The association of triglyceride to high-density lipoprotein cholesterol ratio with high-risk coronary plaque characteristics determined by CT angiography and its risk of coronary heart disease

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Abstract

Triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio is an independent risk index of cardiovascular events. The aim of this study was to evaluate the association between TG/HDL-C ratio and coronary plaque characteristics that increase the likelihood of cardiovascular events as determined by coronary computed tomography angiography (CCTA). A total of 935 patients (mean age; 64 years, men; 55 %) who underwent CCTA for suspected coronary artery disease (CAD) were included. High-risk plaques (HRP) were defined by three characteristics: positive remodeling; low-density plaques; and spotty calcification. Significant stenosis was defined as a luminal narrowing of >70%. Patients with higher TG/HDL-C ratio showed significantly greater prevalence of HRP and significant stenosis compared with patients with low TG/HDL-C ratio ($p<0.01$, respectively). The multivariate logistic analysis demonstrated that TG/HDL-C ratio significantly associated with the presence of HRP ($p<0.01$), but not significant coronary stenosis ($p=0.24$). During the median follow-up period of 4.1 years, 78 cardiovascular occurred. the highest tertile of TG/HDL-C was associated with cardiovascular events with the lowest TG/HDL-C tertile as the reference (hazard ratio, 2.28; 95% confidence interval, 1.18-4.36). A high TG/HDL-C ratio was associated with the presence of CCT-verified HRP, which can lead to cardiovascular events in patients with suspected CAD.

Introduction

Abnormalities in serum lipids, including elevated blood low-density lipoprotein cholesterol (LDL-C), decreased high-density lipoprotein cholesterol (HDL-C), and increased blood triglyceride (TG) levels, are well-known risk factors for coronary artery disease (CAD) (1,2). Although LDL-C is considered the most important risk factor, The TG/HDL-C ratio, known as an atherogenic index of plasma, provides additional risk stratification beyond the one provided by LDL-C (3). Previous studies showed that TG/HDL-C ratio was associated with CAD related outcomes either in general populations (4-6) or in high-risk patients with known CAD (7-9). Although the relation between TG/HDL-C ratio and CAD is well known, its relationship with coronary plaque morphology remains unclear.

Coronary computed tomography angiography (CCTA) allows for the identification of high-risk coronary plaque characteristics as well as coronary atherosclerotic burden both of which are involved in acute coronary syndrome(10-12). A previous study showed that the presence of low attenuation plaques, positive remodeling, and spotty calcification were predictors of acute coronary syndrome (10). Thus, the presence of high-risk plaque features and severe coronary stenosis determined by CCTA are useful for assessing risk for CAD.

The aim of this study was to evaluate (1) the association between TG/HDL-C ratio and coronary plaque characteristics that increase the likelihood of acute coronary events, and (2) the association between TG/HDL-C ration and the incidence of coronary events in patients with suspected CAD.

METHODS

Study population

This study included patients with suspected coronary artery disease who underwent coronary CT angiography at Okayama University Hospital (Okayama, Japan) between August 2011 and August 2015. Exclusion criteria were prior percutaneous coronary intervention, or prior coronary bypass surgery graft, severe heart failure (New York Heart Association classification $\geq$ III), and allergy to iodinated contrast agent, and known severe renal failure (estimated glomerular filtration rate < 30 $mL^{-1}min^{-1}1.73\ m^2$), missing information regarding one or more traditional coronary risk factors or laboratory data, poor image due to motion artifact or inadequate contrast filling. As shown in Figure 1, 935 patients were analyzed in this study. The study protocol was approved by the institutional ethics committee on human research of Okayama University. The requirement for informed consent was waived. The investigation conformed to the principles outlined in the Declaration of Helsinki.

CT image acquisition

CT scans were performed using a 128-slice CT scanner (SOMATOM Definition Flash; Siemens Medical Solutions, Erlangen, Germany) as described previously (13). The initial bolus of contrast agent (Omnipaque 350; Daiichi Sankyo, Tokyo, Japan) was calculated as body weight × 0.07 mL and injected over 10 s. A CT acquisition protocol using a test bolus was carried out at the level of the ascending aorta after administration of 10 ml of the contrast medium (Omnipaque 350; Daiichi Sankyo, Tokyo, Japan), then 15 ml of physiologic (0.9%) saline. A low-dose image was obtained every 1 s. The delay before formal imaging was calculated as the time to peak enhancement in the ascending aorta plus 3 s to ensure enhancement of the contrast agent was 12 s, and was followed by a second bolus of the contrast agent that had been diluted 1:1 with

physiologic saline for an additional 8 s. then, the contrast agent was “chased” with a bolus of physiologic saline (20ml). The flow rate for all injections was equal to (body weight) × 0.07 ml/s. All patients arrived at the hospital 1 h before the scheduled CT scanning time, and those with a persistent high heart rate of > 60 beats per min received oral metoprolol (20–40 mg). If the heart rate did not sufficiently decrease to < 60 beats per min before the scheduled CT scanning time, patients received intravenous landiolol hydrochloride (0.125 mg/kg) until the heart rate was < 60 beats per min.

