Impact of the Triglyceride Level on Coronary Plaque Components in Female Patients with Coronary Artery Disease Treated with Statins

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Abstract

Several studies have reported that elevated triglyceride (TG) levels may be more strongly associated with an increased risk of coronary artery disease (CAD) in females than in males. We examined gender differences in the relationship between TG levels and coronary atherosclerosis using integrated backscatter intravascular ultrasound (IB IVUS) in CAD patients treated with statins. Three hundred seventy-eight CAD patients (105 females and 273 males) who underwent percutaneous coronary intervention using IB IVUS, and who were already receiving statin treatment, were included. Gray-scale and IB IVUS examinations were performed for the non-culprit segment of a coronary artery, and fasting serum TG concentrations were measured. We found that TG levels were significantly correlated with increased lipid ($r=0.40$, $p<0.001$) and decreased fibrous ($r=-0.37$, <0.001) plaque components in females, but not in males. Low-density lipoprotein cholesterol and high-density lipoprotein cholesterol levels were not related to either the gray-scale or IB IVUS parameters in both genders. After adjustment for conventional coronary risk factors by a multivariate stepwise regression analysis, higher TG levels in females were independently associated with increased lipid ($\beta=0.31$, $p=<0.001$) contents in coronary plaques. In conclusion, among CAD patients treated with statins, TG levels were associated with lipid-rich coronary plaques in females, but

not in males. TG levels may be more important indicators of residual risk after statin treatment in females than in males.

Key words: Triglyceride; Coronary plaque; Intravascular ultrasound; Gender difference

Introduction

Elevated triglyceride (TG) levels are associated with an increased risk for cardiovascular disease morbidity and mortality [1-3]. Although statin is a standard treatment for the prevention of cardiovascular diseases [4], TG is an independent risk factor of coronary artery disease (CAD) in subjects at all levels of low-density lipoprotein cholesterol (LDL-C) [5], and even in the setting of low total cholesterol [3, 6]. Large-scale prospective studies have reported that LDL-C is not a very strong predictor of CAD in females [7, 8], and high TG levels are better predictors of CAD than LDL-C levels in females [7]. In addition, a meta-analysis of population-based prospective study [9] and cohort studies [10, 11] have reported that TG levels have a greater impact on the risk of CAD in females than in males. Elevated TG levels in females may be more strongly associated with an increased risk of CAD than those in males [12].

Conventional gray-scale intravascular ultrasound (IVUS) is a useful intravascular imaging modality for evaluating coronary atherosclerotic plaques. However, conventional IVUS cannot evaluate coronary plaque components accurately. Recently, integrated backscatter IVUS (IB IVUS) has been developed for quantitative characterization of tissue in coronary plaques [13, 14]. An increased lipid component in

coronary plaques as evaluated by IB IVUS is a useful predictor of future cardiovascular events in CAD patients [15, 16].

At present, it is not yet clear whether TG levels are associated with coronary atherosclerosis as assessed by IB IVUS in CAD patients treated with statins. It is also not clear whether there is a gender difference in the relationship between TG levels and coronary plaque. Therefore, we aimed to examine these issues using IB IVUS in male and female CAD patients who were already receiving statins.

Materials and methods

Patients and study design

A total of 1351 patients with CAD who received percutaneous coronary intervention (PCI) at Fukuoka University Hospital from December 2011 to February 2016 were screened for this retrospective single-center study. Of these, patients who did not undergo PCI using IB IVUS or who were not receiving statin treatment before PCI were excluded. The remaining patients were excluded according to the following exclusion criteria: (1) patients with unanalyzable IVUS images [17]; (2) familial hypercholesterolemia; (3) contraindication to statins or antiplatelet agents; (4)

cardiogenic shock; (5) severe infection; and (6) recent surgery or trauma. Ultimately, 378 CAD patients who were already receiving statin therapy before PCI were included in this study.

Statin treatment was conducted in all of the study subjects according to the Japan Atherosclerosis Society guidelines for the diagnosis and prevention of atherosclerotic cardiovascular diseases, with a target LDL-C level of <100 mg/dL [18]. All of the patients received a standard antiplatelet therapy before PCI according to the Japanese guidelines for the secondary prevention of myocardial infarction [19]. Fasting blood samples for the measurement of clinical laboratory data were obtained before the PCI and IVUS procedures.

This study was approved by the ethics committee of Fukuoka University Hospital (EC/IRB: 15-7-14). We performed this study according to the Declaration of Helsinki regarding investigations in humans.

IVUS procedure and analysis

IVUS examination was performed for the non-culprit segment (<50% stenosis evaluated by coronary angiography) of a coronary artery using an imaging catheter and a console (View IT and VISIWAVE, Terumo, Tokyo, Japan) after IVUS-guided PCI of the culprit

lesion. The IVUS catheter was inserted into the distal side of the culprit lesion, and pulled back automatically at a speed of 0.5 mm/sec. To prevent coronary spasm, an optimal dose of nitroglycerin was injected into the coronary artery just before IVUS examination. The most diseased 10-mm segment (containing the greatest plaque volume) that was located >5 mm proximal or distal to the PCI site was selected for IVUS analysis, as described previously [20, 21] (Fig. 1). A total of 11 IVUS frames were extracted at an interval of 1.0 mm for a total length of 10 mm at the selected segment by a motorized pullback system.

