Research Article

Eating Quickly is Associated with Ultrasound-Diagnosed Non-Alcoholic Fatty Liver Disease in Japanese Adults

Koichiro Irie[1], Tetsuji Azuma[2], Takatoshi Yonenaga[2], Minako Hada[2], Kazutoshi Watanabe[3], Fumiko Deguchi[3], Akihiro Obora[3], Takao Kojima[3] and Takaaki Tomofuji[2]*

[1]*Department of Oral Health and Preventive Dentistry, Meikai University School of Dentistry, Japan*

[2]*Department of Community Oral Health, School of Dentistry, Asahi University, Japan*

[3]*Asahi University Hospital, Japan*

*Corresponding Author: Takaaki Tomofuji, Department of Community Oral Health, School of Dentistry, Asahi University, Mizuho, Japan.

Abstract

   Non-alcoholic fatty liver disease (NAFLD) is a major global health problem. The aim of the present cross-sectional study was to investigate the relationship between eating quickly and NAFLD in Japanese adults. A total of 8556 participants underwent a health checkup. Abdominal ultrasonography was applied to diagnose NAFLD, and information on eating speed was obtained using a self-administrated questionnaire. Of the study participants, 2570 (30.0%) had ultrasound diagnosed NAFLD. The participants who reported eating quickly had a higher prevalence of NAFLD when compared to those who did not report eating quickly. The presence of NAFLD was significantly associated with male sex (odds ratio [OR] = 3.163, 95% confidence interval [CI] = 2.800 - 3.573), age ≥ 65 years (OR = 1.426, 95%CI = 1.076 - 1.889), high body mass index (≥ 25 kg/m^2; OR = 9.615, 95%CI = 8.511 - 10.863), hypertension (OR = 1.659, 95%CI = 1.424 - 1.931), high hemoglobin A1c values (≥ 6.5%; OR = 4.096, 95%CI = 3.080 - 5.446), the presence of regular exercise habits (OR = 0.605, 95%CI = 0.522 - 0.701), and eating quickly (OR = 1.146, 95%CI = 1.023 - 1.283) after adjusting for confounding factors. These results indicated that lifestyle factors, including eating quickly, is positively associated with NAFLD in Japanese adults independently of overweight and obesity.

Keywords: Eating Behaviors; Eating Speed; Fatty Liver; Cross-Sectional Study; Japanese

Abbreviations

BMI: Body Mass Index; DBP; Diastolic Blood Pressure; HbAlc: Hemoglobin A1c; NAFLD: Non-Alcoholic Fatty Liver Disease; SBP: Systolic Blood Pressure

Introduction

   Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease and a major global health threat due to its growing incidence and prevalence [1]. NAFLD is defined as the accumulation of lipids, mainly triacylglycerol, in the hepatocytes of individuals who do not consume significant amounts of alcohol and in whom other known causes of steatosis, such as certain chronic liver diseases (hepatitis A, B, and C) or medications, have been excluded [2,3]. The prevalence of NAFLD in Japanese adults is approximately 20% to 30% [4]. Nevertheless, effective pharmacological treatments for NAFLD have not been established in Japan. Therefore, investigations on various approaches to prevent and/or improve NAFLD are continuing.

   Previous studies have demonstrated that lifestyle factors are closely associated with NAFLD [5-8]. For instance, it has been reported that a poor dietary composition [9] and Western dietary

pattern [10] are important factors in the progression of NAFLD. It is also known that physical exercise is related to improvements of NAFLD [7]. However, the relationship between lifestyle and NAFLD is still not completely understood, and additional clinical studies are needed. In particular, literature on the relationship between eating behaviors and NAFLD is sparse.

Eating quickly is an inadequate eating behavior, and it has been revealed as a risk factor for overweight and obesity [11-15]. Because obesity is a cause of NAFLD [6], eating quickly may also be associated with NAFLD. However, the relationship between eating quickly and NAFLD remains unclear. We hypothesized that eating quickly is correlated to NAFLD.

Purpose of the Study

The purpose of the present cross-sectional study was to investigate the relationship between eating speed and NAFLD in Japanese adults.