Coronary CT angiography analysis

CT data were transferred to an office image analysis workstation. We used axial and curved multiplanar reformatted images to evaluate the morphology of coronary-artery plaques with commercially available cardiac reconstruction software (Virtual Place; Raijin, AZE Inc., Tokyo, Japan) (14). One experienced senior cardiologist evaluated the images on a per-segment basis with 16 segments examined as described previously using the segment model developed by the American Heart Association (15), and the presence and characteristics of coronary artery plaques on CT angiography were evaluated. Coronary plaques were defined as structures of >1 mm2 within the coronary arteries that differed in density from the contrast-enhanced vessel lumen. The definitions of calcified plaques were a minimum CT density of > 130 Hounsfield units, or noncalcified plaques < 130 HU, or low-density plaques < 50 HU. Coronary artery remodeling was assessed by calculation of the difference in vessel diameter at the plaque site compared with a reference site in a normal-appearing segment proximal to the legion, with positive remodeling defined as an index of >1.05. Spotty calcification was defined as length of calcium burden <3/2 of vessel diameter and width <2/3 of vessel diameter. We defined the term “high-risk plaque” as the presence of positive remodeling, low-density plaque, and spotty calcification. We confirmed

high-risk plaques when all plaque characteristics, including positive remodeling, low-density plaques, and spotty calcification, were present (16). Significant coronary artery stenosis was defined as luminal obstruction of > 70% of the diameter of the vessel.

Assessment of other risk factors

Medical histories were investigated for all patients. A blood sample was drawn after an overnight fast or more than 4 hours after breakfast at the central laboratory of the Okayama university hospital. Coronary risk factor was defined as follows; Diabetes mellitus was defined as diagnosis in the past or self-reported history of, hemoglobinA1c level of > 6.5 % (17), or current or past using of hypoglycemic agents. Dyslipidemia was defined as current or past using of lipid-lowering agents, or a LDL-C level of ≥ 140 mg/dl, TG level of ≥ 150 mg/dl, or HDL-C level of < 40 mg/dl in a fasting blood sample. Hypertension was defined as those whose sitting blood pressure of ≥ 140/90 mmHg or current or past using of antihypertensive agents (18). Smoking status was defined as subjects who smoked regularly at the time of CT. TG/HDL-C ratio was calculated as TG (mg/dl) divided by HDL-C (mg/dl) (19).

Follow-up methods

Follow-up clinical information was obtained from review of the medical records or telephone interviews by attending physicians. MACE was defined as the composite of cardiovascular death, nonfatal myocardial infarction, or late coronary revascularization over 90 days after the indexed CT acquisition. Patients who underwent scheduled revascularization within 90 days after the indexed CT were censored at the time of the first revascularization.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation or median with interquartile range, depending on the Shapiro–Wilks test for normality. Dichotomous variables are expressed as numbers (proportion). Categorical data were compared using $\chi 2$ analysis or Fisher's exact test among the groups. We used one-way analysis of variance to compare normally distributed continuous variables, and Bonferroni correction was used for post hoc testing. The Kruskal-Wallis test was used to compare non-normally distributed continuous variables among the groups. Logistic analysis was performed to determine the odds ratio (OR) with 95% confidence intervals (95%CI) for TG/HDL-C associated with high-risk plaque and significant stenosis. Cumulative survival estimates were calculated using the Kaplan–Meier method and compared with the log-rank test. To ascertain the associations of TG/HDL-C ratio with MACE, we performed univariate and multivariate Cox regression analyses, and the results were reported as hazard ratio (HR) with 95%CI. To avoid the overfitting in a multivariate Cox regression analysis, the model 1 included TG/HDL ratio, age, male, hypertension, diabetes mellitus, current smoking, and the use of statin, and model 2 included HRP and significant stenosis in addition to the variables in the model 1. All reported p-values were two-sided, and statistical significance was set at $p<0.05$. Statistical analyses were performed using SPSS statistical software (Version 28; IBM Corp., Armonk, NY, USA).