A quantitative IVUS analysis system (VISIATLAS, Terumo, Tokyo, Japan), which measures both the volume and content of coronary plaque, was used for gray-scale and IB IVUS analysis. The validity and reliability of this IVUS analysis system has been reported to be suitable for the accurate measurement of coronary arteries [22]. External elastic membrane (EEM) cross-sectional area (CSA) and lumen CSA were manually traced at 1-mm axis intervals for a length of 10 mm for quantitative IVUS analysis, and atheroma CSA (EEM CSA minus lumen CSA) was automatically calculated [20, 21] (Fig. 1). Vessel and lumen volume were calculated automatically using the IB IVUS analysis system as Σ EEM CSA and Σ lumen CSA, respectively. Total atheroma volume (TAV) was calculated as vessel volume – lumen volume.

Percent atheroma volume (PAV), which indicates plaque burden at a non-culprit segment, was calculated as 100 × TAV / vessel volume.

The components of coronary plaques evaluated by the software for IB IVUS were classified into major 4 categories: lipid, fibrosis, dense fibrosis, and calcification, as reported previously [13]. The area and volume of each plaque component were calculated automatically by the IB IVUS software, and these parameters are presented as percentages.

An experienced physician who was blinded to the patient characteristics performed the IVUS analysis according to the criteria described in the American College of Cardiology Clinical Expert Consensus document on IVUS [17].

Clinical laboratory examinations

Fasting blood samples were collected before IB IVUS-guided PCI for the measurement of the clinical data. LDL-C, high-density lipoprotein cholesterol (HDL-C), TG, creatinine, blood sugar and Hemoglobin A1C (HbA1c) levels were measured at the Fukuoka University Hospital Laboratory Unit. Estimated glomerular filtration rate (eGFR) was calculated as follows: $194 \times \text{serum creatinine}^{-1.094} \times \text{age}^{-0.287}$ (male), $194 \times \text{serum creatinine}^{-1.094} \times \text{age}^{-0.287} \times 0.739$ (female).

Statistical data analysis

For statistical data analysis, the SAS software package (version 9.4, SAS Institute) at Fukuoka University (Fukuoka, Japan) was used. Categorical variables are presented as numbers and percentages. Normally distributed continuous variables are presented as mean ± SD, and continuous variables with skewed distributions are presented as median values (interquartile range). The chi-square test or Fisher's exact test was used to compare frequency distributions of categorical variables including gender, risk factors for CAD, and medications between females and males. Differences in continuous variables between females and males were compared using the Student t test when the variables showed normal distributions and Wilcoxon's signed-rank sum test when the variables showed skewed distributions. The Spearman correlation or Pearson correlation was used to examine the correlations among continuous variables including lipid profiles and IVUS parameters according to the distributions of the variables. To identify the factors that were associated with the percentage of lipid volume of coronary plaque, a multivariate stepwise regression analysis was performed among conventional risk factors [age, body mass index (BMI), hypertension, diabetes mellitus and current smoking] and serum levels of LDL-C, HDL-C and TG. A P value

of less than 0.05 was considered to be significant unless indicated otherwise.

Results

Characteristics of the patients and clinical laboratory data

Table 1 shows the patient characteristics in this study. Females were significantly older than males. There were no significant differences in the frequencies of hypertension, diabetes mellitus, dyslipidemia and chronic kidney disease between the groups. The frequencies of current smoking, history of myocardial infarction and the use of angiotensin-converting enzyme inhibitor in males were significantly higher than those in females. All of the patients were already receiving statins before PCI and IVUS examination. None of the patients were receiving fibrates.

Table 2 shows the clinical laboratory data of the subjects in this study. Although serum levels of LDL-C and TG and TG/HDL-C ratio were similar between the groups, the HDL-C level in females was significantly higher than that in males. eGFR in females was significantly lower than that in males. While there was no significant difference in systolic blood pressure between the groups, diastolic blood pressure was significantly lower in females than in males.

Gray-scale and IB IVUS parameters at the non-culprit segment

Gray-scale and IB IVUS parameters at the non-culprit segment are shown in Table 3. TAV was significantly lower in females than in males, while there was no significant difference in PAV between the groups. The percentage of lipid volume was significantly lower in females than in males. The percentages of fibrosis volume, dense fibrosis volume and calcification volume were significantly higher in females than in males.

Associations between clinical data and coronary plaques

Figure 2 shows the associations between TG levels and gray-scale IVUS parameters at the non-culprit segment. In females, although TAV (r=0.28, p=0.004) and vessel volume (r=0.22, p=0.03) were positively correlated with TG levels (Fig. 2B and 2C), plaque burden presented as PAV (Fig. 2A) was not associated with TG levels (r=0.15, p=0.14). There was no significant association between TG and any of the gray-scale IVUS parameters in males (Fig. 2D-2F). While HbA_{1c} levels in males were positively correlated with PAV (data not shown), there were no significant correlations between the other clinical data and PAV in either gender (data not shown).

