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Complete List of Authors:	Conzelmann, Michael; BASF Corporate Health Management, Dept. of Human Toxicology; Rudolf Boehm Institute of Pharmacology and Toxicology, Postgraduate Study "Toxicology and Environmental Toxicology" Hoidis, Anne; University Hospital Heidelberg, Dept. of Gastroenterology Bruckner, Thomas; Heidelberg University Hospital, Institute for Medical Biometry and Informatics Popp, Erik; University Hospital Heidelberg, Dept. of Anaesthesiology Koschny, Ronald; University Hospital Heidelberg, Gastroenterology

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Glasgow Coma Scale predicts aspiration risk in acute alcohol intoxication

Michael Conzelmann [1,2], Anne Hoidis [3], Thomas Bruckner [4], Erik Popp [5], Ronald Koschny [3]

[1] Dept. of Human Toxicology, BASF Corporate Health Management, Carl-Bosch-Str. 38, D-67056 Ludwigshafen, Germany

[2] Postgraduate Study "Toxicology and Environmental Toxicology", Rudolf Boehm Institute of Pharmacology and Toxicology, University of Leipzig, Haertelstrasse 16-18, 04107 Leipzig, Germany.

[3] Dept. of Gastroenterology, University Hospital Heidelberg, INF 410, D-69120 Heidelberg, Germany

[4] Institute for Medical Biometry and Informatics, Heidelberg University Hospital, INF 130.3, D-69120 Heidelberg, Germany

[5] Dept. of Anaesthesiology, University Hospital Heidelberg, INF 420, D-69120 Heidelberg, Germany

✉ Corresponding author — Prof. Dr. med. Ronald Koschny

⊗ Present address — Dept. of Internal Medicine
Im Neuenheimer Feld 410
D-69120 Heidelberg, Germany
Email: ronald.koschny@med.uni-heidelberg.de
Tel.: +49 6221 5637969, Fax: +49 6221 565255

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Key words: alcohol intoxication, airway management, aspiration, intubation, Glasgow Coma Scale, protective airway reflex

Abstract

Objectives In patients with acute alcohol intoxication the decision for or against airway protection by endotracheal intubation can be challenging. It is often based on the Glasgow Coma Scale (GCS), although the GCS has not been validated for non-traumatic intoxicated patients. Data on risk factors for aspiration in alcohol monointoxication are scarce. This study aimed to analyze the aspiration risk in relation to the GCS and clinical parameters in patients with severe acute alcohol monointoxication.

Setting In this monocentric, retrospective study, we analyzed alcoholized patients admitted to a german intensive care unit between 2006 and 2020.

Participants n=458 admissions with acute alcohol intoxication were identified. A total of n=411 admissions between the age of 15 and 75 years were eligible for our analysis. n=47 admissions were excluded due to missing data or severe interfering medical conditions.

Primary and secondary outcome measures The following data were extracted from the medical records: age, gender, admission time, blood alcohol level, blood glucose level, initial outpatient (prehospital) Glasgow Coma Scale (1^{st} GCS), GCS at admission to the hospital (2^{nd} GCS), initial vital signs (systolic blood pressure, heart rate, breathing rate, peripheral capillary oxygen saturation (SpO_2)), clinical and prehospital signs of aspiration and airway management measures.

Results The mean age at admission was 35 years and 72% of the patients were male. The mean blood alcohol level was 2.7 g/l ±1.0 with a maximum of 5.9 g/l. The blood alcohol level did not correlate with the GCS but with the age of the patient. In univariate analysis, the aspiration risk correlated with blood alcohol level, age, GCS, oxygen saturation, respiratory rate, and blood glucose level and was significantly higher in male patients, upon vomiting, and in patients requiring airway measures, especially secretion suction (54% aspiration rate) and intubation (55% aspiration rate). Aspiration rate was 45.4% in patients without vs. 5.8% in patients with preserved protective reflexes. In multivariate analysis, only age and GCS were significantly associated with the risk of aspiration. However, the positive predictive value of GCS=3 for aspiration was only 16%.

Conclusion Although the aspiration rate in alcohol monointoxicated patients correlates with GCS and protective reflexes, the decision for endotracheal intubation should be based on the presence of different risk factors for aspiration.

Strengths and limitations of this study

- Analysis of the so far largest cohort of alcohol monointoxicated patients for risk factors of aspiration.
- GCS does not correlate with the blood alcohol level. The aspiration risk correlates with GCS and age in a multivariate analysis.
- Identification of further risk factors which indicate aspiration and could guide clinical diagnostic and therapeutic work up.
- Due to the retrospective nature of the study, we cannot provide direct clinical recommendations.
- Since we focused on severely alcohol-intoxicated patients admitted to an intensive care unit, data might not be extrapolated to a general emergency department.

Introduction

Patients with acute ethanol intoxication frequently require medical treatment, observation and diagnostics by paramedics, emergency physicians, emergency departments as well as intensive care units (ICU) [1]. Up to 12% of the attendances at the emergency department of an inner-city hospital in the United Kingdom were alcohol-related, mostly due to acute intoxication [2]. In Ontario, Canada, 5.1% of visits to the emergency department were attributable to alcohol use [3]. Besides respiratory depression, an elevated risk of aspiration due to impaired consciousness after alcohol consumption can cause life-threatening complications [4, 5]. In trauma patients with impaired consciousness, a GCS of 8 or less is widely accepted as indication for an airway protection by endotracheal intubation [6]. Although alcohol intoxicated patients often present with impaired consciousness and a GCS of less than 8 the reported intubation rate is low (0-2.3%) [7-9], maybe because the clinical benefit of intubating intoxicated patients with a GCS≤8 in order to prevent aspiration is still controversially discussed [8-12]. Differences of aspiration and intubation rates between mixed intoxications and alcohol monointoxications suggest, that these clinical conditions might not be comparable regarding the necessity of airway protection. In contrast to mixed intoxication, data regarding airway hazard in acute alcohol monointoxication are very scarce. The aim of this study was to analyze the aspiration risk in adolescent and adult atraumatic patients who required admission to our intensive care unit due to severe acute alcohol monointoxication. We hypothesized that aspiration is a rather rare event in this group of patients. We analyzed the blood alcohol level and the consciousness status according to the GCS in correlation with a clinically suspected or proven aspiration to identify risk factors for aspiration.

Material and Methods

Study Design and Population

For this retrospective study, all patients who had been admitted to the intensive and intermediate care unit of the Department of Gastroenterology at the University Hospital of Heidelberg between January 2006 and December 2020 were screened for acute mono-intoxication with alcohol (ethanol). The study was approved by the local ethics board of Heidelberg University (S-329/2013). Mixed intoxication was assumed when reported by the patient or relatives or in case of indicative prehospital scenarios (empty blisters, visible injection signs) or positive toxicology screening upon admission to the hospital (see "Measurements"). These patients were excluded from the study. Ethanol intoxication was defined as impaired consciousness due to a blood alcohol level ≥0.8 g/l, which is the legal definition for alcohol intoxication in many states [13]. Patients with missing data regarding blood alcohol level or GCS were excluded, as well as patients with severe comorbidities or medical conditions interfering with consciousness, airway situation, aspiration risk or breathing rate. Details of excluded patients are given in Figure 1. Deep therapeutic sedation was defined as sedation by the emergency physician resulting in an iatrogenic GCS≤8. Severe hypothermia was defined by a core temperature ≤34°C. Hypoglycemia was defined as any blood glucose level <65mg/dl as the lower level of normal regarding our standard point-of-care-testing (POCT) devices. Concomitant use of common medication at therapeutic doses was permitted. The following data were extracted from the medical records: age, gender, admission time, blood alcohol level, blood glucose level, initial outpatient (prehospital) Glasgow Coma Scale (1st GCS), GCS at admission to the hospital (2nd GCS), initial vital signs (systolic blood pressure, heart rate, breathing rate, peripheral capillary oxygen saturation (SpO_2)), clinical and prehospital signs of aspiration and airway management measures. When patients were prehospitally intubated, only the first GCS before intubation was recorded, since the second GCS was narcosis-induced (usually GCS=3). Aspiration was rated positive if proven by bronchoscopy or if clinical suspicion was supported by at least one of the following factors: coughing up aspirate, coarse crackles on auscultation, new opacities on chest x-ray, development of fever or laboratory signs of inflammation (CRP, leukocytosis) without other overt reasons. Patients without clinical signs of aspiration or normal bronchoscopy were rated negative.

Measurements

Except for prehospital measurements of blood glucose levels by point-of-care-testing (POCT) according to the emergency medical service (EMS), blood samples were obtained immediately after the patient´s admission to our hospital for venous blood gas analysis (RAPIDLab 1200, Siemens Healthcare Diagnostics, Eschborn, Germany), measurement of blood alcohol level and standard laboratory tests including glucose. When indicated by the patient´s history or clinical data, a qualitative urine toxicology screen (Triage 8 Drugs of Abuse Panel, Alere Diagnostics, Cologne, Germany) was performed to exclude mixed intoxications. This test detects the following components: amphetamine, barbiturates, benzodiazepines, cocaine, methadone, opiates, tetrahydrocannabinol (THC), and tricyclic antidepressants. Due to the low specificity, sensitivity and clinical benefit, urine toxicology test was not performed on a regular basis [14].

Statistical Analysis

Data entry was performed with help of Microsoft Excel (Version 14.0), for the statistical analysis SAS Version 9.4 WIN (SAS Institute GmbH, Heidelberg, Germany) was used. The empirical distribution of continuous data was described with mean, standard deviation and range, in case of categorical data with absolute and relative frequencies. Spearman‘s correlation coefficient was calculated to describe associations between blood alcohol level and laboratory values. Possible differences between patients with and without aspiration were tested with t-test for continuous data and chi-square-tests for categorical data. Binary multivariable logistic regression analysis was used to find possible risk factors for aspiration. Statistical graphics were used to visualize the findings.

Patient and Public Involvement

No patient involved.

Results

A total of n=411 admissions to our intermediate and intensive care unit for acute alcohol monointoxication comprising n=327 different patients were eligible for our analysis. Patient´s age ranged between 15 and 74 years. The baseline characteristics of the enrolled patients and their vital parameters are listed in Table 1.

Table 1 Baseline characteristics of the study population at admission

Total number of admissions	411
Number of different patients	327
Patients with more than 1 admission	33
Patients with 2 admissions	21
Patients with 3 admissions	7
Patients with 4 admissions	4
Patients with 5 admissions	1
Gender, males/females (%)	294/117 (72%/28%)
Age, mean ±SD], (range) [y]	35 ±15 (15-74)
Blood alcohol level, mean ±SD, (range) [g/l]	2.7 ±1.0 (0.9-5.9)
Peripheral oxygen saturation (SpO_2), mean ±SD, (range) [%]	96 ±6 (47-100)
Heart rate, mean ±SD (range) [bpm]	92 ±20 (35-180)
Systolic blood pressure, mean ±SD (range) [mmHg]	121 ±22 (70-200)
Respiratory rate, mean ±SD] (range) [1/min]	15 ±5 (0-35)

Figure 2A shows the age distribution for male and female admissions. Most patients (72%) were male. The mean age at admission was 35 years without a significant difference between male and female patients (p=0.122) with a mean age of 36 years (±14 years, range 15-74) for male and 33 years (±15 years, range 15-74) for female patients.

The mean blood alcohol level of all patients admitted to our intensive care unit was 2.7 g/l ±1.01 with a maximum of 5.89 g/l. The distribution of the blood alcohol level is depicted in Figure 2B. The mean alcohol level did not significantly differ between male (2.7±0.95 g/l) and female (2.5±1.14 g/l) patients (p=0.132). The maximum blood alcohol level was 5.89 g/l and 5.85 g/l in male and female patients, respectively. In Figure 2C, the blood alcohol levels are shown according to age and gender. The blood alcohol level strongly correlated with patient´s age (r=0.43, p<0.0001) in the total population, as well as in male (r=0.46, p<0.0001) and female patients (r=0.33, p=0.003).

In order to analyze the fluctuating consciousness in acute alcohol intoxication, we compared the first GCS of the patient upon arrival of the emergency team with the second GCS at admission of the patient to the hospital approximately 30-60 minutes later. Prehospitally intubated patients (iatrogenic GCS=3 at hospital admission) were excluded from this analysis, resulting in a population of n=329 eligible patients with available data regarding first and second GCS. The median GCS improved from 10 to 13 between prehospital presentation and admission to the ICU. Figure 3 visualizes the strong correlation between the first and second GCS (r=0.77, p<0.0001). Dots on the diagonal line correspond to patients with identical first and second GCS. We considered a change of ±3 GCS points (ΔGCS) as clinically relevant. Most patients (n=258, 78.5%) did not show a relevant change of GCS (-2 ≤ ΔGCS ≤ +2). While n=61 (18.5%) demonstrated an improvement of their consciousness level during their transport to the hospital (ΔGCS ≥ +3), only n=10 (3.0%) patients showed a relevant deterioration (ΔGCS ≤ -3).

To rule out any bias due to mixed GCS records (i.e. pooled first and second GCS), all following analyses regarding GCS were performed with the first GCS only. The median first GCS did not differ between male and female patients (10 vs. 10, p=0.864). Blood alcohol levels did neither correlate with the initial GCS in the general population (r=-0.05, p=0.279), nor for male (r=-0.05, p=0.331) or female (r=-0.04, p=0.673) patients. Nevertheless, very high blood alcohol levels (>5 g/l) were measured only in patients with a first GCS ≤11 (Figure 4). The highest blood alcohol levels of 5.89 and 5.85 g/l were found in 2 patients with a GCS of 3 and 8, respectively.

Within the total population of n=411 patients, aspiration was found in n=21 (5.1%). Aspiration was diagnosed by a positive bronchoscopy in n=5 (24%) of these patients. In the remaining n=16 patients, diagnosis of aspiration was based on the presence of at least one of the following criteria: coarse crackles on auscultation (n=9), new opacities on chest x-ray (n=6), development of fever or laboratory signs of inflammation (CRP elevation, leukocytosis) without overt alternative reasons (n=6). In order to identify risk factors for aspiration in alcohol intoxicated patients, we compared the cohorts with and without aspiration regarding demographic characteristics, vital signs, blood alcohol level, blood glucose level and airway management. In univariate analysis of continuous risk factors for aspiration, patients with aspiration were significantly older (mean age 47.4 vs. 34.6 years), had a higher blood alcohol level (mean 3.4 versus 2.6 g/l), a lower first GCS (median 3 vs. 11), a lower peripheral oxygen saturation (SpO_2, mean 90 vs 96%), and a lower respiration rate (mean 13/min vs. 15/min) (Table 2).

Table 2 Univariate analysis of continuous risk factors for aspiration

Parameter	**Patients w/o aspiration** Mean ±SD (range)	**Evaluable patients**	**Patients with aspiration** Mean ±SD (range)	Evaluable patients	**p-value**
Age [y]	34.6 ±14.5 (15-74)	390	47.4 ±9.3 (32-65)	21	<0.0001
Blood alcohol level [g/l]	2.6 ±1.0 (0.9-5.9)	390	3.4 ±1.3 (1.7-5.5)	21	0.017
Initial GCS	11 (median) ±4 (3-15)	378	3 (median) ±2 (3-9)	20	<0.0001
SpO_2 [%]	96 ±6 (47-100)	365	90 ±8 (73-100)	21	0.006
Systolic blood pressure [mmHg]	121 ±22 (70-200)	371	122 ±20 (96-160)	21	0.772
Heart rate [bpm]	92 ±20 (35-180)	377	89 ±20 (50-120)	21	0.580
Respiratory rate [1/min]	15 ±5 (0-35)	302	13 ±3 (8-18)	19	0.014
Blood glucose level [mg/dl]	109 ±40 (65-487)	388	139 ±60 (72-335)	21	0.028

Furthermore, univariate results of binary risk factors revealed a significantly higher risk for aspiration for male patients, patients with documented vomiting as well as for the necessity of secretion suction, oxygen supply, Guedel tube application and mask ventilation, although the last two measures were rarely applied (n=10) (Table 3).

Table 3 Univariate analysis of binary risk factors for aspiration

Parameter	Manifestation	Patients w/o aspiration [%]	Patients with aspiration [%]	Evaluable patients	p-value
Gender	Male	93.5	6.5	294	0.048
	Female	98.3	1.7	117	
Vomiting	No	96.4	3.7	329	0.017
	Yes	89.9	10.1	79	
Oxygen supply	No	99.2	0.8	265	<0.0001
	Yes	86.9	13.1	145	
Guedel tube application	No	95.5	4.5	400	0.0003
	Yes	70.0	30.0	10	
Mask ventilation	No	95.8	4.2	400	<0.0001
	Yes	60.0	40.0	10	
Protective airway reflexes (at GCS ≤8)	No	54.6	45.4	22	0.0001
	Yes	94.2	5.8	52	
Secretion suction	No	96.5	3.5	396	<0.0001
	Yes	46.1	53.9	13	
Intubation	No	98.4	1.6	384	<0.0001
	Yes	44.4	55.6	27	

Intubated patients showed a significantly higher aspiration rate than patient´s without intubation (56% vs. 1.6%). Since many emergency physicians base their decision for protective intubation in patients with a GCS≤8 on the presence or absence of the swallowing and gag reflex, the presence of these protective reflexes was correlated with the risk of aspiration. A total of n=152 patients had a first GCS≤8. Data regarding protective reflexes were available in n=74 (48.7%) of these patients. Protective reflexes in patients with GCS≤8 were present in n=52 (70.3%), but absent in n=22 (29.7%). The absence of protective reflexes was significantly associated with a higher risk of aspiration: 45.4% aspiration rate in patients without vs. 5.8% in patients with protective reflexes (p=0.0001, Table 3).

Some of these factors are interdependent: low oxygen saturation (<92%) will imply oxygen supply, vomiting will imply secretion suction, oxygen saturation inversely correlates with age. On multivariate analysis of the risk factors gender, age, blood alcohol level, first GCS, and oxygen saturation, only age (OR 1.06) and GCS (OR 0.71) significantly correlated with the risk of aspiration (Table 4).

Table 4 Odds ratio estimates in multivariate analysis of risk factors for aspiration.

Risk factor	OR	95% confidence limits		p-value
Gender (male versus female)	3.29	0.67	16.03	0.141
Age	1.06	1.02	1.10	0.005
Blood alcohol level	1.26	0.80	2.00	0.320
First GCS	0.71	0.60	0.84	<0.0001
Oxygen saturation	0.98	0.93	1.03	0.397

Due to the low number of complete data sets, presence of protective reflexes could not be included in the multivariate analysis. The difference of age and GCS between aspirated and non-aspirated patients is visualized in Figure 5A & B. The respective box plot analysis is shown in Figure 5C & D. However, GCS=3 had a low sensitivity (60%) and a moderate specificity (83%) for aspiration, with a positive predictive value (PPV) of only 16% and very high negative predictive value (NPV) of 98%.

