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Possible increased risk of colonic diverticular disease from alcohol intoxication or abuse

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Abstract

Alcohol consumption has been suggested as a potential risk factor for diverticular diseases. This study investigated the association between alcohol intoxication or abuse and colonic diverticular disease (CDD).

Using the National Health Insurance Research Database of Taiwan from January 1, 2000, to December 31, 2008, 51, 866 subjects newly diagnosed with alcohol intoxication were enrolled in this study as the alcohol intoxication cohort. The control (nonalcohol intoxication) cohort was frequency-matched 1:4 by age, sex and index year. Data were analyzed using a Cox proportional hazards model.

The overall incidence of CDD (per 10,000 person-years) for the alcohol intoxication and control cohorts was 16.4 and 3.46, respectively. Compared with patients in the control cohort (95% confidence interval [CI] = 2.76–3.74), those with alcohol intoxication exhibited a 3.21-fold risk of CDD; the risk was particularly higher in male patients (adjusted hazard ratio [aHR] = 3.19, 95% CI = 2.72–3.74) and in those aged <45 years (aHR = 4.95, 95% CI = 3.91–6.27). The alcohol intoxication still had higher risk of CDD than nonalcohol intoxication, regardless of subjects without comorbidity (aHR = 3.38, 95% CI = 2.77–4.11) or with (aHR = 2.85, 95% CI = 2.25–3.61).

There was a significant relationship between alcohol intoxication or abuse and CDD.

Abbreviations: aHR = adjusted hazard ratio, CDD = colonic diverticular disease, CI = confidence interval, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, LHID2000 = longitudinal health insurance database 2000, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database.

Keywords: acute pancreatitis, alcohol abuse, alcohol consumption, alcohol intoxication, anxiety, colonic diverticular disease (CDD), depression, liver cirrhosis, sleep disorder

Key Points

- Alcohol intoxication is a potential risk factor for colonic diverticular disease (CDD); however, data on the association between alcohol intoxication and CDD are insufficient.
- The risk of CDD was higher in patients with alcohol intoxication and was particularly higher in male patients and in those aged <45 years.

1. Introduction

Alcohol abuse and dependence remain highly prevalent.[1] Among working-age adults, approximately10% of deaths result from excessive alcohol consumption.[2] Alcohol can be a significant contributing factor to many medical conditions.[3] The medical consequences of drinking alcohol may manifest in any organ system of the body.[4] An estimated 4% to 40% of medical and surgical patients experience problems related to alcohol intoxication or abuse.[5] Alcohol consumption is increasing in many developing countries, which face increasing alcohol-related health problems.[6]

Colonic diverticular disease (CDD) affects increasingly more developing countries worldwide.[7] Its prevalence in South Asia is between 8% and 25%.[7–9] Its incidence increases with age, reaching a peak during the fifth decade of life.[7,10,11] In Japan, the prevalence of CDD in the 1960s was 2.1%, but it increased to

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28% in 1997.[7,9,11–13] In South Korea, the prevalence was 12% in 2010.[14] The pathogenic mechanisms and predisposing factors of CDD are not completely understood. However, the increased prevalence of CDD in Asian countries has shown that factors related to the environment and lifestyle play crucial roles in pathogenesis.[7,14–16]

A low-fiber or high-fiber diet, constipation, and high bowel movement frequency are widely considered the etiological factors for CDD.[7,15–19] Recent studies have proposed alcohol consumption as a new risk factor for uncomplicated diverticulosis.[14,20] Therefore, our study aimed to determine the relationship between alcohol intoxication or abuse and CDD.

2. Methods

2.1. Data source

The National Health Insurance Research Database (NHIRD) involves all the claims data from the Taiwan National Health Insurance (NHI) program. The Taiwan NHI, launched in March 1995, is a single-payer and compulsory health insurance program for Taiwan's 23 million residents, of whom the insurance coverage rate reached 99% in 1998.

