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Body mass index and triglyceride-to-HDL-cholesterol ratio in relation to risk of diabetes: The Nagasaki Islands study

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Body mass index (BMI) is well known as an independent risk factor for insulin resistance. In addition, lower BMI and lower insulin levels are recognized as specific characteristics of Asian diabetes patients. Since the triglyceride-to-HDL-cholesterol ratio (TG-HDL) is positively associated with insulin level, but inversely associated with insulin sensitivity, we supposed that diabetes combined with high but not with low TG-HDL might be positively associated with BMI. We therefore conducted a cross-sectional study of 2,431 Japanese subjects (905 men and 1,526 women) aged 30-79 years, who underwent a general health check, to investigate associations between BMI, diabetes and its subtypes that we defined on the basis of TG-HDL levels, which in turn were categorized according to sex-specific tertiles. Among the 172 diabetic patients identified in the study group, 45 showed low TG-HDL and 82 high TG-HDL. We found a significant inverse association between low-TG-HDL diabetes and BMI, and a significant positive association between high-TG-HDL diabetes and BMI. The multivariable-adjusted odds ratio and 95%CI for a 1SD increment in BMI (3.03 kg/m^2 for men and 3.44 kg/m^2 for women) for low-TG-HDL diabetes was 0.53 (95%CI: 0.36-0.77) and 1.57 (95%CI: 1.24-2.01) for high-TG-HDL diabetes. These findings demonstrated that for Japanese subjects associations between diabetes and BMI are strongly influenced by the TG-HDL status. Since a previous study of ours found that diabetes combined with high TG-HDL ratios constitutes a risk for atherosclerosis, these findings may serve as an effective tool for estimating risk of atherosclerosis for diabetes patients.

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Key words: TG-HDL ratio, diabetes, BMI, cross-sectional study, risk.

1. Introduction

Asian type 2 diabetes patients are reportedly characterized by lower body mass index (BMI) and lower serum insulin levels than Mexican-American or African-American type 2 diabetes patients.[1-3] In addition, the association between BMI and impaired glucose tolerance is well documented in cases of overweight and obesity.[4] It has been well established that the primary defect in lean subjects with diabetes is β-cell dysfunction while that in their obese counterparts is β-cell dysfunction as well as high insulin resistance.[5] Asians are considered to have less compensatory β-cell function and have type2 diabetes at lower BMI than people in Western countries.[6] Although not only insulin resistance with reduced compensatory β-cell function but also absolute values of insulin deficiency without insulin resistance are well known as causes of diabetes, no study has reported on the association between BMI and diabetes while taking

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these causes of diabetes into account. Diabetes resulting from the first cause, insulin resistance with reduced compensatory β-cell dysfunction, may produce higher concentrations of insulin level while diabetes resulting from the cause, absolute insulin deficiency, may reduce insulin concentration levels.

On the other hand, insulin concentration was found to be inversely associated with serum high-density-lipoprotein (HDL) cholesterol concentration[7] and positively associated with serum triglyceride (TG) concentration.[8] Furthermore, previous studies reported that TG-to-HDL-cholesterol ratio (TG-HDL) reflects the level of insulin resistance in a general study population,[9] overweight individuals,[10,11] and type2 diabetes,[12] while a higher level of insulin sensitivity was found to be associated with a lower level of TG-HDL in overweight patients.[8] Other studies reported that insulin sensitivity and insulin secretion were linked through a negative feedback loop, whereby pancreatic β-cells compensate for change in whole-body insulin sensitivity through a proportionate and reciprocal change in insulin secretion, which suggests that higher levels of insulin secretion may occur when insulin sensitivity is low than when it is high.[13,14] These findings and observations suggest that diabetes of individuals with high TG-HDL is mainly caused by insulin resistance with reduced compensatory β-cell function, while that of patients with low TG-HDL is mainly caused by absolute β-cell dysfunction.

Since absolute β-cell dysfunction may cause under-nutrition, which results in lower BMI, and insulin resistance may be caused by over-nutrition, we hypothesize that BMI is inversely associated with a prevalence of low-TG-HDL diabetes but positively associated with high-TG-HDL diabetes. Since a previous study of ours found that diabetes combined with high TG-HDL ratios constitutes a risk for atherosclerosis,[15] the aforementioned associations may constitute an efficient tool for estimating risk of atherosclerosis for diabetes patients. To examine this hypothesis, we analyzed the data for Japanese who underwent a general medical check between 2008 and 2011.

