

## **Treatment profile and one-year mortality among non-traumatic intensive care unit patients with alcohol-related health problems**

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## **Treatment profile and one-year mortality among non-traumatic intensive care unit patients with alcohol-related health problems**

*Background:* Long-term excessive use of alcohol leads to severe complications, which often require treatment in intensive care unit (ICU). The aim was to study the associations between alcohol-related health problems and treatment profile, as well as one-year mortality among patients with non-trauma-related ICU admissions.

*Methods:* Information on the history of alcohol-related health problems or excessive alcohol use, and ICU treatment were collected retrospectively from electronic medical records and ICU patient data management system at the Oulu University Hospital, Finland. Information on one-year mortality was obtained from the Finnish Population Register Center.

*Results:* According to the medical records, 32.9% (n=296) of the total of 899 admissions the patient had a history of alcohol-related problems. In the alcohol group, intoxications were more frequent and respiratory and cardiovascular causes less frequent, compared to those without alcohol-related problems. The patients without alcohol-related problems had higher rate of previous comorbidities compared with the alcohol group. There were no differences concerning age, severity-of-illness scores, length of stay, or intensive care outcome. The mortality during the one-year follow-up was 32.8% in total; 35.1% among those without alcohol-related history, and 28.0% in the alcohol group (P=0.041). The difference in mortality appeared during the first month from the admission and remained throughout the follow-up period. The highest one-year mortality (59.3%) was observed among patients with alcohol-related liver disease.

*Conclusion:* Every third patient admitted to ICU had excessive alcohol use or alcohol-related diseases, and the patients with alcohol-related liver disease had the poorest one-year survival rate. We found higher long-term mortality in non-alcohol-related admissions which can be explained by the case mix including lower rate of chronic diseases, such as malignancies and coronary artery

disease and higher rate of low-risk admission diagnoses in the alcohol group.

**Keywords:** Alcohol, Intensive Care, Outcome, Mortality

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## **Introduction**

Alcohol misuse is a substantial health problem globally.<sup>1,2</sup> In Finland, alcohol-related deaths comprised 14.5% of total mortality in the working population in year 2014.<sup>3</sup> Long-term excessive use of alcohol leads to severe somatic complications, such as liver cirrhosis, pancreatitis, dilated cardiomyopathy, hepatic encephalopathy and gastrointestinal (GI) hemorrhage.<sup>4,5</sup> Preoperative alcohol consumption has also been associated with admission to intensive care unit.<sup>6</sup> Previous studies have reported the proportion of alcohol-related ICU admissions ranging from 12% to 34%.<sup>7-9</sup> Most of the patients were admitted with intoxication or neurological diagnosis, and also GI complications and traumas were more common in this patient group.<sup>9</sup>

Excessive alcohol use increases the risk of postoperative complications and severe infections, such as sepsis and pneumonia, during the intensive care.<sup>4,6-8,10</sup> However, the previous studies concerning mortality among ICU patients misusing alcohol have shown mixed results. Some studies have reported that mortality is substantially increased among patients with alcohol misuse<sup>7-8,11</sup> whereas other studies have found no significant difference when compared with ICU patients without alcohol misuse.<sup>9,12</sup> However, alcohol related liver disease has been associated with poor short- and long-term outcome in several previous studies.<sup>13-15</sup>

Understanding the clinical features and prognosis pertaining to the patients with alcohol misuse is essential to ensure accurate treatment and resource management in the health services. The aims of the present study were 1) to examine the associations between clinical features and alcohol misuse and alcohol-related disease among the non-trauma-related ICU admissions, and 2) to compare one-year mortality among ICU patients with alcohol misuse to those without.

## Materials and methods

### *Setting*

This retrospective study, based on medical records, was conducted in Oulu University Hospital, in Finland. The setting is a tertiary, academic teaching hospital with 26 ICU beds. The population of the referral area of the hospital district included approximately 400 000 inhabitants in 2014. Patients are admitted also outside of this hospital district from all Northern Finland when university hospital– level care is required, including neurosurgery, cardiac surgery and advanced trauma care. Due to the retrospective design of the study, no statement from the ethics committee was obtained, following the local policy. The study protocol was approved by the hospital administration (reference no. 209/2014) and the study was registered in Ombudsman’s office.

