

Original Article

Difference between Fasting and Nonfasting Triglyceridemia; the Influence of Waist Circumference

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Aim: Postprandial hypertriglyceridemia is recognized as an independent risk factor for cardiovascular disease. The aim of this study was to identify differences between fasting and postprandial TG levels, focusing on the influence of waist circumference.

Methods: Subjects included 1,505 men and 798 women aged 38–65 years who were not taking medications for diabetes or dyslipidemia. Fasting TG levels were measured after an overnight fast, and postprandial TG levels were measured 2 hours after a standardized rice-based lunch (total 740 kcal, 20 g fat, 30 g protein, and 110 g carbohydrates) in the afternoon on the same day.

Results: Fasting and postprandial TG levels were highly correlated in both men ($r=0.86$, $p<0.001$) and women ($r=0.84$, $p<0.001$). Waist circumference was positively correlated with fasting TG ($r=0.38$ in men and $r=0.36$ in women) and postprandial TG ($r=0.42$ in men and $r=0.45$ in women), respectively. On multiple regression analyses, the association of waist circumference with postprandial TG was still significant (standardized $\beta=0.10$ in men and standardized $\beta=0.15$ in women, $p<0.001$) after the inclusion of HbA1c, age, high-density-lipoprotein (HDL)-cholesterol, alcohol consumption, and fasting TG in the regression model.

Conclusion: Postprandial TG has a better relation with waist circumference than fasting TG.

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Key words; Postprandial hyperlipidemia, Triglyceride, Waist circumference

Introduction

Recently, two large-scale, long-term prospective cohort studies on the importance of the prandial state when measuring triglyceride (TG) levels were reported, in which nonfasting triglyceridemia was superior to fasting triglyceridemia for predicting cardiovascular risk^{1, 2}. Consistent with prior cross-sectional analyses^{3, 4} and case-control studies^{5, 6}, these reports seem

to have established postprandial hypertriglyceridemia as an independent risk factor for cardiovascular disease. Although most of these studies were confined to Western populations, relatively smaller prospective studies in Japanese⁷ and Asian⁸ populations have also linked postprandial triglyceridemia with cardiovascular events.

Postprandial TG response is influenced not only by diet composition⁹ but also by the characteristics of the subjects, including gender¹⁰, genotypes¹¹, age¹², menopausal status¹³, glycemic status^{14, 15}, and visceral fat deposition^{10, 16}. In a previous work, we demonstrated that postprandial TG levels were significantly higher in men with impaired glucose tolerance (IGT) than in those with normal glucose tolerance (NGT)¹⁵;

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however, the difference in postprandial TG concentrations between IGT and NGT was diminished after adjusting for waist circumference, suggesting that their difference was not the consequence of the glycemic status but might be attributable to accompanying abdominal obesity.

Waist circumference has been often used to diagnose central obesity in clinical practice since its adoption as a component of the criteria of metabolic syndrome^{17, 18}). In this study, we investigated the influence of waist circumference on postprandial TG levels in Japanese men and women. Other relevant variables were also analyzed.

Subjects and Methods

Study Subjects

Hokuriku Central Hospital has a special department where public school teachers can receive annual medical checkups. Regular health checkups for employees are legally mandated in Japan, and most of the checkup costs are paid by their mutual aid association. Of subjects who had medical checkups in 2005, 2,510 persons were initially recruited for this study. Two hundred seven subjects were excluded because they had received treatment for diabetes or hyperlipidemia ($n=144$), received hormone replacement therapy ($n=8$), were in a post-gastrectomy state ($n=28$), had renal impairment (serum creatinine >1.5 mg/dL) ($n=2$), or were missing the history of alcohol consumption ($n=25$). Thus, the study included 2,303 Japanese adults (1,505 men, 798 women). At gynecological examinations, the menopausal status was asked by nurses. Alcohol consumption was defined by the number of days per week of drinking regardless of its amount. Those reporting no menses for at least 6 months were considered as being menopausal, and subjects who had received hysterectomies were considered postmenopausal if they were over the age of 51, which was the average menopausal age of this sample.

The study was approved by the hospital review board, and informed consent was obtained from all subjects.