Discussion

Acute alcohol intoxication constitutes a frequent medical problem with a considerable socio-economic and health care system burden. The demographic analysis of our cohort shows a predominance of young male patients (72%, mean age 35 years), which is comparable to other demographic studies [15, 16]. However, our ICU cohort showed a younger age distribution than another retrospectively analyzed cohort of patients admitted to an emergency department [1]. With a mean alcohol level of 2.7 g/l, our cohort showed higher blood alcohol levels than many other studies [17-20], which might be due to the selection of ICU patients. In contrast to Vereslt et al. [1], a higher age was associated with a higher blood alcohol level in our cohort. Figures 2A & C impressively illustrate the clinical relevance of acute alcohol intoxication as an important differential diagnosis in unconscious elderly patients.

Since the prehospital care of alcoholized patients comprises a rather short period, one would expect – if at all – a deterioration of the GCS between the first patient contact and the admission to the hospital due to an ongoing alcohol resorption in the alimentary tract. However, 19% of our patients showed an improvement of more than 2 GCS points during their prehospital care, but only 3% of patients showed a relevant deterioration. Overall, we found a strong correlation between the first and second GCS. The GCS of head injured trauma patients with additional alcohol intoxication (blood alcohol level >0.8g/l) also improved between prehospital care and the emergency department [21]. This implies that the measurement time point of GCS during the prehospital care should be exactly defined and pooling GCS data from different phases of care should be avoided. Slight changes in GCS might not necessarily reflect a clinically relevant change of consciousness level of alcoholized patients. We, therefore, considered only an arbitrarily defined ΔGCS of ≥3 as clinically relevant.

Most data on the influence of alcohol on the GCS were derived from trauma patients. Some studies showed a correlation between blood alcohol level and GCS [22], while others did not [23-25]. Interestingly, data on a correlation between blood alcohol level and GCS in alcohol-intoxicated patients without concomitant trauma are very scarce and the clinical consequence of low GCS values is unclear. In a cohort of alcohol-intoxicated patients without trauma from the Oktoberfest in Munich the blood alcohol level was not predictive for the need of hospitalization [26]. Concordantly, in our study on non-traumatic alcoholized patients, the blood alcohol level did not correlate with the GCS, even at a considerably high mean blood alcohol level of 2.7 g/l. Nevertheless, n=8 patients of our cohort with an extremely high blood alcohol level of ≥5 g/l demonstrated a reduced median GCS of 5. This cohort, however, was too small for a subgroup analysis. In contrast, in adolescent patients (13-17 years of age) with rather mild alcohol intoxication (mean 1.6g/l) Mick et al. found a significant correlation between the blood alcohol level and the GCS (mean GCS 12.2) [17]. One might speculate that adolescents and younger adults have not yet undergone habituation to regular alcohol consumption. However, even in the youngest subgroup (15-25 years) of our study, there was no significant correlation between blood alcohol level and GCS (n=136 patients, mean blood alcohol level 2.1 g/l, median GCS 10, p=0.061).

One of the most challenging clinical problems in unconscious alcohol-intoxicated patients is the decision for or against airway protection by intubation. Many studies were performed in heterogeneous cohorts of mixed intoxication [7, 9, 27-29], in trauma patients [8, 30] or without any data on the risk of aspiration [8, 27]. While some authors and recommendations refer to a GCS≤8 as an indication for intubation in alcohol intoxicated patients, the association of a low GCS with a higher risk of aspiration has not been sufficiently substantiated in these patients. In their prospective observational study, Duncan et al. did not find a higher rate of aspiration in patients with a GCS≤8 [7]. However, only n=22 of 73 patients had alcohol monointoxication and only n=12 patients of the entire cohort demonstrated a GCS≤8. Comparing n=12 intubated (mean GCS 5.9) with n=14 not-intubated (mean GCS 5.5) patients with mixed intoxication, Donald et al. did not detect a difference in laboratory or physiological parameters. However, the aspiration rate was not analyzed [9]. None of the intubated patients had an alcohol intoxication. In patients with a mixed intoxication, the risk of aspiration pneumonia did not significantly differ (p=0.48) between patients with GCS≤8 versus GCS>8 [11]. In another prospective study on n=224 drug-intoxicated patients, there was no correlation between the GCS and the risk of aspiration [29]. A GCS≤8 was not considered as essential for an increased risk of aspiration. However, the aspiration rate in that drug-intoxicated cohort was very high (29%) compared to our study (5%). This indicates that mixed intoxication and alcohol monointoxication might not be comparable regarding the risk of aspiration.

In our study on non-traumatic alcohol-monointoxicated patients, we found a strong correlation between the GCS and the risk of aspiration, even in a multivariate regression model. However, n=133 of the 152 patients (87.5%) with GCS≤8 did not aspirate. Thus, even for a GCS=3 the PPV is too low (16%) to guide the decision for intubation. However, Sauter et al. described that a GCS≤8 was the main reason for emergency teams to decide for intubation in intoxicated patients [8]. In our cohort, emergency physicians – according to their emergency protocols – made a more differentiated decision for intubation based on GCS, presence of the gag reflex, vomiting and the suspicion of aspiration.

An alternative parameter to estimate the risk for aspiration is the presence of the gag or cough reflex. However, in a very small cohort of patients with pharmacologically induced coma the cough reflex did not correlate with the GCS, as n=4 of 12 patients (33%) with GCS=3 had an unimpaired cough reflex. On the other hand, 3 of 5 patients (60%) with GCS=8 had an impaired cough reflex [27]. These data are supported by the detection of a depressed gag reflex in drug-intoxicated patients even at a GCS≥8 [28]. Of note, none of these studies has been performed in alcohol monointoxicated patients. In our study, we could obtain information on the gag or cough reflex (often referred to as „protective airway reflexes“ by the emergency physician) in n=74 patients. The absence of protective airway reflexes did significantly correlate with an increased risk of aspiration in a univariate analysis (Table 3). Furthermore, all airway measures (oxygen supply, Guedel tube application, mask ventilation, secretion suction) significantly correlated with the rate of aspiration (Table 3). For instance, the necessity of secretion suction or intubation (on the discretion of the emergency physician) were each associated with an aspiration rate of >50%. Our data are in line with a smaller retrospective study on n=155 patients with mixed intoxication in which patients with reduced GCS or an impaired gag reflex had a higher risk for an aspiration pneumonitis [10]. An absent or reduced gag reflex was found in 96% of their patients with aspiration. However, the high aspiration rate of 15% in their cohort of mixed intoxication might be related to the application of gastric lavage and charcoal administration which is not applied in alcohol monointoxication. Our study impressively shows that the execution of some airway measures (e.g. oxygen supply) or encountered vomiting indicated only a low risk of aspiration, while other measures (e.g. mask ventilation, secretion suction, intubation) and the lack of protective airway reflexes indicate a high incidence for aspiration in these patients. This would imply a thorough diagnostic (e.g. X-ray, bronchoscopy) or therapeutic (e.g. antibiotic treatment) work up in these high-risk patients upon ICU admission. However, a GCS≤8 alone should not warp the emergency physician into endotracheal intubation.

Although herewith we present - to the best of our knowledge - the most comprehensive analysis of the aspiration risk in alcohol monointoxicated patients, our study has some limitations. Due the retrospective nature of our study, we cannot provide direct clinical recommendations. Since the protective airway reflexes were evaluated by the emergency team only in subset of patients, there might be a bias towards reporting rather impaired than normal reflexes. However, since both preserved and impaired protective reflexes were listed as the reason against and in favor of intubation, respectively, we could not detect unilateral under- or over-reporting. Since we focused on severely alcohol-intoxicated patients admitted to the intensive care unit of our hospital, our finding might not be extrapolated to the general population of alcohol monointoxication in an emergency department.

Conclusion

In our retrospective study, we found that the blood alcohol level did correlate with the patient´s age but not with the GCS. However, both age and GCS did correlate with the risk of aspiration (synopsis in Figure 6). Of clinical relevance, we identified risk factors for aspiration in alcohol monointoxicated patients which could guide the decision for airway protection measures: Guedel tube application, mask ventilation, loss of protective airway reflexes, secretion suction. However, a GCS=3 has a very low PPV for aspiration and should per se not trigger tracheal intubation. On the other hand, since only 6% of patients with preserved gag reflexes had aspirated, in this patient subgroup the risk of intubation might prevail its benefits. The high prevalence of aspiration in intubated patients suggests an aggressive diagnostic workup (e.g. X-ray or bronchoscopy) and a liberate use of prophylactic antibiotic treatment for aspiration pneumonitis upon admission to the intensive care unit within this cohort.

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Statements

a. Ethics approval: Not applicable

b. Clinical Trial Registration: Not applicable

c. Funding statement: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

d. Competing Interest: None declared.

e. Data sharing statement: No additional data available.

f. Contributorship Statement

Planning of the study: MC, AH, EP, RK

Data acquisition: MC, AH, EP, RK

Statistical analysis: TB

Manuscript writing and editing: MC, AH, EP, TB, RK

Submission: RK

Figure 1

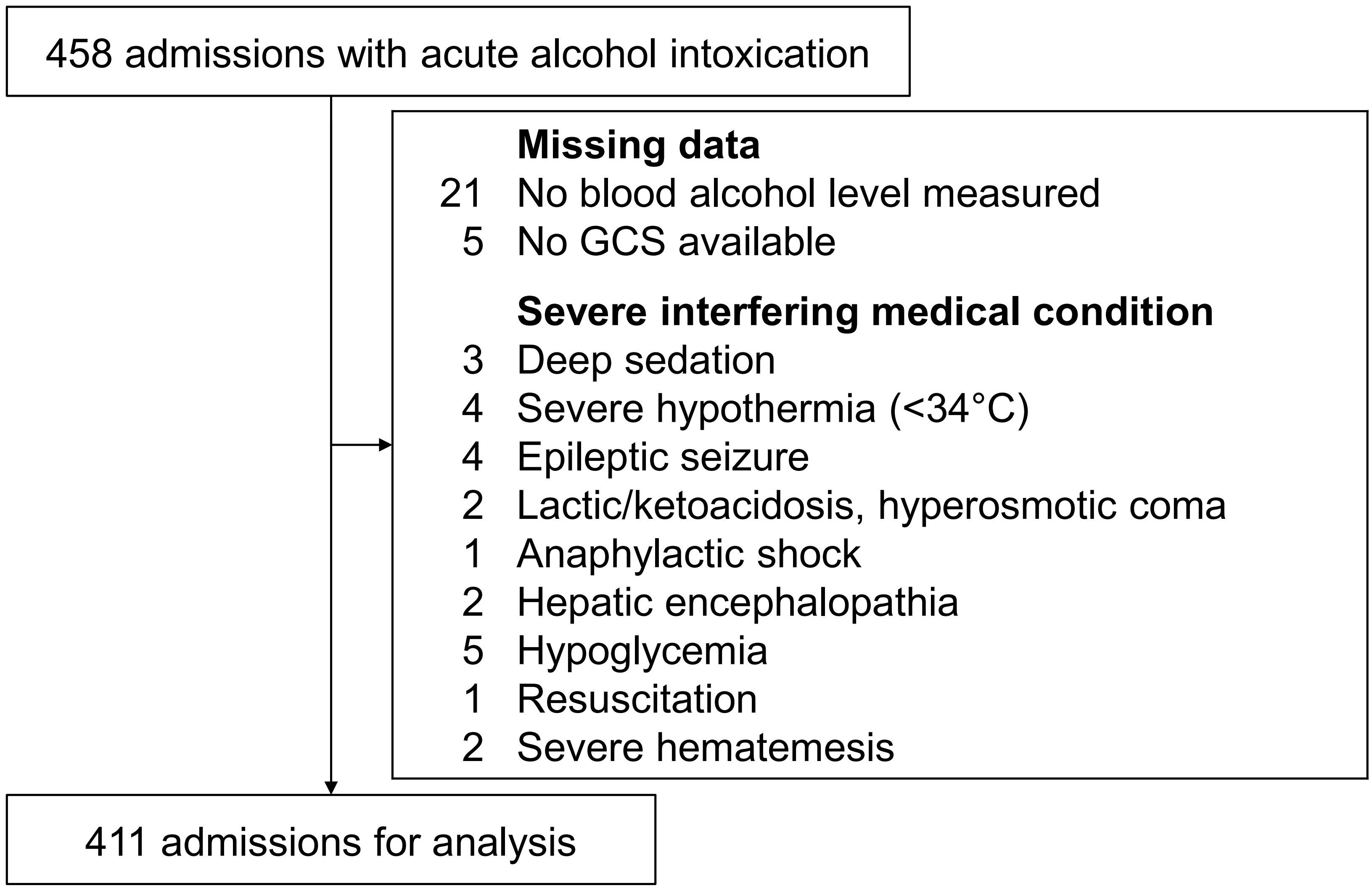

458 admissions with acute alcohol intoxication
Missing data
21 No blood alcohol level measured
5 No GCS available
Severe interfering medical condition
3 Deep sedation
4 Severe hypothermia (<34°C)
4 Epileptic seizure
2 Lactic/ketoacidosis, hyperosmotic coma
1 Anaphylactic shock
2 Hepatic encephalopathia
5 Hypoglycemia
1 Resuscitation
2 Severe hematemesis
411 admissions for analysis

Figure 2A

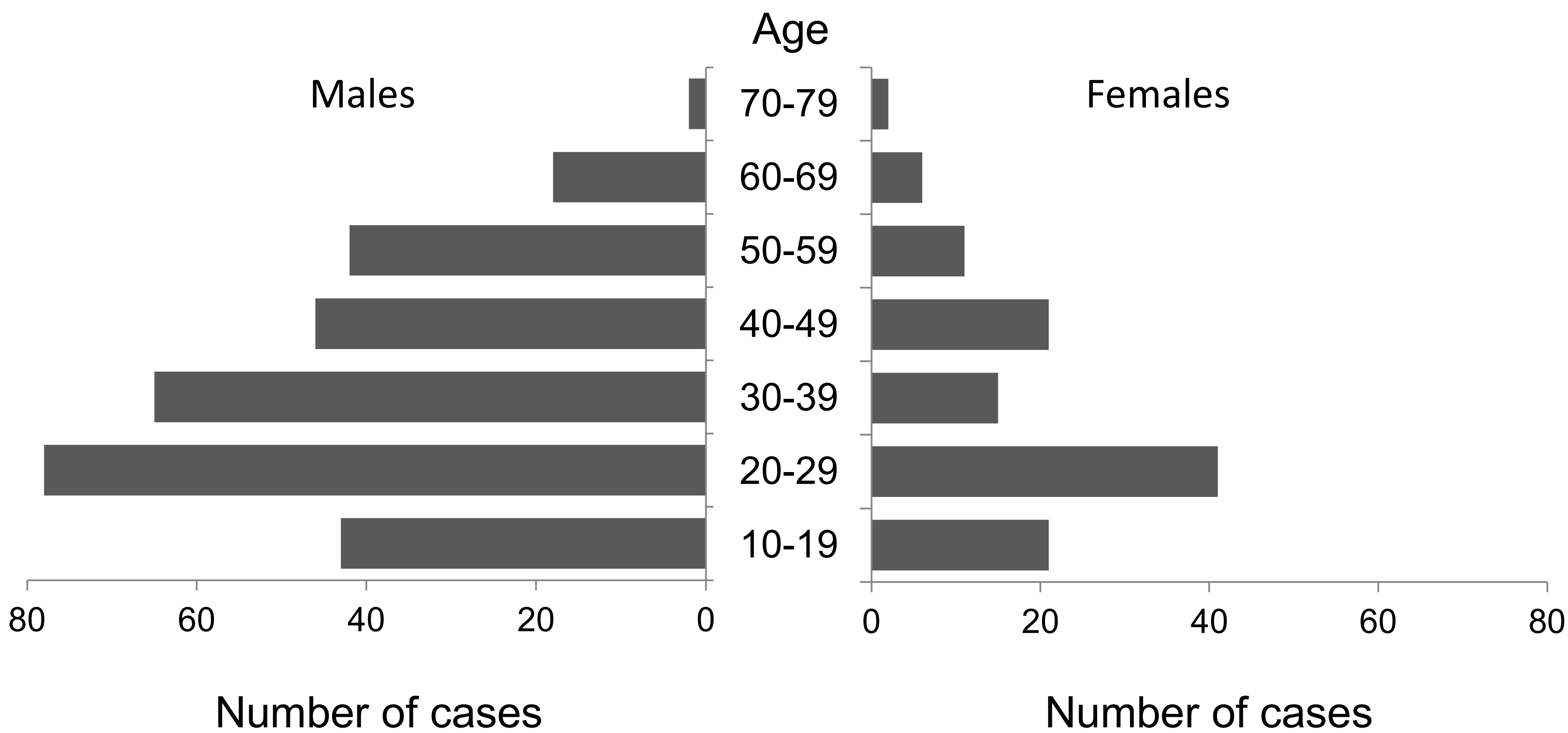

Age
Males
Females
70-79
60-69
50-59
40-49
30-39
20-29
10-19
80
60
40
20
0
0
20
40
60
80
Number of cases
Number of cases

Figure 2B

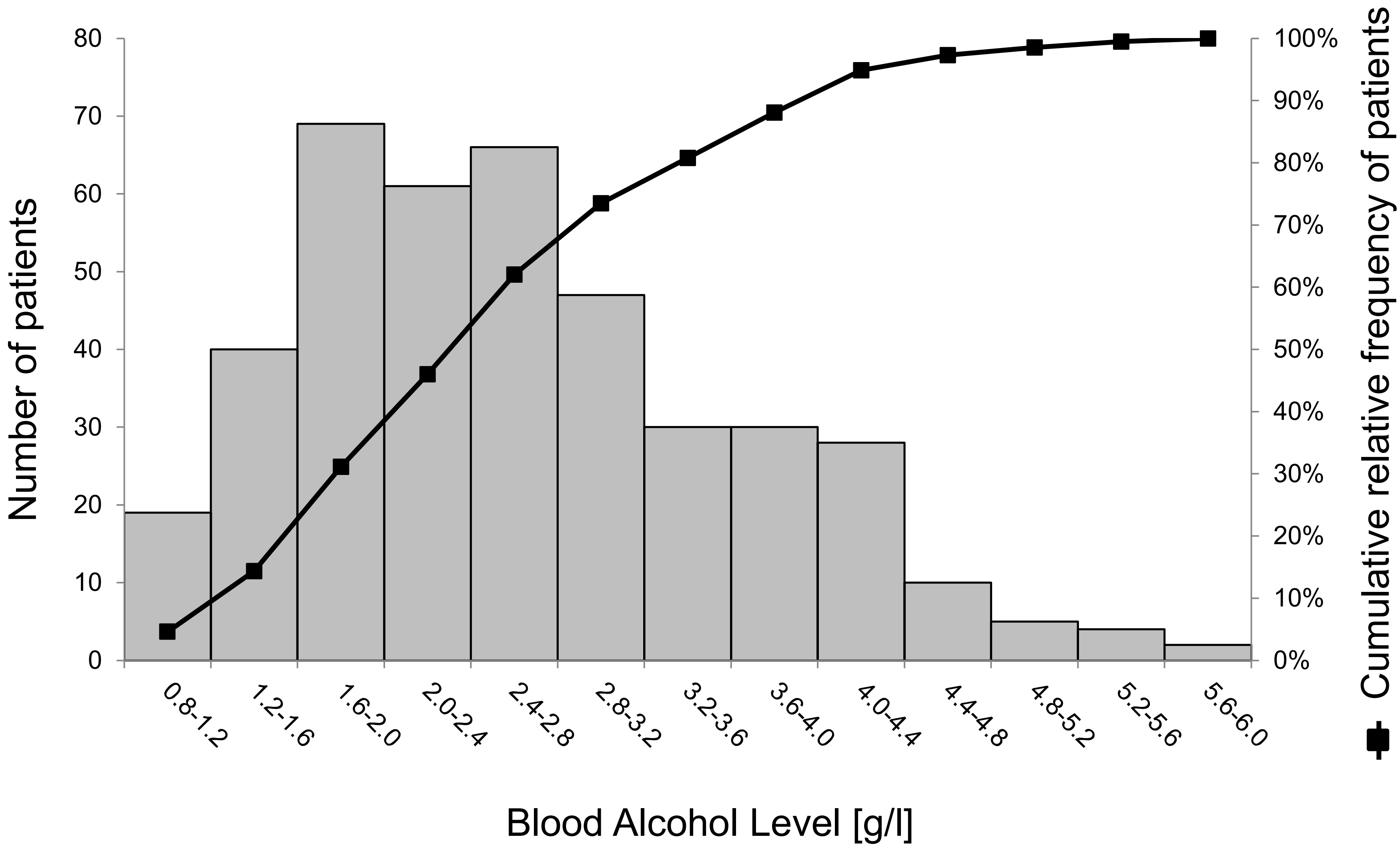

Number of patients
80
70
60
50
40
30
20
10
0
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Cumulative relative frequency of patients
0.8-1.2
1.2-1.6
1.6-2.0
2.0-2.4
2.4-2.8
2.8-3.2
3.2-3.6
3.6-4.0
4.0-4.4
4.4-4.8
4.8-5.2
5.2-5.6
5.6-6.0
Blood Alcohol Level [g/l]