Figure 3 and Table 4 show the associations between clinical data including TG

levels and IB IVUS parameters at the non-culprit segment. As shown in Fig. 3A, 3B and 3C, TG levels in females were positively correlated with the percentage of lipid volume ($r=0.40$, $p<0.001$) and negatively correlated with both the percentage of fibrosis volume ($r=-0.37$, $p<0.001$) and dense fibrosis volume ($r=-0.23$, $p=0.02$). In contrast, there was no significant association between TG levels and plaque composition in males (Fig. 3E-3H). In addition, the TG/HDL-C ratio in females was positively correlated with the percentage of lipid volume ($r=0.34$, $p<0.001$) and negatively correlated with the percentage of fibrosis volume ($r=-0.32$, $p<0.001$), whereas these correlations were not found in males (Table 4). As shown in Table 4, LDL-C and HDL-C levels were not related to the IB IVUS parameters in either gender. In females, age and BMI were significantly associated with the lipid and fibrous coronary plaque components, but these relations were not observed in males. Diabetes mellitus was significantly associated with increased lipid and decreased fibrosis components of coronary plaques in both genders.

Table 5 shows the results of a multivariate stepwise regression analysis to identify the factors that were associated with the percentages of lipid volume at the non-culprit lesion in females and males. After adjustment for conventional coronary risk factors including HDL-C, higher TG levels in females were independently and most

strongly associated with the increased lipid (β=0.31, $p<0.001$) contents in coronary plaques. In males, diabetes mellitus was independently associated with the increased lipid components (β=0.19, $p=0.002$), whereas TG levels were not.

Discussion

The main finding of this study is that higher TG levels were significantly associated with increased lipid and decreased fibrous plaque components as evaluated by IB IVUS in females, while these associations were not observed in males. After adjustment for conventional coronary risk factors and confounders, higher TG levels in females were independently associated with increased lipid and decreased fibrosis components of coronary plaques in CAD patients who were already receiving statins (Fig. 3A and 3B and Tables 4 and 5).

Most TG in the blood stream are carried by very low-density lipoproteins (VLDL) and chylomicrons. Since VLDL and chylomicrons are both large, TG cannot penetrate the arterial wall. Therefore, TG may not directly cause the formation of atherosclerosis. However, elevated TG levels cause an increase in TG-rich lipoproteins (TRLs) such as VLDL and chylomicrons [23]. These remnant lipoproteins can

accumulate in the arterial wall due to their impaired clearance, and contribute to lipid accumulation in the vessel wall [24]. Increased remnants can also promote an inflammatory response in the vascular wall [25]. Thus, the accumulation of TRLs and their remnants promotes the formation of atherosclerotic plaque. TG levels are associated with the risk of cardiovascular diseases [1-3]. However, it is not clear whether TG levels are related to coronary plaque compositions as assessed by IVUS. Recently, a study using IVUS demonstrated that serum remnant-like cholesterol levels are associated with lipid-rich coronary plaque components in CAD patients [26]. In addition, Puri et al. reported that an increase in TG levels was significantly associated with coronary atheroma progression as evaluated by IVUS [27]. The improvement in plaque components probably occurs earlier than plaque regression in CAD patients treated with statin [28]. Given these reports, TG levels may be associated with the coronary plaque composition.

In general, in a younger population, serum TG levels are higher in males than in females. However, TG levels in females tend to increase with age, and TG levels in postmenopausal females are higher than those in premenopausal females [29]. Although females are at a lower risk of CAD than males in a younger population, the risk of CAD increases after a menopause [30]. Females with an early menopause have been reported

to have an increased risk of CAD [31, 32]. Estrogen, the female ovarian sex hormone, is considered to have protective effects on lipid metabolism and atherosclerosis [33]. Sarac et al. reported that postmenopausal females had a higher level of VLDL2-TG production than males who were matched for fasting TG levels [34]. $VLDL_2$-TG itself may promote the development of atherosclerosis, and higher $VLDL_2$-TG production could generate more intermediate-density lipoprotein (IDL). Higher IDL levels have been reported to be associated with the progression of atherosclerosis in humans [35]. Another study reported that natural menopause in females is associated with a delayed clearance of remnant lipoproteins [36]. The Framingham heart study reported that remnant-like particle cholesterol is an independent risk factor for CAD in females [37].

