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Increased risk of pyogenic liver abscess in patients with alcohol intoxication: A population-based retrospective cohort study

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ABSTRACT

We designed a population-based retrospective cohort study to investigate the association between the event of alcohol intoxication and the risk of pyogenic liver abscess. The present study enrolled 245,076 patients with a history of alcohol intoxication from 2000 to 2010 and matched each of them with four comparison patients, with similar mean age and sex ratios. We determined the cumulative incidences and adjusted hazard ratios (aHRs) of liver abscess. A significant association was observed between alcohol intoxication and liver abscess. The incidence density rate of liver abscess was 3.47-fold greater in the alcohol intoxication (AI) cohort than in the non-AI cohort (12.2 vs. 3.43 per 10,000 person-years), with an adjusted HR (aHR) of 2.64 (95% CI = 2.26 to 3.08). This population-based study positively associated the event of alcohol intoxication with increased risk of liver abscess. Our findings warrant further large-scale and in-depth investigations in this area.

Introduction

Pyogenic liver abscess as a potentially grave illness is the most common type of visceral abscess (Altemeier, Culbertson, Fullen, & Shook, 1973). The annual incidence of liver abscess has been estimated at 17.6 cases per 100,000 persons in Taiwan (F–C. Tsai, Huang, Chang, & Wang, 2008). Its risk factors include diabetes mellitus, hepatobiliary or pancreatic disease, and need for liver transplant (Chan et al., 2005; Huang et al., 1996; Mohsen, Green, Read, & McKendrick, 2002; Thomsen, Jepsen, & Sørensen, 2007).

Many people drink beverages containing ethanol. Alcohol intake in moderation appears to lower the risk of myocardial infarction and associated cardiovascular diseases. However, alcohol abuse and acute alcohol intoxication are associated with numerous adverse complications. Alcohol is absorbed in the gastrointestinal system and then metabolized primarily in the liver by alcohol dehydrogenase (Lieber, 1982). Currently, the strongest evidence of alcohol being a potential cause of liver disease comes from epidemiologic data. Furthermore, the volume of alcohol ingestion and the duration of alcohol abuse are positively correlated with increased risk of alcoholic liver disease (Lelbach, 1975; Zakim, Boyer, & Montgomery,

Abbreviations: aHR, adjusted hazard ratio; AI, alcohol intoxication; BNHI, Bureau of National Health Insurance; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; NHI, National Health Insurance; NHIRD, National Health Insurance Research Database; HRs, hazard ratios; PLA, pyogenic liver abscess; SD, standard deviation.

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1990).

Therefore, this study was conducted to investigate the association between alcohol intoxication and the risk of pyogenic liver abscess via a population-based retrospective cohort study. The data are from the database of National Health Insurance of Taiwan.

Materials and methods

Data source

The Taiwan National Health Insurance (NHI) program was established in 1995, and the coverage rate reached 99% of 23.74 million Taiwan citizens (National Health Research Institutes [NHRI]). In cooperation with the Bureau of National Health Insurance (BNHI), the National Health Research Institutes (NHRI) established several datasets for public use. The details of the NHI program have been previously documented (Chung & Lin, 2016; Tsai et al., 2015). In this cohort study, disease history of the insured people was collected from inpatient files. Diseases are coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). To prevent researchers from attempting to identify a particular patient, the identities of the insured people were scrambled. This study was approved by the Ethics Review Board of China Medical University and Hospital in Taiwan (CMUH-104-REC2-115).

Study participants

Patients aged 20 years and older, who were newly diagnosed with a history of alcohol intoxication (AI) from 2000 to 2010 (ICD-9-CM codes 303, 305.0, V113) were identified as the AI cohort. For each AI case, we randomly selected four persons without medical claims for AI care (non-AI cohort), with frequencies matched for ages (every 5-year span), sex, index year, and history of diabetes. The patients diagnosed at the baseline with pyogenic liver abscess (PLA) (ICD-9-CM code 572.0) and amoebic liver abscess (ICD-9-CM 006.3) were excluded from the study.

Outcome measures and comorbidity

The AI and the non-AI cohorts were followed until the PLA appeared, or were censored from the study because of failure to follow-up, death, or the end of 2011. Patients with a history of diabetes (ICD-9-CM code 250), hypertension (ICD-9-CM codes 401–405), hyperlipidemia (ICD-9-CM code 272), cancer (ICD-9-CM codes 140–208), chronic obstructive pulmonary disease (COPD) (ICD-9-CM codes 491, 492, 496), heart failure (ICD-9-CM code 428), biliary stones (ICD-9-CM code 574), alcoholic liver damage (ICD-9-CM codes 571.0, 571.1, and 571.3), and cirrhosis (ICD-9-CM codes 571.2, 571.5, and 571.6) identified at the baseline were considered as comorbidities.