Figure 2C

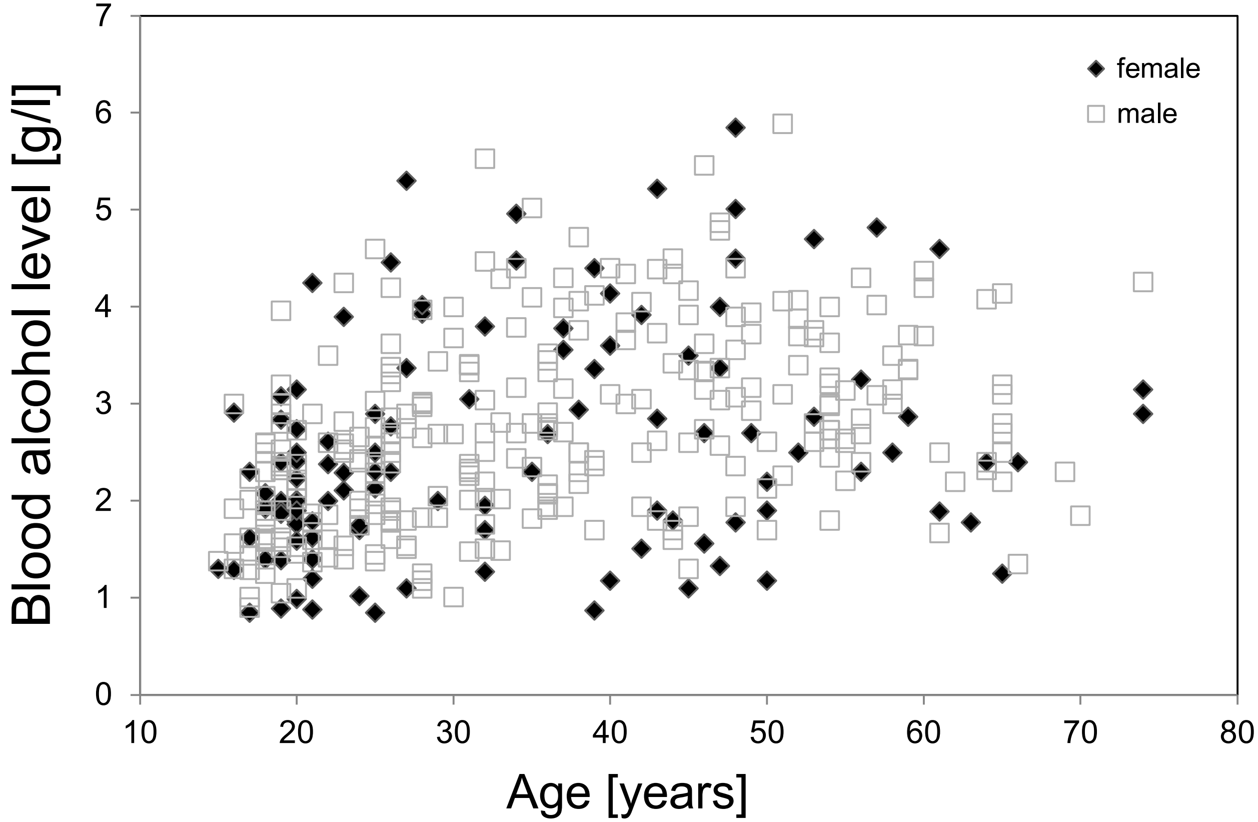

female
male
Blood alcohol level [g/l]
0
1
2
3
4
5
6
7
10
20
30
40
50
60
70
80
Age [years]

Figure 3

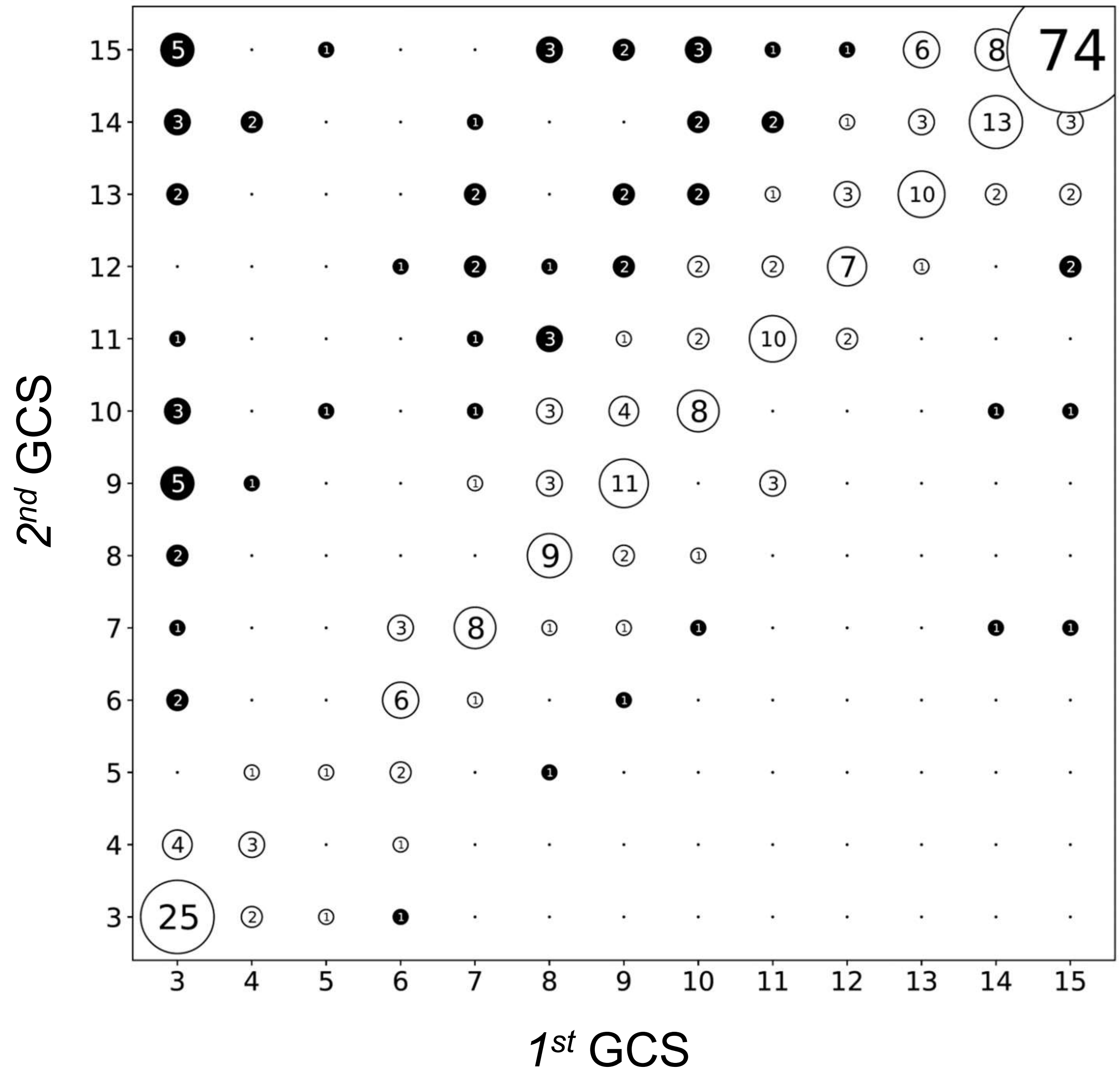
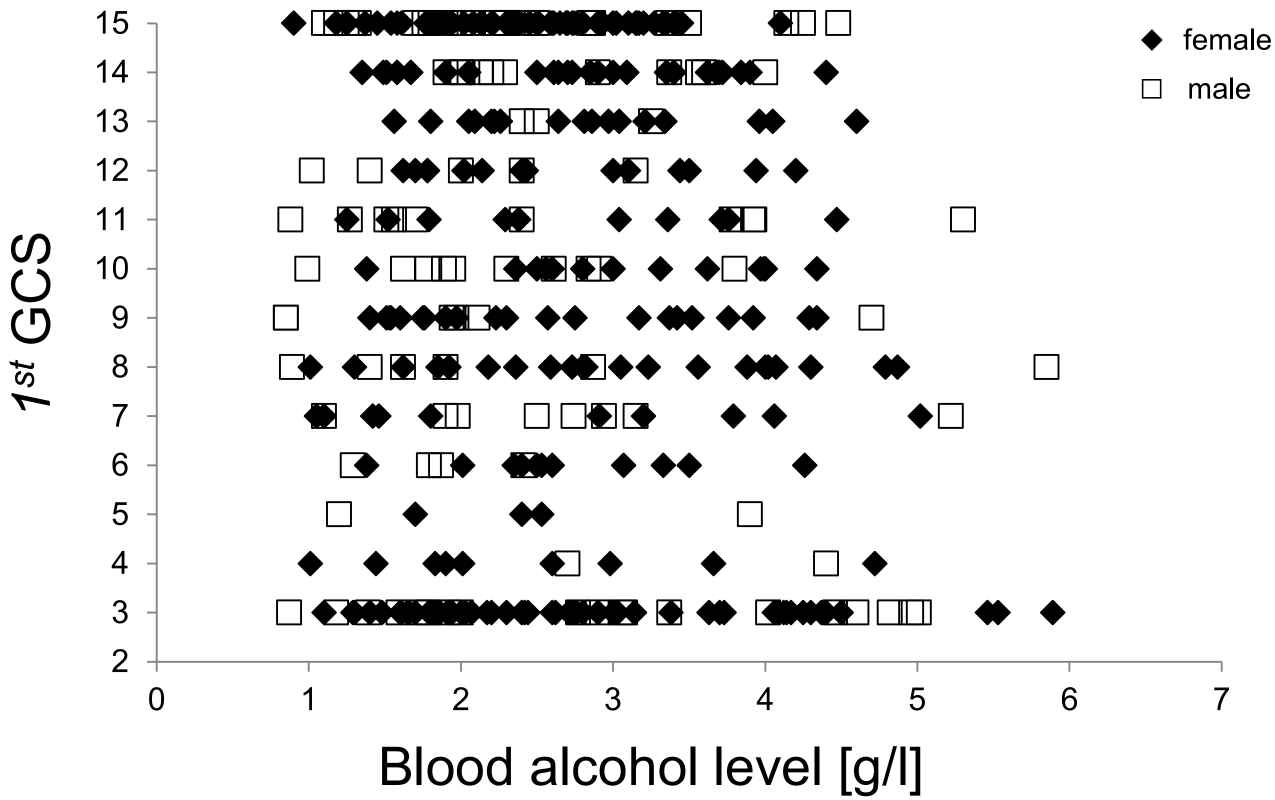


Figure 4



1st GCS
15
14
13
12
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
6
7
Blood alcohol level [g/l]
female
male

Figure 5A

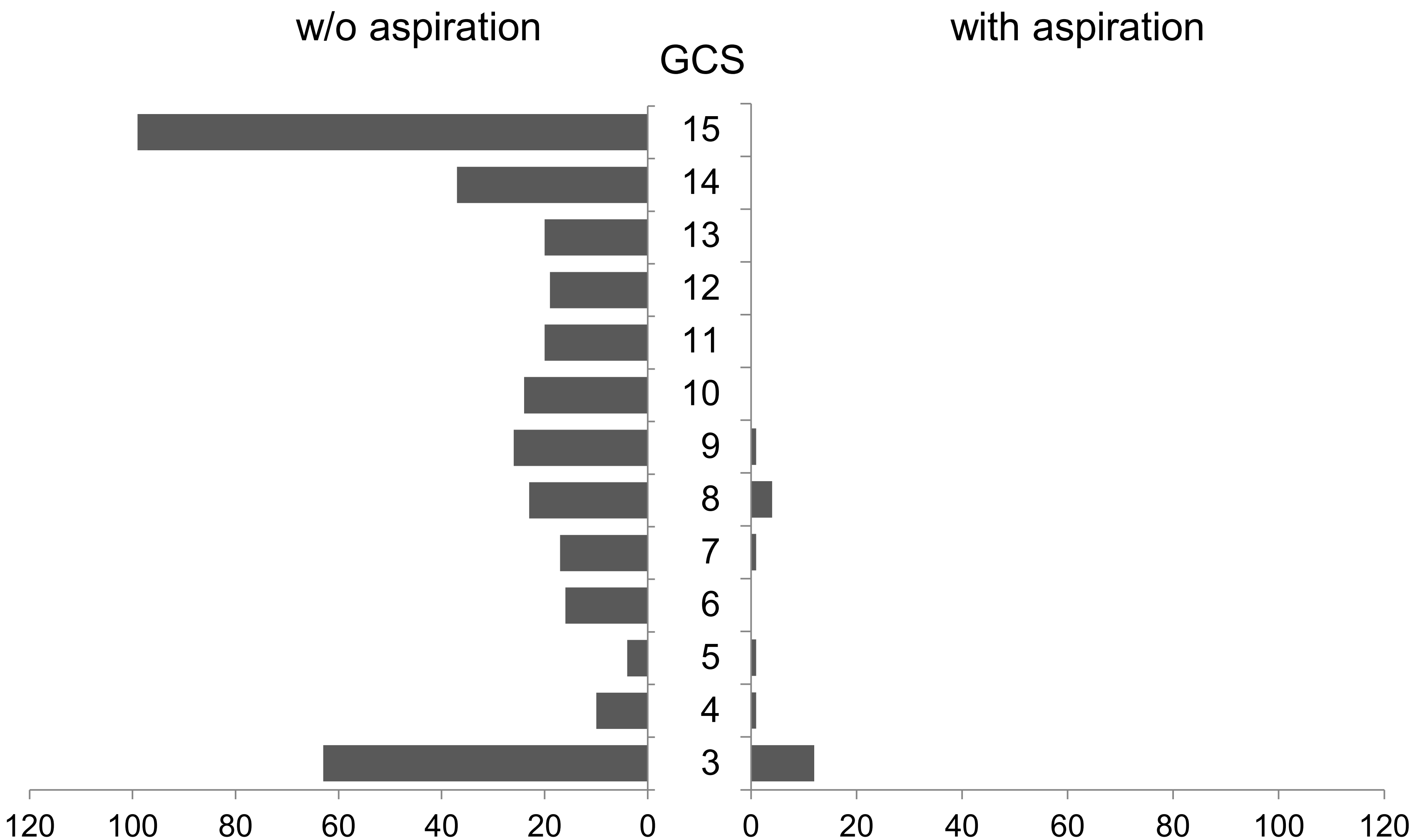

w/o aspiration
with aspiration
GCS
15
14
13
12
11
10
9
8
7
6
5
4
3
120 100 80 60 40 20 0
0 20 40 60 80 100 120

Figure 5B

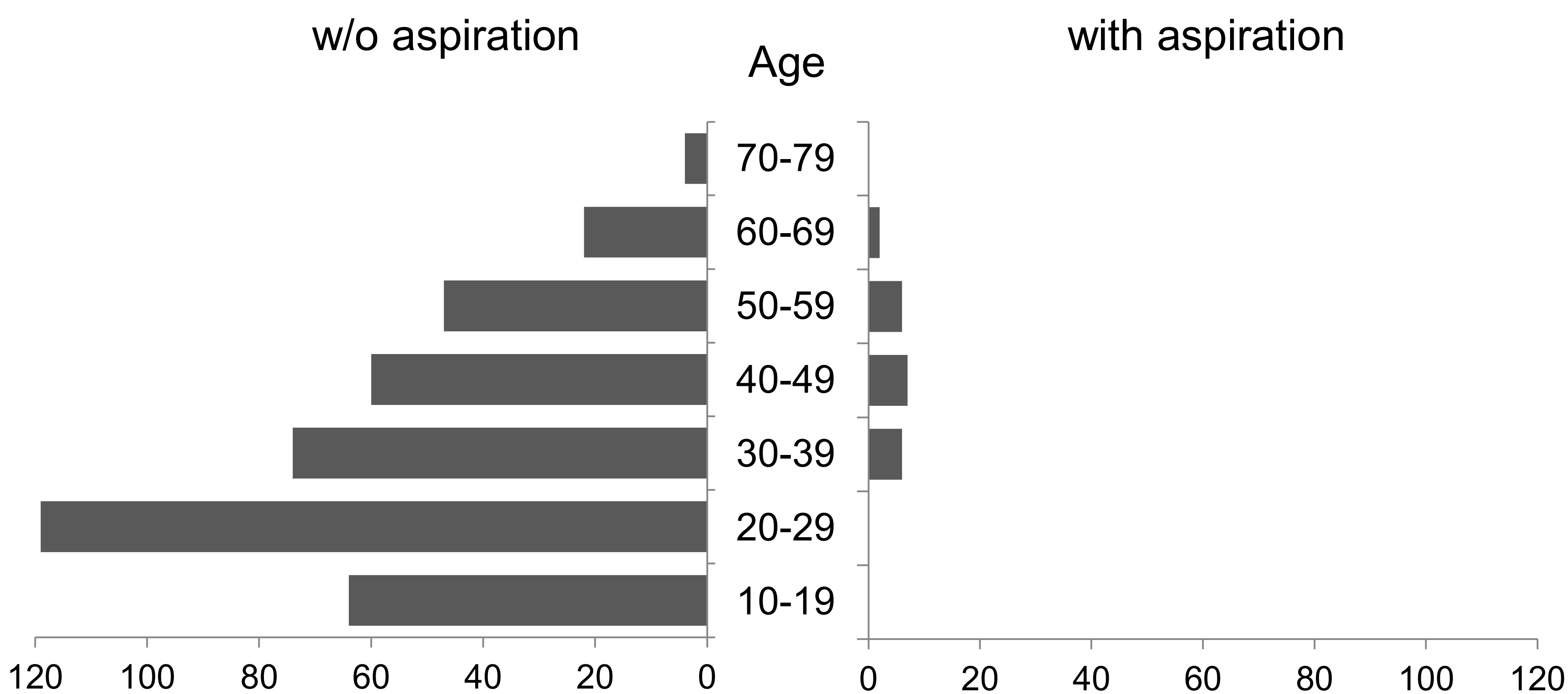

w/o aspiration
Age
with aspiration
70-79
60-69
50-59
40-49
30-39
20-29
10-19
120
100
80
60
40
20
0
0
20
40
60
80
100
120