### *Patients*

All non–trauma-related admissions, except post–cardiac surgery admissions and elective post-operative admissions, to ICU were included in the study. The demographic data, including age, gender, cause of ICU admission, the number of previous admissions within four years before the ICU admission due to traumas, intoxications or pancreatitis, as well as any previous alcohol-related admissions to ICU, were obtained from the electronic medical records in the hospital information system. The data on laboratory markers including blood ethanol concentration (EtOH) on admission, mean corpuscular volume (MCV), aminotransferases (AST, ALT), gamma-glutamyltransferase ( $\gamma$ GT), international normalized ratio (INR) and albumin were obtained from the hospital’s electronic laboratory records when available. The ICU patient data management system (PDMS) was used to obtain data during the ICU stay, including severity-of-illness scores on Acute Physiology and Chronic Health Evaluation (APACHE II)<sup>16</sup>, Sequential Organ Failure Assessment (SOFA)<sup>17</sup> and Therapeutic Intervention Scoring System (TISS) (cumulative score).<sup>18</sup>

The data concerning immunosuppression, malignancies, delirium during the ICU stay, the need of organ support, the length of ICU and hospital stay, and the ICU and hospital outcome were retrieved from the PDMS. A patient was considered having delirium if amnesia, disorientation, delusions, or hallucinations had been recorded during the ICU stay. The follow-up period concerning mortality lasted until the end of the year 2015. The Finnish Population Register Centre provided the dates of death of the non-survivors.

#### *History of alcohol-related health problems*

The admission was considered alcohol-related if the admission diagnosis was alcohol-related liver disease, alcohol-related pancreatitis or alcohol intoxication. Medical records were reviewed to discover previous alcohol-related diagnoses or reference to excessive use of alcohol. The patients with alcohol-related admission, history of excessive use of alcohol, or previous alcohol-related diagnosis were considered having a history of alcohol-related health problems, referred later as ‘alcohol group’. Respectively, the patients without a history of alcohol-related health problems formed the non-alcohol group. The patients whose medical records were not extensive enough to provide this information were excluded from the study. To ensure the reliability of the screening process, laboratory markers indicating high alcohol consumption, such as blood EtOH-concentration on admission, AST, ALT, INR,  $\gamma$ GT, albumin and MCV values, were reviewed.

#### *Statistical analysis*

Statistical analysis was performed using SPSS software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Categorical data are expressed in numbers (N) and percentages (%) and continuous variables are presented as medians and 25th-75th percentiles (25th-75th PCT). Two-tailed *P* values less than 0.05 were considered statistically significant. The categorical data was tested using Pearson’s chi-square, and Mann-Whitney test was

used to compare medians across the groups. Kaplan-Meier analysis was used to compare survival following the ICU stay. Standardized mortality ratios (SMRs) were calculated according to the APACHE II risk score (rAPACHE), and the data are presented with 95% confidence intervals (CIs).

## Results

### *Patient demographics*

There were a total of 2158 ICU admissions during the study period **between January 1 and December 31, 2014**. For the analysis, we excluded 631 (29.2%) post-cardiac surgery admissions, 329 (15.2%) elective, post-surgery admissions and 213 (9.9%) trauma admissions leaving 985 non-trauma-related emergency admissions (45.6% of all ICU admissions). Information on patient's alcohol-related health problems was available for 899 (91.3%) of these 985 admissions, and these cases were included in the analyses. In 296 (32.9%) of these 899 admissions the patient was identified to have a history of alcohol-related health problems (Table 1). The 899 ICU admissions included 847 individual patients, 268 in alcohol group and 579 in non-alcohol group ( $P<0.001$ ). Readmissions during the hospital stay were recorded in 12 (4.2%) of 296 admissions in alcohol group in contrast to 40 (7.1%) of 603 admissions in non-alcohol group ( $P=0.119$ ). In 52 (5.8%) of the admissions classification code F10.1, the harmful use of alcohol, was recorded as side diagnosis.

There were no differences in age, APACHE II or APACHE chronic health point-scores or cumulative TISS scores between alcohol and non-alcohol groups. The SOFA scores on admission and the maximum SOFA scores during the ICU stay were higher in the alcohol group (6 vs 5,  $P=0.002$ , and 8 vs 7,  $P=0.003$ ). The difference remained also in the admission SOFA score when Glasgow Coma Scale (GCS) score was excluded (non-GCS SOFA scores) (5 vs 4,  $P=0.049$ ). Patients in the alcohol group had a higher rate of previous traumas, acute alcohol

pancreatitis, psychiatric diagnoses and intoxications compared with the non-alcohol group. The patients in the non-alcohol group had a higher rate of hematological malignancies, coronary artery disease, use of corticosteroids and ongoing chemotherapy (Table 1). Patients in the alcohol group had higher MCVs and plasma  $\gamma$ GT values compared with the non-alcohol group (Table 2).

