Original Article

Comparison of the relationships of alcoholic and nonalcoholic fatty liver with hypertension, diabetes mellitus, and dyslipidemia

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We compared the relationships of alcoholic fatty liver and nonalcoholic fatty liver with hypertension, diabetes mellitus, and dyslipidemia. Using a nationwide Japanese survey, we collected data on subjects with biopsy-proven alcoholic fatty liver or nonalcoholic fatty liver. Multiple logistic regression analysis was performed to determine whether alcoholic fatty liver and nonalcoholic fatty liver are associated factors for these diseases. Data on 191 subjects (65, alcoholic fatty liver; 126, nonalcoholic fatty liver) were analyzed. Alcoholic fatty liver (odds ratio, 2.54; 95% confidence interval, 1.06–6.32; $p = 0.040$), age ≥55 years, and body mass index ≥25 kg/m² were correlated with hypertension, whereas nonalcoholic fatty liver (odds ratio, 2.32; 95% confidence interval, 1.08–5.20; $p = 0.035$) and serum γ-glutamyl transpeptidase levels ≥75 IU/l were correlated with dyslipidemia. Furthermore, we found that there were biological interactions between alcoholic fatty liver and body mass index ≥25 kg/m² in ≥55-year-old subjects (attributable proportion due to interaction, 0.68; 95% confidence interval, 0.19–1.17), as well as between alcoholic fatty liver and age ≥55 years in subjects with body mass index ≥25 kg/m² (attributable proportion due to interaction, 0.71; 95% confidence interval, 0.24–1.18). Alcoholic fatty liver was more strongly associated with hypertension than nonalcoholic fatty liver and nonalcoholic fatty liver was more strongly associated with dyslipidemia than alcoholic fatty liver. Moreover, alcoholic fatty liver, obesity, and older age may interact to influence hypertension status.

Key Words: **alcoholic fatty liver, nonalcoholic fatty liver, hypertension, diabetes mellitus, dyslipidemia**

Fatty liver disease (FLD) is the most prevalent form of liver disease worldwide.[1,2] Overnutrition and excessive alcohol consumption are 2 major causes of FLD.[3] Overnutrition can induce nonalcoholic fatty liver disease (NAFLD), a spectrum of conditions raging from simple steatosis [or nonalcoholic fatty liver (NAFL)] to nonalcoholic steatohepatitis and cirrhosis.[1,4] NAFLD is considered the hepatic manifestation of the metabolic syndrome,[5,6] and many studies have revealed strong relationships between NAFLD and hypertension (HT), type 2 diabetes mellitus (DM), and dyslipidemia (DL).[7] In contrast, excessive alcohol consumption can lead to alcoholic liver disease (ALD), which includes simple steatosis [or alcoholic fatty liver (AFL)], alcoholic hepatitis, hepatic fibrosis, and cirrhosis.[2] Less data are available on the relationship between ALD and HT, DM, and DL than that between NAFLD and such diseases. However, accumulating evidence indicates a positive relationship between excessive alcohol consumption and HT, DM, and DL.[8–11] These findings indicate that ALD may also be closely linked to these diseases.

In the comprehensive management of FLD, it is important to understand the relationships between FLD and HT, DM, and DL in detail. To the best of our knowledge, no study has analyzed these relationships according to the FLD type. The goal of the present study was to compare AFL and NAFL, the most common FLD types, using data from a nationwide Japanese survey on FLD.

Materials and Methods

A nationwide survey. We conducted a nationwide Japanese survey on the status of FLD between 2009 and 2010 by sending a questionnaire to 894 institutions that employed medical specialists in gastroenterology and hepatology. The questionnaire contained questions regarding how histories were taken to assess alcohol consumption and what values were used as the upper limit of alcohol consumption for the purpose of defining social drinking. We also sent data sheets for subjects with biopsy-proven AFL, NAFL, or nonalcoholic steatohepatitis. The data sheets included details regarding age, gender, anthropometric measurements, blood pressure, liver function tests, data regarding the presence or absence of HT, DM, and DL, and laboratory test values associated with these diseases. Data obtained around the time of liver biopsy were collected. Written informed consent was obtained from each patient at the time of biopsy. This study was performed in accordance with the Declaration of Helsinki.