RESULTS

Patient characteristics

The baseline characteristics of 935 patients according to the tertile of TG/HDL-C ratio are summarized in Table1. Of all, the mean age of all patients was 64 years old, and 55% of patients were male; 59%, 50%, and 33% of patients had hypertension, dyslipidemia, and diabetes mellitus, respectively. Next, patients were divided into tertile based on TG/HDL-C ratio (T1, n = 315,

TG/HDL-C ratio ≤ 1.56; T2, n =315, TG/HDL-C ratio ≥ 1.57 and ≤ 2.66; T3, n = 305, TG/HDL-C ratio ≥ 2.67). Among the three groups, the proportion of male, body mass index, the prevalence of hypertension, dyslipidemia, diabetes mellitus, and current smoking were significantly increased as the TG/HDL-C ratio increased. The levels of LDL-C, TG, and hemoglobinA1c were increased, and HDL-C levels and eGFR were decreased as the TG/HDL-C ratio increased. With respect to medications, as TG/HDL-C ratio increased, the proportions of patients using angiotensin converting enzyme inhibitors or angiotensin receptor blockers, and antidiabetic agents were increased.

CTA plaque characteristics

Table 2 shows coronary artery plaque characteristics analysis with CTA. HRP and significant stenosis were detected in 15% and 21% of patients. Among the three groups, as TG/HDL-C ratio increased, the prevalence of calcified plaques, noncalcified plaques, positive remodeling, low density plaque, spotty calcification, high-risk plaque, and significant stenosis were increased. Agatston score was also significantly increased as TG/HDL-C ratio increased.

Next, the association of TG/HDL-C ratio with HRP and significant stenosis were evaluated using logistic regression models. In the univariate analysis, HRP was significantly associated with TG/HDL-C ratio as well as age, male, hypertension, dyslipidemia, diabetes mellitus, currents smoking, the use of statin, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, calcium channel blockers, and antidiabetic agents. In the multivariate analysis, the association between HRP and TG/HDL-C ratio remains significant. In addition, in the univariate analysis, significant stenosis was significantly associated with TG/HDL-C ratio as well as age, male, hypertension, dyslipidemia, diabetes mellitus, the use of statin, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, calcium channel blockers, and

antidiabetic agents. However, in the multivariate analysis, the association between significant stenosis and TG/HDL-C ratio was not significant.

3.3 TG/HDL-C and of cardiovascular events

During the median follow-up period of 4.1 years, 78 MACEs (4 cardiovascular death, 17 nonfatal myocardial infarction, 57 late coronary revascularization) occurred in study patients. The univariate Cox analysis showed that the highest and middle tertile groups were associated with cardiovascular events with the lowest tertile as the reference ($p = 0.02$ and $p < 0.01$, respectively). HRP ($p < 0.001$) and significant stenosis ($p < 0.001$) were also significant risk factors associated with MACE. In the multivariate Cox model 1 including TG/HDL-C ratio and clinical variables, the highest group was significantly associated with MACE ($p = 0.03$). Furthermore, in the multivariate Cox model 2 including HRP and significant stenosis in addition to the model 1, the highest group was not significant of MACE ($p = 0.06$).

4. Discussion

The major finding of this study is that high TG/HDL-C ratio was significantly associated with the presence of CCTA-verified HRP. To our knowledge, this is the first detailed study to evaluate the association between TG/HDL-C ratio and coronary plaque characteristics in patients with suspected CAD. Furthermore, the increased TG/HDL-C ratio was shown to be a significant predictor of adverse coronary events after adjustment of traditional risk factors, suggesting the TG/HDL ratio is a potential biomarker to assess CAD risk.

This study showed that increased TG/HDL-C ratio, but not LDL-C was associated with the presence of high-risk coronary plaque, which may predict future acute coronary syndrome (20). In line with this study, we have reported that increased levels of oxidized LDL or oxidized HDL, but not the levels of LDL-C were associated with the presence of high-risk coronary plaque in