Study Protocol

The study protocol was described previously¹⁹). Briefly, after an overnight fast, blood samples were drawn at 9:00 a.m. to measure the levels of fasting TG, total-cholesterol (T-Chol), high-density-lipoprotein (HDL)-cholesterol, plasma glucose (PG), and HbA1c. After a 75 g oral glucose tolerance test (OGTT) in the morning and at noon, each subject ate a standardized rice-based lunch composed of 220 g boiled

rice, one main dish of meat or fish, two dishes of vegetables and a piece of fruit (total 740 kcal, 20 g fat, 30 g protein, and 110 g carbohydrates). Two hours after the start of the meal, postprandial TG levels were measured. Subjects were not allowed to eat after the OGTT and their meals but were allowed free access to water.

Anthropometric Measurements

All evaluations were performed at the health check department of Hokuriku Central Hospital. Anthropometric measurements of individuals wearing light clothing and no shoes were conducted by well-trained nurses. Weight was measured to the nearest 0.1 kg, and height was measured to the nearest 0.1 cm. Body mass index (BMI) was calculated by dividing weight (kg) by height squared (m^2). Waist circumference was measured to the nearest 0.5 cm with the tape measure placed horizontally at the level of the umbilicus while the participant exhaled gently.

Laboratory Assays

All assays were conducted at the laboratory of Hokuriku Central Hospital. TG, T-Chol, and HDL-cholesterol were measured enzymatically (Autoanalyzer BioMajesty JCA-BM1650; JEOL Ltd., Tokyo, Japan). PG was determined using the glucose oxidase method (Automatic Glucose Analyzer ADAMS Glucose GA-1160; Arkray, Kyoto). HbA1c was measured by high performance liquid chromatography (HPLC) (Automatic Glycohemoglobin Analyzer ADAMS A1c HA-8160; Arkray, Kyoto) with a reference range between 4.3% and 5.8%.

Statistical Methods

All statistical analyses were conducted using SPSS software version 11.0 for Windows (SPSS Inc., Japan), including the means, frequencies, simple (Pearson's) correlations, and multiple regression analyses. The mean values were compared between men and women using the unpaired Student's *t*-test or Mann-Whitney test. Correlation coefficients were compared after Fisher's *z*-transformation. Multiple regression analyses were performed to quantify the independent contributions of waist circumference, age, HbA1c, HDL-cholesterol, and fasting TG on the variance of postprandial TG. All regression models included alcohol consumption (three-level variable: drinking everyday/drinking 1–6 days per week/ drinking less than 1 day per week) as a covariate. In the analyses of fasting TG and postprandial TG, the data were transformed to logarithmical values. A *p* value of <0.05 was considered significant for all analyses.

Table 1. Physical and metabolic characteristics of the subjects

Variables	Men (n=1,505)	Women (n=798)
Age (years)	49.1 ± 7.6	50.7 ± 7.2*
Height (cm)	170.5 ± 5.9	157.2 ± 5.5*
Weight (kg)	70.9 ± 10.3	56.1 ± 8.2*
Body mass index (kg/m ²)	24.3 ± 3.1	22.7 ± 3.1*
Waist circumference (cm)	85.2 ± 7.8	78.4 ± 8.8*
Fasting plasma glucose (mg/dL)	97.6 ± 15.7	92.3 ± 9.6*
HbA1c (%)	5.3 ± 0.6	5.3 ± 0.4
Fasting total cholesterol (mg/dL)	209.3 ± 33.1	214.1 ± 34.5*
Fasting HDL-cholesterol(mg/dL)	55.9 ± 13.5	65.9 ± 13.9*
Fasting TG (mg/dL)	116 [81-164]	78 [59-107]*
Postprandial TG (mg/dL)	139 [96-193]	87 [61-125]*
NGT/IFG+IGT/DM (%)	73.6/22.3/4.1	82.3/15.8/1.9*
Drinking everyday (%)	33.2	9.6*
Drinking 1-6 days per week (%)	42.3	30.9*
Menopause (%)		49.0

Values are expressed as the means ± SD or median [interquartile range]. HDL, high-density lipoprotein; TG, triglyceride; NGT, normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; DM, diabetes mellitus. * $p < 0.001$.

