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ORIGINAL ARTICLE—LIVER, PANCREAS, AND BILIARY TRACT

Alcohol drinking patterns and the risk of fatty liver in Japanese men

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Abstract
Background Alcohol is considered to be a major cause of fatty liver (FL). In contrast, however, recent investigations have suggested that moderate alcohol consumption is protective against FL. To clarify the role of alcohol consumption in FL development, we examined the association between drinking patterns and FL prevalence.
Methods We enrolled 9,886 male participants at regular medical health checks. Each subject's history of alcohol consumption was determined by questionnaire. The subjects were classified according to alcohol consumption as non-, light, moderate, and heavy drinkers (0, <20, 20–59, and ≥60 g/day, respectively). FL was defined by ultrasonography. Independent predictors of FL were determined by logistic regression analysis.
Results The prevalence of FL displayed a "U-shaped curve" across the categories of daily alcohol consumption (non-, 44.7%; light, 39.3%; moderate, 35.9%; heavy drinkers, 40.1%; $P < 0.001$). The prevalence of FL was associated positively with body mass index and other obesity-related diseases and inversely with alcohol consumption (light, odds ratio [OR] 0.71, 95% confidence interval [CI] 0.59–0.86; moderate, OR 0.55, CI 0.45–0.67; heavy, OR 0.44, CI 0.32–0.62) as determined by multivariate analysis after adjusting for potential confounding variables. In addition, examination of drinking patterns (frequency and volume) revealed that the prevalence of FL was inversely associated with the frequency of alcohol consumption (≥21 days/month) (OR 0.62, CI 0.53–0.71) but not with the volume of alcohol consumed.
Conclusions Our observations suggest that alcohol consumption plays a protective role against FL in men, and consistent alcohol consumption may contribute to this favorable effect.

Keywords Fatty liver · Alcohol consumption · Nonalcoholic fatty liver disease · Metabolic syndrome

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Introduction

Fatty liver (FL) disease is commonly divided into nonalcoholic (NAFLD) and alcoholic (AFLD) FL disease categories. NAFLD is an increasingly recognized condition, predominantly linked to metabolic syndrome, which, in turn, is associated with obesity and insulin resistance [1–4]. The clinical importance of NAFLD is due to its wide

spectrum of histological damage, ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), which can lead to cirrhosis, hepatocellular carcinoma, and hepatic failure [5]. Alcohol dehydrogenase-mediated ethanol metabolism generates a reduced form of nicotinamide adenine dinucleotide (NADH), which promotes steatosis by stimulating the synthesis of fatty acids and opposing their oxidation. The hepatic lipogenic pathway is activated after the consumption of 24 g of ethanol per day [6]. Alcohol intake is a risk factor for both hypertriglyceridemia and FL [7, 8], and daily intake as low as 20–30 g of alcohol per day may be sufficient to cause alcohol-induced liver disease in some cases.

In contrast, recent investigations have reported a protective role of moderate alcohol consumption against FL [9–13]. Light to moderate alcohol consumption is associated with lower cardiovascular mortality [14–16] and a reduced risk of developing type 2 diabetes [17–19]. Mechanisms proposed to explain this observation include improved lipid profiles, especially high-density lipoprotein-cholesterol [15], and increased insulin sensitivity [19–21]. The mechanism of protection against FL, however, remains unclear.

In this study, to elucidate the relationship between the quantity and patterns of alcohol consumption and FL prevalence, we conducted a cross-sectional study of a male Japanese population.

Subjects, materials, and methods

Study population

The study subjects were Japanese men aged 30–69 years, who participated in regular health check-ups from April 2000 to March 2007. Of the initial 10,283 candidates, 204 (2.0%) hepatitis B virus surface antigen (HBsAg)-positive and 195 (1.9%) hepatitis C virus antibody (HCV Ab)-positive subjects were excluded from the analysis (two subjects were positive for both HBsAg and HCV Ab). The remaining 9,886 men were enrolled in this study. Serological testing for HBsAg and HCV Ab was performed by enzyme immunoassay and enzyme-linked immunosorbent assay, respectively. This study, conducted at Kagoshima Kouseiren Medical Health Care Center, was approved by the ethics committee of the Kagoshima Prefectural Federation of Agricultural Cooperatives for Health and Welfare.

A diagnosis of FL was made, using ultrasonography (SSA-250A and SSA-700A; Toshiba, Tokyo, Japan; Logic 400; GE Healthcare Japan, Tokyo, Japan), from findings of bright liver (increased echogenicity) with liver–kidney contrast (increased echogenicity of the liver in comparison to the right kidney). Body mass index (BMI) was calculated from the equation: body weight (kg)/height^2 (m^2). Body composition was categorized according to the Western Pacific Region of WHO criteria pertaining to obesity (WPRO criteria): BMI <18.5 kg/m^2 (underweight), 18.5–22.9 kg/m^2 (normal weight), 23.0–24.9 kg/m^2 (overweight), and 25 kg/m^2 or more (obese). Venous blood samples were taken from all subjects before nine o'clock after an overnight fast and were analyzed immediately. Alanine aminotransferase (ALT), aspartate aminotransaminase (AST), and γ-glutamyl transpeptidase (γ-GTP) activities and the concentrations of total cholesterol, triglycerides, and glucose were measured by standard laboratory procedures. High-density lipoprotein cholesterol (HDL-C) levels were determined by direct homogeneous assay of serum samples using detergents (Sekisui Medical, Tokyo, Japan).

The subjects were investigated for the presence of concomitant metabolic abnormalities. Hypertension was defined as being present in patients on medication for hypertension, those with systolic blood pressure >130 mmHg, and/or those with diastolic blood pressure >85 mmHg. Dyslipidemia was defined as being present in patients on medication for dyslipidemia, those with total cholesterol >220 mg/dl, triglycerides >150 mg/dl, and/or HDL-C <40 mg/dl. Diabetes mellitus (DM) was considered to be present in patients on medication for DM and/or in those with fasting blood glucose >125 mg/dl. ALT or AST elevations were defined as levels over 30 IU/L.

Using a common questionnaire, a history of alcohol intake was determined by a public health nurse without knowledge of the status of FL. Each subject reported their current frequency of alcohol consumption (A, 0; B, 1–5; C, 6–10; D, 11–20; E, ≥21 days/month) and volume of alcohol drunk per day (a, <20; b, 20–39; c, 40–59; d, 60–99; e, ≥100 g/day). All participants except former drinkers were divided into four groups according to the frequency (A–E) and volume (a–e) of alcohol consumption, as follows: non-drinkers, A; light drinkers, B-a–e, C-a–c, D-a or -b, E-a; moderate drinkers, C-d or -e, D-c or -d, E-b or -c; and heavy drinkers, D-e, E-d or -e (daily volumes consumed by non-, light, moderate, and heavy drinkers were approximately 0, <20, 20–59, and ≥60 g/day, respectively).

Statistical analysis

The distributions of each variable were compared between FL subjects and non-FL subjects. Continuous variables, including age, BMI, ALT, AST, γ-GTP, triglycerides, and HDL-C, were analyzed by t-test, and categorical variables were examined by the χ^2 test. In addition, associations of alcohol consumption (non-, light, moderate, and heavy drinkers) with clinical factors and smoking status were

examined by analysis of variance (ANOVA) or the χ^2 test. Maximum likelihood odds ratios (ORs) for FL risk and their 95% confidence intervals (95% CIs) were calculated using logistic regression models. Statistical analyses were performed using STATA version 9.2 (StataCorp, TX, USA). All *P* values presented are two-sided.