patients with suspected CAD (18,21). Although LDL-C is considered the most important risk factor, emerging evidence suggest that TG/HDL-C ratio provides additional risk stratification beyond the one provided by LDL-C (3). The pathophysiological implications of elevated TG and low HDL-C levels have been reported. High TG/HDL-C values were associated with the metabolic syndrome, insulin resistance (8,22) and more in general of a diabetic or pre-diabetic state(23). Patients with high values of TG/HDL-C ratio had high values of remnant-C, which has been implicated in atherogenesis, inflammation(24). TG-rich lipoproteins carry cholesterol in addition to TGs and this, together with LDL-C, is considered to be the atherogenic agent that feeds the development of arterial wall plaques. In addition, elevated TG is associated with lower levels of HDL-C and formation of small, dense LDL particles (25). Recent study of intracoronary imaging using optical coherence tomography revealed that high levels of small dense LDL-C are associated with the presence of vulnerable plaque (26). Meanwhile, TG/HDL-C ratio was positively correlated with insulin resistance (25). Emerging data are linking TG/HDL-C ratio to metabolic syndrome, nonalcohol fatty liver disease, and diabetes mellitus (27-29). Previous studies showed that the prevalence of high-risk plaque detected by CCTA in patients with diabetes mellitus and metabolic syndrome (16,30,31). Thus, cardiometabolic abnormality reflecting TG/HDL-C may also explain the link this maker with high-risk coronary plaque.

The relationship between TG/HDL-C ratio and CAD related outcomes has been previously described either in general populations (4-6) or in high-risk patients with known CAD(7) (8) (9). Cheng et al. reported that, in general population, the highest tertile of TG/HDL ratio had almost 1.5-fold of atherosclerotic cardiovascular events with the lowest TG/HDL-C tertile as the reference (6). Rohullah et al. reported that, in high-risk patients, TG/HDL-C ratio ≥2.5 was associated with almost three increase in cardiovascular events during a 5 years follow-up, independently of traditional coronary risk factors and angiographic CAD severity (9). In line

with these studies, we demonstrated that the highest tertile of TG/HDL-C ratio (≥2.66) had two-fold of cardiovascular events in patients with suspected CAD after adjustment of traditional risk factors with the lowest TG/HDL-C tertile as the reference. Taken together, TG/HDL-C ratio can be easily calculated, based on commonly available parameters and yield strong prognostic significance in the general population as well as high-risk patients with CAD risk factors.

Patients with a high TG/HDL-C ratio generally had other metabolic risk factors including the diagnostic criteria of metabolic syndrome. Although LDL-C can be reduced by statins substantially, first step of these individuals to increase HDL-C levels and decrease TG levels is a lifestyle modification such as physical activity to reduce body weight (32). The pharmacological interventions should be taken into consideration if the above aims are not achieved. Fibrates are commonly used to decrease triglyceride levels, while triglyceride-lowering therapy with fibrates has not been shown to offer considerable cardiovascular disease risk reduction in large, randomized control trials (33). Further studies are warranted to establish the management of patients with a high TG/HDL-C ratio to reduce cardiovascular events.

Our study has several limitations. First, this is a retrospective single center study. Patient selection may have been biased and a prospective study would be preferable. Second, we included only Asian patients with suspected CAD; the results cannot be applied to other ethnic groups and the general population. Third, information on change in medications after CCTA was not available. The intention or intensification of lipid lowing therapy and during follow-up may weaken the association between TG/HDL-C ratio and cardiovascular events.

In conclusion, this study demonstrated that an increase in the TG/HDL-C was significantly associated with the presence of high-risk plaque determined by coronary CT angiography in patients with suspected stable CAD. The TG/HDL-C ratio may be a potential biomarker to assess CV risk. Further studies are required to identify the best method with which to improve a risk of

patients with high TG/HDL-C ratio for protection against cardiovascular events.

Author Contributions

Conceptualization, Y.K. and T.M. (Toru Miyoshi); methodology, Y.K. and T.M. (Toru Miyoshi); formal analysis, Y.K. and T.M. (Toru Miyoshi); investigation, Y.K., T.N., M.N., K.I. and T.M. (Takashi Miki); writing—original draft preparation,Y.K. and T.M. (Toru Miyoshi); writing—review and editing, H.I. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the ethics committees of the Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences (2203-024).

Informed Consent Statement

The requirement for informed patient consent was waived owing to the low-risk nature of the study and the inability to obtain consent directly from all study subjects.

Data Availability Statement

The data presented in this study are available upon request from the corresponding author. The

data is not publicly available because of privacy concerns.

Conflicts of Interest

All authors declare no conflict of interest associated with this manuscript.

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Table1. Baseline characteristics of subjects and according to the TG/HDL ratio tertile in patients in all patients.