Subjects. In this study, we analyzed data from subjects with AFL or NAFL. AFL was diagnosed according to the following criteria of the Alcohol and Liver Research Group of the Ministry of Education: alcohol consumption ≥60 g/day for >5 years for men and ≥40 g/day for >5 years for women.[12] For the diagnosis of NAFL, we adopted ≤20 g/day as the upper limit of alcohol consumption, a value that is accepted by most researchers.[5,13]

Criteria for HT, DM, and DL. The diagnosis of HT, DM, and DL was made on the basis of treatments for these diseases or their respective criteria defined below. HT was defined according to the following Japanese Society of Hypertension guidelines for the management of hypertension: a systolic blood pressure ≥140 mmHg or a diastolic blood pressure ≥90 mmHg.[14] DM was defined by the following criteria of the Japan Diabetes Society: fasting blood glucose levels ≥126 mg/dl or random blood glucose levels ≥200 mg/dl.[15] DL was defined as serum low-density-lipoprotein (LDL) cholesterol levels ≥140 mg/dl, serum high-density-lipoprotein (HDL) cholesterol levels <40 mg/dl, or serum triglyceride levels ≥150 mg/dl, according to the criteria of the Japan Atherosclerosis Society.[16] Serum LDL cholesterol levels were calculated using the Friedewald equation (LDL cholesterol =

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total cholesterol – HDL cholesterol – triglycerides/5) for subjects with serum triglyceride levels <400 mg/dl.[17]

Statistical analysis. Data are expressed as medians (ranges) or percentages. The chi-square test or Fisher's exact probability test were used to compare categorical variables, and the Mann–Whitney *U* test was used to compare continuous variables. A multiple logistic regression analysis was performed to determine whether the FLD types were associated factors for HT, DM, DL or combinations thereof (HT + DM, HT + DL, DM + DL, HT + DM + DL, and all combinations of ≥2 of the 3 diseases). The following potential confounding variables were included in the analysis: age (≥55 years, <55 years), gender (male, female), body mass index (BMI) (≥25 kg/m^2, <25 kg/m^2), serum aspartate aminotransferase (AST) levels (≥40 IU/L, <40 IU/L), and serum γ-glutamyl transpeptidase (γ-GTP) levels (≥75 IU/L, <75 IU/L). BMI ≥25 kg/m^2 is defined as obesity in Japan.[18] A p value <0.05 was considered statistically significant. If the FLD types and other variables were simultaneously identified as associated factors, stratified and biological interaction analyses were conducted. Three indices were employed to assess biological interaction: the relative excess risk due to interaction (RERI), the attributable proportion due to interaction (AP), and the synergy index (S).[19,20] Methods for calculating the indices and their 95% confidence intervals (CI) are described by Andersson *et al.*[21] RERI = 0, AP = 0, or S = 1 indicated an additive interaction; RERI >0, AP >0, or S >1 indicated a synergistic interaction; and RERI <0, AP <0, or S <1 indicated an antagonistic interaction.[22] Analyses were performed using STATA ver 11.1 (STATA Corp., College Station, TX).

Results

Answers to the questionnaire were obtained from 101 (11.3%) of the 894 institutions and data on FLD were obtained from 66 hospitals (7.4%). The numbers of patients with FLDs were as follows: AFL, 71; NAFL, 131; nonalcoholic steatohepatitis, 494. Of the 202 subjects with AFL or NAFL, 6 with AFL and 5 with NAFL were excluded because of a lack of anthropometric data or information on the presence/absence of HT, DM, and DL. Thus, this study was conducted using data for 191 subjects (65, AFL; 126, NAFL).