The claims data of the NHIRD include a registry of beneficiaries, disease records, and other medical services. The database is renewed every year. In this study, disease history data for the study patients were collected from the inpatient file. The Taiwan NHI uses the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) to establish its disease record system. To maintain patient privacy, all personal identification numbers were encrypted before the databases were released to the public. This study was approved by the Ethics Review Board of China Medical University Hospital (CMUH104-REC2-115).

2.2. Study population

In this study, we established an alcohol intoxication cohort and a control cohort, and observed these cohorts for CDD development. The alcohol intoxication cohort consisted of patients newly diagnosed with alcohol intoxication (ICD-9-CM 303, 305.0, and V113) from January 1, 2000 to December 31, 2008, whereas the comparison cohort comprised randomly selected patients without a history of alcohol intoxication. The cohorts were frequency matched 1:4 according to age and sex. The index date for the alcohol intoxication cohort was set on the first day of alcohol intoxication diagnosis, and that for the control cohort was randomly assigned a month and day within the same year of the matched cases. We excluded patients with a history of CDD (ICD-9-CM 562.1) before the index date. We started observing both study cohorts from the index date, and terminated follow-up for a patient when he or she withdrew from the health insurance, in the event of CDD occurrence, or on December 31, 2011.

Patients with comorbidity were defined as those diagnosed with comorbidity before the end of the follow-up. The comorbidities in this study included hypertension (ICD-9-CM 401–405), hyperlipidemia (ICD-9-CM 272), diabetes (ICD-9-CM 250), depression (ICD-9-CM 296.2, 296.3, 296.82, 300.4, and 311), anxiety (ICD-9-CM 300.00), fibromyalgia (ICD-9-CM 729.1), sleep disorder (ICD-9-CM 307.4, 780.5), acute pancreatitis (ICD-9-CM 577.0), cirrhosis (ICD-9-CM 571.2, 571.5, and 571.6), hepatitis B (ICD-9-CM V02.61, 070.20, 070.22, 070.30, and 070.32), and hepatitis C (ICD-9-CM V02.62, 070.41, 070.44, 070.51, and 070.54).

2.3. Statistical analysis

To present the distribution of the study patients, we showed the mean and standard deviations (SDs) for age, number of years, percentage of sex, and comorbidity. The *t* test and Chi-square test were used to test the distribution difference between the study cohorts. The incidence density of CDD was measured as the number of CDD events divided by the sum of the follow-up time (per 10,000 person-year). The Kaplan–Meier method and log-rank test were used respectively to estimate cumulative incidence curves for the 2 study cohorts and to test the curve difference. The incidence rate ratio (IRR) of CDD in the alcohol intoxication and nonalcohol intoxication cohorts was measured for these variables by using Poisson regression analysis, which presented by IRR and 95% confidence intervals (95% CIs). By using a Cox proportional hazards model, the adjusted hazard ratios (aHRs) and 95% CIs were estimated for patients with alcohol intoxication and for those in the control cohort (as a reference for comparison). To consider the effect of the severity of alcohol intoxication, a trend analysis was applied using a Cox proportional hazards model. Statistical analyses were performed using SAS 9.4 software (SAS Institute, Cary, NC). The incidence curves were plotted using R software (R Foundation for Statistical computing, Vienna, Austria). A 2-sided $P < .05$ was considered significant.

3. Results

The number of enrolled patients with alcohol intoxication was 51,866, whereas that in the control cohort was 207,464 (Table 1). Ninety percent of the study patients were men. The mean age was 44 years (SD = 12), and the majority age group was 35 to 65 years old. The comorbidity proportions in the alcohol intoxication cohort were greater than those in the control cohort ($P < .0001$).