2. Material and Methods

2.1 Participants

The surveyed population included 2,556 individuals aged 30 to 79 years, who were residents of the western a rural community in the Goto Islands in western Japan and participated in this study between 2008 and 2011. A total of 125 individuals with missing data were excluded. There were no differences in diabetic risk factors such as systolic blood pressure, antihypertensive medication use, antihyperlipidemic medication use, current drinker, and current smoker between participants with measured serum data and those without. The remaining 2,431 subjects with a mean age of 65.4 years (±9.6 SD; range 36-79) were enrolled in this study.

2.2 Data collections and laboratory measurements

Body weight and height were measured with an automatic body composition analyzer (BF-220; Tanita, Tokyo, Japan) at the time of drawing blood.

Serum separated from fasting blood samples was centrifuged after blood coagulation. Serum samples were also collected in a siliconized tube. Serum TG and serum creatinine were measured with the enzyme method, serum HDL with the direct method, HbA1c with the latex agglutination method, while serum alanine aminotransferase (ALT) and serum γ-glutamyltransferase (γ-GTP) were measured with the JASCC standardization method. Trained interviewers obtained information on smoking status, drinking status, medical history, as well as on use of antihypertensive agents, medication for diabetes mellitus, and medication for dyslipidemia. GFR was estimated by using the established method but with three variations recently proposed by a working group of the Japanese Chronic Kidney Disease initiative.[16] According to this adaptation, GFR (ml/min/1.73 m^2) = 194× (serum creatinine (enzyme method))$^{-1.094}$ × (age)$^{-0.287}$ × (0.739 for women). HbA1c (NGSP: National Glycohemoglobin Standardization Program) was calculated with the following equation, which was recently proposed by a working group of the Japanese Diabetes Society (JDS): HbA1c (NGSP) = HbA1c (JDS) + 0.4%.[17]

2.3 Diagnosis of diabetes and classification of its subtypes

Diabetes was diagnosed on the basis of HbA1c (NGSP) ≥ 6.5% and/or initiation of glucose-lowering medication or insulin therapy.[18] We further classified subtypes of diabetes by calculating sex-specific tertiles of TG-HDL for all the participants (median tertiles of TG-HDL ratio (traditional units) were 0.91, 1.57, and 3.34 for men, and 0.80, 1.41. and 2.61 for women) as detailed in a previous study of ours (Shimizu's diabetes classification).[15] The subtypes were low TG-HDL diabetes (diabetes with the lowest TG-HDL levels: 0.82 (±0.25 SD) for men and 0.74 (±0.20 SD) for women), intermediate TG-HDL diabetes (diabetes with more than the lowest but less than the highest levels of TG-HDL: 1.62

(±0.31 SD) for men and 1.41 (±0.22 SD) for women), and high TG-HDL diabetes (diabetes with the highest TG-HDL levels: 4.80 (±5.3 SD) for men and 3.91 (±2.68 SD) for women).

2.4 Statistical analysis

The clinical characteristics reported here were expressed as follows. TG-HDL categories for all the subjects were established on the basis of the of TG-HDL tertiles. Differences in sex- and age-adjusted mean values of diabetic risk factors according to TG-HDL categories for diabetes patients were analyzed by using covariance or general linear models. Logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI) of diabetes in association with BMI.

A sex-combined model was constructed and two different approaches were used for making adjustments for confounding factors. For the first approach, we adjusted only for sex and age and for the second, we included other possible confounding factors, namely, smoking status (never smoker, former smoker, current smoker), alcohol consumption [non-drinker, and current light to moderate drinker (1-6 times/week), current heavy drinker (every day)], systolic blood pressure (mmHg), antihypertensive medication use (no, yes), antihyperlipidemic medication use (no, yes), antidiabetic medication use (no, yes), body mass index (kg/m^2), ALT (IU/L), γ-GTP (IU/L), and estimated GFR (mL/min/1.73m^2).

All statistical analyses were performed with the SAS system for Windows (version 9.3; SAS Inc., Cary, NC). All p-values for statistical tests were two-tailed, and values of <0.05 were regarded as statistically significant.

3. Results

Of the 2,431 participants, 172 were diagnosed with diabetes, and 45 of whom showed low TG-HDL levels, 45 intermediate TG-HDL levels, and 82 high TG-HDL levels. The clinical characteristic of the participants of this study are summarized in Table 1. "No. at risk" refers to the total number of participants at risk of diabetes and men accounted for 37.2% of them.