In this study, a higher TG/HDL-C ratio was also associated with the increased lipid components in females, but not in males (Table 4). An elevated TG/HDL-C ratio is a simple and useful marker for identifying the presence of small, dense low-density lipoprotein (LDL) particles [38]. An elevated TG level is a major factor associated with smaller LDL particle size [39]. Small, dense LDL exhibits decreased hepatic clearance by the LDL receptor, increased binding to cell surface proteoglycans [40] and greater susceptibility to oxidation [41]. In addition, small, dense LDL can be taken up more easily by arterial tissue compared with larger LDL [42]. Thus, smaller, denser LDL is

more atherogenic than normal-size LDL. In fact, the TG/HDL-C ratio and small, dense LDL particles have been reported to be associated with the risk of CAD [43, 44]. It has been demonstrated that small, dense LDL cholesterol concentrations in menopausal females are higher than those in premenopausal females [45]. In the present study, since the females had a median age of 72 (Table 1), almost all of the female patients can be assumed to be postmenopausal. In addition, although there was no significant difference in TG levels between genders (Table 2), TG levels were associated with increased lipid components of coronary plaques in females, but not in males. Impaired lipid metabolism in a postmenopausal status may contribute to an increase in vulnerability of coronary plaque in female CAD patients.

A large-scale clinical trial, the Fenofibrate Intervention and Event Lowering in Diabetes study (the FIELD study), reported that the TG-lowering agent fenofibrate reduced the risk of cardiovascular events in females, but not in males [46]. Another clinical study has reported that LDL-C in females is not a very strong predictor of future cardiovascular events, and TG is a better predictor than LDL-C in females [7]. In the present study, all of the patients were receiving an appropriate lipid-lowering therapy using statins, and higher TG levels were associated with lipid-rich coronary plaques in females, but not in males. The reduction of TG levels in females may have a greater

impact on the prevention of cardiovascular events, suggesting that higher TG levels in females may be a more important residual risk after statin treatment.

There were no significant associations between serum levels of LDL-C and HDL-C and plaque components in this study. Although both LDL-C and HDL-C are involved in the development of CAD [4, 47], little is known about the relationship between these factors and the tissue characteristics of coronary plaque as assessed by IVUS. Several studies using IVUS showed that LDL-C and HDL-C levels were related to coronary plaque components [48, 49], whereas these relations were not found in other studies [26, 50]. In this study, all of the patients were already receiving statins before the IB IVUS examination. This may influence the associations between serum levels of LDL-C and HDL-C and plaque compositions. The relationships between lipid profiles and coronary plaque components may be affected by patient characteristics such as gender and the status of lipid-lowering therapy.

We measured fasting TG levels instead of non-fasting levels. In general, non-fasting TG levels are very strongly correlated with fasting TG levels [51, 52]. However, several studies have reported that non-fasting TG levels may be a more useful predictor of the risk of CAD than fasting TG levels [53, 54]. Further studies will be needed to examine the relationship between non-fasting TG levels and coronary atherosclerosis in

male and female CAD patients.

Our study has several limitations. First, the sample size of the present study is relatively small. A large-scale study using IB IVUS will be required to confirm our results. Second, CAD patients who had unanalyzable IB IVUS images or who did not undergo IB IVUS-guided PCI were not included in this study. Therefore, there may be a selection bias and the results may not be applicable to all CAD patients. Third, the assessment of multiple plaques using IVUS in 3-vessel coronary trees could not be performed due to ethical considerations, since there were concerns regarding complications of the IVUS examination such as transient ischemia or coronary spasm. Fourth, we did not examine the relationships between the changes in TG levels and coronary plaque compositions. A prospective study using serial IB IVUS examinations will be needed. Fifth, although all of the patients were already receiving statins, the type, dose and duration of statin treatment before IVUS examination are unclear. These factors may affect the coronary plaque components.

In conclusion, among CAD patients who were already receiving statins, higher TG levels were associated with lipid-rich coronary plaques in females, but not in males. TG levels in females may be more important indicators of residual risk after statin treatment than those in males.

Conflict of interest

KS and SM are Directors of NPO Clinical and Applied Science, Fukuoka, Japan. KS and SM received a grant from the Public Interest Incorporated Foundation of "Clinical Research Promotion Foundation" in Fukuoka, Japan, and part of this work was transferred to NPO Clinical and Applied Science, Fukuoka, Japan. KS has an Endowed Department of Molecular Cardiovascular Therapeutics (SM), Fukuoka University, supported by MSD Co., Ltd, and an Endowed Department of Community and Emergency Medicine (MS, HN, SM), Fukuoka University, supported by Izumi City, Kagoshima, Japan.

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Figure legends

Figure 1. Representative coronary angiography and IVUS images of the evaluated vessel in gray-scale and IB IVUS analysis. The target segment for IVUS analysis had to be located >5mm proximal or distal from the PCI site, and its length was 10mm. IVUS, intravascular ultrasound; IB, integrated backscatter; PCI, percutaneous coronary intervention.

Figure 2. Associations between TG levels and gray-scale IVUS parameters in both genders. PAV (A), TAV (B) and vessel volume (C) in females and PAV (D), TAV (E) and vessel volume (F) in males. TG, triglyceride; IVUS, intravascular ultrasound; PAV, percent atheroma volume; TAV, total atheroma volume.