Results

Subject description

Among the 9,886 subjects, 3,816 men (38.6%) met the criteria for FL (Table 1). The subjects' characteristic

Table 1 Characteristic features of study subjects

	All	Fatty liver		*P* value
		(−)	(+)	
Number (%)	9886 (100%)	6070 (100%)	3816 (100%)	
Age (years)	50.7 [50.5, 50.9]	51.4 [51.2, 51.7]	49.5 [49.2, 49.8]	<0.001*
30–39	12.0%	11.4%	12.8%	<0.001**
40–49	31.2%	28.2%	36.0%	
50–59	32.5%	32.6%	32.5%	
60–69	24.3%	27.8%	18.6%	
BMI	23.7 [23.6, 23.7]	22.5 [22.5, 22.6]	25.6 [25.5, 25.7]	<0.001*
<18.5	2.4%	3.9%	0.1%	<0.001**
18.5–22.9	37.7%	51.9%	15.2%	
23.0–24.9	26.9%	27.3%	26.4%	
25–	33.0%	17.0%	58.4%	
Laboratory data				
ALT (IU/L)	25.7 [25.5, 36.7]	21.6 [21.4, 21.8]	33.9 [33.3, 34.4]	<0.001*
AST (IU/L)	24.7 [24.5, 24.9]	23.4 [23.2, 23.6]	27.0 [26.7, 27.3]	<0.001*
γ-GTP (IU/L)	36.2 [35.6, 36.7]	30.7 [30.1, 31.3]	47.0 [45.9, 48.1]	<0.001*
Triglycerides (mg/dl)	120 [119, 122]	102 [100, 103]	156 [153, 159]	<0.001*
HDL-C (mg/dl)	53.9 [53.6, 54.2]	57.0 [56.7, 57.4]	49.3 [48.9, 49.6]	<0.001*
Presence of clinical manifestation				
Fatty liver	38.6%			
ALT elevation	32.7%	18.8%	54.8%	<0.001***
AST elevation	21.2%	15.3%	30.5%	<0.001***
Hypertension	46.5%	42.1%	53.5%	<0.001***
Dyslipidemia	55.9%	45.9%	71.8%	<0.001***
Diabetes mellitus	11.4%	7.9%	16.8%	<0.001***
Smoking status				
Never smoker	29.4%	29.7%	28.8%	0.001***
Former smoker	31.2%	29.9%	33.3%	
Current smoker	39.4%	40.4%	37.9%	
Alcohol consumption				
Never drinker	8.6%	7.7%	10.0%	<0.001***
Former drinker	2.9%	2.6%	3.3%	
Light drinker	45.9%	45.4%	46.7%	
Moderate drinker	39.1%	40.8%	36.4%	
Heavy drinker	3.5%	3.4%	3.6%	

Data are presented as geometric means [corresponding 95% confidence intervals] or proportions

BMI body mass index, *ALT* alanine aminotransferase, *AST* aspartate aminotransaminase, *γ-GTP* γ-glutamyl transpeptidase, *HDL-C* high-density lipoprotein cholesterol

* *P* values were obtained by *t* test

** *P* values for trend were obtained by likelihood ratio test using a logistic regression model

*** *P* values were obtained by χ^2 test

features and the differences in biological parameters in relation to FL are summarized in Table 1. There were 1,131 (11.4%) non-drinkers, including 284 former drinkers; 4,540 (45.9%) light drinkers, 3,868 (39.1%) moderate drinkers; and 347 (3.5%) heavy drinkers.

The subjects with FL were significantly younger than the the subjects without FL ($P < 0.001$). BMI was significantly higher in FL (+) subjects in comparison to FL (−) subjects ($P < 0.001$). ALT, AST, and two parameters typically increased in association with alcohol consumption, γ-GTP and triglycerides, were significantly higher in FL (+) subjects in comparison to those who were FL (−) (all $P < 0.001$). In contrast, HDL-C, another parameter correlated with alcohol consumption, was lower in the FL (+) subjects than in FL (−) subjects ($P < 0.001$).

There was a U-shaped association between the prevalence of FL and categories of alcohol consumption ($P < 0.001$; Table 2). The prevalence of FL was highest in never drinkers among the five categories of alcohol consumption. AST, γ-GTP, triglycerides, and HDL-C, which

Table 2 Comparison of characteristic features across the categories of alcohol consumption

	Never drinker	Former drinker	Light drinker	Moderate drinker	Heavy drinker	*P* value
Number	847 (100%)	284 (100%)	4,540 [100%)	3,868 (100%)	347 (100%)	
Age (years)	51.6 [50.9, 52.3]	54.0 [52.8, 55.2]	50.4 [50.1, 50.7]	50.7 [50.4, 51.0]	48.1 [47.3, 48.9]	<0.001*
30–39	11.5%	7.8%	14.0%	10.0%	11.8%	<0.001**
40–49	28.7%	23.9%	30.6%	32.4%	39.2%	
50–59	30.0%	27.8%	29.4%	36.4%	40.6%	
60–	29.9%	40.5%	26.0%	21.2%	8.4%	
BMI (kg/m^2)	23.7 [23.5, 24.0]	23.6 [23.2, 24.0]	23.7 [23.6, 23.8]	23.6 [23.5, 23.7]	23.9[23.5, 24.2]	0.031*
<18.5	2.6%	4.2%	2.5%	2.0%	2.9%	0.048**
18.5–22.9	37.4%	38.4%	37.0%	38.9%	34.0%	
23.0–24.9	24.6%	25.0%	26.6%	27.9%	28.2%	
25.0–	35.4%	32.4%	33.9%	31.2%	34.9%	
Laboratory data						
ALT (IU/L)	25.4 [24.6, 26.8]	28.0 [26.2, 29.8]	25.4 [25.0, 25.7]	25.6 [25.2, 26.0]	30.5 [28.9, 32.3]	<0.001**
AST (IU/L)	22.7 [22.2, 23.1]	24.3 [23.3, 25.4]	23.7 [23.5, 23.9]	26.0 [25.7, 26.3]	30.5 [29.1, 32.0]	<0.001**
Fatty liver (−)	21.1 [20.6, 21.6]	22.4 [21.3, 23.6]	22.4 [22.1, 22.6]	24.7 [24.4, 25.0]	28.5 [27.1, 30.0]	<0.001***
Fatty liver (+)	24.7 [23.9, 25.6]	27.0 [25.2, 28.9]	25.8 [25.5, 26.2]	28.5 [28.0, 29.1]	33.8 [31.1, 36.8]	<0.001***
γ-GTP (IU/L)	22.5 [21.6, 23.3]	25.8 [23.9, 27.9]	30.2 [29.6, 30.8]	48.1 [46.9, 49.2]	67.1 [61.4, 73.4]	<0.001**
Fatty liver (−)	18.1 [17.3, 18.9]	21.2 [19.3, 23.3]	25.3 [24.8, 26.0]	40.8 [39.6, 42.0]	57.0 [50.9, 63.8]	<0.001***
Fatty liver (+)	29.2 [27.6, 31.0]	33.4 [29.9, 37.3]	39.7 [38.5, 40.9]	64.5 [62.1, 67.0]	85.8 [74.9, 98.3]	<0.001***
Triglycerides (mg/dl)	116 [111, 120]	107 [100, 113]	115 [113, 116]	127 [124, 130]	147 [137, 158]	<0.001**
HDL-C (mg/dl)	48.2 [47.5, 48.9]	49.8 [48.3, 51.2]	52.4 [52.0, 52.7]	57.1 [56.6, 57.5]	58.2 [56.6, 59.7]	<0.001**
Presence of clinical manifestation						
ALT elevation	32.4%	37.3%	31.2%	33.0%	45.5%	<0.001**
AST elevation	13.8%	20.4%	17.1%	26.3%	37.2%	<0.001**
Dyslipidemia	60.3%	56.3%	53.8%	56.8%	62.5%	<0.001**
Fatty liver	45.1%	43.7%	39.3%	35.9%	40.1%	<0.001**
Hypertension	37.4%	44.7%	42.6%	52.2%	58.5%	<0.001**
Diabetes mellitus	11.3%	18.0%	10.2%	12.3%	11.5%	<0.001**
Smoking status						
Never smoker	37.5%	36.6%	36.8%	19.6%	15.6%	<0.001**
Former smoker	24.1%	39.8%	30.0%	33.6%	30.3%	
Current smoker	38.4%	23.6%	33.2%	46.8%	54.2%	

Data are presented as geometric means [corresponding 95% confidence intervals] or proportions

BMI body mass index, *ALT* alanine aminotransferase, *γ-GTP* γ-glutamyl transpeptidase, *AST* aspartate aminotransaminase, *HDL-C* high-density lipoprotein cholesterol

* *P* values obtained by analysis of variance (ANOVA) after logarithmic transformation of each data

** *P* values obtained by χ^2 test

*** *P* values obtained by likelihood ratio test

are known factors associated with alcohol consumption, were significantly increased across the categories with increasing alcohol consumption (all $P < 0.001$). In addition, AST and γ-GTP were significantly higher in FL (+) subjects in comparison with FL (−) subjects in each category of alcohol consumption, and these parameters increased across the categories with increasing alcohol consumption in subjects both with and without FL.