Table 1 shows the baseline characteristics of the subjects. The female-to-male ratio, BMI, and diastolic blood pressure were lower in subjects with AFL than in those with NAFL. Laboratory tests revealed that levels of serum AST, γ-GTP, and fasting blood glucose were higher in subjects with AFL than in those with NAFL, whereas levels of serum total cholesterol and LDL cholesterol were lower in subjects with AFL than in those with NAFL. There were no significant differences in prevalence of HT, DM, DL, HT + DM, HT + DL, DM + DL, HT + DM + DL, and any combination of ≥2 of the 3 diseases between subject groups.

Table 2 lists factors associated with HT, DM, or DL for the entire cohort. Regarding FLD types, AFL was an associated factor for HT whereas NAFL was one for DL. Age ≥55 years was identified as a significant factor for HT, DM, and all combinations of the diseases. BMI ≥25 kg/m^2 was significantly associated with HT and HT + DL. Serum γ-GTP ≥75 IU/L was another factor associated with DL.

Stratified analysis was performed with regard to the 3 associated

Table 1. Baseline characteristics of the subjects

	Total cohort (n = 191)	AFL (n = 65)	NAFL (n = 126)	p value*
Age, years	54 (15–85)	56 (23–80)	53.5 (15–85)	0.541
Gender, male/female	115/76	50/15	65/61	0.0007
BMI, kg/m^2	24.9 (13.2–61.3)	24.4 (18.0–35.3)	25.4 (13.2–61.3)	0.026
Systolic blood pressure, mmHg	124 (84–186)	123 (100–186)	125 (84–168)	0.727
Diastolic blood pressure, mmHg	76 (46–114)	74 (58–114)	78 (46–107)	0.010
AST, IU/L	41 (15–675)	61 (17–675)	35 (15–310)	<0.0001
ALT, IU/L	49 (12–1123)	49 (12–1123)	48.5 (13–377)	0.827
γ-GTP, IU/L	72 (10–3028)	156 (24–3028)	50 (10–646)	<0.0001
Fasting blood glucose, mg/dL	103 (67–310)	111.5 (70–176)	100 (67–310)	0.005
Hemoglobin A1c, %	5.8 (3.7–10.6)	5.9 (3.7–9.1)	5.8 (4.4–10.6)	0.450
Total cholesterol, mg/dL	192 (37–454)	166 (37–454)	201 (88–349)	<0.0001
LDL cholesterol, md/dL†	114 (5–246)	89 (5–210)	119 (51–246)	<0.0001
HDL cholesterol, mg/dL	49 (3–131)	47 (3–131)	50 (20–129)	0.182
Triglycerides, mg/dL	118 (21.5–879)	110 (25–879)	120 (21.5–407)	0.731
HT, n (%)	60 (31.4)	25 (38.5)	35 (27.8)	0.132
untreated, n (%)	18 (30.0)	10 (40.0)	8 (22.9)	
under treatment, n (%)	42 (70.0)	15 (60.0)	27 (77.1)	
DM, n (%)	47 (24.6)	19 (29.2)	28 (22.2)	0.287
untreated, n (%)	18 (38.3)	10 (52.6)	8 (28.6)	
under treatment, n (%)	29 (61.7)	9 (47.4)	20 (71.4)	
DL, n (%)	71 (37.2)	21 (32.3)	50 (39.7)	0.318
untreated, n (%)	43 (60.6)	15 (71.4)	28 (56.0)	
under treatment, n (%)	28 (39.4)	6 (28.6)	22 (44.0)	
HT + DM, n (%)	26 (13.6)	12 (18.5)	14 (11.1)	0.184
HT + DL, n (%)	34 (17.8)	12 (18.5)	22 (17.5)	0.864
DM + DL, n (%)	26 (13.6)	6 (9.2)	20 (15.9)	0.267
HT + DM + DL, n (%)	16 (8.4)	5 (7.7)	11 (8.7)	1.000
≥2 of the 3 diseases, n (%)	53 (27.7)	20 (30.8)	33 (26.2)	0.503

AFL, alcoholic fatty liver; NAFL, nonalcoholic fatty liver; BMI, body mass index; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transpeptidase; HT, hypertension; DM, diabetes mellitus; DL, dyslipidemia; LDL, low-density lipoprotein; HDL, high-density lipoprotein. *AFL vs NAFL. Chi-square test or Fisher's exact probability test for categorical variables, Mann–Whitney *U* test for continuous variables. †The Friedewald equation was used. Data excluded 4 subjects with AFL and 1 with NALF whose serum triglyceride levels were ≥400 mg/dL.