Table 2 shows the characteristics of the study population according to TG-HDL levels, which were divided into sex-specific tertiles of TG-HDL. HbA1c and BMI were found to be positively associated with TG-HDL levels for total subjects as well as for diabetic and non-diabetic participants.

The odds ratios (OR) and 95% confidence intervals (CI) for overall diabetes by BMI quartile showed J-shaped associations (Table 3).

Table 1. Clinical characteristics of the study population

Parameters	Total subjects
No. at risk	2,431
Men, (n(%))	905 (37.2)
Age, year	65.4 ± 9.6
Serum HDL-cholesterol, mg/dL	60 ± 15
Serum triglycerides, mg/dL	103 ± 64
TG-HDL ratio, traditional units	1.94 ± 1.68
Systolic blood pressure, mmHg	141 ± 21
Diastolic blood pressure, mmHg	83 ± 11
Antihypertensive medication use,(n(%))	806(33)
HbA1C, %	5.3 ± 0.5
Diabetes (HbA(1c) ≥6.5%), (n(%))	172(7.1)
Severe diabetes (HbA(1c) ≥8.0%),(n(%))	41(1.7)
Antidiabetic medication use, (n(%))	109(4.5)
Antihyperlipidemic medication use, (n(%))	305(12.5)
Body mass index, kg/m^2	23.2 ± 3.3
Current smoker, (n(%))	249(10)
Current drinker,(n (%))	534(22)
Serum alanine aminotransferase (ALT), IU/L	20 ± 12
Serum γ-glutamyltranspeptidase (γGTP), IU/L	30 ± 42
Serum creatinine, mg/dL	0.71 ± 0.19
Glomerular Filtration Rate (GFR), mL/min/1.73m^2	74.5 ± 15.1

Values are given as mean ± standard deviation

Table 3 also shows the odds ratios (OR) and 95% confidence intervals (CI) for subtypes of diabetes by BMI quartile. For low TG-HDL diabetes, we observed an inverse association with BMI, and a positive association for high-TG-HDL diabetes. The multivariable-adjusted OR and 95%CI for a 1SD increment in BMI (3.03 kg/m^2 for men and 3.44 kg/m^2 for women) for low TG-HDL-ratio diabetes and high TG-HDL-ratio diabetes were 0.53 (95%CI: 0.36-0.77) and 1.57 (95%CI: 1.24-2.01), respectively. Intermediate-TG-HDL diabetes featured a J-shaped association. To avoid the influence of under-nutrition, we performed another analysis restricted to participants with BMI≥19kg/m^2 and found almost the same associations. The multivariable-adjusted OR and 95%CI for a 1SD increment in the BMI for low-TG-HDL-ratio diabetes and high-TG-HDL-ratio diabetes were 0.48 (95%CI: 0.29-0.79) and 1.69 (95%CI: 1.29-2.22), respectively.

In addition, we performed a sex-specific analysis for those subjects and found essentially the same associations for men and women. The multivariable-adjusted OR and 95%CI respectively 1SD increment in BMI for low TG-HDL-ratio and high TG-HDL-ratio diabetes were, respectively, 0.55 (95%CI: 0.33-0.93) and 1.85 (95%CI: 1.30-2.64)

Table 2. Sex-and age-adjusted mean values for characteristics in relation to TG-HDL levels of study population and participants with diabetes