### *Causes of the admissions*

Neurological diagnoses were the most common causes for ICU admissions, recorded in 201 (22.4%) of the 899 admissions. Respiratory and cardiovascular causes as well as need for surgery were more frequent in the non-alcohol group compared with the alcohol group, whereas intoxications were more frequent in the alcohol group (Tables 1 and 3). In the alcohol group 27 (9.1%) of the patients were admitted due to alcohol-related liver disease. Pancreatitis, included in the other category, was the cause of the admission in 17 (1.9%) cases, and 9 (52.9%) of these cases occurred in the alcohol group ( $P=0.08$ ).

### *Adverse events and outcome*

In the alcohol group signs of delirium were recorded more frequently (Table 4). There were no significant differences between the groups in terms of the ICU length of stay or intensive care outcome. The median hospital stay was shorter in the alcohol group (8.2 [3.0-15.2] vs 9.1 [5.0-17.0],  $P=0.003$ ). The standardized mortality ratio during the hospital stay was 0.49 for all admissions (95% CI, 0.41-0.58), and 0.40 for the alcohol group admissions (95% CI, 0.28-0.55) and 0.53 for the non-alcohol group admissions (95% CI, 0.44-0.65) (Table 4).

### *One-year mortality in follow-up*

Of the 847 patients, 278 (32.8%) died during the one-year follow-up: 75 of 268 patients (28.0%) in the alcohol group and 203 of 579 patients (35.1%) in the non-alcohol group ( $P=0.041$ ) (Table 4).



The difference in mortality appeared during the first month from the admission and remained throughout the follow-up period (Figure 1). The difference between the groups was present in patients with APACHE II score below 25 when no difference was found in patients with higher APACHE II scores (Figures 2 and 3).

The highest one-year mortality was observed in patients who had been admitted due to alcohol-related liver disease (16 of 27, 59.3%), cardiovascular causes (49 of 109, 44.9%), and respiratory conditions (67 of 177, 37.9%). In contrast, one-year mortality in patients admitted due to intoxication was only 5.8% (3 of 52). Among the 203 non-survivors in the non-alcohol group the ICU admissions were most often due to respiratory causes (61 of 203, 30.0%) and cardiovascular causes (40 of 203, 19.7%), whereas in the alcohol group the patients were admitted for neurological causes (15 of 75, 20.0%) and alcohol-related liver disease (16 of 75, 21.3%) ( $P<0.001$ ) (Tables 3 and 5).

## Discussion

The main finding of the present study is that one-third of the patients admitted to ICU had an alcohol-related admission, history of excessive alcohol use, or previous alcohol-related diagnosis. There were no differences in short-term outcome between the groups, but less-severely ill patients in the alcohol group (severity of illness measured by the APACHE II score on admission) had better long-term survival, which was a surprising finding. This difference can be explained by differences in diagnostic groups and patients' chronic conditions. However, the highest one-year mortality (59.3%) was observed among patients with alcohol-related liver disease.

Acute and chronic abuse of alcohol is a generally known occurrence in ICUs.<sup>4</sup> However, only few studies have been conducted that focus primarily on the prevalence of alcohol-related admissions to the ICU.<sup>7,9,11,19</sup> However, there seems to be a considerable variation between the results, which is mainly explained by diverse definitions alcohol-related conditions, study-specific inclusion criteria and divergent sociocultural factors. In most of the previous studies specific alcohol abuse classifications according to ICD-10 classification were not used.<sup>9,11,19</sup> A previous Finnish study<sup>9</sup> reported that 24% of intensive care admissions were directly alcohol-related. Correspondingly, in the study performed in the UK in 2002 alcohol-related admissions comprised 28% of all admissions<sup>19</sup>, and in the recent Scottish series more than 30%.<sup>7</sup> In turn, the Danish register-based study from 2012 estimated that 7.3% of all ICU patients were alcoholics.<sup>11</sup>

We were not able to find any major differences between alcohol group and non-alcohol group in ICU length of stay or short-term outcome. This is in line with reports from the previous studies that the patients with a history of alcohol abuse had shorter stays in the ICU than the patients in the control group and that no major differences were found in the short-term outcome.<sup>9,12,20</sup> However, we found a significant difference during the one-year follow-up period between the groups. The difference in long-term outcome occurred approximately one month from

the admission and held through the follow-up period. This finding differs from the results of the recent Scottish study<sup>7</sup> that showed worse long-term survival in alcohol abusers. The difference between the present results and the Scottish series can be partly explained by the patient demographics. The patients in the Scottish study were younger (57 vs 62), and septic shock occurred in 20% of the patients.<sup>7</sup> In our study the proportion of patients with septic shock was only 9.8%, which may, for one thing, explain the differences in the long-term results between these studies.