Figure 3. Associations between TG levels and IB IVUS parameters in both genders. Lipid volume (A), fibrosis volume (B), dense fibrosis volume (C) and calcification volume (D) in females and lipid volume (E), fibrosis volume (F), dense fibrosis volume (G) and calcification volume (H) in males. TG, triglyceride; IB, integrated backscatter; IVUS, intravascular ultrasound.

Table 1. Patient characteristics

	All patients (n=378)	Females (n=105)	Males (n=273)	P value (Female vs. Male)
Age, yrs	70 (64-75)	72 (67-77)	69 (62-75)	0.02
BMI, kg/m^2	24.1 (21.9-26.6)	24.5 (21.6-27.1)	24.0 (22.0-26.4)	0.33
Hypertension, n (%)	337 (89)	96 (91)	241 (88)	0.49
Diabetes mellitus, n (%)	251 (66)	68 (65)	183 (67)	0.77
Dyslipidemia, n (%)	332 (88)	92 (88)	240 (88)	1.0
Current smoking, n (%)	84 (22)	7 (7)	77 (28)	<0.001
CKD, n (%)	177 (47)	57 (54)	120 (44)	0.09
Previous MI, n (%)	84 (22)	15 (14)	69 (25)	0.03
Previous PCI, n (%)	148 (39)	33 (31)	115 (42)	0.07
Previous CABG, n (%)	16 (4)	5 (5)	11 (4)	0.78
Type of CAD, n				
Stable CAD/ACS	339/39	94/11	245/28	1.0
# of diseased vessel, n				
1/2/3	190/115/73	52/32/21	138/83/52	0.98
Target vessel, n				
RCA/LAD/LCx/LMT	119/176/81/2	30/57/18/0	89/119/63/2	0.27
Medications, n (%)				
Statins	378 (100)	105 (100)	273 (100)	-
Fibrates	0 (0)	0 (0)	0 (0)	-
Ezetimibe	12 (3)	3 (3)	9 (3)	1.0
EPA	28 (7)	7 (7)	21 (8)	0.90
CCB	224 (59)	70 (67)	154 (56)	0.09
ARB	251 (66)	70 (67)	181 (66)	1.0
ACE-I	35 (9)	4 (4)	31 (11)	0.04
β-blocker	102 (27)	22 (21)	80 (29)	0.13
Diuretics	62 (16)	16 (15)	46 (17)	0.82
Long acting nitrate	42 (11)	13 (12)	29 (11)	0.76

Data are presented as number (%) or median (interquartile range).

BMI, body mass index; CKD, chronic kidney disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CAD, coronary artery disease; ACS, acute coronary syndrome; RCA, right coronary artery; LAD, left anterior descending; LCx, left circumflex; LMT; left main trunk.; EPA,

eicosapentaenoic acid; CCB, calcium channel blocker; ARB, angiotensin II receptor blocker; ACE-I, angiotensin-converting enzyme inhibitor.

Table 2. Clinical laboratory data

	All patients (n=378)	Females (n=105)	Males (n=273)	P value (Female vs. Male)
LDL-C, mg/dL	87 (75-106)	87 (76-104)	87 (74-108)	0.82
HDL-C, mg/dL	45 (39-54)	48 (41-58)	45 (38-51)	0.004
TG, mg/dL	119 (84-172)	127 (95-175)	117 (81-171)	0.27
TG/HDL-C ratio	2.7 (1.8-4.3)	2.7 (1.8-4.4)	2.6 (1.7-4.2)	0.99
FBS, mg/dL	102 (90-119)	100 (89-116)	103 (90-119)	0.51
HbA_{1c}, %	6.5 (5.9-7.4)	6.7 (5.7-7.6)	6.5 (6.0-7.4)	0.79
eGFR, mL/min/1.73m^2	60.0 ± 20.5	55.5 ± 20.1	61.7 ± 20.4	0.009
SBP, mmHg	128 (118-140)	127 (116-142)	130 (118-140)	0.55
DBP, mmHg	71 (62-80)	68 (60-77)	72 (64-80)	0.003

Data are presented as mean ± SD or median (interquartile range).

LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; FBS, fasting blood sugar; HbA_{1c}, hemoglobin A_{1c}; eGFR, estimate glomerular filtration rate; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 3. Gray-scale and IB IVUS parameters

	All patients (n=378)	Females (n=105)	Males (n=273)	P value (Female vs. Male)
Gray-scale IVUS				
TAV, mm^3	59.9 (40.8-82.2)	56.1 (37.3-72.6)	63.7 (42.1-85.6)	0.04
Vessel volume, mm^3	142 (96-183)	142 (92-170)	144 (100-189)	0.09
PAV, %	43.6 (35.4-51.6)	41.6 (33.2-51.3)	43.8 (35.7-51.6)	0.24
IB IVUS				
Lipid volume, %	48.4 ± 16.5	44.4 ± 16.2	50.0 ± 16.5	0.003
Fibrosis volume, %	44.2 ± 12.8	46.4 ± 12.3	43.3 ± 12.8	0.03
Dense fibrosis volume, %	4.0 (2.3-6.6)	4.6 (3.2-8.0)	3.6 (2.2-6.2)	0.004
Calcification volume, %	1.4 (0.7-2.6)	2.1 (1.0-3.2)	1.1 (0.6-2.4)	<0.001

Data are presented as mean ± SD or median (interquartile range).