Independent predictors of fatty liver

Independent predictors significantly affecting the prevalence of FL were identified by logistic regression analysis (Table 3). FL risk tended to decrease with age and increase with BMI. A significant elevation of FL risk was observed in subjects with ALT elevation, hypertension, dyslipidemia, and DM. Multivariate analysis revealed that alcohol

Table 3 Predictive factors of fatty liver by logistic regression analysis

	All subjects		Limited subjects[c]
	Univariate OR [95% CI]	Multivariate OR [95% CI][a]	Multivariate OR [95% CI][b]
Age (years)			
30–39	1.0 (referent)	1.0 (referent)	1.0 (referent)
40–49	1.14 [0.99, 1.30]	1.27 [1.07, 1.52]	1.41 [0.82, 2.41]
50–59	0.89 [0.78, 1.02]	1.14 [0.95, 1.36]	0.92 [0.52, 1.64]
60–69	0.59 [0.51, 0.69]	0.84 [0.69, 1.02]	0.94 [0.50, 1.76]
P for trend	<0.001	<0.001	0.333
BMI (kg/m^2)			
<18.5	0.05 [0.01, 0.19]	0.06 [0.01, 0.25]	–[d]
18.5–22.9	1.0 (referent)	1.0 (referent)	1.0 (referent)
23.0–24.9	3.30 [2.93, 3.72]	2.42 [2.12, 2.75]	3.15 [2.04, 4.86]
>25	11.8 [10.5, 13.2]	6.01 [5.27, 6.84]	5.50 [3.40, 8.89]
P for trend	<0.001	<0.001	<0.001
Presence of clinical manifestation			
ALT elevation	5.23 [4.78, 5.73]	2.46 [2.19, 2.77][b]	–
Hypertension	1.59 [1.46, 1.72]	1.18 [1.06, 1.32]	–
Dyslipidemia	3.00 [2.75, 3.27]	1.19 [1.05, 1.35]	–
Diabetes mellitus	2.34 [2.06, 2.65]	1.88 [1.61, 2.20]	–
Smoking status			
Never smoker	1.0 (referent)	1.0 (referent)	1.0 (referent)
Former smoker	1.15 [1.04, 1.28]	1.07 [0.94, 1.22]	–
Current smoker	0.97 [0.88, 1.07]	0.83 [0.73, 0.95]	0.58 [0.39, 0.87]
P for heterogeneity	0.001	<0.001	
Alcohol consumption			
Never drinker	1.0 (referent)	1.0 (referent)	1.0 (referent)
Former drinker	0.91 [0.72, 1.24]	0.89 [0.63, 1.25]	–
Light drinker	0.79 [0.68, 0.91]	0.71 [0.59, 0.86]	0.71 [0.38, 1.34]
Moderate drinker	0.68 [0.59, 0.79]	0.55 [0.45, 0.67]	0.81 [0.40, 1.62]
Heavy drinker	0.81 [0.63, 1.05]	0.44 [0.32, 0.62]	0.54 [0.15, 2.03]
P for trend	<0.001	<0.001	0.525

P values were obtained by likelihood ratio test

ALT alanine aminotransferase, *BMI* body mass index

[a] Odds ratios (ORs) and corresponding 95% confidence intervals [95% CIs] were obtained by logistic regression models using variables in this table and serum levels of alanine aminotransferase, γ-glutamyl transpeptidase, triglycerides, and high-density lipoprotein cholesterol

[b] ORs and corresponding 95% CIs were obtained by logistic regression models using variables in this table and serum levels of γ-glutamyl transpeptidase, triglycerides, and high-density lipoprotein cholesterol

[c] Subjects were limited to those who had no history of ALT elevation, hypertension, dyslipidemia, and diabetes mellitus. Subjects who stopped drinking or who were ex-smokers were also excluded from the analysis ($n = 1,481$)

[d] There was no subject with fatty liver in this BMI category

consumption was inversely associated with FL risk, after adjusting for the effects of all variables in Table 3, and serum levels of ALT, γ-GTP, triglycerides, and HDL-C (P for trend <0.001). This association was still present when the study subjects were limited to those who were not former smokers or drinkers, and who had no history of ALT elevation, hypertension, dyslipidemia, and DM, although the ORs for alcohol consumption were not statistically significant.

Influence of drinking patterns on FL prevalence

The prevalence of FL was examined in 10 subgroups classified by the frequency of alcohol consumption (0, 1–10, 11–20, and >20 days/month) and volume of alcohol consumed on days subjects drank (0, <20, 20–59, and ≥60 g/day) (Fig. 1). The prevalence of FL in non-drinkers was 44.7%. The prevalences of FL in those who consumed alcohol on 1–10, 11–20, and ≥21 days/month were 41.8, 39.1, and 30.7% (<20 g/day); 52.8, 48.5, and 35.0% (20–59 g/day); and 54.9, 53.6, and 38.4% (≥60 g/day), respectively. The prevalence of FL decreased with increased frequency of alcohol consumption and increased with increasing volumes of alcohol consumed per day (Fig. 1, Table 4).

For current alcohol drinkers, the FL risk was examined based on alcohol drinking patterns, the frequency of alcohol consumption, and the daily volume of alcohol (Table 4). There was a significant inverse association between the frequency of alcohol consumption and the risk

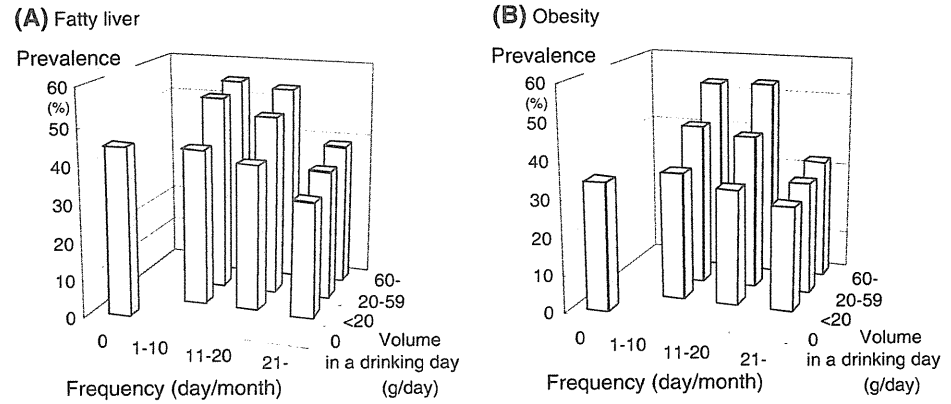

Fig. 1a,b Relationship of drinking patterns (frequency and volume in a drinking day) with the prevalence of fatty liver and obesity

Table 4 Estimated risk of fatty liver and obesity by alcohol drinking patterns among current alcohol drinkers

	Fatty liver		Obesity	
	Number (%)	OR [95% CI][a]	Number (%)	OR [95% CI][b]
Frequency (days/month)				
1–10 (n = 1,953)	921 (47%)	1.0 (referent)	775 (40%)	1.0 (referent)
11–20 (n = 863)	384 (45%)	0.92 [0.75, 1.12]	326 (38%)	1.05 [0.86, 1.27]
21– (n = 5,939)	2,005 (34%)	0.62 [0.53, 0.71]	1,765 (30%)	0.87 [0.76, 1.00]
P value	<0.001[#]	<0.001[##]	<0.001[#]	<0.033[##]
Alcohol volume (g/drinking day)				
1–20 (n = 3,438)	1,206 (35%)	1.0 (referent)	1,042 (30%)	1.0 (referent)
21–59 (n = 4,705)	1,823 (39%)	1.02 [0.90, 1.15]	1,566 (33%)	1.18 [1.05, 1.33]
60– (n = 612)	281 (46%)	0.83 [0.66, 1.04]	258 (42%)	1.41 [1.14, 1.74]
P value	<0.001[#]	0.378[##]	<0.001[#]	<0.001[##]

[#] P values were obtained by χ^2 test

[##] P values for trend were obtained by likelihood ratio test

[a] Odds ratios (ORs) and corresponding 95% confidence intervals [95% CIs] were obtained by logistic regression models using alcohol drinking patterns (frequency/daily alcohol consumption); age; body mass index; height; smoking status; the presence of alanine aminotransferase elevation, hypertension, dyslipidemia, and diabetes mellitus; and serum levels of alanine aminotransferase, γ-glutamyl transpeptidase, triglycerides, and high-density lipoprotein cholesterol

[b] ORs and 95% CIs were obtained by logistic regression models using alcohol drinking patterns (frequency/daily alcohol consumption); age; height; smoking status; the presence of fatty liver, alanine aminotransferase elevation, hypertension, dyslipidemia, and diabetes mellitus; and serum levels of alanine aminotransferase, γ-glutamyl transpeptidase, triglycerides, and high-density lipoprotein cholesterol

of FL (P for trend <0.001). On the other hand, alcohol volume was not related to the risk of FL (P for trend = 0.378).