Materials and Methods

Study design

The present study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of Asahi University (No. 27010). A total of 13778 Japanese adults, aged 29 to 82 years, who received health check-ups at Asahi University Hospital in Gifu, Japan, were recruited from April 2018 to March 2019. Since the present study involved completing a survey, we did not calculate the required sample size for statistical significance. We excluded 912 participants with insufficient data. Participants who tested positive for serum antigen and antibody to hepatitis B or C infection (n = 115) were also excluded. In addition, we excluded participants with an alcohol intake of "≥ 2 go", where "go" is a traditional Japanese unit of volume measurement corresponding to 23 g of ethanol (n = 1244). Accordingly, 8556 participants (4756 men and 3800 women) were eligible for inclusion in this study. All participants provided written informed consent prior to enrollment in the study.

Diagnosis of NAFLD

Three specialists in internal medicine diagnosed NAFLD using ultrasonography (ProSound Alpha 7, Hitachi Aloka Medical, Tokyo, Japan) [16]. An ultrasonographical diagnosis of fatty liver was defined as a bright liver, increased liver echotexture when compared to the kidneys, vascular blurring, and deep attenuation of the liver.

Evaluation of eating speed and other lifestyle factors

Information on eating speed was collected using a self-administered questionnaire, which was developed based on the con-

ventional National Health and Nutrition Examination Survey and questions specified by the Industrial Safety and Health Act [17]. The participants answered "slowly", "normally", or "quickly" to the question "Compared to other people, how fast is your rate of eating?". The questionnaire also included other lifestyle factors, such as current smoking status (yes or no), regular exercise habits (absence or presence), skipping breakfast (< 3 times/week or ≥ 3 times/week), having dinner within 2 hours of bedtime (< 3 times/week or ≥ 3 times/week), and eating snacks after dinner (< 3 times/week or ≥ 3 times/week). The validity and reliability of this questionnaire has already been confirmed, and it has been used in previous studies [17,18].

Measurement of biochemical markers

Fasting venous blood samples were used to measure the serum levels of hemoglobin (Hb) A1c, triglyceride (TG), and high-density lipoprotein (HDL) cholesterol. The serum level of HbA1c was determined using a diabetes item automatic analyzer (DM-JACK, Kyowa Medex, Tokyo, Japan). A HbA1c value ≥ 6.5 was defined as poor glycemic control. The serum levels of TG and HDL cholesterol were measured using a simultaneous multi-item automatic analyzer (Dimension Vista 1500, Siemens Healthineers Japan, Tokyo, Japan).

Assessment of body composition

An automatic height scale with a body composition meter (TBF-110/TBF-210/DC-250, Tanita, Tokyo, Japan) was used to measure the height and body weight of the participants. The body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters. A BMI ≥ 25 kg/m^2 was classified as overweight or obesity [17].

Measurement of blood pressure

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using an automatic blood pressure monitor (HBP-9021/HBP-9020/BP-230RV3, Omron Healthcare, Kyoto, Japan). In this study, a minimum of two readings was taken at intervals of at least 1 minute, and the average of those readings was used to represent the blood pressure. Hypertension was defined as a SBP ≥ 140 mmHg or DBP ≥ 90 mmHg [19].

Statistical analysis

The normality of our data was checked by the Kolmogorov-Smirnov test. Since none of the continuous variables were normally distributed, the variables are presented as medians and interquartile ranges. The chi-square test and the Mann-Whitney U test were used to assess the significance of differences in selected characteristics between the study participants with and without NAFLD and between the different eating-speed groups.

Logistic regression analyses were also performed with the presence or absence of NAFLD as a dependent variable. Because the number of participants who reported eating slowly was small (n = 277), we combined the participants with a slow or normal eating speed into a "not eating quickly" group. Sex (male vs. female), age (< 65 years vs. ≥ 65 years), BMI (< 25 vs. ≥ 25), hypertension (absence vs. presence), HbA1c value (< 6.5% vs. ≥ 6.5%), current smoking status (no vs. yes), regular exercise habits (absence vs. presence), eating speed (not quickly vs. quickly), skipping breakfast (< 3 times/week vs. ≥ 3 times/week), having dinner within 2 hours of bedtime (< 3 times/week vs. ≥ 3 times/week), and eating snacks after dinner (< 3 times/week vs. ≥ 3 times/week) were selected as independent variables. In the multivariable adjusted logistic regression analysis, independent variables were selected when the p value was < 0.05 in the univariate model. In addition, we confirmed that there was no multicollinearity between each variable using Spearman's correlation analysis. Analyses were performed using a statistical package (IBM SPSS statistics version 25, IBM Japan, Tokyo, Japan). The reported p values were considered to be statistically significant if less than 0.05.