	Tertiles of TG-HDL ratio			p
	Low TG-HDL diabetes	Intermediate TG-HDL diabetes	High TG-HDL diabetes	
Total subjects				
No. of cases	808	812	811	
Men (%)	301 (37.2)	302 (37.2)	302 (37.2)	
Age, year	64.6±10.2	65.9±9.6	65.7±9.1	
Serum HDL-cholesterol, mg/dL	72	60	49	<0.001
Serum triglycerides, mg/dL	56	89	164	<0.001
Systolic blood pressure, mmHg	140	141	143	0.007
Diastolic blood pressure, mmHg	82	83	84	<0.001
Antihypertensive medication use, %	26	34	40	<0.001
Antidiabetic medication use, %	4.3	3.3	5.9	0.036
HbA(1c), %	5.2	5.2	5.4	<0.001
Severe diabetes (HbA(1c) ≥ 8.0%), %	1.0	0.6	3.5	<0.001
Antihyperlipidemic medication use, %	4.3	14.8	13.5	0.002
Body mass index, kg/m^2	22.0	23.3	24.3	<0.001
Current smoker, %	7.0	11.3	12.4	<0.001
Current drinker, %	26.8	22.5	16.6	<0.001
ALT, IU/L	19.4	20.1	22.7	<0.001
γGTP, IU/L	26.1	30.8	32.9	0.002
Serum creatinine, mg/dL	0.69	0.71	0.73	<0.001
GFR, mL/min/1.73m^2	76.7	74.1	72.7	<0.001
Participants with diabetes				
No.of cases	45	45	82	
Men (%)	27 (60.0)	26 (57.8)	40 (48.8)	
Age, Year	68.1±7.3	69.3±7.0	67.2±8.4	
Serum HDL-cholesterol,mg/dL	74	56	45	<0.001
Serum triglycerides,mg/dL	56	88	183	<0.001
Systolic blood pressure,mmHg	141	150	148	0.111
Diastolic blood pressure,mmHg	80	83	85	0.090
Antihypertensive medication use,%	31	60	44	0.015
Antidiabetic medication use,%	75.0	59.3	59.2	0.172
HbA(1c),%	6.3	6.4	6.9	0.003
Severe diabetes (HbA(1c) ≥ 8.0%),%	18.2	12.8	33.0	0.020
Antihyperlipidemic medication use,%	22.7	22.0	19.4	0.892
Body mass index,kg/m^2	22.3	25.1	25.5	<0.001
Current smoker,%	16.7	7.1	18.6	0.184
Current drinker,%	33.5	24.2	23.2	0.354
ALT,IU/L	23.2	23.5	26.1	0.578
γGTP,IU/L	43.4	37.9	38.3	0.908
Serum creatinine,mg/dL	0.69	0.74	0.76	0.072
GFR, mL/min/1.73m^2	79.8	73.4	74.2	0.135
Participants without diabetes				
No. of cases	763	767	729	
Men (%)	274 (35.9)	276 (36.0)	262 (36.0)	
Age, year	64.4±10.3	65.7±9.7	65.5±9.2	
Serum HDL-cholesterol, mg/dL	72	60	50	<0.001
Serum triglycerides, mg/dL	57	89	162	<0.001
Systolic blood pressure, mmHg	140	140	143	0.021
Diastolic blood pressure, mmHg	82	82	84	<0.001
Antihypertensive medication use, %	26	32	40	<0.001
Antidiabetic medication use, %	-	-	-	-
HbA(1c), %	5.1	5.1	5.2	<0.001
Severe diabetes (HbA(1c) ≥ 8.0%), %	-	-	-	-
Antihyperlipidemic medication use, %	8.5	14.4	12.9	<0.001
Body mass index, kg/m^2	22.0	23.2	24.2	<0.001
Current smoker, %	6.4	11.6	11.7	<0.001
Current drinker, %	26.3	22.3	16.0	<0.001
ALT, IU/L	19.2	19.9	22.3	<0.001
γGTP, IU/L	25.0	30.4	32.3	<0.001
Serum creatinine, mg/dL	0.69	0.71	0.73	<0.001
GFR, mL/min/1.73m^2	76.6	74.2	72.4	<0.001

ALT:alanine aminotransferase; γGTP: γ-glutamyltranspeptidase; GFR:Glomerular filtration rate; TG-HDL ratio: Triglycerides / HDL-cholesterol ratio; TG-HDL ratio was categorized by sex-specific tertiles of TG-HDL values for total subjects. Median value of tertiles of TG-HDL ratio (traditional units) were 0.91, 1.57, and 3.34 for men, and 0.80, 1.41. and 2.61 for women.

Table 3. Odds ratios (OR) and 95% CI for total diabetes and subtypes in relation to BMI level quartiles