	All	TG/HDL ratio			P value for trend
		Tertile 1 (0.31-1.56)	Tertile 2 (1.57-2.66)	Tertile 3 (2.67-14.69)	
n	935	315	315	305	
Age, years	64±14	63±15	64±15	63±12	0.436
Male	516 (55)	152 (48)	164 (52)	200 (55)	<0.001
Body mass index, kg/m^2	23.8±4.0	22.6±3.9	23.7±4.1	25.1±3.5	<0.001
Hypertension	552 (59)	159 (21)	187 (59)	206 (67)	<0.001
Dyslipidemia	472 (50)	129 (41)	153 (48)	190 (62)	<0.001
Diabetes mellitus	306 (33)	84 (27)	103 (32)	123 (40)	0.001
Current smoking	211 (23)	53 (17)	68 (22)	90 (29)	<0.001
LDL-C, mg/dL	114±31	107±27	114±32	121±32	<0.001
TG, mg/dL	131±74	74±21	114±27	207±79	<0.001
HDL-C, mg/dL	58±16	71±16	56±11	46±10	<0.001
TG/HDL-C	23.8±4.0	22.6±3.9	23.7±4.1	25.1±3.5	<0.001
HemoglobinA1c, %	6.3±1.2	6.1±1.0	6.3±1.2	6.4±1.3	<0.001
eGFR, mL/min/1.73m^2	69.7±18	71.1±19.0	68.4±17.5	68.9±16.7	0.154
Medications					
Statins	318 (34)	92 (29)	112 (35)	114 (37)	0.078
ACEIs or ARBs	355 (38)	102 (32)	127 (40)	126 (41)	0.042
CCBs	317 (34)	95 (30)	109 (35)	113 (37)	0.184
Antidiabetic agents	196 (23)	46 (15)	61 (20)	89 (29)	<0.001

Data are presented as number (%) of patients or mean ± standard deviation.

LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker

Table 2. Numbers of plaques with various characteristics according to the tertile of TG/HDL ratio

	All	TG/HDL ratio			
		Tertile 1 (0.31-1.56)	Tertile 2 (1.57-2.66)	Tertile 3 (2.67-14.69)	P value for trend
n	935	315	315	305	
Calcified plaque	608 (65)	201(56)	206 (65)	219 (72)	0.002
Noncalcified plaque	462 (49)	129 (41)	159 (51)	174 (57)	<0.001
Positive remodeling	373 (40)	95 (30)	132 (42)	146 (48)	<0.001
Low density plaque	277 (30)	66 (21)	100 (31)	111 (36)	<0.001
Spotty calcification	77 (24)	108 (34)	108 (34)	120 (39)	<0.001
High risk plaque	136 (15)	27 (9)	45 (14)	64 (21)	<0.001
Significant stenosis	193 (21)	53 (17)	63 (20)	77 (25)	0.033
Agatston score	20 [0, 245]	5 [0, 210]	33 [0, 286)	26 [0, 225)	0.016

Data are presented as number (%) of patients or median [interquartile range].

TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.

Table 3 Univariable and multivariable associates of high-risk plaque

	Univariate analysis		Multivariate analysis	
	Odds ratio(95%CI)	P value	Odds ratio (95%CI)	P value
Log TG/HDL-C	2.009 (1.514-2.666)	<0.001	1.581 (1.150-2.173)	0.005
LDL-C	0.999 (0.994-1.005)	0.085		
Age, per year	1.032 (1.016-1.048)	<0.001	1.029 (1.011-1.048)	0.002
Male	2.917 (1.925-4.422)	<0.001	2.797 (1.773-4.412)	<0.001
Hypertension	2.543 (1.673-3.876)	<0.001	1.129 (0.654-1.949)	0.664
Dyslipidemia	1.981 (1.358-2.892)	<0.001	1.472 (0.879-2.465)	0.142
Diabetes mellitus	1.998 (1.382-2.889)	<0.001	1.460 (0.803-2.655)	0.214
Current smoking	1.530 (1.020-2.296)	0.040	1.050 (0.655-1.657)	0.834
Statin	1.598 (1.103-2.313)	0.013	1.126 (0.682-1.857)	0.643
ACEIs or ARBs	2.534 (1.751-3.668)	<0.001	1.889 (1.192-2.992)	0.007
CCB	1.665 (1.151-2.409)	0.007	1.079 (0.695-1.675)	0.734
Antidiabetic agents	2.110 (1.414-3.147)	<0.001	1.032 (0.537-1.981)	0.925