Influence of drinking patterns on body composition

The association between alcohol drinking patterns and the prevalence of obesity, which is the most important risk factor for FL, are shown in Fig. 1b and Table 4. The prevalence of FL in non-drinkers was 34.6%. The prevalences of obesity in those who consumed alcohol on 1–10, 11–20, and ≥21 days/month were 34.3, 31.2, and 28.1% (<20 g/day); 43.7, 41.8, and 30.4% (20–59 g/day); and 53.0, 53.7, and 32.6% (≥60 g/day), respectively. As with the prevalence of FL, the prevalence of obesity decreased with increasing frequency of alcohol consumption and increased with the increasing alcohol volume in a drinking day (Table 4).

Logistic regression analysis (Table 4) revealed a significant association between the volume of alcohol in a drinking day and the risk of obesity (P for trend <0.001). In addition, consistent alcohol consumption tended to reduce the likelihood of obesity (OR 0.87, 95% CI 0.76–1.00, P for trend 0.033).

Discussion

This study demonstrated that FL in men was positively associated with factors including the presence of obesity, hypertension, dyslipidemia, and DM, but was negatively associated with age and alcohol consumption. Although our survey was not prospective in nature, these findings confirm that the major risk factors for FL are factors related to adiposity [1–4], not alcohol consumption, findings which agree with recent reports proposing a protective effect of alcohol intake [9–13]. We also confirmed that alcohol consumption tended to be negatively associated with FL in the limited number of subjects who had no history of ALT elevation, hypertension, dyslipidemia, or DM. In addition, our study may provide new evidence to help understand the role of alcohol drinking patterns in the pathogenesis of hepatic steatosis.

While alcohol consumption certainly may be a cause of FL in some cases [7, 8], it potentially plays a protective role against FL regardless of daily alcohol volume. Gunji et al. previously reported that "any drinking" might potentially be protective against FL; light (40–140 g/week) and moderate alcohol (140–280 g/week) consumption decreased the risk of FL, and the prevalence of FL was not increased even by heavy alcohol consumption [12]. Our study is also a report providing evidence of a significant inverse association between FL and alcohol consumption, even in heavy drinkers (≥60 g/day) (Table 3). We consider that alcohol consumption is a double-edged sword in the pathogenesis of hepatic steatosis. The difference in the results of our study and previous studies proposing alcohol consumption as a risk factor for FL may be due to differences in the ethnicity, age, BMI, and lifestyle (drinking style, type of alcohol, dietary habits, etc.) of the subjects in each study.

In the present study, we examined the relationship between drinking patterns (frequency of alcohol consumption and volume of alcohol in a drinking day) and FL. Consistent alcohol consumption (≥21 days/month) reduced the risk of FL independently (Table 4). In addition, consistent alcohol consumption may reduce the likelihood of obesity (Table 4), possibly contributing to a lowered risk of FL. Thus, consistent alcohol consumption may provide a protective effect on FL development in association with or without obesity. Conigrave et al. [22] reported that light to moderate alcohol consumption was inversely associated with an increased risk of DM in men only when consumed frequently (≥5 days/week). Consumption of alcohol on at least 3–4 days per week was associated with a decreased risk of myocardial infarction in men [23]. Consistent alcohol exposure may contribute to the favorable association with FL seen in the present study, as well as contributing to the favorable association with type 2 diabetes and ischemic heart disease reported in the studies cited above [22, 23], suggesting a common mechanism in these metabolic diseases.

We examined the relationship between alcohol volume in a drinking day and FL. Although the prevalence of FL increased with the increase in the daily volume of alcohol consumption (Fig. 1), no significant association between FL prevalence and the daily volume of alcohol consumption could be identified by logistic regression analysis after adjusting for BMI and other factors related to adiposity (Table 4). On the other hand, an increase in the daily volume of alcohol consumption was associated with an increased risk of obesity (Fig. 1; Table 4). We consider that excessive alcohol consumption in a drinking day may cause an alteration of body composition, most likely due to inadequate drinking and eating lifestyles, such as a prolonged duration of eating and increased calorie intake, probably resulting in the increasing prevalence of FL seen in the present study. These factors may influence the conflicting results reported about the relationship between alcohol consumption and the prevalence of FL.

Recent investigations have elucidated some of the mechanisms by which alcohol alters liver metabolism. Two critical nuclear transcription factors, sterol regulatory element binding protein (SREBP) [24] and peroxisome proliferator activated receptor alpha (PPARα) [25], are altered with alcohol consumption. You et al. [26] reported a role

for AMP activated protein kinase activity in the action of ethanol on the liver. In addition, disturbances in the cytokine network, including alterations in the tumor necrosis factor-α (TNF-α) [27] level, were shown to be involved in ethanol-induced steatosis. These pivotal factors, however, appear to be common in the pathogenesis of both NAFLD [28–30] and AFLD. Therefore, the inverse association between FL and alcohol consumption cannot be explained by these alterations alone.

It has been reported that moderate alcohol intake enhances insulin sensitivity [19, 20], contributing to a lower risk of DM. It was shown that moderate alcohol consumption was associated with a lower prevalence of both nonalcoholic steatohepatitis (NASH) and DM [11]. Sierksma et al. [21] hypothesized that the increase in adiponectin after chronic moderate alcohol consumption would cause an increase in insulin sensitivity in relatively insulin-resistant men. In addition, alcohol consumption also alters apolipoprotein profiles. Elevations in HDL cholesterol levels confer a lower risk of chronic heart disease [16]. Recently, studies examining the pathogenesis of NASH have demonstrated an association of hepatic apolipoprotein synthesis/secretion with the development of steatosis [31, 32]. Our study provides evidence that the risk of FL is decreased across the categories of alcohol consumption, despite an increase in serum triglyceride levels. Alcohol dehydrogenase-mediated ethanol metabolism generates a redox shift in the liver, which stimulates the synthesis of fatty acids. Subsequent removal of these fatty acids may be of benefit to prevent the development of FL.

Although the level of AST is considered to be higher than that of ALT in the majority of alcoholic liver diseases, the AST level was similar to that of ALT in moderate and heavy drinkers in our study (Table 2). In addition, our study demonstrated that liver injury assessed by AST and γ-GTP was positively associated with alcohol consumption regardless of the presence or absence of FL (Table 2). It was reported that the distribution of ratios of AST to ALT (AST/ALT) <1 and >1 was not different between healthy non-drinkers and moderate drinkers of normal weight or with obesity [33]. The ALT level was also similar to the AST level in moderate drinkers of normal weight, and it was observed that the effect of moderate alcohol consumption on liver-derived enzymes, including AST, ALT, and γ-GTP, increased with increasing BMI [33]. These results indicate that the relationships between alcohol consumption, BMI, and different serum liver-derived enzymes in drinkers should be considered. We should also pay attention to the finding that the absence of FL assessed by ultrasonography does not necessary rule out liver injury in drinkers.