Results

Characteristics of the study participants

The overall prevalence of NAFLD was 30%. There were significant differences between the participants with and without NAFLD with respect to sex, age, BMI, SBP, DBP, HbA1c, TG, HDL cholesterol, current smoking status, regular exercise habit, eating speed, and frequency of having dinner within 2 hours of bedtime ($p < 0.001$; Table 1).

Prevalence rate of NAFLD

The prevalence of NAFLD in each eating-speed group is shown in table 2. In total, 45.0% of the participants reported eating quickly. The prevalence of NAFLD was higher in the eating-quickly group than in the eating-slowly ($p < 0.05$) and eating-normally ($p < 0.05$) groups.

Logistic regression analysis with the prevalence of NAFLD as the dependent variable

Table 3 shows the results of univariate logistic regression analysis with NAFLD as the dependent variable. The results showed that the odds ratios (OR) for having NAFLD were higher in those of male sex (OR = 3.687, 95% confidence interval [CI] = 3.322 - 4.091) and in those with an age ≥ 65 years (OR = 1.695, 95%CI = 1.346 - 2.135), BMI ≥ 25 kg/m² (OR = 11.434, 95%CI = 10.192 - 12.827), hypertension, high HbA1c (≥ 6.5%; OR = 7.469, 95%CI = 2.418 - 3.109), current smoking status (OR = 1.555, 95%CI = 1.371 - 1.763), the presence of regular exercise habits (OR = 0.783, 95%CI = 0.694 - 0.884), reported eating quickly (OR = 1.589, 95%CI 1.447 - 1.744), and a high frequency of dinner within 2 hours of bedtime (OR = 1.267, 95%CI = 1.149 - 1.397) than in the participants who did not have these factors ($p < 0.001$ for all).

Variables	NAFLD		p value
	Absence (n = 5986)	Presence (n = 2570)	
Male, n (%)	2794 (46.7)	1962 (76.3)	< 0.001
Age, years	50 (44, 56)	53 (47, 58)	< 0.001
BMI, kg/m²	21.4 (19.7, 23.3)	25.5 (23.5, 27.7)	< 0.001
Systolic blood pressure, mmHg	117 (107, 127)	126 (117, 135)	< 0.001
Diastolic blood pressure, mmHg	72 (65, 80)	80.5 (73, 87)	< 0.001
HbA1c, %	5.4 (5.2, 5.5)	5.6 (5.4, 5.9)	< 0.001
TG, mg/dL	56 (41, 78)	96 (70, 134)	< 0.001
HDL-cholesterol, mg/dL	67 (56, 79)	51 (44, 60)	< 0.001
Current smoker, n (%)	755 (12.6)	471 (18.3)	< 0.001
Regular exercise habits, n (%)[1]	1217 (20.3)	428 (16.6)	< 0.001
Eating speed, n (%)[2]	2216 (37.0)	1241 (48.3)	< 0.001
Skipping breakfast, n (%)[3]	615 (10.3)	291 (11.3)	0.156
Dinner within 2 hours of bedtime, n (%)[3]	1795 (30.0)	904 (35.2)	< 0.001
Eating snacks after dinner, n (%)[3]	8 (0.1)	3 (0.1)	1.000

Table 1: Characteristics of the study participants with and without NAFLD.

Continuous variables are expressed as median and interquartile range.

For the significance test, Mann-Whitney U test was used for continuous variables, and Fisher's direct method was used for categories.

[1]: Number (%) of presence; [2]: Number (%) of eating quickly; [3]: Number (%) of 3 or more times/week. Abbreviation: NAFLD: Non-Alcoholic Fatty Liver Disease; BMI: Body Mass Index; HbA1c: Hemoglobin A1c; TG: Triglyceride; HDL: High Density Lipoprotein.

Eating speed	Sample size (n)	Non-alcoholic fatty liver disease		
		Absence (n)	Presence (n)	Prevalence rate (%)
Slowly	277	196	81	29.2
Normal	2340	1443	897	38.3
Quickly	2139	1155	984	46.0

Table 2: Prevalence of non-alcoholic fatty liver disease among the different eating-speed groups.