Results

Physical and metabolic characteristics of men and women are presented in **Table 1**. Men had higher mean BMIs and waist circumferences than women ($p < 0.001$). Gender differences in metabolic parameters were also observed. Men were characterized by

higher fasting TG ($p < 0.001$), lower plasma HDL-cholesterol levels ($p < 0.001$) and a higher proportion of subjects with glucose intolerance than women ($p < 0.001$). More men were consuming alcohol than women. In addition, 49.0 % of women in this sample were postmenopausal.

Fig. 1 shows scatter-plots for fasting TG versus postprandial TG in men and women. As expected, they were highly correlated in both men ($r = 0.86$, $p < 0.001$) and women ($r = 0.84$, $p < 0.001$).

Fig. 2 shows scatter-plots for fasting TG (left) and postprandial TG (right) according to waist circumference, respectively, in men (A) and in women (B). Both fasting and postprandial TG were significantly and positively correlated with waist circumference in both genders ($p < 0.001$).

Table 2 shows the correlation coefficients of metabolic parameters with fasting and postprandial TG levels. Age was positively correlated with both fasting TG ($r = 0.28$, $p < 0.001$) and postprandial TG ($r = 0.29$, $p < 0.001$) in women but not in men. Waist circumference was significantly and positively correlated with fasting and postprandial TG. The coefficient between postprandial TG and waist circumference ($r = 0.45$) was significantly greater than that between fasting TG and waist circumference ($r = 0.36$) in women ($p < 0.05$). In men, the comparison of the correlation coefficients ($r = 0.42$ versus $r = 0.38$) did not reach statistical difference. A stronger correlation with postprandial TG was also observed with BMI and HbA1c in women ($p < 0.05$). HDL-cholesterol was inversely correlated with fasting and postprandial TG in both genders.

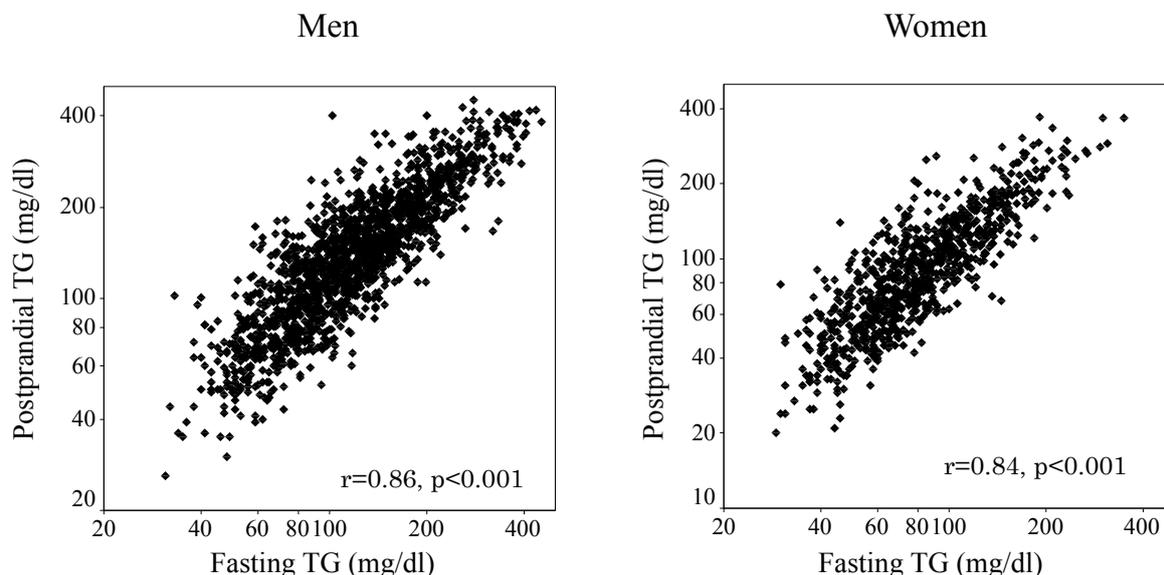


Fig. 1. Scatter-plots of Postprandial TG versus Fasting TG in men (left) and women (right).