Table 2 shows that the IRR of CDD was 4.75-fold greater in the alcohol intoxication cohort than in the control cohort (16.4 vs 3.46 per 10,000 person-year). The cumulative incidence of CDD after an 11-year follow-up was greater in the alcohol intoxication cohort than in the control cohort (log-rank test, $P < .0001$; Fig. 1). After adjustment for age, sex, and comorbidities, patients with alcohol intoxication had a 3.21-fold higher risk of CDD compared with the controls (hazard ratio [HR] = 3.21, 95% CI = 2.76–3.74). Both male and female patients with alcohol intoxication were significantly associated with an increased risk of CDD (men: HR = 3.19; women: HR = 3.44; both men and women: $P < .0001$). In patients aged <45 years, those with alcohol intoxication had a 4.95-fold increased risk of CDD compared with those without alcohol intoxication (HR = 4.95, 95% CI = 3.91–6.27). For patients aged ≥45 years, the HR of CDD was 2.34 (95% CI = 1.89–2.88) for those with alcohol intoxication. For patients in the alcohol intoxication cohort with and without comorbidity, the HRs of CDD were 3.38 (95% CI = 2.77–4.11) and 2.85 (95% CI = 2.25–3.61), respectively.

Table 3 demonstrates the joint effects of alcohol intoxication and comorbidity on the CDD risk. Relative to patients in the control cohort without comorbidity, those in the alcohol intoxication cohort with comorbidity had the highest risk of CDD. The HRs of CDD for patients in the alcohol intoxication

Table 1

Comparison of demographics and history of comorbidity between alcohol intoxication, and nonalcohol intoxication cohorts.

	Alcohol intoxication				
	No (N = 207,464)		Yes (N = 51,866)		
	n	%	n	%	*P*-value
Sex					.99
Women	20,508	9.89	5127	9.89	
Men	186,956	90.1	46739	90.1	
Age, yr					.99
<35	48,784	23.5	12196	23.5	
35–65	144,308	69.6	36077	69.6	
≥65	14,372	6.93	3593	6.93	
Mean (SD)*	44.3 (12.6)		44.3 (12.5)		.5164
Comorbidity					
Hypertension	3088	1.49	1163	2.24	<.0001
Hyperlipidemia	2891	1.39	908	1.75	<.0001
Diabetes	1867	0.90	877	1.69	<.0001
Depression	1512	0.73	9375	18.1	<.0001
Anxiety	723	0.35	1710	3.30	<.0001
Fibromyalgia	652	0.31	1424	2.75	<.0001
Sleep disorder	2348	1.13	5862	11.3	<.0001
Acute pancreatitis	1903	0.92	12033	23.2	<.0001
Cirrhosis	3451	1.66	15823	30.5	<.0001
Hepatitis B	3750	1.81	5746	11.1	<.0001
Hepatitis C	2038	0.98	3971	7.66	<.0001

Chi-square test.
* Student *t*-test.

cohort without comorbidity and for those with comorbidity were between the HRs of CDD for patients in the control cohort and those in the alcohol intoxication cohort with comorbidity. We observed that patients in the alcohol intoxication cohort with acute pancreatitis had a 9.03-fold increased risk of CDD compared with those without acute pancreatitis (HR = 9.03, 94% CI = 7.63–10.7).

Table 4 presents the risk of CDD in patients with different severities of alcohol intoxication. The HRs of CDD were 1.98 (95% CI = 1.64–2.39), 4.73 (95% CI = 3.86–5.79), and 10.3 (95% CI = 8.27–12.7) for patients with mild, moderate, and severe alcohol intoxication, respectively. The results also indicated a significantly increasing trend of the risk of CDD among patients with different severities of alcohol intoxication (*P* for trend <.0001).

4. Discussion

The rate of alcohol dependence and abuse was estimated at 16.2% among people aged 18 to 29 years, 9.7% among those aged 30 to 44 years, 12.4% among men, and 4.9% among women.[1] In our study (Table 1), 90% of the study patients were men, the mean age was 44 years, and the majority age group was 35 to 65 years. Whether being male and middle-aged increases

Table 2

Incidence and adjusted hazard ratio of colonic diverticular disease stratified by sex, age, and comorbidity (yes/no) between both 2 cohorts.