Abbreviation: n: Number.

Variables		Crude odds ratio	95% Confidence interval	p value
Gender	Female	1	(Reference)	< 0.001
	Male	3.687	3.322 - 4.091	
Age, years	< 65	1	(Reference)	< 0.001
	≥ 65	1.695	1.346 - 2.135	
BMI, kg/m^2	< 25	1	(Reference)	< 0.001
	≥ 25	11.434	10.192 - 12.827	
Hypertension	Absence	1	(Reference)	< 0.001
	Presence	2.742	2.418 - 3.109	
HbA1c, %	< 6.5	1	(Reference)	< 0.001
	≥ 6.5	7.469	5.828 - 9.571	
Current smoker	No	1	(Reference)	< 0.001
	Yes	1.555	1.371 - 1.763	
Regular exercise habits	Absence	1	(Reference)	< 0.001
	Presence	0.783	0.694 - 0.884	
Eating speed	Not quickly	1	(Reference)	< 0.001
	Quickly	1.589	1.447 - 1.744	
Skipping breakfast	< 3 times/week	1	(Reference)	0.148
	≥ 3 times/week	1.115	0.962 - 1.293	
Dinner within 2 hours of bedtime	< 3 times/week	1	(Reference)	< 0.001
	≥ 3 times/week	1.267	1.149 - 1.397	
Eating snacks after dinner	< 3 times/week	1	(Reference)	0.841
	≥ 3 times/week	0.873	0.231 - 3.294	

Table 3: Factors associated with NAFLD according to univariate logistic regression analysis.

Abbreviation: NAFLD: Non - Alcoholic Fatty Liver Disease; BMI: Body Mass Index; HbA1c: Hemoglobin A1c.

Table 4 shows the results of the multivariate adjusted logistic regression analysis with NAFLD as the dependent variable. NAFLD was significantly associated with male sex (OR = 3.163, 95%CI = 2.800 - 3.573, p < 0.001), age ≥ 65 years (OR = 1.426, 95%CI = 1.076 - 1.889, p < 0.05), high BMI (≥ 25 kg/m^2; OR = 9.615, 95%CI = 8.511 - 10.863, p < 0.001), hypertension (OR = 1.659, 95%CI = 1.424 - 1.931, p < 0.001), high HbA1c (≥ 6.5%; OR = 4.096, 95%CI = 3.080 - 5.446, p < 0.001), presence of regular exercise habits (OR = 0.605, 95%CI = 0.522 - 0.701, p < 0.001), and eating quickly (OR = 1.146, 95%CI = 1.023 - 1.283, p < 0.05) after adjusting for sex, age, BMI, hypertension, HbA1c, current smoking status, regular exercise habits, eating speed and having dinner within 2 hours of bedtime.

Variables		Multivariable adjusted odds ratio[1]	95% Confidence interval	p value
Gender	Female	1	(Reference)	< 0.001
	Male	3.163	2.800 - 3.573	
Age, years	< 65	1	(Reference)	0.014
	≥ 65	1.426	1.076 - 1.889	
BMI, kg/m^2	< 25	1	(Reference)	< 0.001
	≥ 25	9.615	8.511 - 10.863	
Hypertension	Absence	1	(Reference)	< 0.001
	Presence	1.659	1.424 - 1.931	
HbA1c, %	< 6.5	1	(Reference)	< 0.001
	≥ 6.5	4.096	3.080 - 5.446	
Regular exercise habits	Absence	1	(Reference)	< 0.001
	Presence	0.605	0.522 - 0.701	
Eating speed	Not quickly	1	(Reference)	0.018
	Quickly	1.146	1.023 - 1.283	
Dinner within 2 hours of bedtime	< 3 times/week	1	(Reference)	0.056
	≥ 3 times/week	0.889	0.789 - 1.003	

Table 4: Factors associated with NAFLD according to multivariable adjusted logistic regression analysis.

[1]: Adjusting gender, age, BMI, hypertension, HbA1c, regular exercise habits, eating speed, and dinner within 2 hours of bedtime.

Abbreviation: NAFLD: Non-Alcoholic Fatty Liver Disease; BMI: Body Mass Index; HbA1c: Hemoglobin A1c.