CI, confidence interval; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker

Table 4. Univariable and multivariable associates of significant stenosis

	Univariate analysis		Multivariate analysis	
	Odds ratio (95%CI)	P value	Odds ratio (95%CI)	P value
Log TG/HDL-C	1.551 (1.185-1.927)	<0.001	1.183 (0.893-1.568)	0.242
LDL-C	1.000 (0.995-1.00)	0.981		
Age, per year	1.051 (1.035-1.067)	<0.001	1.055 (1.036-1.074)	<0.001
Male	2.829 (1.988-4.026)	<0.001	3.075 (2.064-4.580)	<0.001
Hypertension	2.051 (1.451-2.898)	<0.001	0.980 (0.617-1.557)	0.932
Dyslipidemia	2.214 (1.591-3.082)	<0.001	2.116 (1.340-3.342)	0.001
Diabetes mellitus	2.017 (1.459-2.789)	<0.001	1.390 (0.811-2.381)	0.231
Current smoking	1.399 (0.975-2.009)	0.069	1.043 (0.687-1.583)	0.843
Statins	1.628 (1.177-2.251)	0.003	0.898 (0.574-1.694)	0.639
ACEIs or ARBs	1.704 (1.237-2.346)	<0.001	1.128 (0.751-1.694)	0.562
Ca blockers	1.778 (1.286-2.457)	<0.001	1.442 (0.969-2.147)	0.071
Antidiabetic agents	2.106 (1.472-3.013)	<0.001	1.182 (0.653-2.139)	0.581

CI, confidence interval; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker

Table 5. Univariable and multivariable associates of major adverse cardiac events

	Univariate analysis		Multivariate analysis: model1		Multivariate analysis: model2	
	Hazard ratio (95%CI)	P value	Hazard ratio (95%CI)	P value	Hazard ratio (95%CI)	P value
TG/HDL-C ratio						
Tertile 1 (0.31-1.56)	reference	–	reference	–	reference	–
Tertile 2 (1.57-2.66)	2.133(1.109-4.103)	0.023	1.843 (0.950-3.578)	0.071	1.762 (0.906-3.427)	0.095
Tertile 3 (2.67-14.69)	2.754 (1.459-5.200)	0.002	2.085 (1.075-4.046)	0.030	1.884 (0.964-3.681)	0.064
LDL-C, per 1 mg/dL			1.005 (0.997-1.012)	0.257	1.004 (0.996-1.012)	0.319
Age, per year	1.032 (1.011-1.053)	0.003	1.033 (1.010-1.056)	0.004	1.027 (1.004-1.051)	0.021
Male	2.311 (1.411-2.786)	<0.001	1.858 (1.083-3.186)	0.024	1.539 (0.887-2.669)	0.125
Hypertension	1.740 (1.062-2.850)	0.028	1.211 (0.711-2.063)	0.480	1.118 (0.656-1.907)	0.682
Dyslipidemia	1.377 (0.874-2.167)	0.168	–	–	–	–
Diabetes mellitus	1.947(1.249-3.036)	0.003	1.750 (1.099-2.789)	0.019	1.642 (1.027-2.625)	0.038
Current smoking	1.875 (1.176-2.990)	0.008	1.552 (0.945-2.547)	0.082	1.552 (0.945-2.555)	0.083
Statin	1.690 (1.225-2.331)	<0.001	0.837 (0.508-1.379)	0.485	0.798 (0.483-1.318)	0.378
ACEIs or ARBs	1.791 (1.149-2.793)	0.01	–	–	–	–
CCBs	1.856 (1.190-2.895)	0.006	–	–	–	–
Antidiabetic agents	1.454 (0.887-2.385)	0.138	–	–	–	–
High-risk plaque	3.033 (1.901-4.840)	<0.001	–	–	1.741 (1.041-2.910)	0.034
Significant stenosis	2.979 (1.897-4.676)	<0.001	–	–	1.706 (1.029-2.828)	0.038

CI, confidence interval; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker

Figure legends

Figure 1. Flow chart of eligibility and exclusion of patients

Figure2. Kaplan-Meier plot of cumulative probability of cardiovascular events by tertiles of the TG/HDL-C ratio.

Time to cardiovascular events, including cardiovascular death, nonfatal myocardial infarction, and late revascularization according to baseline TG/HDL-C ratio. The cumulative incidence rates of the primary outcomes according to the TG/HDL-C ratio were significantly higher in the highest tertile group (CAVI $\geq$ 2.67) than in the first tertile group (CAVI $\leq$ 1.56) (P value for trend $<$ 0.01).