Table 2. Associated factors for HT, DM, DL or their combinations

Disease	Associated factors	*p* value	Adjusted odds ratio*	95% Confidence interval
HT	AFL	0.040	2.54	1.06–6.32
	Age ≥55 years	<0.0001	6.64	3.24–14.49
	BMI ≥25 kg/m^2	0.012	2.49	1.23–5.17
DM	Age ≥55 years	<0.0001	5.46	2.55–12.62
DL	NAFL	0.035	2.32	1.08–5.20
	γ-GTP ≥75 IU/L	0.004	2.85	1.42–5.90
HT + DM	Age ≥55 years	0.0006	7.17	2.55–25.78
HT + DL	Age ≥55 years	0.001	4.20	1.81–10.72
	BMI ≥25 kg/m^2	0.021	2.61	1.18–6.06
DM + DL	Age ≥55 years	0.002	5.14	1.95–15.64
HT + DM + DL	Age ≥55 years	0.006	8.51	2.22–56.32
≥2 of the 3 diseases	Age ≥55 years	0.0001	4.42	2.19–9.41

HT, hypertension; DM, diabetes mellitus; DL, dyslipidemia; AFL, alcoholic fatty liver; BMI, body mass index; NAFL, nonalcoholic fatty liver; γ-GTP, γ-glutamyl transpeptidase. *A multiple logistic regression analysis was performed on the basis of types of fatty liver disease, age, gender, BMI, and serum levels of aspartate aminotransferase and γ-GTP.