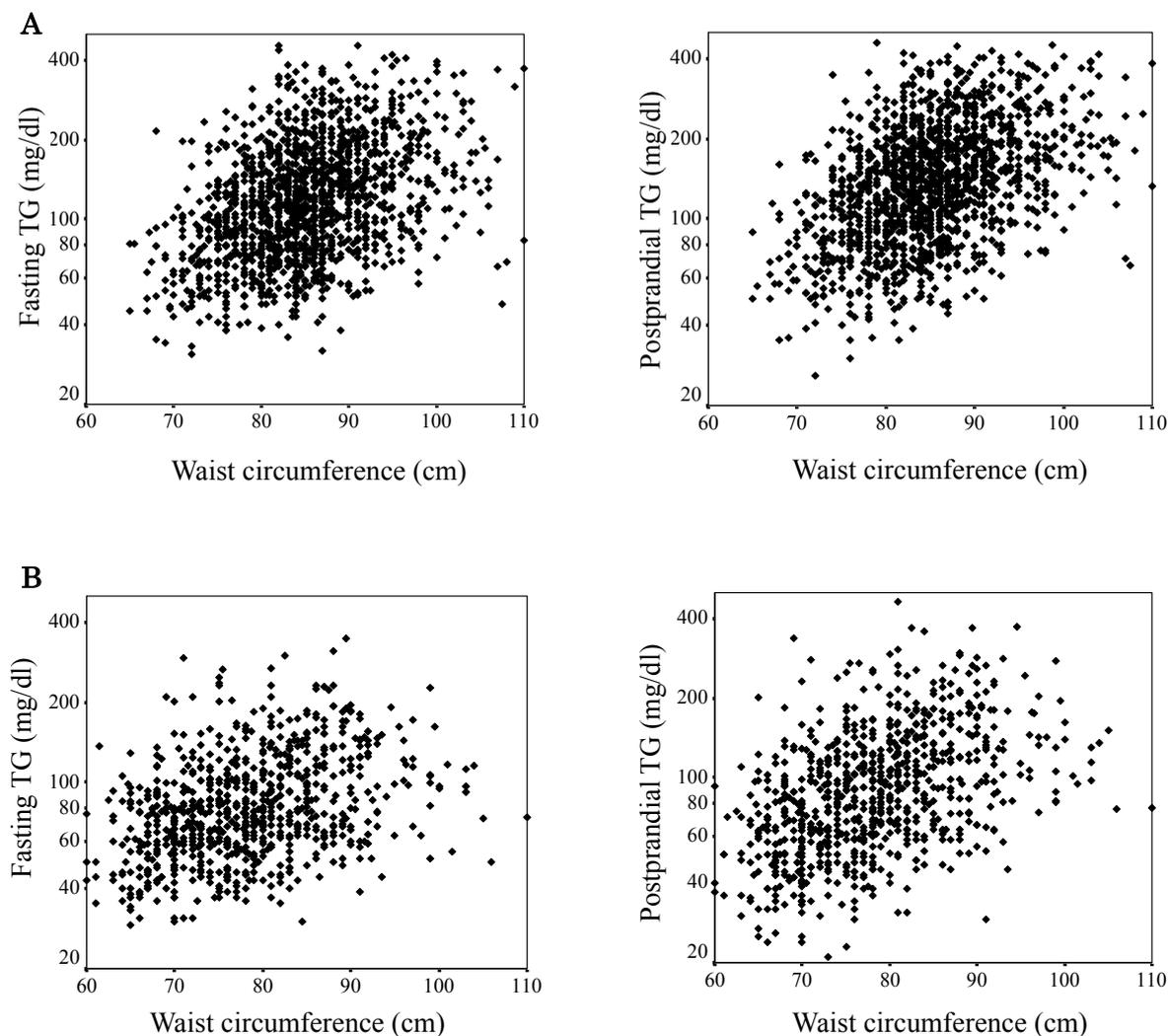


Fig. 2. Scatter-plots of Fasting TG versus waist circumference (left) and Postprandial TG versus waist circumference (right) in men (A) and in women (B).