IB, integrated backscatter; IVUS, intravascular ultrasound; TAV, total atheroma volume; PAV, percent atheroma volume.

Table 4. Univariate factors associated with the percentage of lipid volume and fibrosis volume as evaluated by IB IVUS

	Lipid volume, %		Fibrosis volume, %	
	r	P value	r	P value
Females (n=105)				
Age	-0.21	0.03	0.22	0.02
BMI	0.28	0.004	-0.31	0.001
Hypertension	0.17	0.09	-0.16	0.11
Diabetes mellitus	0.26	0.009	-0.32	0.001
Current smoking	0.06	0.52	-0.09	0.36
LDL-C	0.06	0.56	-0.09	0.38
HDL-C	-0.02	0.80	0.03	0.78
TG	0.40	<0.001	-0.37	<0.001
TG/HDL-C ratio	0.34	<0.001	-0.32	<0.001
Males (n=273)				
Age	-0.02	0.77	0.01	0.82
BMI	0.07	0.28	-0.07	0.28
Hypertension	-0.02	0.79	-0.01	0.82
Diabetes mellitus	0.20	<0.001	-0.24	<0.001
Current smoking	-0.07	0.23	0.10	0.09
LDL-C	0.003	0.96	0.01	0.83
HDL-C	0.07	0.24	-0.08	0.18
TG	0.04	0.51	-0.06	0.35
TG/HDL-C ratio	0.02	0.74	-0.03	0.60

IB, integrated backscatter; IVUS, intravascular ultrasound; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride.

Table 5. Multivariate stepwise regression analysis: independent factors associated with the percentage of lipid volume evaluated by IB IVUS in females and males

Independent factors	β	SE	t value	P value
Females				
1. TG	0.31	0.02	3.42	<0.001
2. Diabetes mellitus	0.21	3.06	2.33	0.04
3. Hypertension	0.19	5.15	2.12	0.04
Males				
1. Diabetes mellitus	0.19	2.09	3.15	0.002

Multivariate stepwise regression analysis was performed using the following variables: age, BMI, hypertension, diabetes mellitus, current smoking, LDL-C, HDL-C and TG.
IB, integrated backscatter; IVUS, intravascular ultrasound; SE, standard error; TG, triglyceride; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Figure 1. Representative IVUS measurement for the non-culprit segment