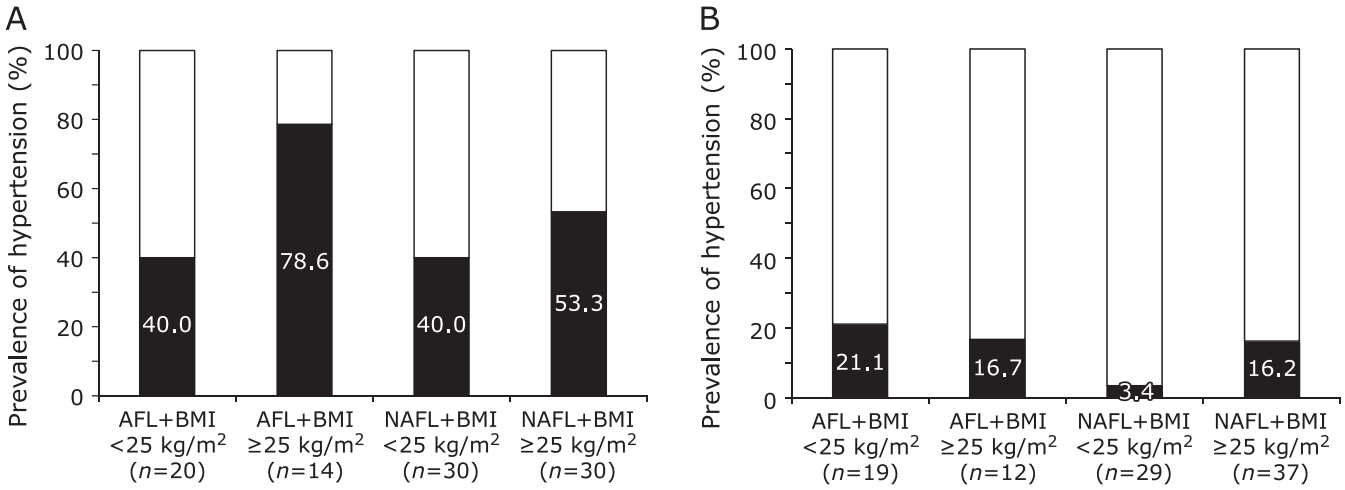

Fig. 1. Comparison of the prevalence of hypertension among subjects stratified by types of fatty liver disease and body mass index in each age subgroup. (A) Subjects aged ≥55 years. $p = 0.082$ (chi-square test). (B) Subjects aged <55 years. $p = 0.284$ (chi-square test). AFL, alcoholic fatty liver; NAFL, nonalcoholic fatty liver; BMI, body mass index ■, presence of hypertension; □, absence of hypertension.

factors (AFL, age ≥55 years, and BMI ≥25 kg/m^2) for HT. First, the entire cohort was divided into 2 subgroups according to age (≥55 years, <55 years), and stratified analysis by FLD type and BMI was performed. Among subjects aged ≥55 years ($n = 94$), the prevalence of HT was the highest in subjects with AFL + BMI ≥25 kg/m^2 (Fig. 1A). After adjusting for other variables, AFL + BMI ≥25 kg/m^2 showed significantly higher odds ratio (OR) for HT compared with NAFL + BMI <25 kg/m^2 (Table 3). In interaction analysis between AFL and BMI ≥25 kg/m^2, AP (0.68, 95% CI, 0.19–1.17) was significant, whereas RERI and S were not. Among subjects aged <55 years ($n = 97$), the prevalence of HT was the highest in subjects with AFL + BMI <25 kg/m^2 (Fig. 1B). There were no significant differences between the relationship of each stratified group with HT (Table 3); moreover, neither RERI, AP, nor S was significant as per the interaction analysis.

We next divided the entire cohort into 2 subgroups according to BMI (≥25 kg/m^2, <25 kg/m^2), and performed stratified analysis by FLD type and age. Among subjects with BMI ≥25 kg/m^2 ($n = 93$), the prevalence of HT was the highest in subjects with AFL + age ≥55 years (Fig. 2A). After adjusting for other variables, AFL + age ≥55 years and NAFL + age ≥55 years showed significantly higher ORs for HT compared with NAFL + age <55 years (Table 4). Regarding interaction analysis between AFL and age ≥55 years, AP (0.71, 95% CI, 0.24–1.18) was significant, whereas RERI and S were not. Among subjects with BMI <25 kg/m^2 ($n = 98$), the prevalence of HT was the highest in subjects with AFL + age ≥55 years (Fig. 2B). After adjustment for other variables, AFL + age ≥55 years and NAFL + age ≥55 years showed significantly higher ORs for HT compared with NAFL + age <55 years (Table 4). Neither RERI, AP, nor S was significant as per the interaction analysis.

The subjects were divided according to the FLD type and serum γ-GTP levels. The prevalence of DL was the highest in subjects with NAFL + γ-GTP ≥75 IU/L (Fig. 3). After adjusting for other variables, NAFL + γ-GTP ≥75 IU/L showed significantly higher ORs for DL than AFL + γ-GTP <75 IU/L (Table 5). A significant interaction between NAFL and γ-GTP ≥75 IU/L was not detected.

Discussion

To the best of our knowledge, this is the first study to analyze the relationships between FLD and HT, DM, and DL according to

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Table 3. Stratified and biological interaction analyses for hypertension in age subgroups

Subgroup	Stratification	*p* value	Adjusted odds ratio*	95% Confidence interval	Measures of interaction	Estimate	95% Confidence interval
Age ≥55 years (*n* = 94)	NAFL + BMI <25 kg/m²		1.00				
	NAFL + BMI ≥25 kg/m²	0.138	2.29	0.77–6.83	RERI	7.48	–9.59–24.56
	AFL + BMI <25 kg/m²	0.294	2.23	0.50–9.96	AP	0.68	0.19–1.17
	AFL + BMI ≥25 kg/m²	0.008	11.00	1.90–63.86	S	3.97	0.62–25.56
Age <55 years (*n* = 97)	NAFL + BMI <25 kg/m²		1.00				
	NAFL + BMI ≥25 kg/m²	0.127	5.46	0.41–72.11	RERI	–6.50	–27.33–14.33
	AFL + BMI <25 kg/m²	0.098	7.26	0.69–76.09	AP	–1.25	–5.50–3.01
	AFL + BMI ≥25 kg/m²	0.216	5.22	0.38–71.32	S	0.39	0.04–3.80