	Alcohol intoxication							
	No			Yes			Compared to nonalcohol intoxication cohort	
Variables	Event	PY	Rate‡	Event	PY	Rate‡	IRR (95% CI)	Adjusted HR† (95% CI)
Overall	518	1,496,031	3.46	495	301,051	16.4	4.75 (4.62–4.88)*	3.21 (2.76–3.74)*
Sex								
Women	35	147,141	2.38	31	32,335	9.59	4.03 (3.69–4.40)*	3.44 (1.91–6.21)*
Men	483	1,348,890	3.58	464	268,716	17.3	4.82 (4.69–4.96)*	3.19 (2.72–3.74)*
Age, yr								
<45	178	861,358	2.07	282	180,108	15.66	7.58 (7.30–7.86)*	4.95 (3.91–6.27)*
≥45	340	634,672	5.36	213	120,943	17.6	3.29 (3.15–3.43)*	2.34 (1.89–2.88)*
Comorbidity								
No	427	1,379,843	3.09	130	117,527	11.1	3.57 (3.44–3.71)*	3.38 (2.77–4.11)*
Yes	91	116,188	7.83	365	183,524	19.9	2.54 (2.36–2.73)*	2.85 (2.25–3.61)*

CI = confidence interval, IRR = incidence rate ratio, PY = person-year, rate = incidence rate (per 10,000 person-years).
* *P* < .001.
† Adjusted HR: multiple analysis including age, sex, and comorbidities.
‡ Rate, incidence rate, per 10,000 person-years.

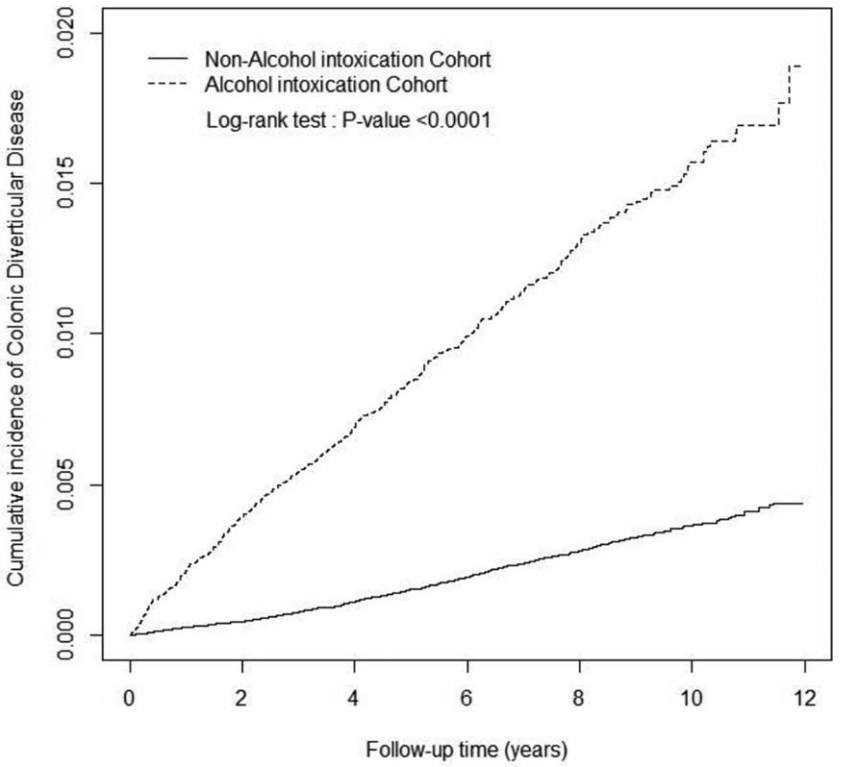

Figure 1. The cumulative incidence of colonic diverticular between alcohol intoxication (dashed line) and nonalcohol intoxication cohorts (solid line).

the likelihood of people consciously or accidentally intoxicating themselves with alcohol requires further research.