Figure 5C

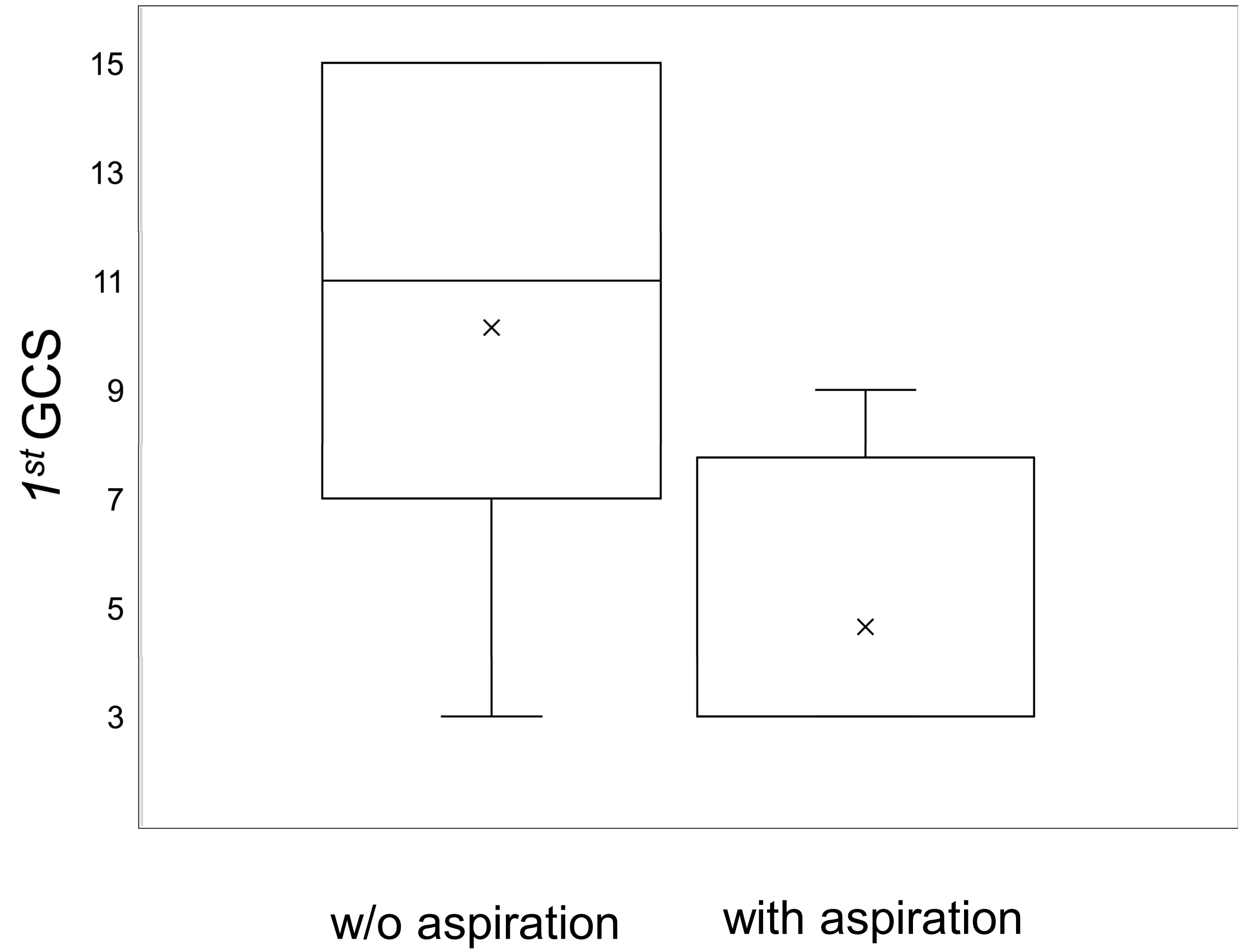


Figure 5D

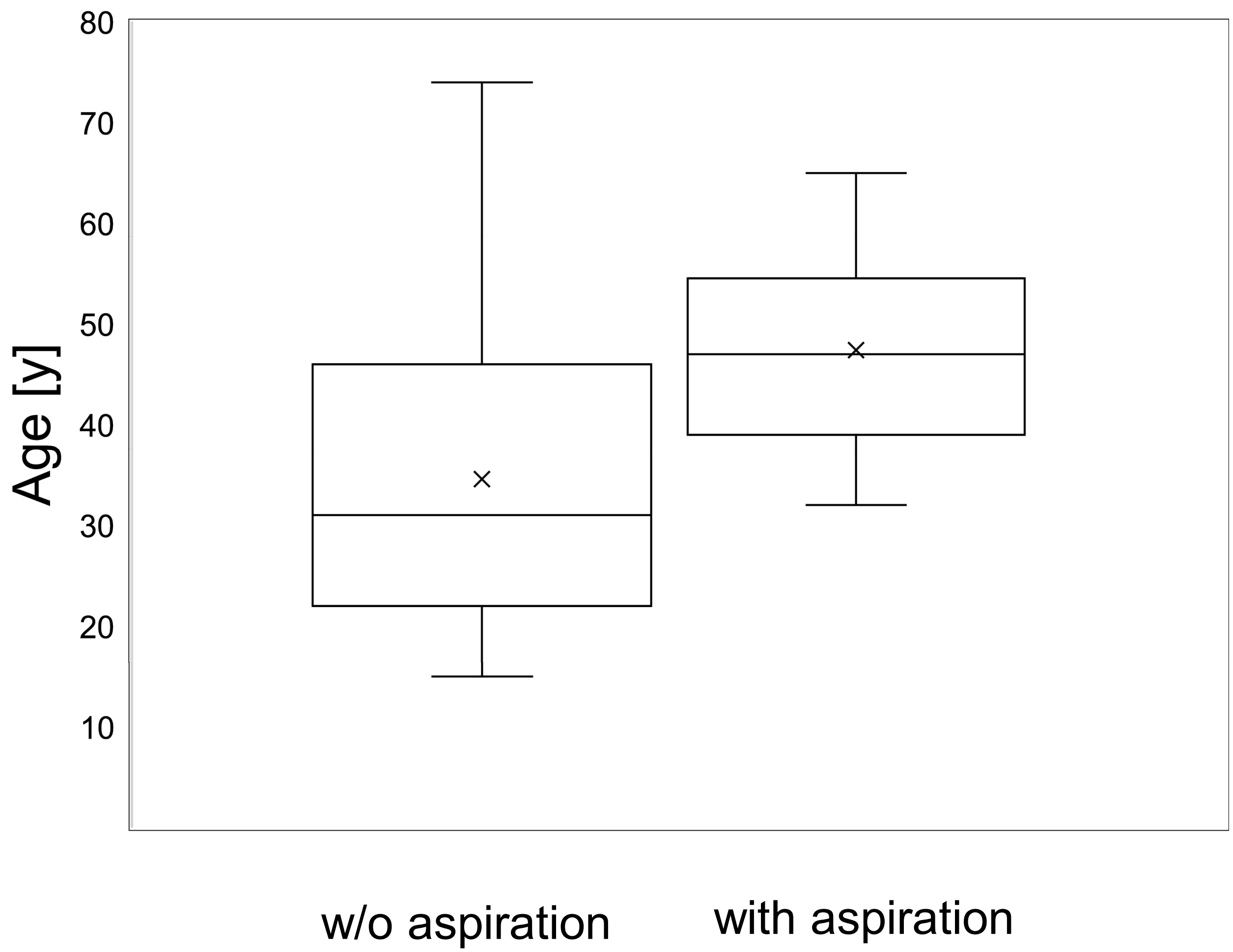
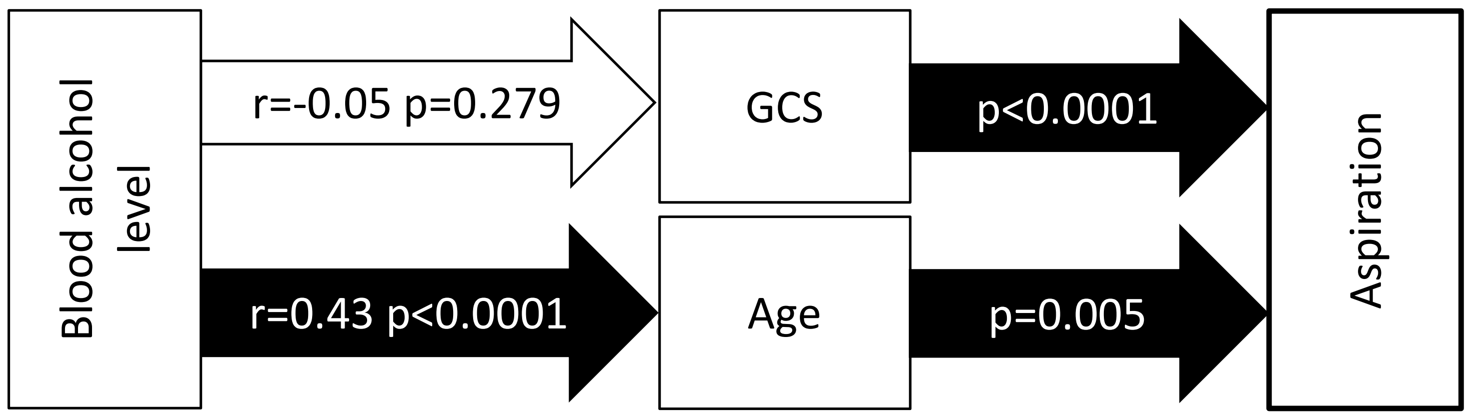


Figure 6


Blood alcohol level
r=-0.05 p=0.279
r=0.43 p<0.0001
GCS
Age
p<0.0001
p=0.005
Aspiration

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-10

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-10
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Aspiration risk in relation to Glasgow Coma Scale score and clinical parameters in patients with severe acute alcohol intoxication: a single-centre, retrospective study

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Aspiration risk in relation to Glasgow Coma Scale score and clinical parameters in patients with severe acute alcohol intoxication: a single-centre, retrospective study

Michael Conzelmann [1,2], Anne Hoidis [3], Thomas Bruckner [4], Erik Popp [5], Ronald Koschny [3]

[1] Dept. of Human Toxicology & Health Risk Assessment, BASF Corporate Health Management, Carl-Bosch-Str. 38, D-67056 Ludwigshafen am Rhein, Germany

[2] Postgraduate Study "Toxicology and Environmental Toxicology", Rudolf Boehm Institute of Pharmacology and Toxicology, University of Leipzig, Haertelstrasse 16-18, 04107 Leipzig, Germany.

[3] Dept. of Gastroenterology, University Hospital Heidelberg, INF 410, D-69120 Heidelberg, Germany

[4] Institute for Medical Biometry and Informatics, Heidelberg University Hospital, INF 130.3, D-69120 Heidelberg, Germany

[5] Dept. of Anaesthesiology, University Hospital Heidelberg, INF 420, D-69120 Heidelberg, Germany

✉ Corresponding author — Prof. Dr. med. Ronald Koschny

⊗ Present address — Dept. of Internal Medicine
Im Neuenheimer Feld 410
D-69120 Heidelberg, Germany
Email: ronald.koschny@med.uni-heidelberg.de
Tel.: +49 6221 5637969, Fax: +49 6221 565255

Abbreviated title: Aspiration risk in severe acute alcohol intoxication

Key words: alcohol intoxication, airway management, aspiration, intubation, Glasgow Coma Scale, protective airway reflex

Abstract

Objectives In alcohol intoxicated patients, the decision for or against airway protection can be challenging and is often based on the Glasgow Coma Scale (GCS). Primary aim of this study was to analyse the aspiration risk in relation to the GCS score and clinical parameters in patients with severe acute alcohol monointoxication. Secondary aim was the association between the blood alcohol level and the GCS score.

Setting Single-centre, retrospective study of alcoholised patients admitted to a German intensive care unit between 2006 and 2020.

Participants n=411 admissions were eligible for our analysis.

Clinical measures and analysis The following data were extracted: age, gender, admission time, blood alcohol level, blood glucose level, initial GCS score, GCS score at admission, vital signs, clinical signs of aspiration and airway management measures. The empirical distribution of continuous and categorical data was calculated. Binary multivariable logistic regression analysis was used to identify possible risk factors for aspiration.

Results The mean age was 35 years. 72% of the patients were male. The blood alcohol level (mean 2.7 g/l ±1.0, maximum 5.9 g/l) did not correlate with the GCS score but with the age of the patient. In univariate analysis, the aspiration risk correlated with blood alcohol level, age, GCS score, oxygen saturation, respiratory rate, and blood glucose level and was significantly higher in male patients, upon vomiting, and in patients requiring airway measures. Aspiration rate was 45% in patients without vs. 6% in patients with preserved protective reflexes (p=0.0001). In multivariate analysis, only age and GCS score were significantly associated with the risk of aspiration.

Conclusion Although in this single-centre, retrospective study the aspiration rate in severe acute alcohol monointoxicated patients correlates with GCS and protective reflexes, the decision for endotracheal intubation might rather be based on the presence of different risk factors for aspiration.

Strengths and limitations of this study

- We provide an analysis of the so far largest homogenous cohort of alcohol monointoxicated non-traumatic ICU patients for risk factors of aspiration.
- Since the aspiration pneumonia could have developed after the discharge of the patient from the hospital in cases with short-time in-hospital care, we might have missed some aspiration events.
- Since a minority of patients were admitted to the hospital more than once, we analysed admissions instead of patients as single events.
- Within our cohort of limited sample size we identified risk factors for aspiration which could help to guide clinical diagnostic and therapeutic work up.
- However, due to the retrospective nature of this single-centre study, we cannot provide direct clinical recommendations.

Introduction

Patients with acute ethanol intoxication frequently require medical treatment, observation and diagnostics by paramedics, emergency physicians, emergency departments as well as intensive care units (ICU) [1]. Up to 12% of the attendances at the emergency department of an inner-city hospital in the United Kingdom were alcohol-related, mostly due to acute intoxication [2]. In Ontario, Canada, 5.1% of visits to the emergency department were attributable to alcohol use [3]. Besides respiratory depression, an elevated risk of aspiration due to impaired consciousness after alcohol consumption can cause life-threatening complications [4, 5]. In trauma patients with impaired consciousness, a GCS score of 8 or less is widely accepted as an indication for an airway protection by endotracheal intubation [6]. Although alcohol intoxicated patients often present with impaired consciousness and a GCS score of less than 8, the reported intubation rate of 0-2.3% is low compared to the overall intubation rate of 3-5% in prehospital emergencies [7-11]. The clinical benefit of intubating intoxicated patients with a GCS score≤8 in order to prevent aspiration is still controversially discussed [8, 9, 12-14]. Apart from adverse events like hypotension and cardiac arrest, prehospital intubation bears a risk of approx. 8% for the development of an intubation-related aspiration pneumonia [15]. Therefore, the risk-benefit ratio of prehospital invasive airway measures needs to be carefully considered. Differences of aspiration and intubation rates between mixed intoxications and alcohol monointoxications suggest that these clinical conditions might not be comparable regarding the necessity for airway protection. In contrast to mixed intoxication, data regarding airway impairment in acute alcohol monointoxication are very scarce.

The primary aim of this study was to search for risk factors for aspiration in adolescent and adult atraumatic patients who required admission to our intensive care unit due to severe acute alcohol monointoxication.. As a secondary aim, we analysed the association between the blood alcohol level and the GCS score.

Material and Methods

Study Design and Population

For this retrospective study, all patients who had been admitted to the intensive care unit of the Department of Gastroenterology at the University Hospital of Heidelberg between January 2006 and December 2020 were screened for acute mono-intoxication with alcohol (ethanol). The study was approved by the local ethics board of Heidelberg University (S-329/2013), which waived the need for an informed consent by the patient. Mixed intoxication was assumed when reported by the patient or relatives or in case of indicative prehospital scenarios (empty blisters, visible injection signs) or positive toxicology screening upon admission to the hospital (see "Measurements"). These patients were excluded from the study. Alcohol intoxication was defined as impaired consciousness due to a blood alcohol level ≥0.8 g/l, which is the legal definition for alcohol intoxication in many countries [16]. Patients with missing data regarding blood alcohol level or GCS score were excluded, as well as patients with severe comorbidities or medical conditions interfering with consciousness, airway situation, aspiration risk or breathing rate. Details of excluded patients are given in Figure 1. Deep therapeutic sedation was defined as sedation by the emergency physician resulting in an iatrogenic GCS score ≤8. Severe hypothermia was defined by a core temperature ≤34 °C. Hypoglycemia was defined as any blood glucose level <65 mg/dl as the lower level of normal regarding our standard point-of-care-testing (POCT) devices. Concomitant use of common medication at therapeutic doses was permitted. The following data were extracted from the medical records: age, gender, admission time, blood alcohol level, blood glucose level, initial GCS score (1st GCS), GCS score at admission to the hospital (2nd GCS), initial vital signs (systolic blood pressure, heart rate, breathing rate, peripheral capillary oxygen saturation (SpO_2)), clinical and prehospital signs of aspiration and airway management measures. When patients were prehospitally intubated, only the first GCS score before intubation was recorded, since the second GCS score was narcosis-induced (usually GCS score=3). Aspiration was rated positive if proven by bronchoscopy or if clinical suspicion was supported by at least one of the following factors: coughing up aspirate, coarse crackles on auscultation, new opacities on chest x-ray, development of fever or laboratory signs of inflammation (CRP, leukocytosis) without other overt reasons. Patients without clinical signs of aspiration or normal bronchoscopy were rated negative.

Measurements

Except for prehospital measurements of blood glucose levels by point-of-care-testing (POCT) according to the emergency medical service (EMS), blood samples were obtained immediately after the patient´s admission to our hospital for venous blood gas analysis (RAPIDLab 1200, Siemens Healthcare Diagnostics, Eschborn, Germany), measurement of blood alcohol level and standard laboratory tests including glucose. When indicated by the patient´s history or clinical data, a qualitative urine toxicology screen (Triage 8 Drugs of Abuse Panel, Alere Diagnostics, Cologne, Germany) was performed to exclude mixed intoxications. This test detects the following components: amphetamine, barbiturates, benzodiazepines, cocaine, methadone, opiates, tetrahydrocannabinol (THC), and tricyclic antidepressants. Due to the low specificity, sensitivity and clinical benefit, urine toxicology test was not performed on a regular basis [17].

Statistical Analysis

Data entry was performed with help of Microsoft Excel (Version 14.0), for the statistical analysis SAS Version 9.4 WIN (SAS Institute GmbH, Heidelberg, Germany) was used. The empirical distribution of continuous data was described with mean, standard deviation and range, in case of categorical data with absolute and relative frequencies. Spearman‘s correlation coefficient was calculated to describe associations between blood alcohol level and laboratory values. Possible differences between patients with and without aspiration were tested with t-test for continuous data and chi-square-tests for categorical data. Binary multivariable logistic regression analysis was used to find possible risk factors for aspiration. Statistical graphics were used to visualise the findings.