NAFL, nonalcoholic fatty liver; BMI, body mass index; AFL, alcoholic fatty liver; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; S, synergy index. *Odds ratios for hypertension were calculated after adjustment for gender and serum levels of aspartate aminotransferase and γ-glutamyl transpeptidase.

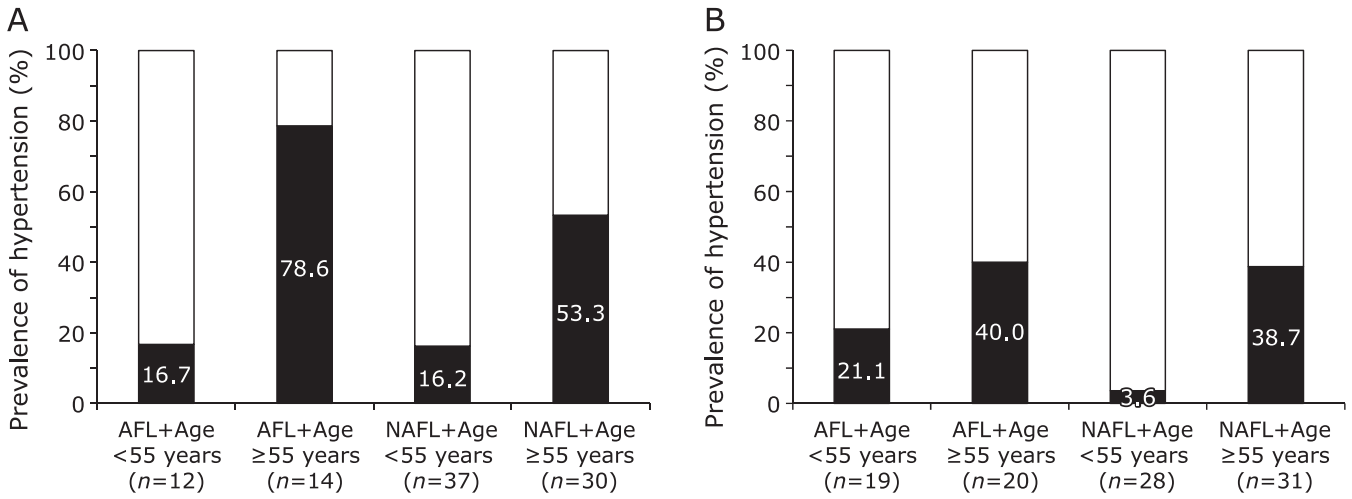

Fig. 2. Comparison of the prevalence of hypertension among subjects stratified by types of fatty liver disease and age in each body mass index (BMI) subgroup. (A) Subjects with BMI ≥25 kg/m². $p<0.0001$ (chi-square test). (B) Subjects with BMI <25 kg/m². $p = 0.006$ (chi-square test). AFL, alcoholic fatty liver; NAFL, nonalcoholic fatty liver; ■, presence of hypertension; □, absence of hypertension.