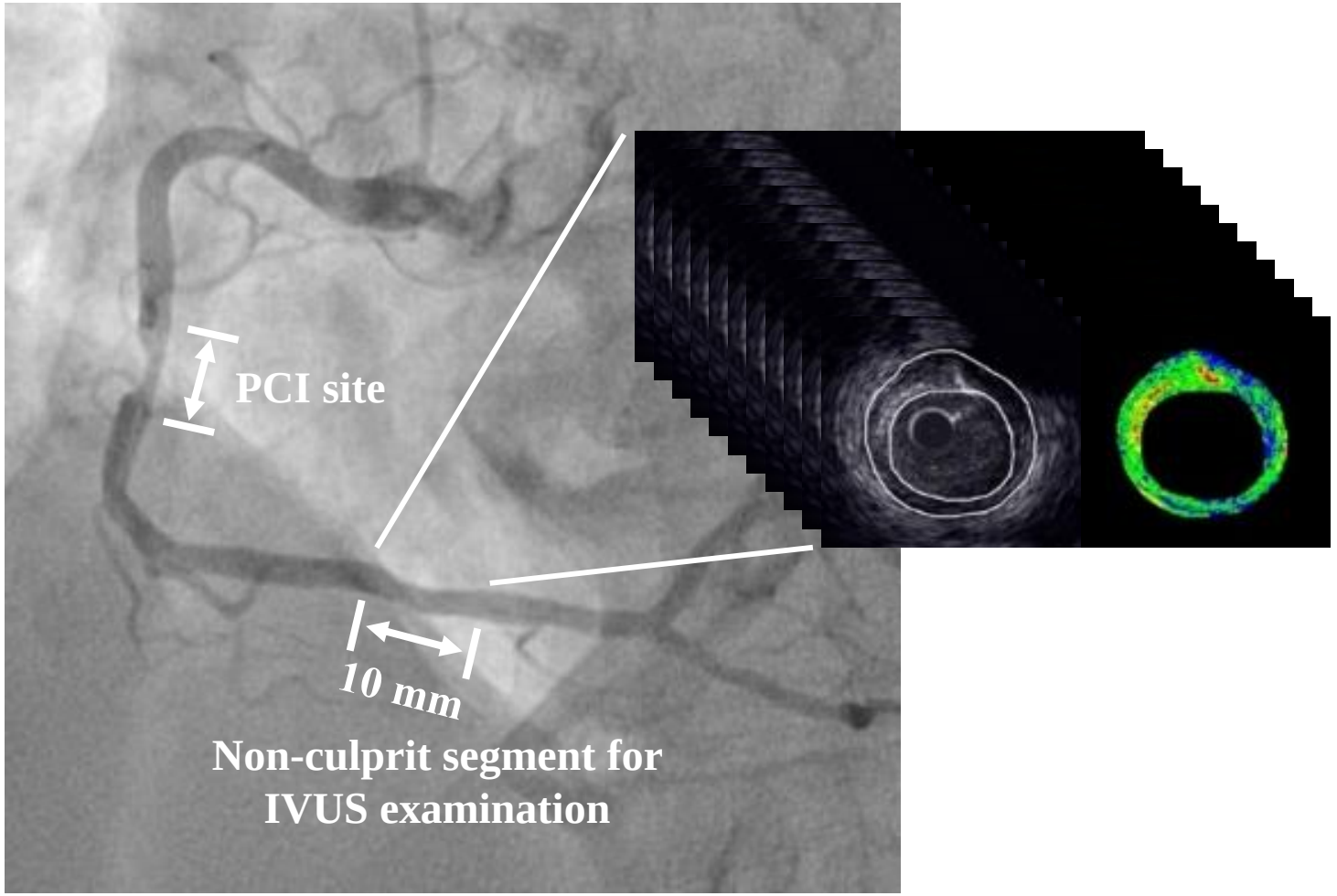
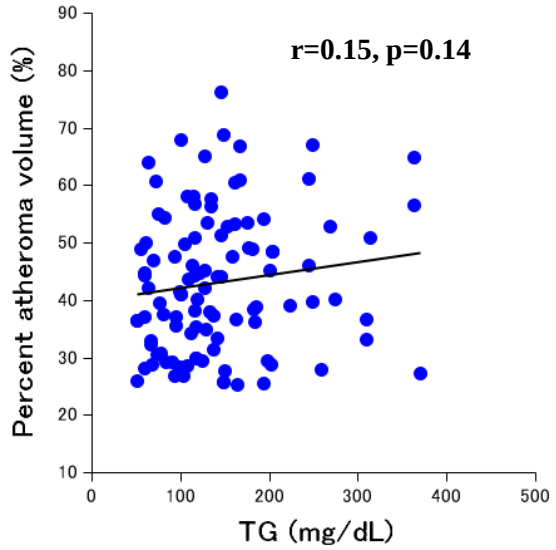


Figure 2. Associations between TG levels and gray-scale IVUS parameters in both genders

Female

A



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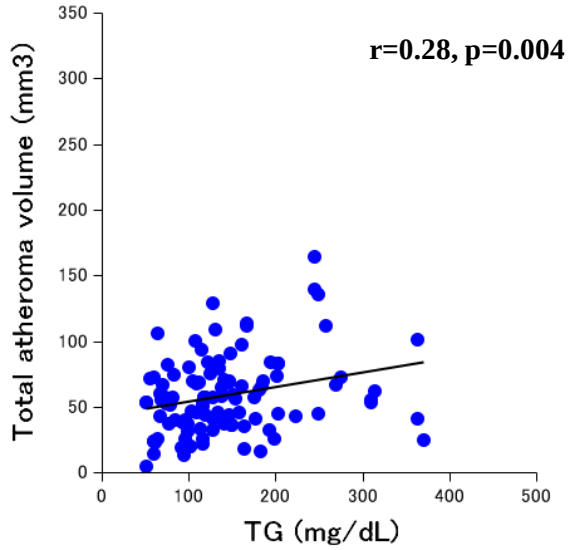

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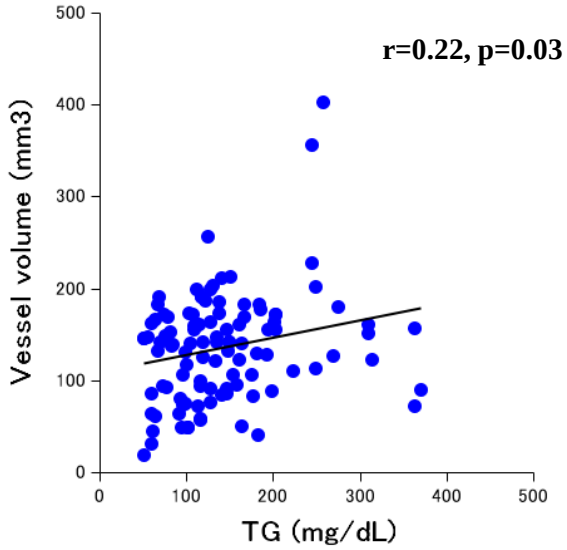
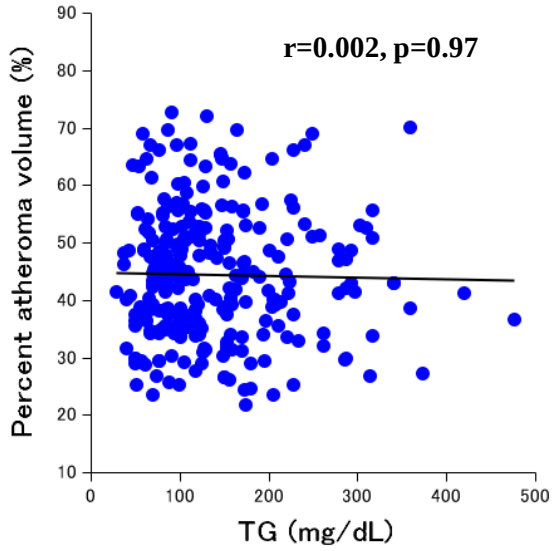