The comorbidity proportions in the alcohol intoxication cohort were greater than those in the control cohort (Table 1). Medication for alcohol intoxication should be prescribed carefully. Current use of opiate analgesics (odds ratio [OR]= 2.16, 95% CI=1.55–3.01) or oral corticosteroids (OR=2.74, 95% CI=1.63–4.61) was associated with an increased risk of diverticular perforation.[21]

On the basis of multivariate analysis, some studies have reported that alcohol consumption is significantly associated with diverticulosis. The adjusted OR was 1.91 (1.36–2.69) in the United States[20]; the adjusted OR was 2.195 (95% CI=1.091–4.416) in South Korea.[14] After adjustments for age, physical activity, and energy intake of dietary fiber and total fat, a study reported that alcohol intake was only weakly or nonsignificantly associated with the risk of symptomatic diverticular disease (relative risk [RR]=1.36, 95% CI=0.94–1.97, *P* for trend =.37).[22] In 1994, Aldoori et al mentioned that for men on a high-total-fat, he RR was 2.35 compared with those on a low-total-fat, high-fiber diet, and for men on a high-red-meat, low-fiber diet the RR was 3.32 compared with those on a low-red-meat, high-fiber diet.[23] Men in the lowest quintile for both dietary fiber and physical activity were also associated with an increased risk of symptomatic diverticular disease compared with those in the highest quintile (RR 2.56, 95% CI=1.36–4.82).[24] Obesity in men in the highest quintile of waist circumference compared with those in the lowest quintile showed an increased risk of symptomatic diverticular disease (RR diverticulitis 1.56, 95% CI=1.18–2.07; RR diverticular bleeding 1.96, 95% CI= 1.30–2.97).[25] Women smokers appeared to have an increased risk of perforated diverticulitis and diverticular abscess compared with nonsmokers (OR 1.89, 95% CI=1.15–3.10).[26] In addition, compared with nonusers, users of aspirin and non-steroidal anti-inflammatory drugs had an increased risk of diverticulitis (HR 1.25, 95% CI=1.05–1.47).[27] In the present study, patients with alcohol intoxication exhibited a 3.21-fold higher risk of CDD (95% CI=2.76–3.74) compared with those in the control cohort (nonalcohol intoxication). This result suggests a strong association between alcohol intoxication and CDD. Compared with the incidence of CDD for patients in the control cohort, that for younger patients (aged <45 years) with alcohol intoxication was as much as 4.95-fold higher, and that for female patients was as much as 3.44-fold higher (Table 2). In addition, the incidence of CDD was as much as 3.38-fold higher for patients with no comorbidity and 2.85-fold higher for patients in the alcohol intoxication cohort with comorbidity (Table 2).

Further analysis of comorbidities among hypertension, hyperlipidemia, diabetes, fibromyalgia, and hepatitis C revealed no increased risk associated with CDD. Depression, anxiety, sleep disorder, acute pancreatitis, liver cirrhosis, and hepatitis B were associated with an increased risk of CDD. When patients with alcohol intoxication simultaneously had sleep disorder, acute pancreatitis, or liver cirrhosis, they were determined to be at a significantly higher risk of developing CDD (Table 3). The relationship between these diseases and CDD still requires further evaluation. However, except for hepatitis B, depression,[28,29] anxiety,[30,31] sleep disorder,[32–36] pancreatitis,[37,38] and liver cirrhosis,[39] all diseases were associated with alcoholic consumption. Heavy drinkers seem to be at a higher risk of depression than consumers who do not drink regularly.[28]

Table 3

The join effect between alcohol intoxication and each different comorbidity for risk of colonic diverticular disease.