There are several limitations in our study. Firstly, we did not enroll women subjects, although 7097 women subjects were investigated, because most of the women did not drink, or they drank 20 g/day at most; the number of subjects who drank more than 20 g/day was only 153 and the number of subjects with FL was 33. Thus, the sample size was insufficient to elucidate the association between alcohol drinking patterns and FL risk in women by the methods used in the present study. Secondly, subjects with other liver diseases, including autoimmune hepatitis and primary biliary cirrhosis, were not excluded. In addition, the association between alcohol consumption and FL prevalence was estimated by multivariate analysis after adjusting for age; BMI; the presence of hypertension, dyslipidemia, or DM; and smoking status. However, it is possible that additional factors for which we did not adjust may have influenced the results. One such factor is adult-onset type II citrullinemia (CTLN2) [34], an inherited metabolic disease caused by a deficiency of mitochondrial aspartate/glutamate carrier protein. Because of an impairment of cytosolic NADH oxidation, CTLN2 patients show both steatohepatitis and alcohol intolerance [35]. Thus, there may have been some differences in metabolic background, such as the capacity for alcohol oxidation or NAD^+/NADH metabolism, across the categories of alcohol consumption that could have affected the prevalence of FL. Thirdly, drinking habits are influenced by a polymorphism in the aldehyde dehydrogenase 2 (*ALDH2*) gene, and this polymorphism may affect our analysis. However, our study did not examine this polymorphism, and the alcohol-flushing response, which can be used to roughly estimate the presence of this polymorphism, was not investigated in the questionnaire. Furthermore, although treatment with an angiotensin II type 1 receptor blocker or peroxisome proliferator-activated receptor agonists is known to alleviate FL, we did not obtain information from the subjects about their use of these medications. Fourthly, the diagnosis of FL was made using abdominal ultrasonography, which defines the presence or absence of fatty steatosis. Diagnosis by ultrasonography may overlook a subset of advanced AFLD or NAFLD, so called "burnt-out steatohepatitis", in which fatty steatosis is reduced. Lastly, although direct interviews were carried out by trained medical staff, self-reported information on alcohol consumption may lead to under- or over-reporting. The influence of the type of alcoholic beverage was also not taken into account in this study. Further studies will be needed to clarify these issues.

In conclusion, this study demonstrates that the major risk factors for FL in Japanese men are factors related to adiposity, not alcohol consumption, and that consistent consumption of alcohol may play a protective role against FL. These results suggest that lifestyle modifications aimed at fighting central obesity and metabolic abnormalities should be the most important recommendations for the management of FL. In addition, it seems unlikely that the

risk of FL can be reduced by the discontinuation and/or reduction of alcohol consumption alone. Further studies are required to better understand FL pathogenesis and management.

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厚生労働科学研究費補助金（わが国における飲酒の実態ならびに飲酒に関連する生活習慣病、公衆衛生上の諸問題とその対策に関する総合的研究事業
平成23年度　分担研究報告書

アルコール性肝障害における生活習慣病の関与　―性差・積算飲酒量・酒種との関連―

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研究要旨；【背景】わが国の生活習慣病の有病率は増加している。生活習慣病はアルコール性肝障害(ALD)にも合併しその病態を修飾する。また、生活習慣病の病態は性・年齢で大きく異なる。今回、性差を踏まえた上で、生活習慣病がALDの病態に及ぼす影響に関して検討した。【対象と方法】当科で1987年から2011年に経験したALD514例のうち、飲酒量の詳細な検討が可能な入院加療例420例（女性55例、男性365例）に対し、1)ALDの性別、積算飲酒量別（t/bodyで0.5未満/0.5～1/1～1.5/1.5～2/2以上）に群別した生活習慣病の合併率　2)ALDにおける全例および積算飲酒量で層別した肝硬変に関与する因子　をcross-sectional studyで検討した。【成績】1）男女別では、年齢(中央値) 女47/男59歳、積算飲酒量(中央値) 0.7 / 1.3 t/body、BMI21/23 kg/m^2、肥満(BMI≧25) 11/27%、II型糖尿病(DM)11 / 40%、高血圧(HTN)15 / 29%、脂質異常症(DL)33 / 22%で、女性は男性より若年で積算飲酒量が少なく、年齢の影響も加わり肥満・DMの合併が少なかった。積算飲酒量別では、女性は生活習慣病合併と積算飲酒量に明らかな傾向はなく、男性ではDMは積算飲酒量の増加に伴い増加した。2) ALD全例の肝硬変の有無別多変量ロジスティック解析では、積算飲酒量（Odds比1.822）・DM（Odds比1.674）・DL（Odds比0.268）・肥満（Odds比0.322）が有意因子であった。積算飲酒量で層別し肝硬変に関与する因子を検討すると、肥満は一貫して負の因子として抽出された。【結論】ALDにおいて、肥満は肝硬変合併に関与する負の因子であった。

A. 研究目的

飽食の時代を迎えた我が国では、肥満・糖尿病などの生活習慣病の急増に伴い、生活習慣病の肝病変である非アルコール性脂肪性肝疾患(NAFLD)が増加している。日本人の約20%がNAFLDを合併していると考えられる現状では、NAFLDは様々な他の肝疾患に合併し、その病態を修飾していると推測される。また、生活習慣病・NAFLDに性差があることが明らかにされている。我々は、若年女性においては精神疾患合併がNAFLDの最も重要な危険因子であることを報告した。

一方、アルコール性肝障害(ALD)に性差があることも以前から広く知られており、女性では男性より少ない飲酒量・飲酒期間で病態が進行すると報告されている。かつて我が国においては、女性飲酒者は非常に少なかった。しかし近年、若年層の単純飲酒者人口は女性が男性より多数であると報告される。このような社会的背景の変化に伴い、若年女性の問題飲酒者の増加など、新たな問題が生じている。

現在までALD病態における生活習慣病の影響に関し、性差との関連を踏まえ検討した報告はない。そこで、ALDにおける生活習慣病の関与と性差の関連を明らかにすることを目的として検討を行った。

B. 研究方法

1987 年から 2011 年に当科に入院し、HBs 抗原陰性、HCV 抗体陰性、自己免疫性肝疾患など既知の疾患が否定され臨床病理学的に ALD と診断された 514 例のうち、飲酒量の詳細な検討が可能な入院加療例 420 例（女性 55 例、男性 365 例）に対し、1)ALD の性別、積算飲酒量別（t/body で 0.5 未満 /0.5～1/1～1.5/1.5～2/2 以上）に群別した生活習慣病の合併率　2)ALD における全例および積算飲酒量で層別した肝硬変に関与する因子　を cross-sectional study で検討した。検討項目は、年齢、body mass index(BMI)、臨床検査値、肝硬変・生活習慣病（高血圧・糖尿病・脂質異常症)・肥満（BMI>25kg/m^2）の各合併率である。数値は Mann-Whitney U 検定、比率はカイ 2 乗検定、多変量解析は二項 logistic 回帰分析にて解析し、p 値が 0.05 未満を有意差ありとした。

（倫理面への配慮）

本研究では、ヒトゲノム・遺伝子情報は取り扱わない。全症例に関するデータは症例番号のみで管理され個人を特定する情報は収集していない。解析用データファイルはアクセスにパスワードを設け、管理責任者を決めて管理した。

C. 研究結果

1)性別・積算飲酒量別検討

男女別年齢分布を図 1 に示す。

年齢(中央値) 女 47 /男 59 歳、積算飲酒量(中央値) 0.7 / 1.3 t/body、BMI21 /23 kg/m^2、肥満(BMI ≧ 25) 11/ 27％、II 型糖尿病(DM)11 / 40%、高血圧(HTN)15 / 29%、脂質異常症(DL)33 / 22%であった。全アルコール性肝障害の性別・年齢別積算飲酒量を表 1 に示す。30 代から 60 代において女性は男性より積算飲酒量が少なかった。酒種では女性でワイン飲酒者が多く、高齢男性でウイスキー飲酒者が多かった（図 2)。全アルコール性肝障害・アルコール性肝硬変における性別・積算飲酒量別肥満・生活習慣病合併率を示す（図 3, 4)。女性では生活習慣病合併と積算飲酒量に明らかな傾向はなかった。男性では DM 合併率が積算飲酒量と正の相関を示した。酒種と肥満・生活習慣病が合併率では一定の傾向は示さなかった（図 5, 6)