Statistical analysis

According to the previous inclusion criteria, we first demonstrated the characteristics distinguishing the AI cohort and the non-AI cohort. The mean age and follow-up time were presented via mean and standard deviation (SD); the mean age and average follow-up time difference were tested with the Student's *t*-test. The category variables, such as age, group, gender, and PLA-associated comorbidities between cohorts, were demonstrated by number and percentage and were tested for the difference by Chi-square test. We used the Kaplan–Meier method to measure cumulative incidence of PLA curves for each cohort and tested the curves using a log-rank test. We calculated the overall, gender-specific, age-specific, comorbidity-specific, and follow-up-specific incidence density rates of PLA with person-years in each cohort. Univariable and multivariable Cox proportional hazards regression models were used to assess the hazard ratios (HRs) and 95% confidence intervals (CIs) for PLA associated with AI. Further data analyses of interactions were separately performed to evaluate the joint effect for PLA risk between AI and PLA-associated comorbidities. We used SAS 9.4 software (SAS Institute, Cary, NC, USA) to manage data and to perform statistical analysis. The significance level was set at less than 0.05 as p value for a two-tailed t-test.

Results

We identified 61,269 patients in the AI cohort and 245,076 patients in the non-AI cohort with similar distributions in age, sex, and comorbidity of diabetes (Table 1). There were 47.9% of subjects in the age 35–49 group and more male subjects (90.1%). The mean ages of the AI and non-AI cohorts were 44.8 ± 12.3 and 44.5 ± 12.8 years, respectively. Compared with the non-AI cohort, the AI cohort had a higher prevalence of hypertension, hyperlipidemia, cancer, COPD, heart failure, biliary stones, alcoholic liver damage, and cirrhosis (all p values < 0.001). The average follow-up periods for AI and non-AI cohorts were 5.17 (SD = 3.33) and 6.24 (SD = 3.26) years, respectively. The results of Kaplan–Meier analysis showed that the AI cohort had a 0.74% higher cumulative incidence of PLA than the non-AI cohort (log-rank test, p value < 0.001) (Fig. 1).

The incidence density rate of PLA was 3.47-fold greater in the AI cohort than in the non-AI cohort (12.2 vs. 3.43 per 10,000 person-years), with an adjusted HR (aHR) of 2.64 (95% CI = 2.26 to 3.08) (Table 2). The PLA incidence was greater in men than in women and was increased with age and comorbidity in both cohorts. The relative risks of PLA in sex-specific AI cohorts compared to non-AI cohorts were significantly higher for both women (aHR = 2.53, 95% CI = 1.28–5.03) and men (aHR = 2.64, 95% CI = 2.25–3.09). Regardless of the age or the presence of comorbidity, the risk for PLA was higher in the AI cohort than in the non-AI cohort.

Compared with the non-AI patients without these comorbidities, those with only alcohol intoxication had a higher risk of PLA (aHR = 4.37, 95% CI = 3.49–5.48) (Table 3). Moreover, compared

Table 1
Comparison of demographics and comorbidity between alcohol intoxication patients and controls.

	Alcohol intoxication		
	Yes (N = 61,269)	No (N = 24,5076)	*p* Value
	n (%)	n (%)	
Age, years			0.99
20–34	13,535 (22.1)	54,140 (22.1)	
35–49	29,356 (47.9)	117,424 (47.9)	
>50	18,378 (30.0)	73,512 (30.0)	
Mean (SD)[a]	44.8 (12.3)	44.5 (12.8)	<0.001
Gender			0.99
Female	6050 (9.9)	24,200 (9.9)	
Male	220,876 (90.1)	55,219 (90.1)	
Comorbidity			
Diabetes	8816 (14.4)	35,264 (14.4)	0.99
Hypertension	10,773 (17.6)	18,488 (7.5)	<0.001
Hyperlipidemia	7385 (12.1)	8838 (3.6)	<0.001
Cancer	1370 (2.2)	4259 (1.7)	<0.001
COPD	2486 (4.1)	2733 (1.1)	<0.001
Heart failure	1134 (1.9)	2031 (0.8)	<0.001
Biliary stone	3403 (5.6)	3281 (1.3)	<0.001
Alcoholic liver damage	14,047 (22.9)	1884 (0.8)	<0.001
Cirrhosis	12,119 (19.8)	2742 (1.1)	<0.001

Chi-square test examined categorical data.
[a] *t*-Test examined continuous data.