Variable		N	Event	Adjusted HR (95% CI)
Alcohol intoxication	Hypertension			
No	No	204,376	507	1.00
No	Yes	3088	11	1.14 (0.63–2.07)
Yes	No	50,703	481	4.91 (4.33–5.57)‡
Yes	Yes	1163	14	5.11 (3.01–8.70)‡
Alcohol intoxication	Hyperlipidemia			
No	No	204,573	508	1.00
No	Yes	2891	10	1.18 (0.63–2.20)
Yes	No	50,958	481	4.88 (4.31–5.53)‡
Yes	Yes	908	14	6.76 (3.97–11.5)‡
Alcohol intoxication	Diabetes			
No	No	205,597	510	1.00
No	Yes	1867	8	1.38 (0.68–2.77)
Yes	No	50,989	483	4.90 (4.33–5.55)‡
Yes	Yes	877	12	6.10 (3.44–10.8)‡
Alcohol intoxication	Depression			
No	No	205,952	502	1.00
No	Yes	1512	16	3.99 (2.43–6.57)‡
Yes	No	42,491	398	4.87 (4.27–5.56)‡
Yes	Yes	9375	97	5.75 (4.62–7.16)‡
Alcohol intoxication	Anxiety			
No	No	206,741	511	1.00
No	Yes	723	7	3.11 (1.48–6.56)†
Yes	No	50,156	476	4.93 (4.35–5.58)‡
Yes	Yes	1710	19	5.63 (3.56–8.91)‡
Alcohol intoxication	Fibromyalgia			
No	No	206,812	514	1.00
No	Yes	652	4	2.15 (0.80–5.74)
Yes	No	50,442	475	4.87 (4.30–5.52)‡
Yes	Yes	1424	20	6.70 (4.29–10.5)‡
Alcohol intoxication	Sleep disorder			
No	No	205,116	501	1.00
No	Yes	2348	17	2.50 (1.54–4.07)†
Yes	No	46,004	415	4.73 (4.15–5.39)‡
Yes	Yes	5862	80	7.15 (5.64–9.06)‡
Alcohol intoxication	Acute pancreatitis			
No	No	205,561	501	1.00
No	Yes	1903	17	3.18 (1.96–5.17)‡
Yes	No	39,833	304	3.93 (3.41–4.54)‡
Yes	Yes	12,033	191	9.03 (7.63–10.7)‡
Alcohol intoxication	Cirrhosis			
No	No	204,013	499	1.00
No	Yes	3451	19	2.21 (1.40–3.50)†
Yes	No	36,043	300	4.09 (3.54–4.72)‡
Yes	Yes	15,823	195	7.70 (6.52–9.09)‡
Alcohol intoxication	Hepatitis B			
No	No	203,714	500	1.00
No	Yes	3750	18	1.91 (1.19–3.05)†
Yes	No	46,120	444	4.93 (4.34–5.61)‡
Yes	Yes	5746	51	5.51 (4.12–7.36)‡
Alcohol intoxication	Hepatitis C			
No	No	205,426	513	1.00
No	Yes	2038	5	0.82 (0.34–1.97)
Yes	No	47,895	460	4.89 (4.31–5.54)‡
Yes	Yes	3971	35	5.02 (3.56–7.07)‡

Model adjusted for age and sex.

CI = confidence interval, HR = hazard ratio, Ref = reference group.

† $P < .01$.

‡ $P < .001$.

Table 4

Incidence rate and hazard ratio for colonic diverticular disease stratified by severity of alcohol intoxication.

Severity of alcohol intoxication	Event	Rate	Adjusted HR† (95% CI)
Nonalcohol intoxication cohort	518	3.46	1.00
Alcohol intoxication cohort			
Mild (T_1)	169	9.01	1.98 (1.64–2.39)*
Moderate (T_2)	164	22.05	4.73 (3.86–5.79)*
Severe (T_3)	162	41.44	10.3 (8.27–12.7)*
P for trend			<.0001

Severity of alcohol intoxication = (total length of hospital stay due to alcohol intoxication during the follow-up duration) ÷ (length of follow-up duration).