2) ALD 全例の肝硬変の有無別多変量ロジスティック解析では、積算飲酒量（Odds 比 1.822)・DM (Odds 比 1.674)・DL (Odds 比 0.268)・肥満（Odds 比 0.322）が有意因子であった。積算飲酒量で層別し肝硬変に関与する因子を検討すると、肥満は一貫して負の因子として抽出された。

まとめ；1) 全 ALD において、女性は男性より若年で積算飲酒量が少なく、年齢の影響も加わり肥満・DM の合併が少なかった。積算飲酒量別では、女性は生活習慣病合併と積算飲酒量に明らかな傾向はなく、男性は DM が積算飲酒量の増加に伴い増加した。2) ALD における肝硬変合併に関与する因子では、DM と積算飲酒量が正の因子、肥満が負の因子であった。

D. 考察

本班研究における昨年度までの我々の検討として、１）アルコール性肝障害における肝細胞癌合併と生活習慣病の関与、２）全国アンケート調査による肝細胞癌の基礎館病変としてのアルコール性、非アルコール性脂肪性肝疾患、原因不明群の位置付け　３）ALD 病態の肥満・生活習慣病による修飾の実態を明らかにすることを検討してきた。本年度は、３）に関連し、性・年齢の関与を踏まえたうえで、

ALDにおける肥満・生活習慣病の合併を、積算飲酒量別、酒種別など飲酒様態の詳細な分類を含めて検討した。今回の検討では、全ALDにおいて、女性は男性より若年で積算飲酒量が少なく、肥満・DMの合併が少なかった。積算飲酒量別生活習慣病との関連に関して、女性では生活習慣病と積算飲酒量に明らかな傾向はなく、男性では積算飲酒量の増加に伴いDM合併率が増加した。従来より、飲酒量が同等の場合は女性でALDが進行しやすく男性より短期間・少飲酒量で肝硬変に進展することが報告されている。今回の検討はほぼこれに矛盾しない結果を示した。また、積算飲酒量で層別し肝硬変に関与する因子の検討で、肥満は一貫して負の因子として抽出された。肥満・生活習慣病がALDの進行に関わる正の因子として抽出されることが予想されたが、これに相反する結果が出たことの原因として、今回の検討対象が入院を要する比較的重篤なALDであることから、一定量以上の飲酒量が有る場合、アルコールの影響が圧倒的に大きく、関連する他の因子が抽出されないことが推測される。従って、生活習慣病などの病態修飾が大きいのは、アルコール性肝障害の定義に達しない程度の中間的飲酒量の患者層であることが予想され、このような患者層において、飲酒量や酒種の影響などを詳細に検討していきたい。また、今後さらに、飲酒と肝発癌に関しても、性差・積算飲酒量・禁酒の有無を含む飲酒実態・生活習慣病合併などの観点から詳細に検討する予定である。

今回の検討の問題点として、ALDでは女性の頻度が極端に低く女性症例数の少なさから統計解析が困難であること、特に女性において飲酒の自己申告量が過少である傾向があり、正確で偏りのない評価が困難であることなどが挙げられる。今後、精神科や心療内科など他診療科と連携し、ブリーフミーティングや自己評価シートなど他科で用いられる飲酒の正確な評価法などを積極的に取り入れ、消化器内科におけるアルコール性肝障害の診療をブラッシュアップし、また、実態を把握して社会に発信・啓発し、我が国のアルコール性臓器障害を解決していく一助としたい。

E.結論

ALDにおいて、肥満は肝硬変合併に関与する負の因子であった。

F. 研究発表

＜論文発表＞

・ Roles of gender, obesity, and lifestyle-related diseases in alcoholic liver disease: Obesity does not influence the severity of alcoholic liver disease.
Taniai M, Hashimoto E, Tokushige K, et al.
Hepatol Res. 2012; 42 :359-67.

・Hepatocellular carcinoma in Japanese patients with nonalcoholic fatty liver disease, alcoholic liver disease, and chronic liver disease of unknown etiology.
Tokushige K, Hashimoto E, Taniai M, et al.
J Gastroenterol. 2011; 46 :1230-7.

G. 知的財産権の出願・登録状況

1．特許取得　　なし

2．実用新案登録　なし

図1 全アルコール性肝障害の性別 年齢分布

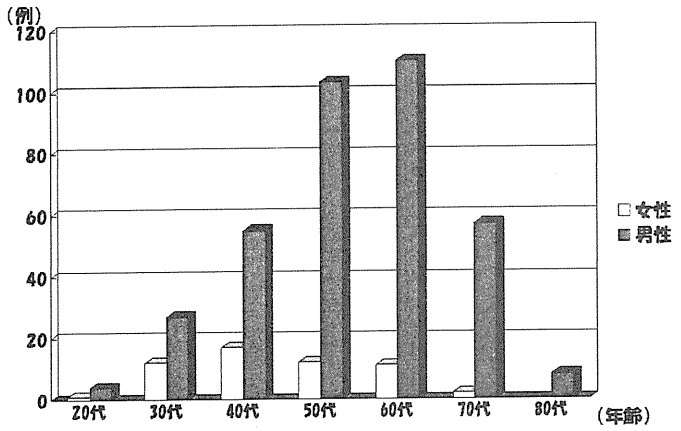


表1 全アルコール性肝障害の性別年齢別積算飲酒量

	20代	30代	40代	50代	60代	70代	80代
女性	0.8 n=1	0.3 (0.1-0.9) n=12	0.4 (0.1-1.5) n=17	0.8 (0.3-5.5) n=12	1.0 (0.3-1.8) n=11	2.0 (1.7-2.7) n=2	
男性	0.5 (0.4-0.7) n=4	0.5 (0.1-2.0) n=27	0.9 (0.1-4.7) n=55	1.0 (0.2-8.0) n=103	1.3 (0.3-6.0) n=110	1.3 (0.1-4.9) n=57	1.7 (0.5-2.4) n=8

(ton/body)