Table 3 shows the results of multiple regression analyses to quantify the independent contributions of waist circumference, age, HbA1c, HDL-cholesterol, and fasting TG to the variance of postprandial TG. Waist circumference alone explained as much as 17.8% and 20.5% of the variability in TG levels in men and in women, respectively (Model 1). When age, HbA1c, and HDL-cholesterol were included as the second, third, and fourth variables in models after entering waist circumference, each variable was statistically significant ($p < 0.001$), and the R^2 value of the model improved (Model 2–4). Finally, when fasting TG was forced into the regression model (Model 5), the regression coefficient of waist circumference was markedly reduced but was still significant as an independent variable in both genders ($p < 0.001$). The

association of HDL-cholesterol with postprandial TG persisted in men ($p < 0.05$) but no significant association was observed in women after the inclusion of fasting TG in the model. Models including BMI in place of waist circumference as an independent variable did not yield higher R^2 values than models that included waist circumference (data not shown). Similar results were found when diabetic subjects, as defined by OGTT, were not included in multiple regression analysis. Because the replacement of HbA1c by fasting PG or 2-h PG did not provide higher R^2 values than the model with HbA1c and there was high collinearity among them, regression with fasting PG or 2-h PG was not pursued.

Table 2. Simple correlations of metabolic parameters with Fasting TG and Postprandial TG

	Men (<i>n</i> =1,505)		Women (<i>n</i> =798)	
	Fasting TG	Postprandial TG	Fasting TG	Postprandial TG
Age	-0.01	-0.07 [§]	0.28*	0.29*
Waist circumference	0.38*	0.42*	0.36*	0.45*
Body mass index	0.36*	0.41*	0.35*	0.44*
HbA1c	0.13*	0.16*	0.21*	0.31*
Fasting plasma glucose	0.12*	0.14*	0.20*	0.24*
HDL-Cholesterol	-0.45*	-0.43*	-0.42*	-0.39*

[§]*p*<0.01, **p*<0.001. HDL, high-density lipoprotein; TG, triglyceride. Analyses of fasting TG and postprandial TG were performed after logarithmical transformation.

Table 3. Standardized partial regression coefficients on the multiple regression analysis of Postprandial TG as a dependent variable

Independent variable	Men (<i>n</i> =1,505)					Women (<i>n</i> =798)				
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 1	Model 2	Model 3	Model 4	Model 5
Waist	0.42*	0.42*	0.41*	0.30*	0.10*	0.44*	0.40*	0.37*	0.30*	0.15*
Age		-0.05 [§]	-0.067 [§]	-0.07 [§]	-0.06*		0.19*	0.14*	0.13*	0.00
HbA1c			0.12*	0.10*	0.05*			0.17*	0.16*	0.11*
HDL-C				-0.32*	-0.03 [§]				-0.26*	0.00
Fasting TG					0.80*					0.76*
Model R ² (%)	17.8	18.0	19.3	28.4	76.1	20.5	24.0	26.2	32.3	74.6

[§]*p*<0.05, **p*<0.001. The analyses of fasting TG and postprandial TG were performed after logarithmical transformation.

Discussion

In this large-scale cross-sectional study, we examined differences between fasting and postprandial TG levels in middle-aged Japanese men and women with a focus on the associations with waist circumference. Consistent with previous reports²⁰⁻²², these two measurements of TG levels on the same day were indeed strongly correlated; however, we were able to demonstrate a modest but significant association of waist circumference with postprandial TG levels independent of fasting TG levels. This indicates that subjects with a larger waist circumference may have higher levels of postprandial TG than those with a smaller waist circumference and similar fasting levels. It is noteworthy that these results were observed after physiological fat load in free-living subjects, excluding those receiving treatments for diabetes and dyslipidemia.