CI = confidence interval, HR = adjusted hazard ratio, Rate = incidence rate, per 10,000 person-years, T_1 = first tertile, T_2 = second tertile, T_3 = third tertile.

* $P < .001$.

† Adjusted for age, sex, and comorbidities.

Among patients treated for alcohol addiction, changes in depression were considered predictors of changes in alcohol consumption.[29] Drinking may be a potential risk factor for non-recovery from anxiety and depression.[30] Clinicians should consider a patient's alcohol consumption before prescribing or dispensing sedative/anxiolytic drugs.[31] Herein, sleep disorders according to ICD-9-CM include insomnia (307.4) and sleep apnea (SA) (780.5). Insomnia and alcohol dependence can be considered co-occurring disorders.[32] Alcohol dependence can be accompanied by primary and/or secondary mood disorder or sleep disorder.[34] After adjustments for gender and age, insomnia was associated with alcohol consumption (adjusted OR = 1.21, CI 95% = 1.03–1.41) and depressive symptoms (adjusted OR = 3.59, CI 95% = 3.04–4.24).[35] Chronic insomnia was associated with alcoholic disorder (OR = 4.83, CI 95% = 1.89–12.37).[36] Current and past alcohol consumers had significantly higher odds of having SA (OR = 1.52, 95% CI = 1.03–2.23; OR = 1.65, 95% CI = 1.09–2.49) than those of nonalcohol drinkers.[33] In this study, we demonstrated that alcohol intoxication or abuse was a strong risk factor for CDD. Furthermore, patients with depression, anxiety, sleep disorder, acute pancreatitis, cirrhosis, and hepatitis B were found to be predisposed to CDD.

A stratified analysis (Table 4) of different severities of alcohol intoxication reveals that the adjusted HR of CDD increased as the alcohol intoxication of patients changed from mild to moderate to severe. The results also indicate a significantly increasing trend of risk of CDD among patients with different severities of alcohol intoxication (*P* for trend <.0001). There was a significantly positive correlation between alcohol intoxication or abuse and CDD.

5. Limitations

This study had some limitations. First, the NHIRD provides no information about patients' lifestyle, living habits, body mass index, physical activity, socioeconomic status, or details of family history, all of which were possible confounders in our study. Second, the general methodological quality of the evidence obtained from cohort studies is lower than that of randomized trials. Cohort studies are relevant because confounding factors cause the necessary adjustments to result in considerable prejudice. Despite the well-designed study of control and adequate confounders, bias can be maintained because there may be unknown or unmeasured confounders. Third, the NHI

registration of claims is mainly used for administrative fees and research purposes. Because of the anonymity of the identification number, obtaining additional information directly from patients was not possible. The accuracy claims of medical coding data may affect the validity of the data. However, the diagnostic data regarding the NHIRD are highly reliable, and the insurance system has a mechanism for monitoring insurance claims. Finally, there was a tendency for patients with alcohol intoxication to undergo examination such as computed tomography or colonoscopy examinations. But there is no conclusion whether the presence of gastrointestinal symptoms increases the diagnosis of CDD, or uncomplicated diverticular disease can also cause gastrointestinal symptoms.[40] Several studies report there is significantly increased risk of CDD in alcohol drinkers.[7,20,41]

Our study had the following advantages: It had a population-based design, the obtained results are universal, the number of samples was large, and the study and control groups included population-based data and NHIRD records. In addition, the NHIRD is a highly representative sample: it covers nearly all of Taiwan's total population because the reimbursement policy is universal and operated by a single buyer, the government of Taiwan. All insurance claims to be reimbursed to medical experts are subject to peer review.

Author contributions

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