図2 全アルコール性肝障害の性別年齢別酒種

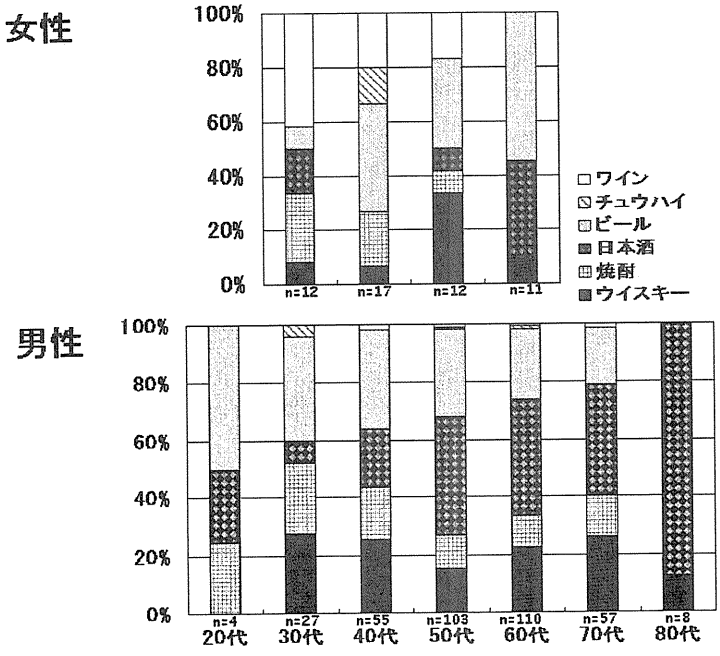


図3　全アルコール性肝障害における積算飲酒量別生活習慣病合併率

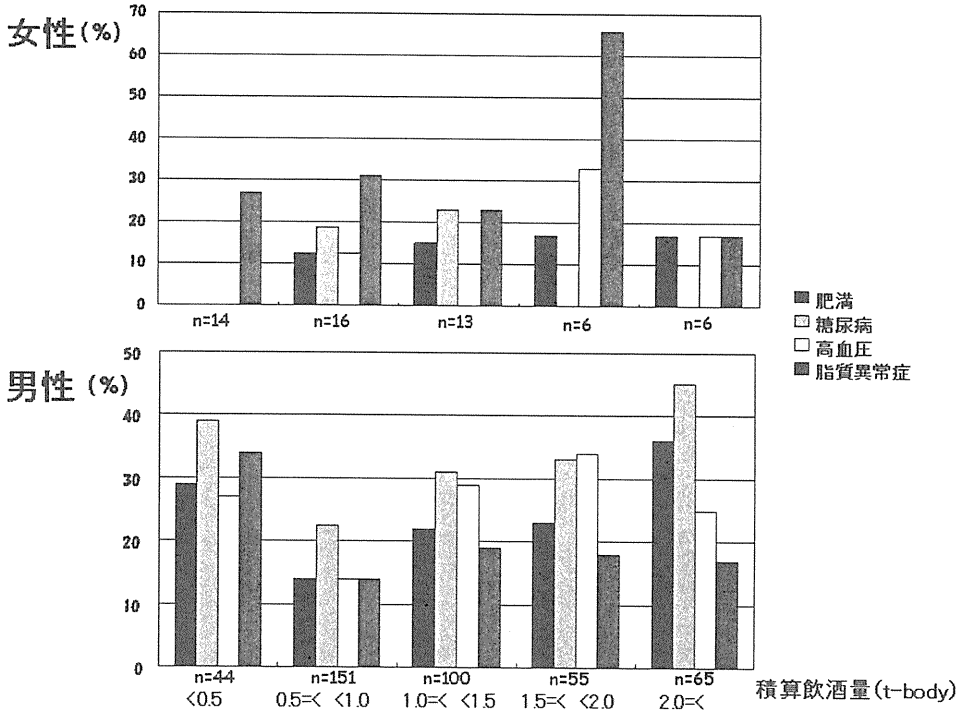


図4　アルコール性肝硬変における積算飲酒量別生活習慣病合併率

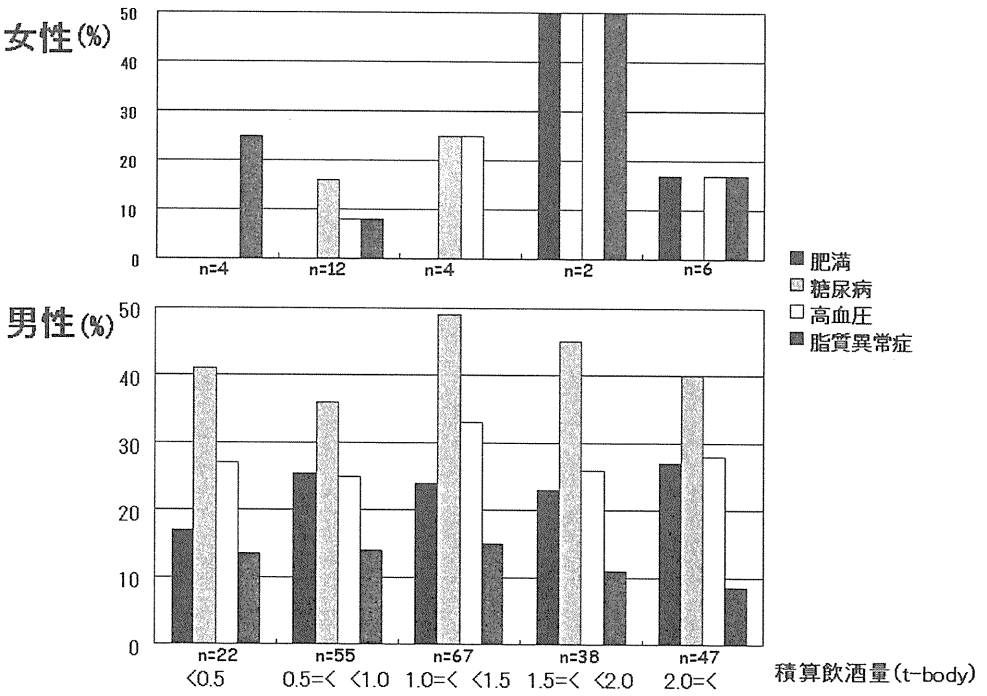


図5　全アルコール性肝障害における酒種別生活習慣病合併率

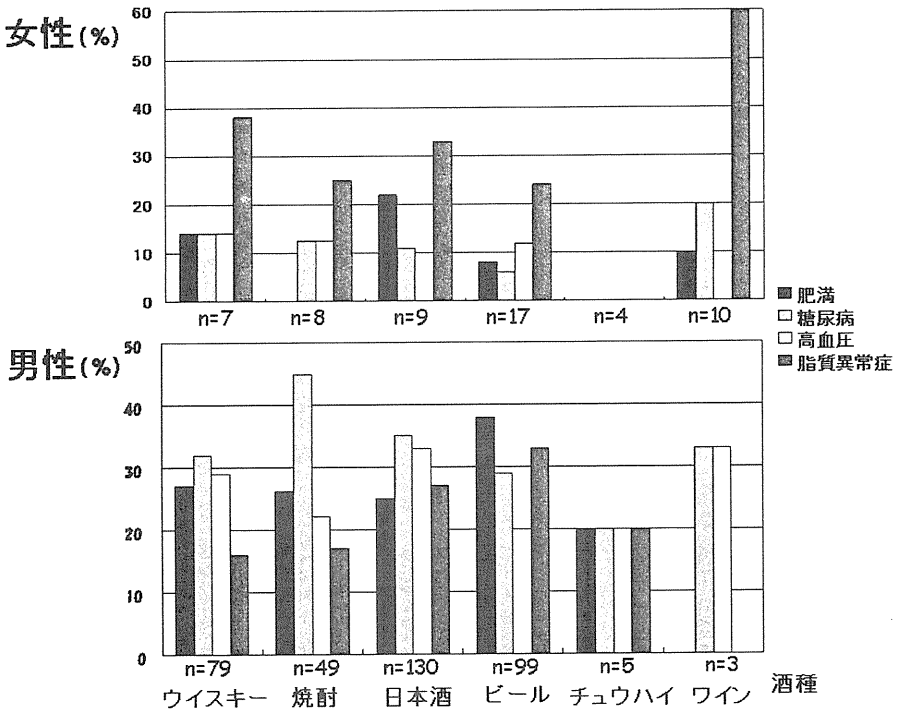
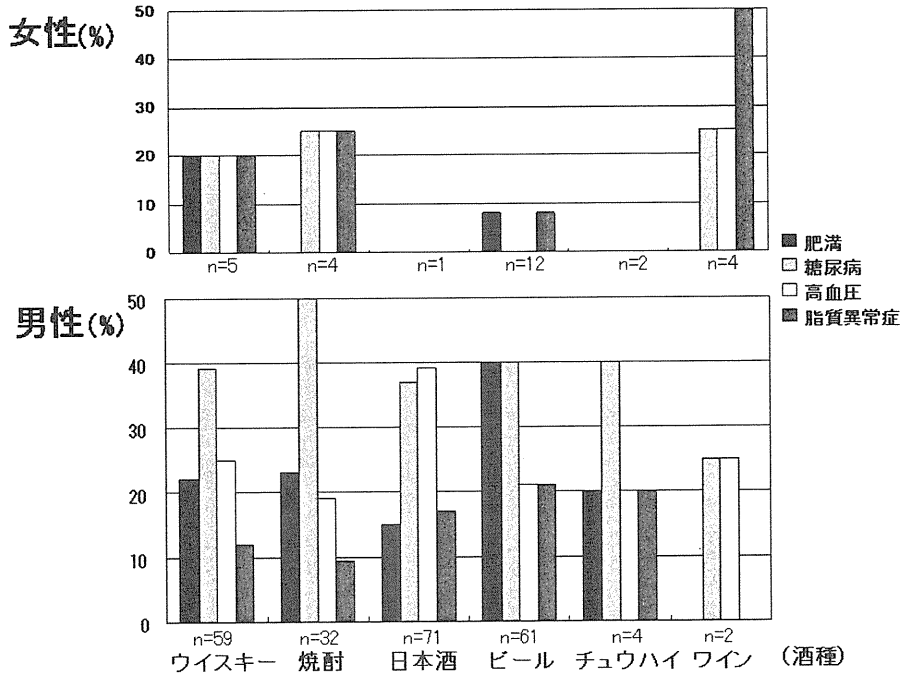