Patient and Public Involvement

No patient involved.

Results

A total of n=411 admissions to our intensive care unit for acute alcohol monointoxication comprising n=360 different patients were eligible for our analysis. The baseline characteristics of the enrolled patients and their vital parameters are listed in Table 1.

Table 1 Baseline characteristics of the study population at admission

Total number of admissions	411
Number of different patients	360
Patients with more than 1 admission	33
Patients with 2 admissions	21
Patients with 3 admissions	7
Patients with 4 admissions	4
Patients with 5 admissions	1
Gender, males/females (%)	294/117 (72%/28%)
Age, mean ±SD, (range) [y]	35 ±15 (15-74)
Blood alcohol level, mean ±SD, (range) [g/l]	2.7 ±1.0 (0.9-5.9)
Peripheral oxygen saturation (SpO_2), mean ±SD, (range) [%]	96 ±6 (47-100)
Heart rate, mean ±SD (range) [bpm]	92 ±20 (35-180)
Systolic blood pressure, mean ±SD (range) [mmHg]	121 ±22 (70-200)
Respiratory rate, mean ±SD (range) [1/min]	15 ±5 (0-35)

The mean blood alcohol level did not significantly differ between male (2.7±0.95 g/l) and female (2.5±1.14 g/l) patients (p=0.132). The maximum blood alcohol level was 5.89 g/l and 5.85 g/l in male and female patients, respectively. In Figure 2, the blood alcohol levels are shown according to age and gender. The blood alcohol level strongly correlated with patient´s age (r=0.43, p<0.0001) in the total population, as well as in male (r=0.46, p<0.0001) and female patients (r=0.33, p=0.003).

In order to analyse the fluctuating consciousness in acute alcohol intoxication, we compared the first GCS score of the patient upon arrival of the emergency team with the second GCS score at admission to the hospital approximately 30-60 minutes later. The median GCS score improved from 10 to 13 between prehospital presentation and admission to the ICU. Figure 3 visualises the strong correlation between the first and second GCS score (r=0.77, p<0.0001). Dots on the diagonal line correspond to patients with identical first and second GCS scores. We considered a change of ±3 GCS points (ΔGCS) as clinically relevant. Most patients (n=258, 78.5%) did not show a relevant change of the GCS score (-2 ≤ ΔGCS ≤ +2). While n=61 admissions (18.5%) demonstrated an improvement of their consciousness level during their transport to the hospital (ΔGCS score ≥ +3), only n=10 patients (3.0%) showed a relevant deterioration (ΔGCS score ≤ -3).

To rule out any bias due to mixed GCS records (i.e. pooled first and second GCS scores), all following analyses regarding GCS scores were performed with the first GCS score only. The median first GCS score did not differ between male and female patients (10 vs. 10, p=0.864). Blood alcohol levels did neither correlate with the initial GCS score in the general population (r=-0.05, p=0.279), nor for male (r=-0.05, p=0.331) or female (r=-0.04, p=0.673) patients. Nevertheless, very high blood alcohol levels (>5 g/l) were measured only in patients with a first GCS score ≤11 (Figure 4). The highest blood alcohol levels of 5.89 and 5.85 g/l were found in 2 patients with a GCS score of 3 and 8, respectively.

Within the total population of n=411 patients, aspiration was found in n=21 (5.1%). Aspiration was diagnosed by a positive bronchoscopy in n=5 (24%) of these patients. In the remaining n=16 patients, diagnosis of aspiration was based on the presence of at least one of the following criteria: coarse crackles on auscultation (n=9), new opacities on chest x-ray (n=6), development of fever or laboratory signs of inflammation (n=6). In order to identify risk factors for aspiration in alcohol intoxicated patients, we compared the cohorts with and without aspiration regarding demographic characteristics, vital signs, blood alcohol level, blood glucose level and airway management. In univariate analysis of continuous risk factors for aspiration, patients with aspiration were significantly older (mean age 47.4 vs. 34.6 years), had a higher blood alcohol level (mean 3.4 vs. 2.6 g/l), a lower first GCS score (median 3 vs. 11), a lower peripheral oxygen saturation (SpO_2, mean 90 vs. 96%), a lower respiration rate (mean 13/min vs. 15/min), and a higher blood glucose level (139 vs. 109 mg/dl) (Table 2).

Table 2 Univariate analysis of continuous risk factors for aspiration

Parameter	**Patients w/o aspiration** Mean ±SD (range)	**Eligible patients**	**Patients with aspiration** Mean ±SD (range)	**Eligible patients**	**p-value**
Age [y]	34.6 ±14.5 (15-74)	390	47.4 ±9.3 (32-65)	21	<0.0001
Blood alcohol level [g/l]	2.6 ±1.0 (0.9-5.9)	390	3.4 ±1.3 (1.7-5.5)	21	0.017
Initial GCS score	11 (median) ±4 (3-15)	378	3 (median) ±2 (3-9)	20	<0.0001
SpO_2 [%]	96 ±6 (47-100)	365	90 ±8 (73-100)	21	0.006
Systolic blood pressure [mmHg]	121 ±22 (70-200)	371	122 ±20 (96-160)	21	0.772
Heart rate [bpm]	92 ±20 (35-180)	377	89 ±20 (50-120)	21	0.580
Respiratory rate [1/min]	15 ±5 (0-35)	302	13 ±3 (8-18)	19	0.014
Blood glucose level [mg/dl]	109 ±40 (65-487)	388	139 ±60 (72-335)	21	0.028

Furthermore, univariate results of binary risk factors revealed a significantly higher risk for aspiration for male patients, patients with documented airway measures as listed in Table 3.

Table 3 Univariate analysis of binary risk factors for aspiration

Parameter	Manifestation	Patients w/o aspiration [%]	Patients with aspiration [%]	Evaluable patients	p-value
Gender	Male	93.5	6.5	294	0.048
	Female	98.3	1.7	117	
Vomiting	No	96.4	3.7	329	0.017
	Yes	89.9	10.1	79	
Oxygen supply	No	99.2	0.8	265	<0.0001
	Yes	86.9	13.1	145	
Guedel tube application	No	95.5	4.5	400	0.0003
	Yes	70.0	30.0	10	
Mask ventilation	No	95.8	4.2	400	<0.0001
	Yes	60.0	40.0	10	
Protective airway reflexes (at GCS score ≤8)	No	54.6	45.4	22	0.0001
	Yes	94.2	5.8	52	
Secretion suction	No	96.5	3.5	396	<0.0001
	Yes	46.1	53.9	13	
Intubation	No	98.4	1.6	384	<0.0001
	Yes	44.4	55.6	27	

Intubated patients showed a significantly higher aspiration rate than patient´s without intubation (56% vs. 1.6%). Since many emergency physicians base their decision for intubation in patients with a GCS score ≤8 on the presence or absence of the swallowing and gag reflex, the presence of these protective reflexes was correlated with the risk of aspiration. A total of n=152 patients had a first GCS score ≤8. Data regarding protective reflexes were available in n=74 (48.7%) of these patients. Protective reflexes in patients with GCS score ≤8 were present in n=52 (70.3%), but absent in n=22 (29.7%). The absence of protective reflexes was significantly associated with a higher risk of aspiration: 45.4% aspiration rate in patients without vs. 5.8% in patients with protective reflexes (p=0.0001, Table 3).

On multivariate analysis of the risk factors gender, age, blood alcohol level, first GCS score, and oxygen saturation, only age (OR 1.06) and GCS score (OR 0.71) significantly correlated with the risk of aspiration (Table 4).

Table 4 Odds ratio estimates in multivariate analysis of risk factors for aspiration.

Risk factor	OR	95% confidence limits		p-value
Gender (male versus female)	3.29	0.67	16.03	0.141
Age	1.06	1.02	1.10	0.005
Blood alcohol level	1.26	0.80	2.00	0.320
First GCS score	0.71	0.60	0.84	<0.0001
Oxygen saturation	0.98	0.93	1.03	0.397

Due to the low number of complete data sets, presence of protective reflexes could not be included in the multivariate analysis. The difference of age and GCS score between aspirated and non-aspirated patients is visualized as box plots in Figure 5A & B. However, a

GCS score=3 had a low sensitivity (60%) and a moderate specificity (83%) for aspiration, with a positive predictive value (PPV) of only 16% and very high negative predictive value (NPV) of 98%. Since information on the preservation of protective airway reflexes in these patients were rather scarce, the PPV and NPV were calculated for a GCS score=3, irrespective of the gag reflex.

Discussion

Acute alcohol intoxication constitutes a frequent medical problem with a considerable socio-economic and health care system burden. The demographic analysis of our cohort shows a predominance of young male patients, which is comparable to other demographic studies [18, 19]. However, our ICU cohort showed a younger age distribution than another retrospectively analysed cohort of patients admitted to an emergency department [1]. With a mean alcohol level of 2.7 g/l, our cohort showed higher blood alcohol levels than many other studies [20-23], which might be due to the selection of ICU patients. In contrast to Vereslt et al. [1], a higher age was associated with a higher blood alcohol level in our cohort.

Since the short period of prehospital care of alcoholised patients impedes a relevant alcohol degradation, one would expect – if at all – a deterioration of the GCS between the first patient contact and the admission to the hospital due to an ongoing alcohol resorption in the alimentary tract. However, 19% of our patients showed an improvement of more than 2 GCS score points during their prehospital care, but only 3% of patients showed a relevant deterioration. Overall, we found a strong correlation between the first and second GCS score. The prehospital blood alcohol level is not routinely available to the emergency team. Therefore, we can neither provide data on its kinetics, nor does the clinical decision rely on these data. The GCS score of head injured trauma patients with additional alcohol intoxication also improved between prehospital care and the emergency department [24]. This implies that the measurement time point of the GCS score during the prehospital care should be exactly defined and pooling of GCS data from different phases of care should be avoided. Slight changes in GCS score might not necessarily reflect a clinically relevant change of consciousness level of alcoholised patients. We, therefore, considered only an arbitrarily defined ΔGCS of ≥3 as clinically relevant.

Most data on the influence of alcohol on the GCS score were derived from trauma patients. Some studies showed a correlation between blood alcohol level and GCS score [25], while others did not [26-28]. Interestingly, data on a correlation between blood alcohol level and GCS score in alcohol-intoxicated patients without concomitant trauma are very scarce and the clinical consequence of low GCS values is unclear. In a cohort of alcohol-intoxicated patients without trauma from the Oktoberfest in Munich the blood alcohol level was not predictive for the need of hospitalisation [29]. Concordantly, in our study on non-traumatic alcoholised patients, the blood alcohol level did not correlate with the GCS score even at a considerably high mean blood alcohol level of 2.7 g/l. Nevertheless, n=8 patients of our cohort with an extremely high blood alcohol level of ≥5 g/l demonstrated a reduced median GCS score of 5. This cohort, however, was too small for a subgroup analysis. In contrast, in adolescent patients (13-17 years of age) with rather mild alcohol intoxication (mean 1.6 g/l), Mick et al. found a significant correlation between the blood alcohol level and the GCS score [20]. One might speculate that adolescents and younger adults have not yet undergone habituation to regular alcohol consumption. However, even in the youngest subgroup (15-25 years) of our study, there was no significant correlation between blood alcohol level and GCS score (n=136 patients, mean blood alcohol level 2.1 g/l, median GCS score 10, p=0.061).

One of the most challenging clinical problems in unconscious alcohol-intoxicated patients is the decision for or against airway protection by intubation. Many studies were performed in heterogeneous cohorts of mixed intoxication [7, 9, 30-32], in trauma patients [8, 33] or without any data on the risk of aspiration [8, 30]. While some authors and recommendations refer to a GCS score ≤8 as an indication for intubation in alcohol intoxicated patients, the association of a low GCS score with a higher risk of aspiration has not been sufficiently substantiated in these patients. In their prospective observational study, Duncan et al. did not find a higher rate of aspiration in patients with a GCS score ≤8 [7]. However, only n=22 of 73 patients had alcohol monointoxication and only n=12 patients of their entire cohort demonstrated a GCS score ≤8. Comparing n=12 intubated (mean GCS score 5.9) with n=14 not-intubated (mean GCS score 5.5) patients with mixed intoxication, Donald et al. did not detect a difference in laboratory or physiological parameters. However, the aspiration rate was not analysed [9]. None of the intubated patients had an alcohol intoxication. In patients with a mixed intoxication, the risk of aspiration pneumonia did not significantly differ between patients with a GCS score ≤8 versus a GCS score >8 [13]. In another prospective study on n=224 drug-intoxicated patients, there was no correlation between the GCS score and the risk of aspiration [32]. A GCS score ≤8 was not considered as essential for an increased risk of aspiration. However, the aspiration rate in that drug-intoxicated cohort was very high (29%) compared to our study (5%). This indicates that mixed intoxication and alcohol monointoxication might not be comparable regarding the risk of aspiration.

In our study on non-traumatic alcohol-monointoxicated patients, we found a strong correlation between the GCS score and the risk of aspiration, even in a multivariate regression model. However, n=133 of the 152 patients (87.5%) with GCS score ≤8 did not aspirate. Thus, even for a GCS score =3 the PPV is too low (16%) to guide the decision for intubation. However, Sauter et al. described that a GCS score ≤8 was the main reason for emergency teams to decide for intubation in intoxicated patients [8]. In our cohort, emergency physicians – according to their emergency protocols – made a more differentiated decision for intubation based on GCS score, presence of the gag reflex, vomiting and the suspicion of aspiration.

An alternative parameter to estimate the risk for aspiration is the presence of the gag or cough reflex. However, in a very small cohort of patients with pharmacologically induced coma the cough reflex did not correlate with the GCS score, as n=4 of 12 patients (33%) with a GCS score =3 had an unimpaired cough reflex. On the other hand, 3 of 5 patients (60%) with a GCS score =8 had an impaired cough reflex [30]. These data are supported by the detection of a depressed gag reflex in drug-intoxicated patients even at a GCS score ≥8 [31]. Of note, none of these studies has been performed in alcohol monointoxicated patients. In our study we could obtain information on the gag or cough reflex in n=74 patients. The absence of protective airway reflexes did significantly correlate with an increased risk of aspiration in a univariate analysis (Table 3). Furthermore, all airway measures significantly correlated with the rate of aspiration (Table 3). For instance, the necessity of secretion suction or intubation (on the discretion of the emergency physician) were each associated with an aspiration rate of >50%. Our data are in line with a smaller retrospective study on n=155 patients with mixed intoxication in which patients with reduced GCS scores or an impaired gag reflex had a higher risk for an aspiration pneumonitis [12]. An absent or reduced gag reflex was found in 96% of their patients with aspiration. However, the high aspiration rate of 15% in their cohort of mixed intoxication might be related to the application of gastric lavage and charcoal administration which is not applied in alcohol monointoxication. Our study impressively shows that the execution of some airway measures (e.g. oxygen supply) or encountered vomiting indicated only a low risk of aspiration, while other measures (e.g. mask ventilation, secretion suction, intubation) and the lack of protective airway reflexes indicate a high aspiration incidence in these patients. This would imply a thorough diagnostic (e.g. X-ray, bronchoscopy) or therapeutic (e.g. antibiotic treatment) work-up in these high-risk patients upon ICU admission. However, a GCS score ≤8 alone should not warp the emergency physician into endotracheal intubation.

Although herewith we present - to the best of our knowledge - the most comprehensive analysis of the aspiration risk in alcohol monointoxicated patients, our study has some limitations. Due the retrospective nature of our study, we cannot provide direct clinical recommendations. Since protective airway reflexes were evaluated by the emergency team only in a subset of patients, there might be a bias towards reporting rather impaired than normal reflexes. However, since both preserved and impaired protective reflexes were listed as the reason against and in favor of intubation, respectively, we could not detect unilateral under- or over-reporting. Since we focused on severely alcohol-intoxicated patients admitted to the ICU of our hospital, our finding might not be extrapolated to the general population with alcohol monointoxication in an emergency department.

Conclusion

In our retrospective study, we found that the blood alcohol level did correlate with the patient´s age but not with the GCS score. However, both age and GCS score did correlate with the risk of aspiration . Of clinical relevance, we identified risk factors for aspiration in alcohol monointoxicated patients which could guide the decision for airway protection measures: Guedel tube application, mask ventilation, loss of protective airway reflexes, secretion suction. However, a GCS score =3 has a very low PPV for aspiration and, as a single parameter, might not trigger endotracheal intubation. On the other hand, since only 6% of patients with preserved gag reflexes had aspirated, in this patient subgroup the risk of intubation might prevail its benefits. Based on these single-centre, retrospective data the high prevalence of aspiration in intubated patients suggests that these patients might benefit from an aggressive diagnostic workup (e.g. X-ray or bronchoscopy) and a liberate use of prophylactic antibiotic treatment for potential aspiration pneumonitis upon admission to the ICU.

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Conflict of interests: none

Figure captions

Figure 1. Composition of the study cohort. From the initial cohort of 458 atraumatic patients with acute alcohol monointoxication, 47 admissions were excluded due to missing data or severe interfering medical conditions, resulting in 411 admissions eligible for the final analysis. In 3 cases 2 different exclusion criteria were present.

Figure 2. Blood alcohol levels at admission are plotted as a function of age, separately for n=294 admission of male (□) and n=117 admissions of female (♦) patients.

Figure 3. Correlation between the first GCS score at prehospital presentation and the second GCS score at hospital admission (n=336 complete data sets). The diagonal represents patients with no change in GCS score during their prehospital treatment. The number of patients is inscribed within each dot and reflected by the dot size. A change of ±2 points between first and second GCS score was considered clinically irrelevant (unfilled circles). Patients with changes of their GCS score of 3 or more points are considered clinically relevant (filled circles).

Figure 4. Correlation between first GCS score and blood alcohol level for male (□) and female (♦) patients.

Figure 5. Distribution of the first GCS score (A) and age (B) for patients without aspiration versus proven aspiration, presented as box plots.

Ethics Statement

The study was approved by the local ethics board of Heidelberg University (S-329/2013)

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b. Competing Interest: None declared.