Table 4. Stratified and biological interaction analyses for hypertension in BMI subgroups

Subgroup	Stratification	*p* value	Adjusted odds ratio*	95% Confidence interval	Measures of interaction	Estimate	95% Confidence interval
BMI ≥25 kg/m² (*n* = 93)	NAFL + Age <55 years		1.00				
	NAFL + Age ≥55 years	0.004	5.83	1.79–19.05	RERI	14.43	–16.50–45.35
	AFL + Age <55 years	0.891	1.14	0.17–7.55	AP	0.71	0.24–1.18
	AFL + Age ≥55 years	0.0003	20.40	3.96–104.98	S	3.90	0.66–23.11
BMI <25 kg/m² (*n* = 98)	NAFL + Age <55 years		1.00				
	NAFL + Age ≥55 years	0.011	16.65	1.90–146.17	RERI	–1.21	–34.15–31.74
	AFL + Age <55 years	0.059	9.61	0.92–100.97	AP	–0.05	–1.46–1.36
	AFL + Age ≥55 years	0.006	24.05	2.44–237.10	S	0.95	0.24–3.84

BMI, body mass index; NAFL, nonalcoholic fatty liver; AFL, alcoholic fatty liver; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; S, synergy index. *Odds ratios for hypertension were calculated after adjustment for gender and serum levels of aspartate aminotransferase and γ-glutamyl transpeptidase.

the FLD type. Our results show that the FLD type influences the relationship between FLD and HT or DL. Thus, AFL was more strongly associated with HT than NAFL and NAFL was more strongly associated with DL than AFL. In contrast, the relationship between FLD and DM or the combinations of HT, DM, and DL were found not to be influenced by the FLD type.

Intensive studies have established excessive alcohol consumption as a risk factor for HT.[9] Because hepatic steatosis occurs in almost all subjects who consume alcohol excessively,[23] the close relationship between AFL and HT was expected. However, a full understanding of the influence of the FLD type on the relationship between FLD and HT is still lacking. Studies have revealed various mechanisms by which excessive alcohol consumption induces HT, including increased sympathetic nervous

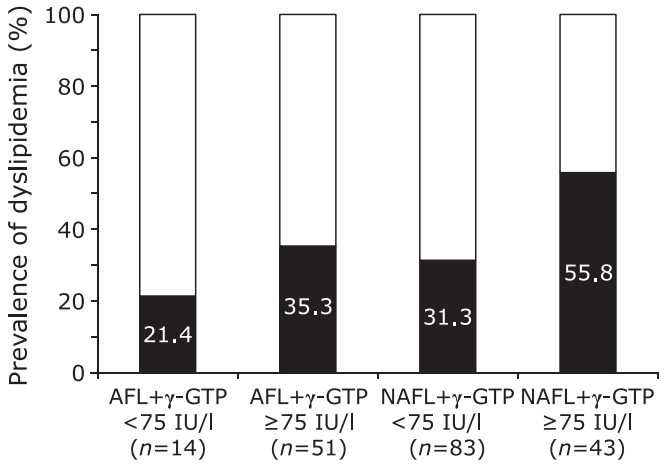

Fig. 3. Comparison of the prevalence of dyslipidemia among subjects stratified by types of fatty liver disease and serum γ-glutamyl transpeptidase level. $p = 0.027$ (chi-square test). AFL, alcoholic fatty liver; NAFL, nonalcoholic fatty liver; γ-GTP, γ-glutamyl transpeptidase; ■, presence of hypertension; □, absence of hypertension.

Table 5. Stratified and biological interaction analyses for dyslipidemia

Stratification	*p* value	Adjusted odds ratio*	95% Confidence interval	Measures of interaction	Estimate	95% Confidence interval
AFL + γ-GTP <75 IU/l		1.00				
AFL + γ-GTP ≥75 IU/l	0.298	2.13	0.51–8.91	RERI	2.30	–1.64–6.23
NAFL + γ-GTP <75 IU/l	0.482	1.65	0.41–6.61	AP	0.45	–0.07–0.97
NAFL + γ-GTP ≥75 IU/l	0.028	5.08	1.19–21.60	S	2.29	0.46–11.40

AFL, alcoholic fatty liver; γ-GTP, γ-glutamyl transpeptidase; NAFL, nonalcoholic fatty liver; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; S, synergy index. *Odds ratios for dyslipidemia were calculated after adjustment for age, gender, body mass index, and serum aspartate aminotransferase levels.

system activity and stimulation of the renin–angiotensin–aldosterone system.[9] These mechanisms also have been reported to be involved in the metabolic syndrome, which is usually accompanied by NAFLD.[24,25] Insulin resistance, a key factor in the development of the metabolic syndrome,[26] is another mechanism in the pathogenesis of HT.[27] Recent studies have found that excessive alcohol consumption does not significantly increase insulin resistance.[28] Nevertheless, our study demonstrates that AFL is the FLD type more closely linked to HT. Potential differences in mechanisms of HT between the FLD types might influence planning therapeutic strategies for HT in subjects with such FLD types.