Male

D



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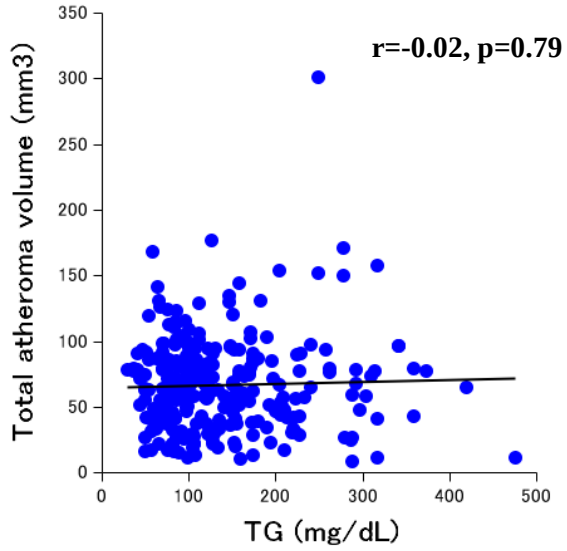

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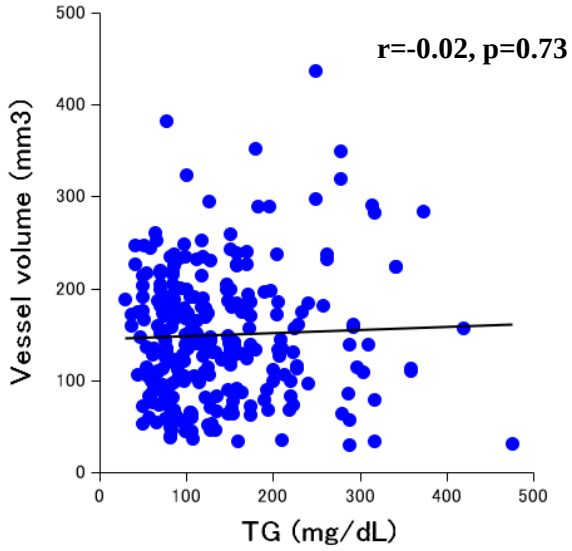
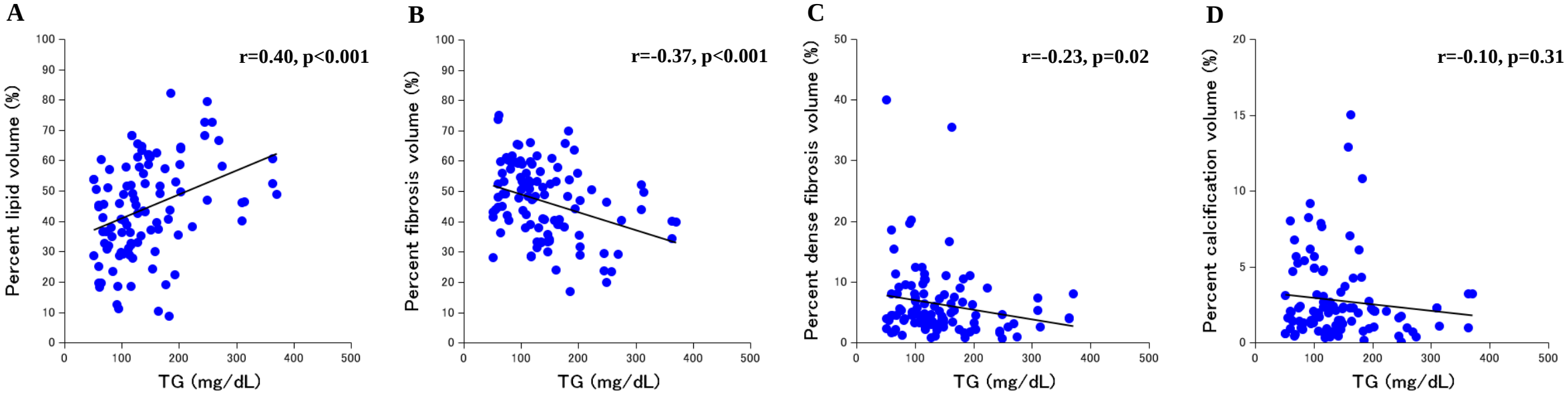


Figure 3. Associations between TG levels and coronary plaque components in both genders

Female



Male