	Height quartiles					1 SD increment in BMI
	Q1 (low)	Q2	Q3	Q4	P for trend	
Total diabetes						
No. at risk	607	608	609	607		
No. of cases (percentage)	36 (5.9)	22 (3.6)	46 (7.6)	68 (11.2)		
Sex-and age-adjusted OR	1.69 (0.97-2.92)	1.00	2.18 (1.29-3.67)	3.35 (2.04-5.51)		
Multivariable OR	1.82 (0.66-5.03)	1.00	3.05 (1.20-7.79)	4.09 (1.63-10.29)		
Diabetes (low TG-HDL ratio)						
No. of cases (percentage)	18 (3.0)	9 (1.5)	12 (2.0)	6 (1.0)		
Sex-and age-adjusted OR	1.00	0.49 (0.22-1.04)	0.65 (0.31-1.37)	0.32 (0.13-0.82)	0.026	0.66 (0.48-0.92)
Multivariable OR	1.00	0.79 (0.29-2.17)	0.62 (0.23-1.67)	0.17 (0.05-0.55)	0.004	0.53 (0.36-0.77)
Diabetes (intermediate TG-HDL ratio)						
No. of cases (percentage)	9 (1.5)	4 (0.7)	10 (1.6)	22 (3.6)		
Sex-and age-adjusted OR	2.22 (0.68-7.31)	1.00	2.50 (0.78-8.02)	5.58 (1.91-16.33)		
Multivariable OR	2.14 (0.50-9.08)	1.00	1.91 (0.55-6.65)	3.65 (1.14-11.73)		
Diabetes (high TG-HDL ratio)						
No. of cases (percentage)	9 (1.5)	9 (1.5)	24 (3.9)	40 (6.6)		
Sex-and age-adjusted OR	1.00	1.00 (0.39-2.53)	2.71 (1.25-5.88)	4.64 (2.23-9.66)	<0.001	1.83 (1.51-2.21)
Multivariable OR	1.00	1.34 (0.48-3.73)	3.12 (1.29-7.58)	4.34 (1.82-10.31)	<0.001	1.57 (1.24-2.01)

Odds ratios and 95% CI obtained from conditional logistic regression models. Multivariable OR: adjusted further for body mass index, smoking status, drinking status, systolic blood pressure, antihypertensive medication use, antidiabetic medication use, antihyperlipidemic medication use, ALT, γGTP and GFR. The median values of BMI quartiles were 20.5kg/m^2, 22.7kg/m^2, 24.0kg/m^2 and 27.2kg/m^2 for men and 19.1kg/m^2, 21.5kg/m^2, 23.7kg/m^2, 26.9kg/m^2 for women.

for men and 0.48 (95%CI: 0.25-0.91) and 1.38 (95%CI: 0.98-1.94) for women.

To eliminate the influence of menopausal status, we further investigated the associations between a 1SD increment in BMI and the risks of low TG-HDL and high TG-HDL diabetes only in elderly women (≥ 60 years) and found essentially the same associations: the multivariable OR and 95%CI of low TG-HDL-ratio diabetes and high TG-HDL-ratio diabetes were 0.42 (95%CI: 0.19-0.95) and 1.58 (95%CI: 1.04-2.40), respectively.

As part of our study, we conducted a further investigation of CAVI (Cardio Ankle Vascular Index) data for 2,414 subjects, which showed a significantly positive association between diabetes categorized by TG-HDL and increased arterial stiffness (mean CAVI≥8.0). The multivariable OR and 95%CI of increased arterial stiffness were 0.94 (95%CI: 0.42-2.12) for low TG-HDL-ratio diabetes, 0.79 (95%CI: 0.38-1.66) for intermediate TG-HDL diabetes, and 2.27 (95%CI: 1.21-4.24) for high TG-HDL-ratio diabetes, respectively.

4. Discussion

A major finding of the present study was that the associations between diabetes and BMI for Japanese people are strongly influenced by the status of TG-HDL.

A random-digit telephone survey of 195,005 adults aged 18 years or older concluded that overweight and obesity were significantly associated with diabetes. Compared with subjects of normal weight, those with a BMI of 40 or higher proved to have an odds ratio (OR) of 7.37 (95%CI: 6.39-8.50) for having been diagnosed with diabetes.[4] However, numerous studies have shown there are striking differences in the average BMI of diabetes patients from different populations: The UK Prospective Diabetes Study (UKPDS) reported that the average BMI of patients with diabetes was 29.4 kg/m^2, whereas the Japan Diabetes Complications Study (JDCS) reported a corresponding value of 23.1 kg/m^2.[19,20] A pooled cross-sectional analysis that was conducted to evaluate the association between baseline BMI and self-reported diabetes status in over 900,000 individuals showed that the prevalence of diabetes in Japan was higher for individuals with lower BMI (22.5 kg/m^2>BMI) than it was in China, Taiwan, Korea, and Singapore, while for individuals with higher BMI, the prevalence was similar.[21] In addition, our analysis showed a J-shaped association between BMI levels and overall risk of diabetes.

Moreover, Asian type 2 diabetes patients are reportedly characterized by lower BMI and lower serum insulin levels than their Mexican-American or African-American counterparts.[1-3] These findings seem to indicate that the risk of

diabetes for those with lower BMI is associated with lower serum insulin levels.