This study identified obesity and older age as other associated factors for HT. These factors are established risk factors for HT.[29,30] In stratified analysis, the combination of AFL and obesity in older subjects and that of AFL and older age in both obese and nonobese subjects showed a significant increase in the ORs for HT. In interaction analysis, the results differed according to the indices for biological interaction. According to the interaction analysis for AFL and obesity in older subjects, AP was significant, whereas RERI and S were not. The relationship between AFL and older age in obese subjects followed this same pattern. However, a study on interaction analysis published in 2006 demonstrates that AP is the most robust measure in a logistic regression model.[31] Hence our results could indicate that AFL, obesity, and older age interact to influence hypertension status.

Cross-sectional studies have suggested an interactive influence of excessive alcohol consumption and obesity on HT.[32,33] Moreover, in overweight men, combined intervention involving restricted alcohol and food consumption leads to decreases in blood pressure more effectively than either intervention alone.[34] We were unable to find any published studies examining the interaction between excessive alcohol consumption and older age in relation to HT. On the basis of the theory of biological interaction,[35] the interactions found in our present study may indicate the presence of at least a pathway toward HT in which AFL, obesity, and older age, are all involved. However, future prospective studies will be necessary to confirm these interactions.

We show here that NAFL and increased serum γ-GTP levels are associated factors for DL, and their combination is most strongly associated with DL. We could not confirm the DL types with which these factors were associated because we did not collect the relevant information. Generally, baseline serum LDL cholesterol levels were higher in subjects with NAFL than in those with AFL, although the results were calculated using data from untreated as well as treated subjects. This finding is consistent with the results in large-scale studies investigating the influence of alcohol consumption on serum lipid levels in which serum LDL cholesterol levels were inversely correlated with alcohol consumption.[36,37] Recent studies of subjects with DM have shown that serum γ-GTP levels are positively associated with DL.[38] Furthermore, elevation of serum γ-GTP levels has been identified as a predictor for cardiovascular diseases[39] as well as a marker of metabolic syndrome.[40] The complexes that form between γ-GTP forms and LDL lipoprotein facilitate the evolution of atherosclerotic plaques toward instability and rupture.[41] Given these findings, the magnitude of risk for cardiovascular diseases in subjects with NAFL with elevated serum γ-GTP levels should be investigated.

There are some limitations to this study. First, because of its cross-sectional design, this study could not determine causality between HT, DM, and DL and associated factors. Second, the number of subjects was relatively small, constraining statistical

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power. Third, data on FLD were obtained from only a limited number of institutions in Japan, which might limit generalizability of the findings. Fourth, this study lacked data on smoking, a potential confounder in particular for HT.[42] Since a close link of excessive alcohol consumption to smoking has been reported,[43] it is possible that in our cohort, the proportion of smokers was higher in subjects with AFL than in those with NAFL. A large-scale study, however, has demonstrated that smoking has a smaller impact on elevation of blood pressure than excessive alcohol consumption in men, no such effect was seen in women.[44] Therefore, although our results should be interpreted with caution, we feel confident in concluding that they would not have changed significantly if smoking had been included as a variable.

The present study demonstrates that the relationships between FLD and HT, DM, and DL partly depend on the FLD type. We believe that these findings may be helpful in managing subjects with FLD. Future studies are needed to confirm our results and clarify mechanisms responsible for the development of HT in which AFL, obesity, and older age play a role.

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Conflict of Interest

We have no financial disclosure or conflict of interest to report.

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