteristics between the intoxicated and the non-alcohol group. The AAI group comprised mainly males and the group was significantly younger than the non-intoxicated group. This observation is in accord with studies describing that young males are more likely to engage in risk-taking behavior, such as binge drinking.^{5,35} The two groups differed in mechanism of injury, as well, as intoxicated patients more frequently sustained falls or violence-related injuries than traffic- or sports-related injuries. This is supported by existing literature showing that AAI raises the risk of injury through impaired motor control (e.g., falls) and interpersonal violence, especially in young males.^{5,7} In our study cohort, further analysis of results showed that intoxicated patients are initially assessed with a lower GCS score and have a higher hospital admittance rate. However, this does not appear to be a precursor of a worse recovery. When controlling for age, gender, and injury severity, the AAI group reports a lower number and less severe complaints 2 weeks post-injury. When looking at the specific

complaints, the AAI group reports fewer complaints of fatigue, concentration, slowness, memory, neck and arm pain, and sleeping through the night, compared with the non-alcohol group. Moreover, AAI patients even have a better outcome 6 months post-injury, compared with the sober patients.

The apparent discrepancy between the initially worse clinical presentation of intoxicated patients and a more favorable outcome may be due to several underlying factors. First, several studies show that AAI can interfere with the initial assessment of injury severity.^{17–19} Patients may be initially judged to have more severe brain injury due to the central nervous system depressant effect of alcohol. This may lead to an erroneous impression of a more rapid improvement and better recovery. However, Lange and colleagues reported that GCS scores were only lowered by high BALs for patients with CT abnormalities.³⁶ Considering the fact that only a minority of CTs from our patient group showed abnormalities, an intoxication is not likely to have influenced the severity assessment in our patient population. Secondly, AAI can lead to an increased use of therapeutic and diagnostic procedures in the acute phase that may have an influence on outcome.¹⁸ This is in line with our finding that intoxicated patients were admitted to the hospital more often. Moreover, a significantly higher number of these admitted intoxicated patients were discharged after just one day, suggesting that these were patients only admitted to “sleep off” their inebriation.²¹

Thirdly, AAI could have exerted a neuroprotective effect in the recovery process following mTBI. Using a rat model, Perez-Polo and colleagues demonstrated that the post-injury inflammatory processes seen in severe TBI also are present in mTBI, and therefore are also influenceable by alcohol.²² However, several studies indicate that the effect of alcohol is dose related, with only moderate concentrations being protective.^{5,37} Considering the fact that we only included clearly intoxicated patients that had an excessive amount of alcohol, this would plead against this mechanism of protection. Moreover, two recent mouse studies on mTBI found no dose-dependent effects; there was no difference between moderate and excessive doses of alcohol intake on outcome.^{19,38}

Our finding that differences in specific complaints are present between the intoxicated and non-alcohol group may provide more insight in the differences between these groups. Sleep dysfunction and fatigue are important complaints to assess since these may aggravate other symptoms and pain.³⁹ A higher percentage of the non-alcohol patients complain about fatigue and sleeping problems, which might partly explain the higher number of other complaints. Moreover, the non-alcohol group has more somatic complaints of neck and arm pain, which has been suggested to be strongly related to pre-existent stress levels and a neurotic personality that may influence the development of complaints.^{39,42} A higher number of post-concussive complaints also is associated with mood disorders and PTSD.^{39,43,44} Despite the fact that we found no differences in the presence of mood disorders and PTSD-related complaints between the intoxicated and the non-alcohol group, the report of more and severe complaints by the non-alcohol group suggests that the impact of the trauma was bigger for this group. The trauma might have had a greater impact on sober patients because they experienced it more vividly in contrast to intoxicated patients, of whom the intensity of the experience was dampened by alcohol.²⁴

There are some limitations to this study. First, no objective measures, such as blood alcohol levels (BAL), were obtained for the majority of patients. BAL is the currently accepted standard to measure alcohol exposure and is used to create a distinction in moderate and excessive alcohol use on the basis of legal limits. However, the clinical significance of these legal limit cut-offs is

unknown, and does not take the variability of individual dependent effects of alcohol into account. Moreover, in several studies, BALs were obtained in less than half of the patients.¹³ Further, several studies report that BALs are not indispensable for an accurate distinction between intoxicated and sober patients. Mahler and colleagues found that emergency physicians were able to correctly identify significant alcohol exposure in blunt trauma patients 96% of the time.⁴⁵ In another study, Puljula and colleagues reported that in 95% of cases, the initial judgement of intoxication by emergency physicians and nurses corresponded correctly with the obtained BALs.³⁵ This study included only patients who were assessed to be clearly intoxicated and compared with patients who had absolutely no alcohol. Patients who drank alcohol but were not intoxicated were excluded, which makes our study a solid comparison of intoxicated versus non-alcohol. The sample size included in the outcome analysis was smaller than the sample size at the 2-week analysis. However, the two groups did not differ on the important clinical and injury characteristics. It is therefore unlikely that the smaller sample size would have had a negative effect on our comparison.

In summary, the current study demonstrates that AAI is inextricably linked to mTBI as part of the cause of injury and as a potential predictor for outcome. The AAI group seems a population to itself and differs from other mTBI patients on important aspects. The majority of intoxicated patients are young males, and the injury is more likely to be caused by falls or violence. Our results support the finding of a better outcome for mTBI patients that were intoxicated with alcohol. Intoxicated patients that initially appeared to have a worse clinical presentation, report a lower number of and less severe complaints after 2 weeks and have a better outcome after 6 months, compared with non-alcohol patients. The clinical implication of our findings is that alcohol forms a high risk factor for the incidence of an mTBI, especially among adolescents and young adults. Routine assessment of recent alcohol use and precise registration of this information by clinicians and effective education targeted at this group might play an important role in the prevention of mTBI, reducing unnecessary hospital admission and related costs.

Author Disclosure Statement

No competing financial interests exist.

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