Conventionally, postprandial lipemia has been evaluated by oral fat-loading tests²³. The concept of using a high-fat load approach is that a large amount of fat can better challenge and bring out postprandial abnormalities than a smaller amount of fat²⁴, because the magnitude of postprandial lipemia increases with the increasing fat content of a meal²⁵. Subsequently,

the capillary measurement method has enabled assessments of diurnal TG profiles under daily conditions^{26, 27}. Diurnal TG profiles with meals containing relatively less fat correlated well with data obtained by standardized high fat-loading tests and could also be informative. Postprandial capillary TG levels significantly increased from fasting levels, and the incremental diurnal TG as expressed by the area under the capillary TG curve (TGc-AUC) was correlated with fasting capillary TG, gender, mean daily intake²⁸ and BMI²⁹. The results of the present study are in line with their observations. Furthermore, our results extend their results showing that even a single evaluation of postprandial TG levels after a normal daily meal could reflect information about an individual's metabolism, in addition to fasting TG levels, including waist circumference.

As for variables other than waist circumference, HbA1c was also an independent predictor of postprandial TG levels, though the contribution of HbA1c to the variance in postprandial TG levels did not exceed that of waist circumference. With regard to HDL-cholesterol, its association with postprandial TG was attenuated after the inclusion of fasting TG in the model, resulting in a modest association in men (*p*<

0.05) and no significant association in women. Of note is that these results were obtained after adjusting for alcohol consumption, which affects both HDL-cholesterol levels and TG levels³⁰. Couillard *et al.* have reported that men with low HDL-cholesterol did not show an exaggerated postprandial TG response after high fat meal unless fasting hypertriglyceridemia was accompanied³¹. Indeed, various phenotypes accompany low HDL-cholesterol and high fasting TG in type 2 diabetic patients or insulin-resistant individuals who show postprandial hyperlipidemia³². In addition, subjects with cholesteryl ester transfer protein (CETP) deficiency have been reported to show a favorable postprandial TG metabolism³³; however, at least in general population studies such as this study, it appears that the association of HDL-cholesterol with postprandial TG levels was subtle, if any, after accounting for fasting TG levels.

What biological mechanisms could underlie this association between waist circumference and postprandial triglyceridemia? It is possible that waist circumference reflects the degree of visceral fat accumulation³⁴. In subjects with increased visceral adiposity and concomitant insulin resistance, increased lipolysis of visceral adipocytes that is presumably caused by insulin resistance contributes to the increase in postprandial delivery of fatty acids to the portal circulation^{16, 35}. Another possible explanation may be that excess liver fat content plays a dominant role in postprandial hypertriglyceridemia in subjects with expanded waist circumference^{36, 37}. It is reported that hepatic TG represents the driving force for very-low-density-lipoprotein (VLDL) assembly and that secretion of large VLDL increases with increasing liver fat content³⁸. Abdominally obese subjects often also have increased synthesis and secretion of VLDL particles, which compete with the catabolic pathways of intestinal particles for their clearance during the postprandial period.

The strengths of this study include its large sample size and measurements of both fasting and postprandial TG levels on the same day in each individual. Nonetheless, the limitations of this study also should be considered. First, a single evaluation of postprandial TG levels 2 hours after lunch could be inappropriate to capture the maximal TG concentration after the meal. Previous studies using a smaller fat load (~30 g) demonstrated peak plasma TG 4 hours after ingestion^{39, 40}. In the cohort study of Bansal *et al.*, postprandial TG levels measured 2–4 hours after the last meal had the strongest association with future cardiovascular events¹. Plasma TG sampled at later time points could have reached even higher levels, and the

impact of waist circumference might have been stronger than observed in the present study; however, this possibility needs to be further examined. Second, the measurements of TG might be only an indicator of the impaired clearance of TG-rich lipoprotein particles. Current evidence suggests that TG-rich remnant lipoproteins are much more atherogenic than large nascent TG-rich particles^{41, 42}. Since the determination of remnant lipoprotein cholesterol (RLP-C) has recently become available in clinical settings, it could be utilized as a direct indicator of postprandial lipaemia.

In conclusion, this study demonstrated that waist circumference was a significant determinant of postprandial TG levels independent of fasting TG levels after loading with a moderate amount of fat, similar to daily meals of Japanese men and women. Postprandial TG has a better relation with waist circumference than fasting TG.

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