Discussion

To our knowledge, this is the first study to investigate the relationship between eating quickly and NAFLD in Japanese adults. In this study, the prevalence of NAFLD was higher in the eating-quickly group than in the eating-slowly group or the eating-normally group. In addition, the logistic regression analyses showed that the presence of NAFLD was significantly correlated to eating quickly as well as to male sex, age ≥ 65 years, high BMI, hypertension, high HbA1c, and absence of regular exercise habits after adjusting for sex, age, BMI, hypertension, HbA1c, current smoking status, regular exercise habits, eating speed, and having dinner within 2 hours of bedtime. These results indicated that there is a positive association between eating quickly and NAFLD in Japanese adults.

Eating quickly and having dinner within 2 hours of bedtime are risk factors for overweight and obesity [20,21]. The recent increase in the prevalence and severity of NAFLD has been linked to the rising trends in obesity [22]. Therefore, it is possible that overweight and obesity overwhelm the effects that eating quickly and having dinner within 2 hours of bedtime have on NAFLD. In our regres-

sion analysis, a significant association between eating quickly and NAFLD remained even after adjusting for overweight and obesity. In contrast, there was no association between having dinner within 2 hours of bedtime and NAFLD after adjusting for overweight and obesity. These results suggested that eating quickly, but not having dinner within 2 hours of bedtime, was associated with NAFLD independently of overweight and obesity.

A possible mechanism by which eating quickly is related to NAFLD is that eating quickly might cause overeating before the stomach can sense fullness [13]. Overeating following eating quickly would lead to being overweight and obesity [15,20-22], and dysfunctional adipocytokine secretion in obese conditions contribute to the development of NAFLD [23]. In our findings, overweight or obesity is strongly associated with the presence of NAFLD. Although the positive association between eating quickly and NAFLD was statistically significant after adjusting for overweight and obesity, it is possible that eating quickly had indirect effects on the presence of NAFLD through overweight and obesity.

Our results also showed that eating quickly was positively associated with poor glycemic control (HbA1c ≥ 6.5%) and hypertension. Poor glycemic control and hypertension can lead to the acceleration of lipolysis in adipose tissues [24,25]. It has been suggested that poor glycemic control and hypertension accompanied by eating quickly may also affect the presence of NAFLD.

In Japan, the Japanese Government started a new health policy of providing specific health checkups followed by specific counseling for individuals diagnosed with metabolic syndrome since 2008. From this project, it was reported that the improvements of BMI and waist circumference in those with metabolic syndrome were greater among those who participated in the specific health guidance than in those who did not participate [26]. Furthermore, it was also revealed that intensive health guidance focusing on eating quickly was more effective for improving BMI, waist circumference, and triglyceride levels than the standard specific health guidance in subjects with metabolic syndrome [27]. These indicated that interventions for eating quickly may have additional effects on preventing and/or improving NAFLD following other lifestyle modifications. However, further studies are needed to clarify this point.

From our observations, eating snacks after dinner was not associated with the presence of NAFLD. Only 11 participants reported eating snacks after dinner in the present population, which may have been too few to show any statistical significance.

In this study, the prevalence of NAFLD was approximately 30%. This value is similar to a previous report, which showed that the prevalence of NAFLD was 20% to 30% in the Japanese general population [4]. In addition, 40.4% of the participants in our study reported eating quickly. This value is also similar to the results of past studies, which have reported the prevalence of eating quickly to be 40% to 50% among Japanese adults [28,29].

The strength of this study is the large sample size that was sufficient for assessing the prevalence of NAFLD among participants who reported eating quickly. However, our study had some limitations. First, all participants had received health checkups at Asahi University Hospital, which may limit our ability to extrapolate the findings to the general population. Second, since the present study was combined with routine health checkups, the amount of data we could collect was limited, and the questionnaire did not include any questions regarding the total energy intake or the eating fre-

quency per day. Third, this study was a cross-sectional study, which prevented conclusions to be reached regarding causal relationships. Additional longitudinal studies are needed to investigate the relationship between eating speed and NAFLD.

Conclusion

Within the limits of our study, eating quickly was positively associated with NAFLD in Japanese adults. Interventions for eating quickly may be beneficial for controlling the risk of NAFLD.

Acknowledgements

Conflict of Interest

The authors declare no conflicts of interest.

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