Our results concerning the long-term outcome are in line with previous Danish study<sup>11</sup> that found better 3-year survival among alcoholic patients without complications. Alternatively, in the Danish study the alcoholic patients with complications had worse long-term outcome compared with the non-alcoholic patients. As expected, also in our study the worst long-term outcome was found in patients with alcohol-related liver disease. Several previous studies<sup>13-15</sup> have shown that end-stage liver disease is hardly managed condition resulting in poor short- and long-term outcomes. However, in our series the prevalence of alcohol-related liver disease was not considerable enough to have impact on alcohol group's survival rate. **All the patients in the alcohol group had alcohol-related health problems but not necessarily alcohol related organ failure, which also explains the alcohol group's unexpected survival rate.** Furthermore, our study shows that low-mortality conditions such as intoxications were more prevalent in the alcohol group whereas the non-alcohol group had a higher tendency for malignant diseases and coronary disease and required operative treatment more often.

In our series there were more severe organ dysfunctions in the alcohol group according to the SOFA scores despite better outcome. We have previously examined the risk factors for prolonged ICU stay and hospital mortality in patients with acute drug poisoning and found that poisonings as causes of organ dysfunctions or failures may be considered self-curing conditions, when considering cardiovascular, respiratory and central nervous system scores.<sup>21</sup> The higher

SOFA scores in the alcohol group in the present study without impact on the outcome could be explained by the higher rate of intoxications in the alcohol group and similarly by the higher rate of respiratory and cardiovascular causes in the non-alcohol group. Moreover, we did not find any major differences in APACHE II scores between the groups, and APACHE II overestimated mortality in the present study, especially in the alcohol group. A difference found in admission GCS scores can partly explain the bias in the APACHE II scoring.

There are a few limitations in the present study. Due to the retrospective study design, we were not able to use structured and validated methods to recognize excessive use of alcohol, and therefore it was determined by reviewing patient history available on the medical records. According to the medical records, only in a minority of cases (5.8%) were diagnosed to have an ICD-10 harmful use of alcohol, most likely due to underdiagnosing and recording alcohol use disorders. Further, no systematic screening using validated questionnaires or diagnostic assessment for alcohol use disorder were performed during the treatment period in the ICU. Therefore it is likely that there are false negative cases among the controls. Also, definition of alcohol-related health problem in the present study comprehends a wide range of alcohol users, which should be noted when interpreting the results. However, this limitation is similar in most of the previous studies.<sup>9,11,19</sup> It is notable that we had access to all data recorded in the hospital, and we could review the medical history of the patients reliably. Moreover, we showed differences between the groups in results of laboratory screenings used to detect excessive use of alcohol, which indicates reliable patient recognition. **Finally, when considering the outcome data, we were not able to grade the patients' alcohol-related organ failure, which can be considered as limitation in the present study. However, in our results, the difference in outcome between the groups can be explained by the differences in the case-mix including the rate of chronic diseases and low-mortality conditions.**

## **Conclusions**

Every third patient admitted to ICU had excessive alcohol use or alcohol-related diseases, and the patients with alcohol-related liver disease had the poorest one-year survival rate. We found higher long-term mortality in non-alcohol-related admissions which can be explained by the case mix including lower rate of chronic diseases, such as malignancies and coronary artery disease and higher rate of low-risk admission diagnoses in the alcohol group.

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## **Declaration of Conflicting Interests**

The Authors declare that there is no conflict of interest.

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< Table 1. Age, gender and treatment profile of the 899 patients admitted to ICU.>

< Table 2. Laboratory markers of 899 patients admitted to ICU.>

< Table 3. Causes of the admissions of 899 patients admitted to ICU.>

< Table 4. Complications and outcome of 899 patients admitted to ICU. >

< Table 5. The cause of the ICU admission and the previous medical conditions of the 278 non-survivors.>

<Fig 1. Kaplan-Meier survival curves of the 899 patients admitted to ICU divided into alcohol and non-alcohol groups>

<Fig 2. Kaplan-Meier survival curves of the 899 patients admitted to ICU with APACHE II score 25 or less divided into alcohol and non-alcoholbuse groups>

<Fig 3. Kaplan-Meier survival curves of the 899 patients admitted to ICU with APACHE II score above 25 divided into alcohol and non-alcohol groups>