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d. Contributorship Statement

MC, AH, EP, RK planned the study and performed the data acquisition. Statistical analysis was performed by TB. Manuscript writing and editing was performed by MC, AH, EP, TB, RK. The manuscript was submitted by MC.

e. Word count

3.742

Figure 1

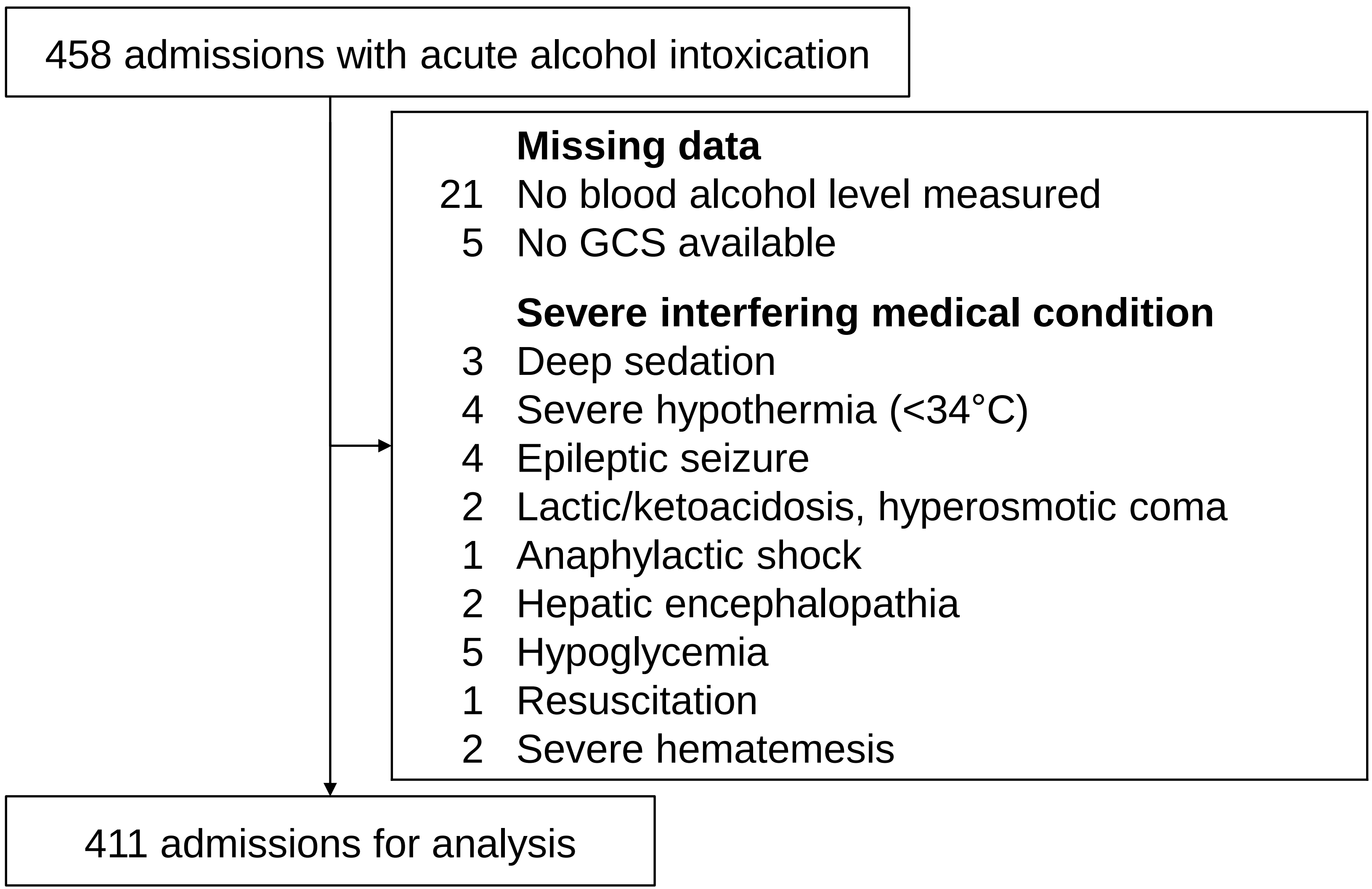
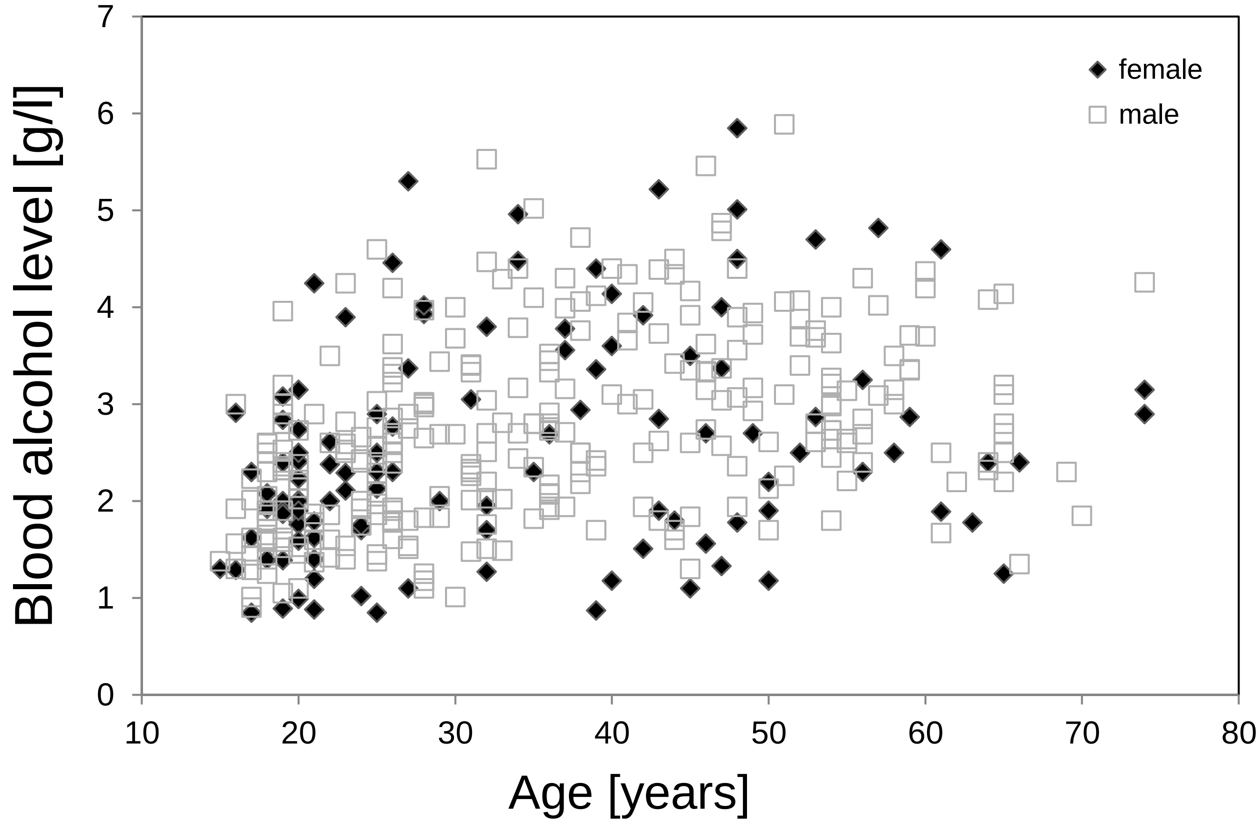

458 admissions with acute alcohol intoxication
Missing data
21 No blood alcohol level measured
5 No GCS available
Severe interfering medical condition
3 Deep sedation
4 Severe hypothermia (<34°C)
4 Epileptic seizure
2 Lactic/ketoacidosis, hyperosmotic coma
1 Anaphylactic shock
2 Hepatic encephalopathia
5 Hypoglycemia
1 Resuscitation
2 Severe hematemesis
411 admissions for analysis

Figure 2


female
male
Blood alcohol level [g/l]
Age [years]
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1
2
3
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60
70
80

Figure 3

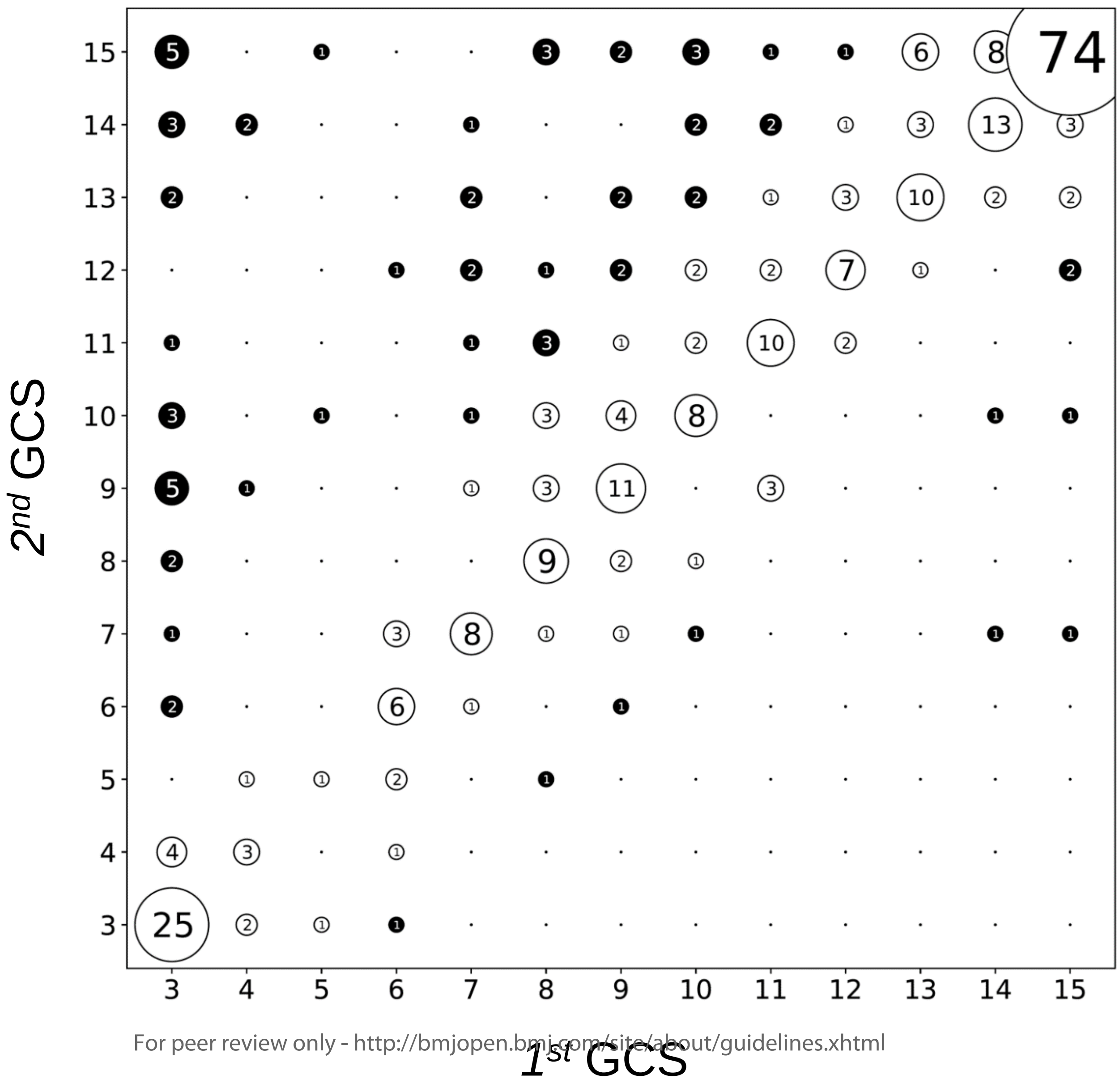

Figure 4


15
14
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12
11
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9
8
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5
4
3
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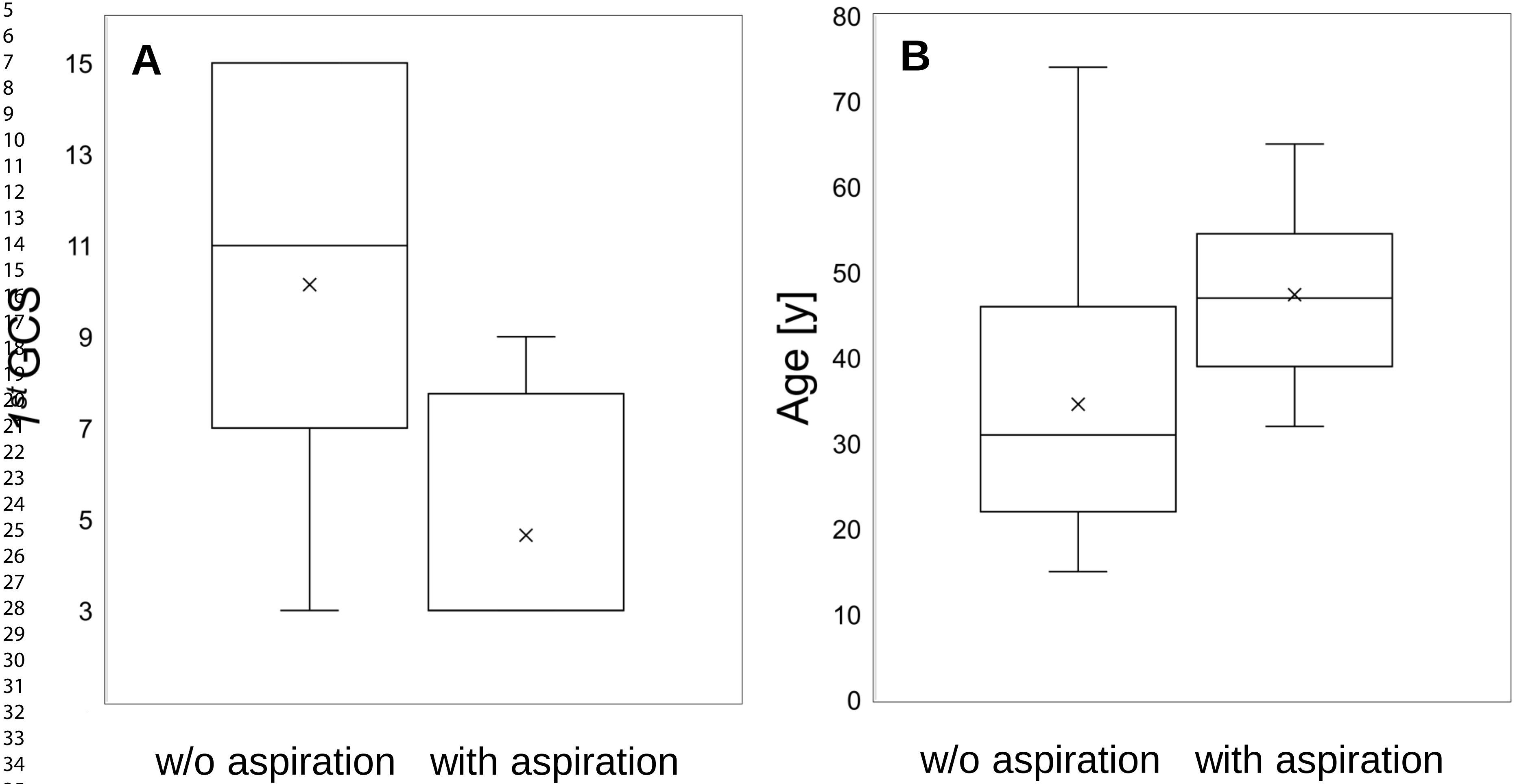
0
1
2
3
4
5
6
7
female
male
1^{st} GCS
Blood alcohol level [g/l]

Figure 5


A
1st GCS
15
13
11
9
7
5
3
w/o aspiration
with aspiration
B
Age [y]
80
70
60
50
40
30
20
10
0
w/o aspiration
with aspiration

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-10

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-10
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Aspiration risk in relation to Glasgow Coma Scale score and clinical parameters in patients with severe acute alcohol intoxication: a single-centre, retrospective study

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Aspiration risk in relation to Glasgow Coma Scale score and clinical parameters in patients with severe acute alcohol intoxication: a single-centre, retrospective study

Michael Conzelmann [1,2], Anne Hoidis [3], Thomas Bruckner [4], Erik Popp [5], Ronald Koschny [3]

[1] Dept. of Human Toxicology & Health Risk Assessment, BASF Corporate Health Management, Carl-Bosch-Str. 38, D-67056 Ludwigshafen am Rhein, Germany

[2] Postgraduate Study "Toxicology and Environmental Toxicology", Rudolf Boehm Institute of Pharmacology and Toxicology, University of Leipzig, Haertelstrasse 16-18, 04107 Leipzig, Germany.

[3] Dept. of Gastroenterology, University Hospital Heidelberg, INF 410, D-69120 Heidelberg, Germany

[4] Institute for Medical Biometry and Informatics, Heidelberg University Hospital, INF 130.3, D-69120 Heidelberg, Germany

[5] Dept. of Anaesthesiology, University Hospital Heidelberg, INF 420, D-69120 Heidelberg, Germany

✉ Corresponding author — Prof. Dr. med. Ronald Koschny

⊗ Present address — Dept. of Internal Medicine
Im Neuenheimer Feld 410
D-69120 Heidelberg, Germany
Email: ronald.koschny@med.uni-heidelberg.de
Tel.: +49 6221 5637969, Fax: +49 6221 565255

Abbreviated title: Aspiration risk in severe acute alcohol intoxication

Key words: alcohol intoxication, airway management, aspiration, intubation, Glasgow Coma Scale, protective airway reflex

Abstract

Objectives In alcohol intoxicated patients, the decision for or against airway protection can be challenging and is often based on the Glasgow Coma Scale (GCS). Primary aim of this study was to analyse the aspiration risk in relation to the GCS score and clinical parameters in patients with severe acute alcohol monointoxication. Secondary aim was the association between the blood alcohol level and the GCS score.

Setting Single-centre, retrospective study of alcoholised patients admitted to a German intensive care unit between 2006 and 2020.

Participants n=411 admissions were eligible for our analysis.

Clinical measures and analysis The following data were extracted: age, gender, admission time, blood alcohol level, blood glucose level, initial GCS score, GCS score at admission, vital signs, clinical signs of aspiration and airway management measures. The empirical distribution of continuous and categorical data was calculated. Binary multivariable logistic regression analysis was used to identify possible risk factors for aspiration.

Results The mean age was 35 years. 72% of the patients were male. The blood alcohol level (mean 2.7 g/l ±1.0, maximum 5.9 g/l) did not correlate with the GCS score but with the age of the patient. In univariate analysis, the aspiration risk correlated with blood alcohol level, age, GCS score, oxygen saturation, respiratory rate, and blood glucose level and was significantly higher in male patients, upon vomiting, and in patients requiring airway measures. Aspiration rate was 45% in patients without vs. 6% in patients with preserved protective reflexes ($p=0.0001$). In multivariate analysis, only age and GCS score were significantly associated with the risk of aspiration.

Conclusion Although in this single-centre, retrospective study the aspiration rate in severe acute alcohol monointoxicated patients correlates with GCS and protective reflexes, the decision for endotracheal intubation might rather be based on the presence of different risk factors for aspiration.

Strengths and limitations of this study

- We provide an analysis of the so far largest homogenous cohort of alcohol monointoxicated non-traumatic ICU patients for risk factors of aspiration.
- Since the aspiration pneumonia could have developed after the discharge of the patient from the hospital in cases with short-time in-hospital care, we might have missed some aspiration events.
- Since a minority of patients were admitted to the hospital more than once, we analysed admissions instead of patients as single events.
- Within our cohort of limited sample size we identified risk factors for aspiration which could help to guide clinical diagnostic and therapeutic work up.
- However, due to the retrospective nature of this single-centre study, we cannot provide direct clinical recommendations.