図6　アルコール性肝硬変における酒種別生活習慣病合併率



「わが国における飲酒の実態ならびに飲酒に関連する生活習慣病、公衆衛生上の諸問題とその対策に関する総合的研究」班

平成23年度　研究報告書

アルコール性膵障害の実態調査

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研究要旨

全国の日本消化器病学会認定、関連施設に対して、平成18年4月1日より平成22年3月31日までの過去4年間に受療した急性膵炎および慢性膵炎患者を対象に症例対照研究をを行った。飲酒量について詳細な記載があった膵炎群976例とその対照群1001例を比較検討した。その結果、急性膵炎の場合、男性ではエタノール換算で1日平均40-59g, 60-79g, >80gを飲酒した者のオッズ比は、それぞれ1.9, 2.1, 4.0と有意に上昇していた。女性ではそれぞれ5.4, 8.6, 7.5といずれも男性より高い危険率であった。慢性膵炎の場合、男性では1日平均40-59g, 60-79g, >80gの飲酒した者のオッズ比はそれぞれ2.6, 9.0, 15.6であった。同量の飲酒量でも男性にくらべ女性のほうが急性膵炎および慢性膵炎の危険率が高かった。膵炎の再発リスクについては1日80g以上の飲酒者でハザード比が6.2と上昇しており、多量の飲酒者に対しての断酒指導が重要であると考えられた。

A. 研究目的

近年、急性膵炎の予後は改善されたとはいえ重症化した場合の致命率はなお高く、治療には膨大な医療資源を要する。また慢性膵炎患者の末期には栄養障害や糖尿病などが主な病態となり、患者のQOLを悪化させるばかりでなく、各種悪性疾患の併発率も高く生命予後も悪化する。難治性膵疾患に関する調査研究班が行った最新の全国疫学調査では、2007年に受療した急性膵炎患者の成因はアルコール性が31%と多く、続いて胆石性が24%、特発性が17%であった[1]。特に男性患者においてはアルコール性が43%を占めていた。また慢性膵炎の成因別頻度でもアルコール性が65%と最も多く、特発性が18%であった。男性患

者では 73%がアルコール性であり、慢性膵炎でよりアルコールの占める割合が高かった [2]。過去の全国調査を比較しても、慢性膵炎患者におけるアルコール性慢性膵炎の割合は、1970年代の 50%から現在の 64%まで増加傾向を示している [2]。

一方、飲酒量に注目し、急性膵炎や慢性膵炎の発症率、膵炎の再発率などを大規模に調査した報告は少ない。飲酒の膵障害の病態に及ぼす影響を明らかにすることは、医学的、社会的に国民の健康を長期的に改善する手立てを考えるうえで意義が大きいと考えられる。本研究によって、急性膵炎や慢性膵炎の病態におけるアルコールの役割を具体的に明らかにすることを目的とする。

B. 研究方法

日本消化器病学会認定ならびに関連施設に対して調査票を送付し、症例対照研究を実施した。平成 18 年 4 月 1 日から平成 22 年 3 月 31 日までの 4 年間に入院した急性および慢性膵炎患者とした。対照は症例 1 例に対し、同じ病院を受診した患者から性、年齢(±5 歳)、初診時年月日(±1 年)を合わせて無作為に抽出した。各症例について年齢や身長、体重、飲酒量、喫煙歴、糖尿病、高血圧などの合併症などについて検討した。統計解析はロジスティック回帰分析を用いて、オッズ比と 95%信頼区間を算出し、各要因と膵炎の関連の強さの指標とした。

また、膵炎患者の予後を調査するため、平成 13 年 4 月 1 日から平成 18 年 3 月 31 日までの 5 年間に入院した急性および慢性膵炎患者を対象に、退院後の飲酒量や喫煙量、膵炎再発の有無と生命予後、血液データなどについて調査した（図 1)。統計解析は膵炎再発リスクについては Cox 比例ハザード回帰モデルを用いてハザード比を算出した。

（倫理面への配慮）

膵疾患に関するアンケート調査では、全体の数や総量、平均値のみの取り扱いとし、個人情報としては取り扱わない。個人調査票については、氏名やイニシャルを用いず、連結不可能匿名化とした。本研究は慶応大学医学部（受付番号 2009-171）ならびに東北大学医学部倫理委員会の承認（承認番号：2009-404）（承認番号：2011-261）のもと行った。

C. 研究結果

1. 飲酒量と膵炎リスクについての症例対照研究

症例は急性膵炎 574 例、慢性膵炎 402 例の計 974 例であり、対照群計 1001 例と比較検討した。急性膵炎の場合、男性ではエタノール換算で 1 日平均 40-59g, 60-79g, >80g を飲酒した者のオッズ比(95%信頼区間)は非飲酒者に比べ、それぞれ 1.9(1.1-3.2), 2.1(1.2-3.5), 4.0 (2.6-6.2) であった（表 1)。女性ではそれぞれ 5.4 (0.6-46.4) , 8.6 (1.1-69.4) , 7.5

(1.7-33.6) といずれも男性より高い危険率であった。慢性膵炎の場合、男性では 1 日平均 40-59g, 60-79g, >80g の飲酒した者のオッズ比(95%信頼区間)はそれぞれ 2.6(1.4-4.9), 9.0 (4.9-16.8), 15.6 (9.0-26.9) であった (表 2)。女性ではそれぞれ 11.7 (1.4-98.4), 11.7 (1.4-98.4), 23.3 (3.0-184.4) といずれも男性より高い危険率であった。1 日飲酒量を 20g ごとに分類し、急性膵炎と慢性膵炎を合わせた全膵炎のリスクを評価したところ 1 日平均<20g, 20-39g, 40-59g, 60-79g, 80-99g, >100g の飲酒した者のオッズ比 (95%信頼区間) はそれぞれ 0.8 (0.6-1.0), 1.4 (1.0-1.9), 1.8 (1.3-2.5), 3.3 (2.3-4.7), 4.5 (2.9-6.9), 6.7 (4.7-9.6) であった (表 3)。

2. 飲酒と膵炎再発リスクについての予後調査

現在症例を集積中である。これまでに集計した膵炎症例計 138 例を用いた解析結果について報告する。症例の成因別分類ではアルコール性が 61 例、特発性が 22 例、胆石性が 22 例、自己免疫性が 7 例、遺伝·家族性が 5 例、高脂血症性が 2 例、その他 19 例であった。膵炎発症後も飲酒していた群は、飲酒をしていなかった群に比べ、膵炎再発率のハザード比 (95%信頼区間) が 2.5(1.2-5.4)と有意に高かった (図 2)。飲酒量別に評価すると 1 日平均 80g 未満の飲酒者のハザード比 (95%信頼区間) は 1.7(0.7-4.0)であるのに対し、80g 以上の飲酒者の場合、ハザード比 (95%信頼区間) は 6.2(1.7-18.1)と有意に高かった (図 3)。

D. 考察

本研究は、全国の消化器病学会の認定施設とその関連施設の協力を得て、膵炎症例を登録し、飲酒の側面から急性膵炎および慢性膵炎の病態やその特徴、および関連性を明らかにしようとする試みである。

膵炎の発症には飲酒が需要な要因となることは周知である、しかし、これまで膵炎リスクの定量化はあまりおこなわれていない。本邦では比較的少数での症例対照研究のみであった[3)]。本研究では膵炎群 974 例とその対照群 1001 例を比較し、飲酒による膵炎リスクを評価した。その結果、急性膵炎の場合、男性ではエタノール換算で 1 日平均 40-59g, 60-79g, >80g を飲酒した者のオッズ比は、それぞれ 1.9, 2.1, 4.0 と有意に上昇していた。女性ではそれぞれ 5.4, 8.6, 7.5 といずれも男性より高い危険率であった。慢性膵炎の場合、男性では 1 日平均 40-59g, 60-79g, >80g の飲酒した者のオッズ比はそれぞれ 2.6, 9.0, 15.6 であった。女性ではそれぞれ 11.7, 11.7, 23.3 といずれも男性より高い危険率であった。同量の飲酒量でも男性にくらべ女性のほうが急性膵炎および慢性膵炎の危険率が高かった。近年、若い世代を中心とした女性飲酒者の増加が指摘されているが、全国調査でも女性患