Since absolute insulin deficiency may cause relative under-nutrition because of a lack of ability to metabolize glucose, which could result in a lower BMI, and insulin resistance, which may be caused by over-nutrition, the association between BMI and diabetes may be confounded by these two different mechanisms. However, and to the best of our knowledge, no studies have been reported on the association between BMI and diabetes while taking these two mechanisms into account.

On the other hand, in the presence of insulin resistance, HDL levels are often found to be reduced[4,22] and TG levels elevated.[8] Furthermore, previous studies reported that TG-HDL also reflected the level of insulin resistance in general participants,[9] overweight individuals,[10,11] and type2 diabetes,[12] while other studies reported that insulin sensitivity and insulin secretion were linked.[13,14] High TG-HDL levels can indicate the presence of insulin resistance, while lower serum insulin levels can be indicated by low TG-HDL levels. In our study, low TG-HDL diabetes showed an inverse association with BMI, while high TG-HDL diabetes showed a positive association with BMI, which can be explained by the mechanisms described above. Furthermore, the association between the prevalence of diabetes in patients with intermediate TG-HDL and BMI, which showed a J-shape, is essentially the same as that between the overall prevalence of diabetes and BMI. These two types of associations can be explained by confounding caused by two different types of diabetes. It is well known that patients with advanced severe diabetes often show low BMI. However, our analysis showed the sex- and age-adjusted prevalence of severe diabetes (HbA1c $\geq$ 8%) was significantly and positively associated with TG-HDL levels. This prevalence was 18.2% for low-TG-HDL diabetes, 12.8% for intermediate-TG-HDL diabetes and 33.0% for high-TG-HDL diabetes (P=0.020).

Certain potential limitations of this study warrant consideration. First, although significant associations were observed in our study of BMI-levels, there was a wide confidence interval due to the small number of incident cases. However, a 1SD increment in BMI showed significant associations with both low- and high-TG-HDL diabetes.

Second, since no data on exercise were available, we could not adjust for the effect of exercise. Third, there might be a difference in patient compliance between low- and high-TG-HDL diabetes patients, which may influence associations between diabetes and BMI. However, our study showed that associations between BMI and risk of subtypes of diabetes remained significant even after adjustment for anti-diabetic and anti-hyperlipidemic medication use. Furthermore, we detected no significant differences in the sex- and age-adjusted prevalence of taking anti-diabetic and anti-hyperlipidemic medication among subtypes of diabetes. Fourth, we had no access to menopausal status data, although menopause is well known as a strong classical risk factor for diabetes among women. However, the previously observed associations remained essentially the same even after we restricted the analysis to women over 60 years old. Fifth, a number of the participants with type1 diabetes were initially diagnosed with type 2 diabetes at disease onset and in our study, too, it was difficult to differentiate type1 from type 2 diabetes.[23] However, most subjects in previous studies were also defined as type 2 diabetes without information on serum insulin levels, urinary C-peptide, anti-glutamic acid decarboxylase and anti-islet cells, which is considered necessary to rule out type1 diabetes.[1-3] What is more, type1 diabetes is also considered to be an independent risk factor for atherosclerosis,[24] while a previous study of ours, on high TG-HDL diabetes, and which did not distinguish between type1 and type 2, identified a significant risk of atherosclerosis for men.[15] Also, and as part of our study, high TG-HDL diabetes was found to be significantly and positively associated with increased arterial stiffness whereas no such association was observed for intermediate and low TG-HDL diabetes. This means that associations between BMI and diabetes in relation to TG-HDL do constitute an efficient tool for estimating risk of atherosclerosis for diabetes patients. And because other Japanese studies have reported that there may be a complex association between drinking status and insulin resistance[25] as well as incidence of diabetes for Japanese men,[26] pancreatic dysfunction may also have an effect on the association between BMI and diabetes in relation to TG-HDL. Since it is known that a high prevalence of drinking is characteristic of Japanese men,[27, 28] the associations discussed here may be affected by sex differences if pancreatic dysfunction is found to have a major influence on those associations. However, our additional analyses found that a 1SD increment in BMI was positively associated with high TG-HDL diabetes and inversely associated with low TG-HDL diabetes for both men and women, that is, regardless of sex. Finally, because this study is a cross-sectional study, we cannot establish any causal relationships.

In conclusion, our findings suggest that the associations between diabetes and BMI for Japanese subjects are strongly influenced by the status of TG-HDL. This indicates that such associations may constitute an efficient tool for estimating risk of atherosclerosis for diabetes patients.

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