Introduction

Patients with acute ethanol intoxication frequently require medical treatment, observation and diagnostics by paramedics, emergency physicians, emergency departments as well as intensive care units (ICU) [1]. Up to 12% of the attendances at the emergency department of an inner-city hospital in the United Kingdom were alcohol-related, mostly due to acute intoxication [2]. In Ontario, Canada, 5.1% of visits to the emergency department were attributable to alcohol use [3]. Besides respiratory depression, an elevated risk of aspiration due to impaired consciousness after alcohol consumption can cause life-threatening complications [4, 5]. In trauma patients with impaired consciousness, a GCS score of 8 or less is widely accepted as an indication for an airway protection by endotracheal intubation [6]. Although alcohol intoxicated patients often present with impaired consciousness and a GCS score of less than 8, the reported intubation rate of 0-2.3% is low compared to the overall intubation rate of 3-5% in prehospital emergencies [7-11]. The clinical benefit of intubating intoxicated patients with a GCS score≤8 in order to prevent aspiration is still controversially discussed [8, 9, 12-14]. Apart from adverse events like hypotension and cardiac arrest, prehospital intubation bears a risk of approx. 8% for the development of an intubation-related aspiration pneumonia [15]. Therefore, the risk-benefit ratio of prehospital invasive airway measures needs to be carefully considered. Differences of aspiration and intubation rates between mixed intoxications and alcohol monointoxications suggest that these clinical conditions might not be comparable regarding the necessity for airway protection. In contrast to mixed intoxication, data regarding airway impairment in acute alcohol monointoxication are very scarce.

The primary aim of this study was to search for risk factors for aspiration in adolescent and adult atraumatic patients who required admission to our intensive care unit due to severe acute alcohol monointoxication. As a secondary aim, we analysed the association between the blood alcohol level and the GCS score.

Material and Methods

Study Design and Population

For this retrospective study, all patients who had been admitted to the intensive care unit of the Department of Gastroenterology at the University Hospital of Heidelberg between January 2006 and December 2020 were screened for acute mono-intoxication with alcohol (ethanol). The study was approved by the local ethics board of Heidelberg University (S-329/2013), which waived the need for an informed consent by the patient. Mixed intoxication was assumed when reported by the patient or relatives or in case of indicative prehospital scenarios (empty blisters, visible injection signs) or positive toxicology screening upon admission to the hospital (see "Measurements"). These patients were excluded from the study. Alcohol intoxication was defined as impaired consciousness due to a blood alcohol level ≥0.8 g/l, which is the legal definition for alcohol intoxication in many countries [16]. Patients with missing data regarding blood alcohol level or GCS score were excluded, as well as patients with severe comorbidities or medical conditions interfering with consciousness, airway situation, aspiration risk or breathing rate. Details of excluded patients are given in Figure 1. Deep therapeutic sedation was defined as sedation by the emergency physician resulting in an iatrogenic GCS score ≤8. Severe hypothermia was defined by a core temperature ≤34 °C. Hypoglycemia was defined as any blood glucose level <65 mg/dl as the lower level of normal regarding our standard point-of-care-testing (POCT) devices. Concomitant use of common medication at therapeutic doses was permitted. The following data were extracted from the medical records: age, gender, admission time, blood alcohol level, blood glucose level, initial GCS score (1st GCS), GCS score at admission to the hospital (2nd GCS), initial (prehospital) vital signs (systolic blood pressure, heart rate, breathing rate, peripheral capillary oxygen saturation (SpO_2)), clinical and prehospital signs of aspiration and airway management measures. When patients were prehospitally intubated, only the first GCS score before intubation was recorded, since the second GCS score was narcosis-induced (usually GCS score=3). Aspiration was rated positive if proven by bronchoscopy or if clinical suspicion was supported by at least one of the following factors: coughing up aspirate, coarse crackles on auscultation, new opacities on chest x-ray, development of fever or laboratory signs of inflammation (CRP, leukocytosis) without other overt reasons. Patients without clinical signs of aspiration or normal bronchoscopy were rated negative.

Measurements

Except for prehospital measurements of blood glucose levels by point-of-care-testing (POCT) according to the emergency medical service (EMS), blood samples were obtained immediately after the patient´s admission to our hospital for venous blood gas analysis (RAPIDLab 1200, Siemens Healthcare Diagnostics, Eschborn, Germany), measurement of blood alcohol level and standard laboratory tests including glucose. When indicated by the patient´s history or clinical data, a qualitative urine toxicology screen (Triage 8 Drugs of Abuse Panel, Alere Diagnostics, Cologne, Germany) was performed to exclude mixed intoxications. This test detects the following components: amphetamine, barbiturates, benzodiazepines, cocaine, methadone, opiates, tetrahydrocannabinol (THC), and tricyclic antidepressants. Due to the low specificity, sensitivity and clinical benefit, urine toxicology test was not performed on a regular basis [17].

Statistical Analysis

Data entry was performed with help of Microsoft Excel (Version 14.0), for the statistical analysis SAS Version 9.4 WIN (SAS Institute GmbH, Heidelberg, Germany) was used. The empirical distribution of continuous data was described with mean, standard deviation and range, in case of categorical data with absolute and relative frequencies. Spearman's correlation coefficient was calculated to describe associations between blood alcohol level and laboratory values. Possible differences between patients with and without aspiration were tested with t-test for continuous data and chi-square-tests for categorical data. Binary multivariable logistic regression analysis was used to find possible risk factors for aspiration. Statistical graphics were used to visualise the findings.

Patient and Public Involvement

No patient involved.

Results

A total of n=411 admissions to our intensive care unit for acute alcohol monointoxication comprising n=360 different patients were eligible for our analysis. The baseline characteristics of the enrolled patients and their vital parameters are listed in Table 1.

Table 1 Baseline characteristics of the study population at admission

Total number of admissions	411
Number of different patients	360
Patients with more than 1 admission	33
Patients with 2 admissions	21
Patients with 3 admissions	7
Patients with 4 admissions	4
Patients with 5 admissions	1
Gender, males/females (%)	294/117 (72%/28%)
Age, mean ±SD, (range) [y]	35 ±15 (15-74)
Blood alcohol level, mean ±SD, (range) [g/l]	2.7 ±1.0 (0.9-5.9)
Peripheral oxygen saturation (SpO_2), mean ±SD, (range) [%]	96 ±6 (47-100)
Heart rate, mean ±SD (range) [bpm]	92 ±20 (35-180)
Systolic blood pressure, mean ±SD (range) [mmHg]	121 ±22 (70-200)
Respiratory rate, mean ±SD (range) [1/min]	15 ±5 (0-35)

The mean blood alcohol level did not significantly differ between male (2.7±1.0 g/l) and female (2.5±1.1 g/l) patients (p=0.132). The maximum blood alcohol level was 5.9 g/l and 5.9 g/l in male and female patients, respectively. In Figure 2, the blood alcohol levels are shown according to age and gender. The blood alcohol level strongly correlated with patient´s age (r=0.43, p<0.0001) in the total population, as well as in male (r=0.46, p<0.0001) and female patients (r=0.33, p=0.003).

In order to analyse the fluctuating consciousness in acute alcohol intoxication, we compared the first GCS score of the patient upon arrival of the emergency team with the second GCS score at admission to the hospital approximately 30-60 minutes later. The median GCS score improved from 10 to 13 between prehospital presentation and admission to the ICU. Figure 3 visualises the strong correlation between the first and second GCS score ($r=0.77$, $p<0.0001$). Dots on the diagonal line correspond to patients with identical first and second GCS scores. We considered a change of ±3 GCS points (ΔGCS) as clinically relevant. Most patients (n=258, 79%) did not show a relevant change of the GCS score ($-2 \leq \Delta GCS \leq +2$). While n=61 admissions (19%) demonstrated an improvement of their consciousness level during their transport to the hospital (ΔGCS score ≥ +3), only n=10 patients (3%) showed a relevant deterioration (ΔGCS score ≤ -3).

To rule out any bias due to mixed GCS records (i.e. pooled first and second GCS scores), all following analyses regarding GCS scores were performed with the first GCS score only. The median first GCS score did not differ between male and female patients (10 vs. 10, $p=0.864$). Blood alcohol levels did neither correlate with the initial GCS score in the general population ($r=-0.05$, $p=0.279$), nor for male ($r=-0.05$, $p=0.331$) or female ($r=-0.04$, $p=0.673$) patients. Nevertheless, very high blood alcohol levels (>5 g/l) were measured only in patients with a first GCS score ≤11 (Figure 4). The highest blood alcohol levels of 5.9 and 5.9 g/l were found in 2 patients with a GCS score of 3 and 8, respectively.

Within the total population of n=411 patients, aspiration was found in n=21 (5%). Aspiration was diagnosed by a positive bronchoscopy in n=5 (24%) of these patients. In the remaining n=16 patients, diagnosis of aspiration was based on the presence of at least one of the following criteria: coarse crackles on auscultation (n=9), new opacities on chest x-ray (n=6), development of fever or laboratory signs of inflammation (n=6). In order to identify risk factors for aspiration in alcohol intoxicated patients, we compared the cohorts with and without aspiration regarding demographic characteristics, vital signs, blood alcohol level, blood glucose level and airway management. In univariate analysis of continuous risk factors for aspiration, patients with aspiration were significantly older (mean age 47 vs. 35 years), had a higher blood alcohol level (mean 3.4 vs. 2.6 g/l), a lower first GCS score (median 3 vs. 11), a lower peripheral oxygen saturation (SpO_2, mean 90 vs. 96%), a lower respiration rate (mean 13/min vs. 15/min), and a higher blood glucose level (139 vs. 109 mg/dl) (Table 2).

Table 2 Univariate analysis of continuous risk factors for aspiration

Parameter	Patients without aspiration Mean ±SD (range)	Eligible patients	Patients with aspiration Mean ±SD (range)	Eligible patients	p-value
Age [y]	34.6 ±14.5 (15-74)	390	47.4 ±9.3 (32-65)	21	<0.0001
Blood alcohol level [g/l]	2.6 ±1.0 (0.9-5.9)	390	3.4 ±1.3 (1.7-5.5)	21	0.017
Initial GCS score	11 (median) ±4 (3-15)	378	3 (median) ±2 (3-9)	20	<0.0001
SpO_2 [%]	96 ±6 (47-100)	365	90 ±8 (73-100)	21	0.006
Systolic blood pressure [mmHg]	121 ±22 (70-200)	371	122 ±20 (96-160)	21	0.772
Heart rate [bpm]	92 ±20 (35-180)	377	89 ±20 (50-120)	21	0.580
Respiratory rate [1/min]	15 ±5 (0-35)	302	13 ±3 (8-18)	19	0.014
Blood glucose level [mg/dl]	109 ±40 (65-487)	388	139 ±60 (72-335)	21	0.028

Furthermore, univariate results of binary risk factors revealed a significantly higher risk for aspiration for male patients, patients with documented airway measures as listed in Table 3.

Table 3 Univariate analysis of binary risk factors for aspiration

Parameter	Manifestation	Patients without aspiration [%] (n)	Patients with aspiration [%] (n)	Evaluable patients (n)	p-value
Gender	Male	93.5 (275)	6.5 (19)	294	0.048
	Female	98.3 (115)	1.7 (2)	117	
Vomiting	No	96.4 (317)	3.7 (12)	329	0.017
	Yes	89.9 (71)	10.1 (8)	79	
Oxygen supply	No	99.2 (262)	0.8 (3)	265	<0.0001
	Yes	86.9 (126)	13.1 (19)	145	
Guedel tube application	No	95.5 (382)	4.5 (18)	400	0.0003
	Yes	70.0 (7)	30.0 (3)	10	
Mask ventilation	No	95.8 (383)	4.2 (17)	400	<0.0001
	Yes	60.0 (6)	40.0 (4)	10	
Protective airway reflexes (at GCS score ≤8)	No	54.6 (12)	45.4 (10)	22	0.0001
	Yes	94.2 (49)	5.8 (3)	52	
Secretion suction	No	96.5 (382)	3.5 (14)	396	<0.0001
	Yes	46.1 (6)	53.9 (7)	13	
Intubation	No	98.4 (377)	1.6 (7)	384	<0.0001
	Yes	44.4 (12)	55.6 (15)	27	

Intubated patients showed a significantly higher aspiration rate than patient´s without intubation (56% vs. 2%). Since many emergency physicians base their decision for intubation in patients with a GCS score ≤8 on the presence or absence of the swallowing and gag reflex, the presence of these protective reflexes was correlated with the risk of aspiration. A total of n=152 patients had a first GCS score ≤8. Data regarding protective reflexes were available in n=74 (49%) of these patients. Protective reflexes in patients with GCS score ≤8 were present in n=52 (70%), but absent in n=22 (30%). The absence of protective reflexes was significantly associated with a higher risk of aspiration: 45% aspiration rate in patients without vs. 6% in patients with protective reflexes (p=0.0001, Table 3).

On multivariate analysis of the risk factors gender, age, blood alcohol level, first GCS score, and oxygen saturation, only age (OR 1.06) and GCS score (OR 0.71) significantly correlated with the risk of aspiration (Table 4).

Table 4 Odds ratio estimates in multivariate analysis of risk factors for aspiration.

Risk factor	**OR**	**95% confidence limits**		**p-value**
Gender (male versus female)	3.29	0.67	16.03	0.141
Age	1.06	1.02	1.10	0.005
Blood alcohol level	1.26	0.80	2.00	0.320
First GCS score	0.71	0.60	0.84	<0.0001
Oxygen saturation	0.98	0.93	1.03	0.397

Due to the low number of complete data sets, presence of protective reflexes could not be included in the multivariate analysis. The difference of age and GCS score between aspirated and non-aspirated patients is visualized as box plots in Figure 5A & B. However, a

GCS score=3 had a low sensitivity (60%) and a moderate specificity (83%) for aspiration, with a positive predictive value (PPV) of only 16% and very high negative predictive value (NPV) of 98%. Since information on the preservation of protective airway reflexes in these patients were rather scarce, the PPV and NPV were calculated for a GCS score=3, irrespective of the gag reflex.

Discussion

Acute alcohol intoxication constitutes a frequent medical problem with a considerable socio-economic and health care system burden. The demographic analysis of our cohort shows a predominance of young male patients, which is comparable to other demographic studies [18, 19]. However, our ICU cohort showed a younger age distribution than another retrospectively analysed cohort of patients admitted to an emergency department [1]. With a mean alcohol level of 2.7 g/l, our cohort showed higher blood alcohol levels than many other studies [20-23], which might be due to the selection of ICU patients. In contrast to Vereslt et al. [1], a higher age was associated with a higher blood alcohol level in our cohort.

Since the short period of prehospital care of alcoholised patients impedes a relevant alcohol degradation, one would expect – if at all – a deterioration of the GCS between the first patient contact and the admission to the hospital due to an ongoing alcohol resorption in the alimentary tract. However, 19% of our patients showed an improvement of more than 2 GCS score points during their prehospital care, but only 3% of patients showed a relevant deterioration. Overall, we found a strong correlation between the first and second GCS score. The prehospital blood alcohol level is not routinely available to the emergency team. Therefore, we can neither provide data on its kinetics, nor does the clinical decision rely on these data. The GCS score of head injured trauma patients with additional alcohol intoxication also improved between prehospital care and the emergency department [24]. This implies that the measurement time point of the GCS score during the prehospital care should be exactly defined and pooling of GCS data from different phases of care should be avoided. Slight changes in GCS score might not necessarily reflect a clinically relevant change of consciousness level of alcoholised patients. We, therefore, considered only an arbitrarily defined ΔGCS of ≥3 as clinically relevant.

Most data on the influence of alcohol on the GCS score were derived from trauma patients. Some studies showed a correlation between blood alcohol level and GCS score [25], while others did not [26-28]. In our study on non-traumatic alcoholised patients, the blood alcohol level did not correlate with the GCS score even at a considerably high mean blood alcohol level of 2.7 g/l.In adolescent patients (13-17 years of age) with rather mild alcohol intoxication (mean 1.6 g/l), Mick et al. found a significant correlation between the blood alcohol level and the GCS score [20]. One might speculate that adolescents and younger adults have not yet undergone habituation to regular alcohol consumption. However, even in the youngest subgroup (15-25 years) of our study, there was no significant correlation between blood alcohol level and GCS score (n=136 patients, mean blood alcohol level 2.1 g/l, median GCS score 10, p=0.061).

One of the most challenging clinical problems in unconscious alcohol-intoxicated patients is the decision for or against airway protection by intubation. Many studies were performed in heterogeneous cohorts of mixed intoxication [7, 9, 29-31], in trauma patients [8, 32] or without any data on the risk of aspiration [8, 29]. While some authors and recommendations refer to a GCS score ≤8 as an indication for intubation in alcohol intoxicated patients, the association of a low GCS score with a higher risk of aspiration has not been sufficiently substantiated in these patients. In their prospective observational study, Duncan et al. did not find a higher rate of aspiration in patients with a GCS score ≤8 [7]. However, only n=22 of 73 patients had alcohol monointoxication and only n=12 patients of their entire cohort demonstrated a GCS score ≤8. Comparing n=12 intubated (mean GCS score 5.9) with n=14 not-intubated (mean GCS score 5.5) patients with mixed intoxication, Donald et al. did not detect a difference in laboratory or physiological parameters. However, the aspiration rate was not analysed [9]. None of the intubated patients had an alcohol intoxication. In patients with a mixed intoxication, the risk of aspiration pneumonia did not significantly differ between patients with a GCS score ≤8 versus a GCS score >8 [13]. In another prospective study on n=224 drug-intoxicated patients, there was no correlation between the GCS score and the risk of aspiration [31]. A GCS score ≤8 was not considered as essential for an increased risk of aspiration. However, the aspiration rate in that drug-intoxicated cohort was very high

(29%) compared to our study (5%). This indicates that mixed intoxication and alcohol monointoxication might not be comparable regarding the risk of aspiration.

In our study on non-traumatic alcohol-monointoxicated patients, we found a strong correlation between the GCS score and the risk of aspiration, even in a multivariate regression model. However, n=133 of the 152 patients (88%) with GCS score ≤8 did not aspirate. Thus, even for a GCS score =3 the PPV is too low (16%) to guide the decision for intubation. However, Sauter et al. described that a GCS score ≤8 was the main reason for emergency teams to decide for intubation in intoxicated patients [8]. In our cohort, emergency physicians – according to their emergency protocols – made a more differentiated decision for intubation based on GCS score, presence of the gag reflex, vomiting and the suspicion of aspiration.

An alternative parameter to estimate the risk for aspiration is the presence of the gag or cough reflex. However, in a very small cohort of patients with pharmacologically induced coma the cough reflex did not correlate with the GCS score, as n=4 of 12 patients (33%) with a GCS score =3 had an unimpaired cough reflex. On the other hand, 3 of 5 patients (60%) with a GCS score =8 had an impaired cough reflex [29]. These data are supported by the detection of a depressed gag reflex in drug-intoxicated patients even at a GCS score ≥8 [30]. Of note, none of these studies has been performed in alcohol monointoxicated patients. In our study we could obtain information on the gag or cough reflex in n=74 patients. The absence of protective airway reflexes did significantly correlate with an increased risk of aspiration in a univariate analysis (Table 3). Furthermore, all airway measures significantly correlated with the rate of aspiration (Table 3). For instance, the necessity of secretion suction or intubation (on the discretion of the emergency physician) were each associated with an aspiration rate of >50%. Our data are in line with a smaller retrospective study on n=155 patients with mixed intoxication in which patients with reduced GCS scores or an impaired gag reflex had a higher risk for an aspiration pneumonitis [12]. An absent or reduced gag reflex was found in 96% of their patients with aspiration. However, the high aspiration rate of 15% in their cohort of mixed intoxication might be related to the application of gastric lavage and charcoal administration which is not applied in alcohol monointoxication. Our study impressively shows that the execution of some airway measures (e.g. oxygen supply) or encountered vomiting indicated only a low risk of aspiration, while other measures (e.g. mask ventilation, secretion suction, intubation) and the lack of protective airway reflexes indicate a high aspiration incidence in these patients. This would imply a thorough diagnostic (e.g. X-ray, bronchoscopy) or therapeutic (e.g. antibiotic treatment) work-up in these high-risk patients upon ICU admission. However, a GCS score ≤8 alone should not warp the emergency physician into endotracheal intubation.

Although herewith we present - to the best of our knowledge - the most comprehensive analysis of the aspiration risk in alcohol monointoxicated patients, our study has some limitations. Due the retrospective nature of our study, we cannot provide direct clinical recommendations. Since protective airway reflexes were evaluated by the emergency team only in a subset of patients, there might be a bias towards reporting rather impaired than normal reflexes. However, since both preserved and impaired protective reflexes were listed as the reason against and in favor of intubation, respectively, we could not detect unilateral under- or over-reporting. Since we focused on severely alcohol-intoxicated patients admitted to the ICU of our hospital, our finding might not be extrapolated to the general population with alcohol monointoxication in an emergency department.

Conclusion

In our retrospective study, we found that the blood alcohol level did correlate with the patient´s age but not with the GCS score. However, both age and GCS score did correlate with the risk of aspiration. A GCS score = 3 has a very low PPV for aspiration. We identified risk factors for aspiration in alcohol monointoxicated patients: Guedel tube application, mask ventilation, loss of protective airway reflexes, secretion suction, intubation. These patients might benefit from an aggressive diagnostic and therapeutic workup. Since only 6% of patients with preserved gag reflexes had aspirated, in this patient subgroup the risk of intubation might prevail its benefits.

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Conflict of interests: none

Figure captions

Figure 1. Composition of the study cohort. From the initial cohort of 458 atraumatic patients with acute alcohol monointoxication, 47 admissions were excluded due to missing data or severe interfering medical conditions, resulting in 411 admissions eligible for the final analysis. In 3 cases 2 different exclusion criteria were present.

Figure 2. Blood alcohol levels at admission are plotted as a function of age, separately for n=294 admission of male (□) and n=117 admissions of female (♦) patients.

Figure 3. Correlation between the first GCS score at prehospital presentation and the second GCS score at hospital admission (n=336 complete data sets). The diagonal represents patients with no change in GCS score during their prehospital treatment. The number of patients is inscribed within each dot and reflected by the dot size. A change of ±2 points between first and second GCS score was considered clinically irrelevant (unfilled circles). Patients with changes of their GCS score of 3 or more points are considered clinically relevant (filled circles).

Figure 4. Correlation between first GCS score and blood alcohol level for male (□) and female (♦) patients.

Figure 5. Distribution of the first GCS score (A) and age (B) for patients without aspiration versus proven aspiration, presented as box plots.

Ethics Statement

The study was approved by the local ethics board of Heidelberg University (S-329/2013)

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Statements

a. Funding Statement: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

b. Competing Interest: None declared.

c. Data Sharing Statement: Data may be obtained from a third party and are not publicly available

d. Contributorship Statement

MC, AH, EP, RK planned the study and performed the data acquisition. Statistical analysis was performed by TB. Manuscript writing and editing was performed by MC, AH, EP, TB, RK. The manuscript was submitted by MC.

e. Word count

3.694

Figure 1

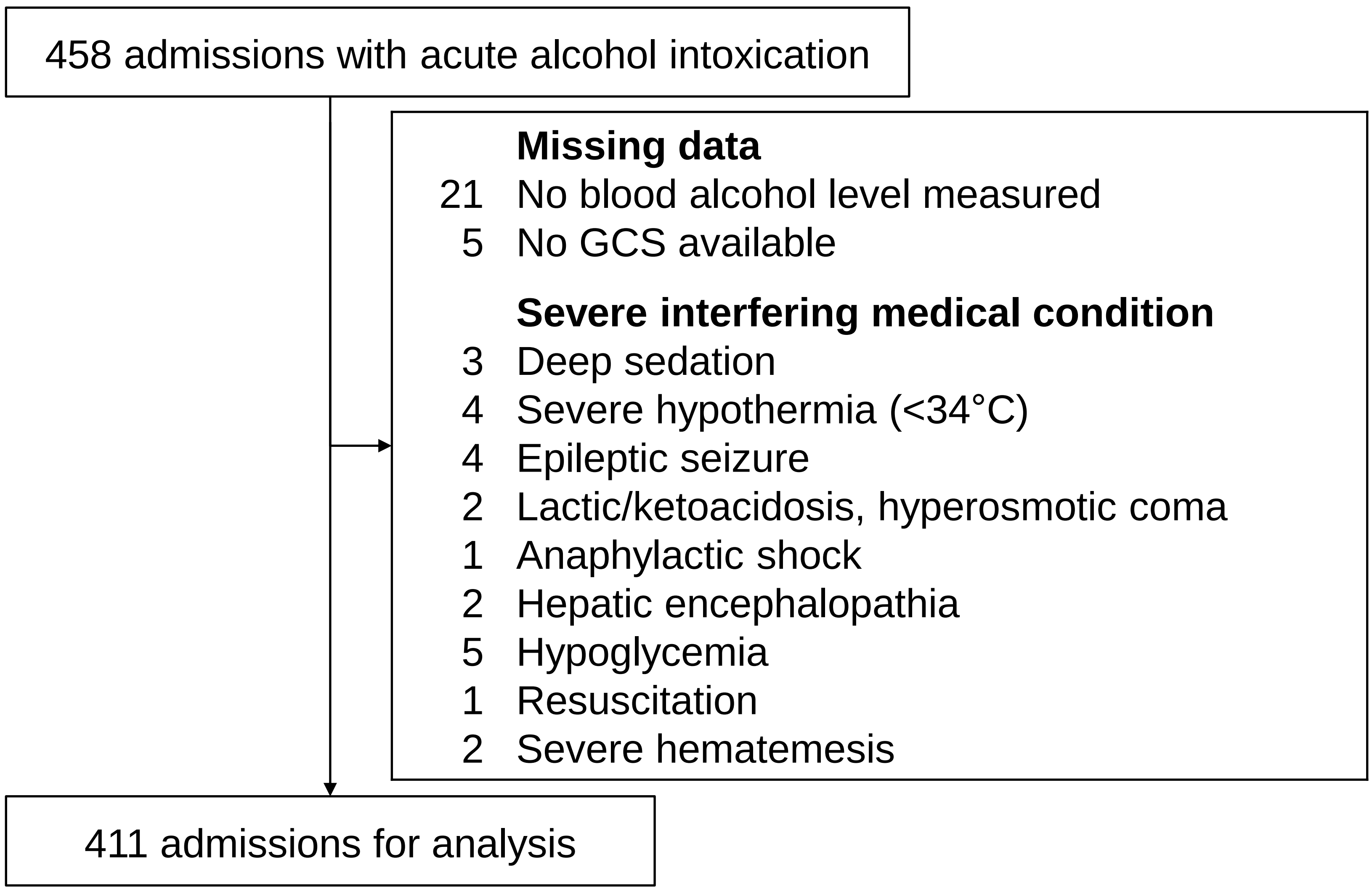

458 admissions with acute alcohol intoxication
Missing data
21 No blood alcohol level measured
5 No GCS available
Severe interfering medical condition
3 Deep sedation
4 Severe hypothermia (<34°C)
4 Epileptic seizure
2 Lactic/ketoacidosis, hyperosmotic coma
1 Anaphylactic shock
2 Hepatic encephalopathia
5 Hypoglycemia
1 Resuscitation
2 Severe hematemesis
411 admissions for analysis

Figure 2

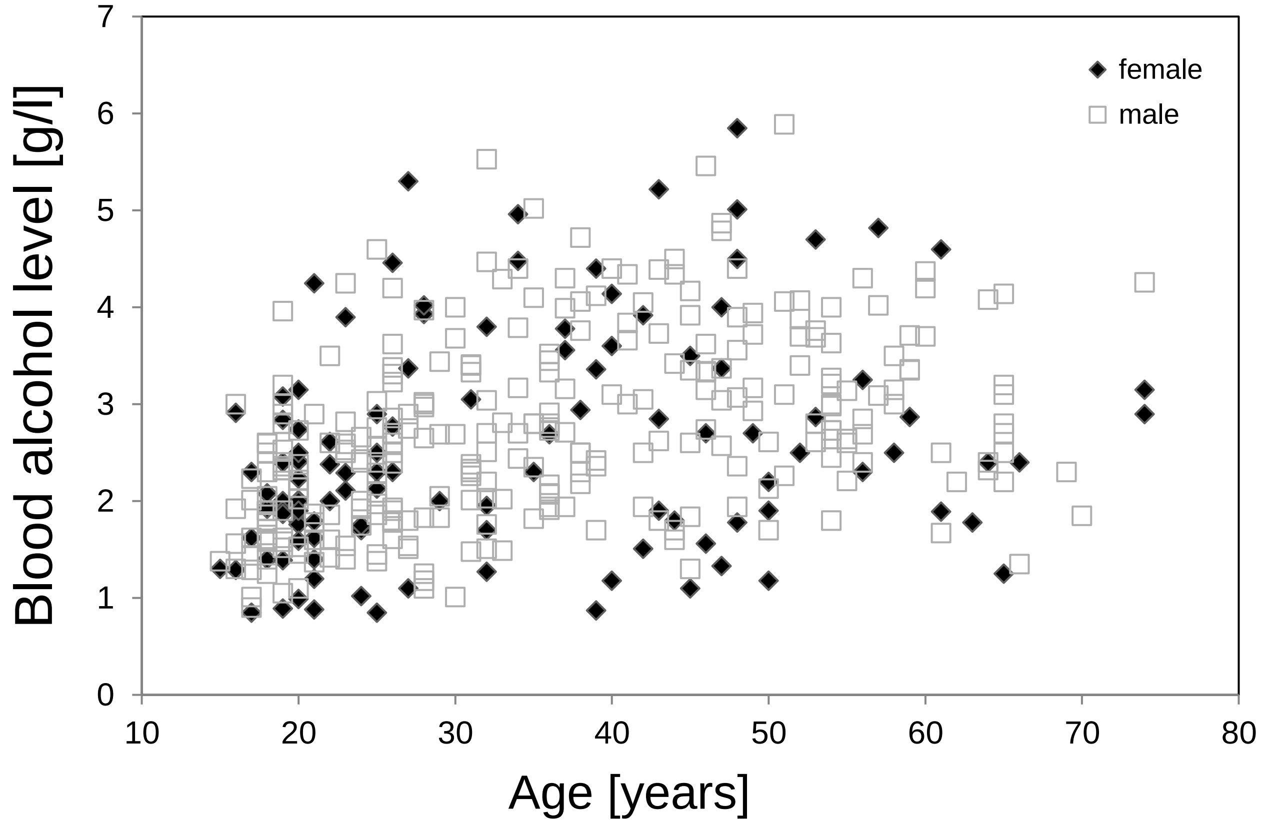

7
6
5
4
3
2
1
0
Blood alcohol level [g/l]
female
male
10
20
30
40
50
60
70
80
Age [years]

Figure 3

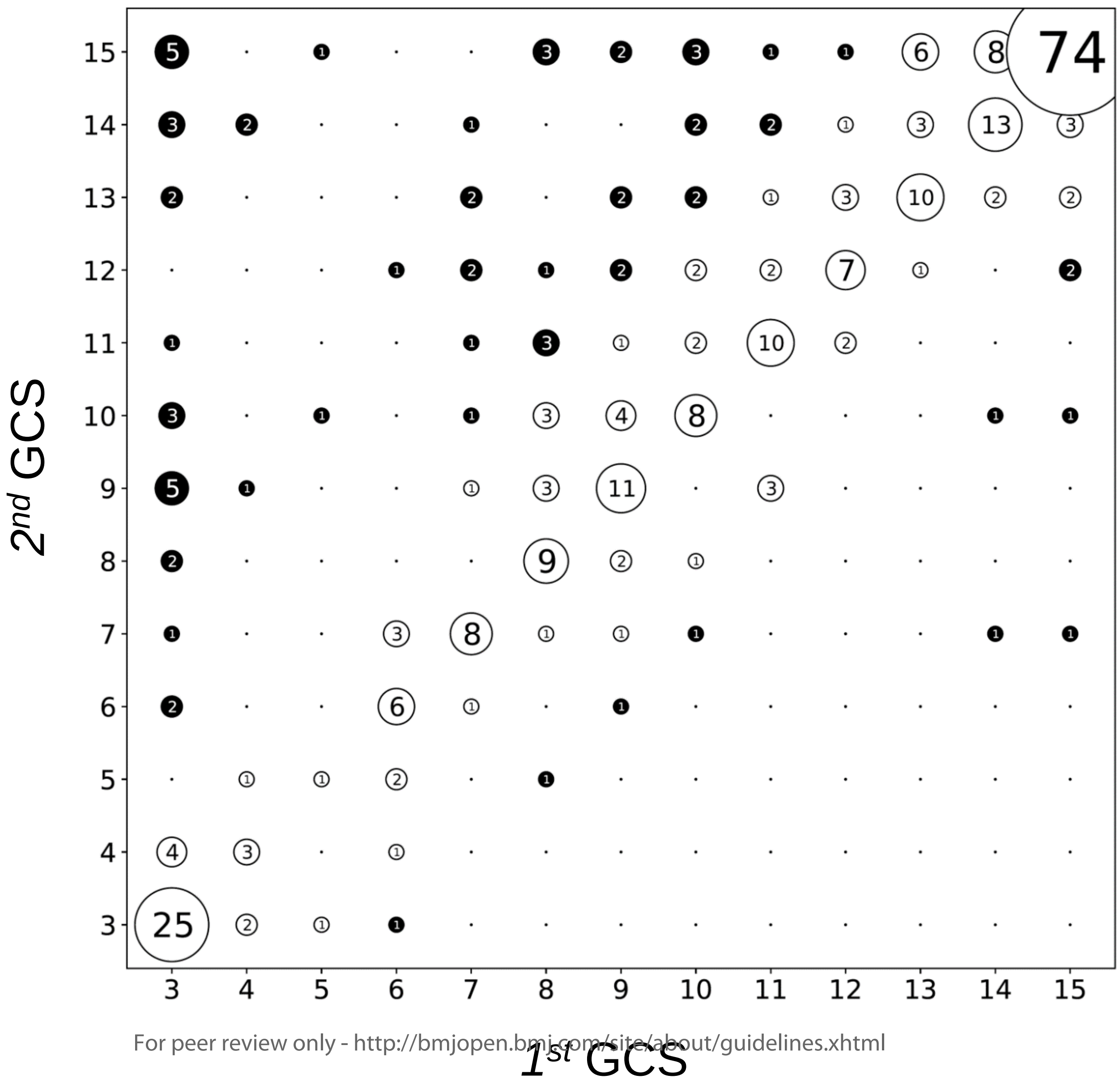
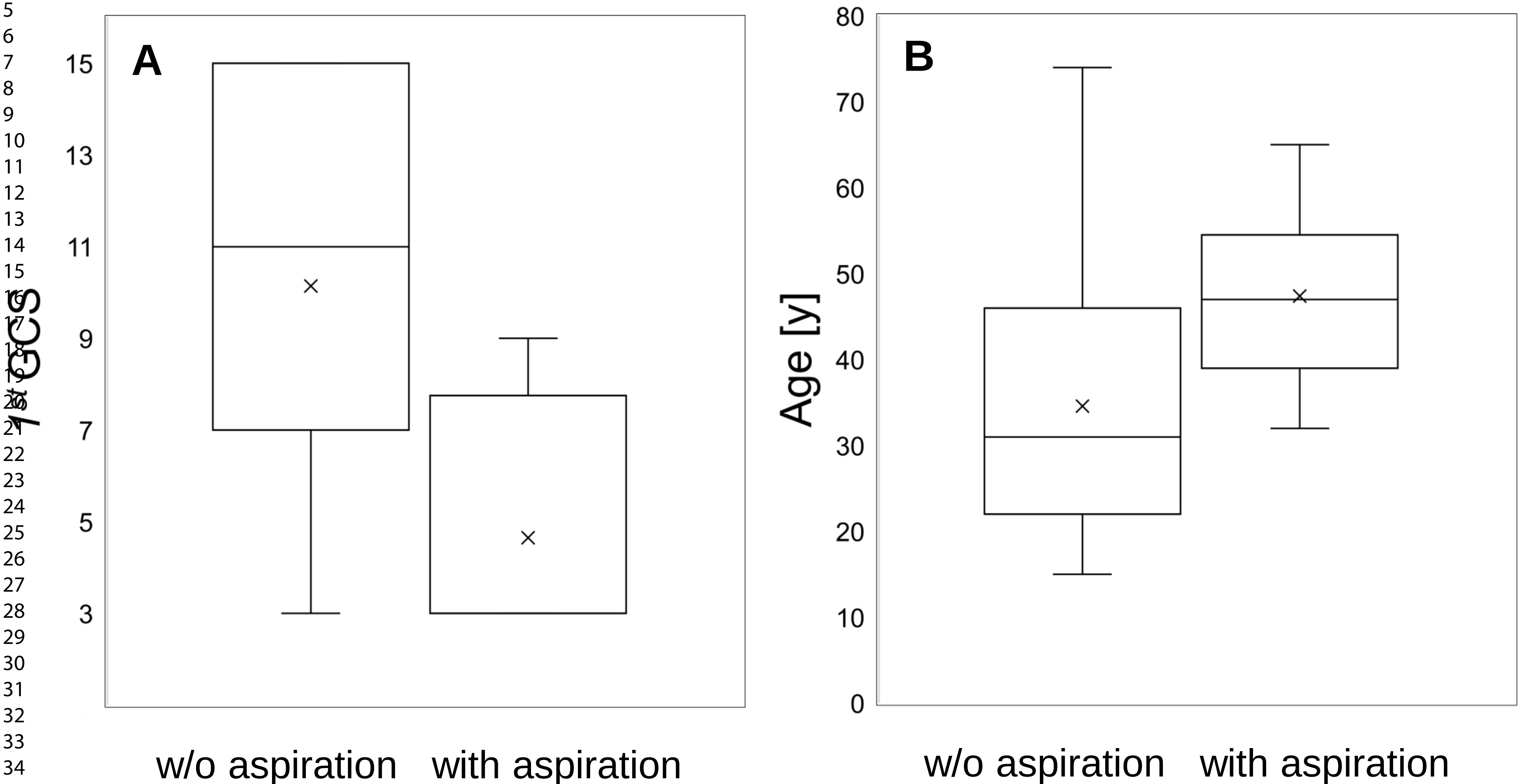


Figure 4


15
14
13
12
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
6
7
female
male
1st GCS
Blood alcohol level [g/l]

Figure 5


A
1st GCS
15
13
11
9
7
5
3
w/o aspiration
with aspiration
B
Age [y]
80
70
60
50
40
30
20
10
0
w/o aspiration
with aspiration

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-10

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-10
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.