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Rationale of decreasing low-density lipoprotein cholesterol below 70 mg/dL in patients with coronary artery disease: A retrospective virtual histology-intravascular ultrasound study

Young Hoon Seo, Duck-Jun Seo, In Geol Song, Ki-Hong Kim, Taek-Geun Kwon, Jang-Ho Bae

Division of Cardiology, Heart Center, Konyang University Hospital, Daejeon, South Korea

Abstract

Background: *The associations between statin and coronary plaque compositional changes were reported according to the use of high dose or not. An evaluation of the impact of low-density lipoprotein cholesterol (LDL-C) < 70 mg/dL by using real world dosages of statin on coronary plaque composition was undertaken.*

Methods: *The study subjects consisted of 61 patients (mean 59.9 years old, 45 males) who underwent percutaneous coronary intervention, baseline and follow-up (F/U; mean 8.4 months) virtual histology-intravascular ultrasound (VH-IVUS) examination. Change of plaque composition at peri-stent area, which was selected in order to measure the identical site at F/U study, was compared according to the F/U LDL-C level.*

Results: *Body mass index, prevalence of dyslipidemia, baseline total cholesterol and baseline LDL-C were significantly lower in F/U LDL-C < 70 mg/dL group (14 segments in 10 patients) than F/U LDL-C ≥ 70 mg/dL group (79 segments in 51 patients). F/U high-density lipoprotein cholesterol (HDL-C, OR 1.06, 95% CI 1.00–1.11, p = 0.054) and F/U LDL-C < 70 mg/dL (OR 3.43, 95% CI 0.97–12.17, p = 0.056) showed strong tendency of regression of necrotic core volume (NCV) ≥ 10%. In multivariable logistic regression analysis, F/U HDL-C (OR 1.07, 95% CI 1.01–1.14, p = 0.020) and F/U LDL-C < 70 mg/dL (OR 8.02, 95% CI 1.58–40.68, p = 0.012) were the independent factors for regression of NCV ≥ 10%.*

Conclusions: *Follow-up LDL-C level < 70 mg/dL with any types of statins and increase of HDL-C were associated with regression of NCV ≥ 10% in patients with coronary artery disease.* (Cardiol J 2018; 25, 6: 674–682)

Key words: cholesterol, LDL, coronary artery disease, intravascular ultrasonography, myocardial ischemia, coronary stenosis

Introduction

According to the National Cholesterol Education Program-Adult Treatment Panel-III (NCEP-ATP-III), target level of low-density lipoprotein cholesterol (LDL-C) in patient with coronary disease or coronary heart disease risk equivalents is less than 100 mg/dL [1]. But accumulating data, since NCEP-ATP-III was reported, supports lower LDL-C which can result in better outcomes [2, 3], and guidelines on treatment of cholesterol in patients with high cardiovascular risk recommends more intensive lipid-lowering therapy, LDL-C less than 70 mg/dL [4, 5].

Address for correspondence: Jang-Ho Bae, MD, PhD, Division of Cardiology, Heart Center, Konyang University Hospital 158, Gwanjeodong-Ro, Seo-Gu, Daejeon, South Korea, 35365, tel: 82-42-600-9400, fax: 82-42-600-9420, e-mail: janghobae@yahoo.co.kr

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Statin is a very important in coronary artery disease (CAD) in terms of coronary plaque regression as well as its own lipid lowering effect. High dose statin such as atorvastatin 80 mg or rosuvastatin 40 mg decreased coronary plaque volume in follow-up (F/U) intravascular ultrasound (IVUS) studies [2, 6]. Recent studies using virtual histology (VH)-IVUS showed that statin therapy draws a favorable coronary plaque modification such as decreased necrotic core volume (NCV) as well as decreased total plaque volume in patients with CAD [7, 8]. However, it was very difficult to compare the exact lesion site when F/U VH-IVUS study is done, even when a specific landmark such as branching point and/or perivascular marking was used. Furthermore, VH-IVUS captures the scanned frames at the end-diastolic point and this is another difficult reason why F/U VH-IVUS cannot exactly capture the same lesion frame with the F/U study.

Till now, associations between statin and coronary plaque compositional changes were reported according to the use of high dose or not. Therefore, the present study sought to evaluate the impact of LDL-C < 70 mg/dL by using any practical dosage of statin on coronary plaque composition, especially the necrotic core which is a key feature of vulnerable plaque, and the peri-stent coronary plaque for measuring the identical site was selected when doing the F/U VH-IVUS study.

Methods

Subjects

Among 298 consecutive patients who underwent percutaneous coronary intervention (PCI) and VH-IVUS for CAD in Heart Center, Konyang University Hospital, 72 patients underwent F/U coronary angiography (CAG) and VH-IVUS at mean 8.4 ± 1.4 months were included. There was no cardiogenic shock or need for intra-aortic balloon pump during the procedure and there were no major cardiovascular events, such as stroke, myocardial infarction or death. Eleven patients who could not take the statin because of side effects or those who showed unavailable lipid level were also excluded. In order to exactly compare the same segment of coronary plaque with F/U VH-IVUS examination, the proximal and distal segment of the implanted stent was used for the analysis. If the reference proximal and distal segment were in the side branch or had no plaque, those segments were excluded from the analysis. Finally, a total of 93 segments of 61 patients were enrolled in this study, specifically 49 proximal segments and 44 distal segments.

Clinical information including past medical history or medication history of patients were obtained by medical records or from patients and their relatives. Informed consent was obtained from each patient. Biochemical laboratory findings were obtained at least 8 h after fasting state at times of the index procedure and F/U procedure. In cases of primary PCI, fasting blood was obtained the following morning. Coronary risk factors included hypertension (blood pressure ≥ 140/90 mmHg based on the average of repeated readings or patients on antihypertensive drugs), dyslipidemia (total cholesterol [TC] > 200 mg/dL and/or triglyceride > 150 mg/dL and/or LDL-C > 130 mg/dL or patients on lipid lowering therapy), diabetes mellitus (controlled diet, oral hypoglycemic agents, or insulin; or fasting glucose level ≥ 126 mg/dL or 2 h oral glucose tolerance test ≥ 200 mg/dL) and current cigarette smoking.

Subjects received standardized treatment including one conventional dose of statin (atorvastatin 10 mg or rosuvastatin 10 mg or pitavastatin 2 mg) during the F/U period and no unnecessary procedures were performed. All study subjects received similar intensity of general advice for medication, diet, exercise and cessation of smoking. This study was approved by the ethics committee of Konyang University Hospital (2016-08-024) and was in accordance with the Declaration of Helsinki.

IVUS examination and analysis

Baseline and F/U VH-IVUS examination were performed during CAG after intracoronary administration of 100–200 μg nitroglycerin using with dedicated 20-MHz, 2.9 F monorail, electronic Eagle Eye Gold IVUS catheter (Volcano Therapeutics, Rancho Cordova, California) and VH-IVUS console (Volcano Therapeutics, Rancho Cordova, California). The IVUS catheter was advanced into the target lesion after wiring or ballooning and automatic pullback at 0.5 mm/s. The VH-IVUS image was recorded on DVD-ROM for subsequent off-line analysis.

Both qualitative and quantitative analyses of gray scale IVUS images were performed according to criteria of the American College of Cardiology's Clinical Expert Consensus Document on IVUS [9]. External elastic membrane (EEM) and cross-sectional area (CSA) was measured with customized software (IVUS Lab., Volcano Therapeutics, Rancho Cordova, CA, USA). The remodeling index

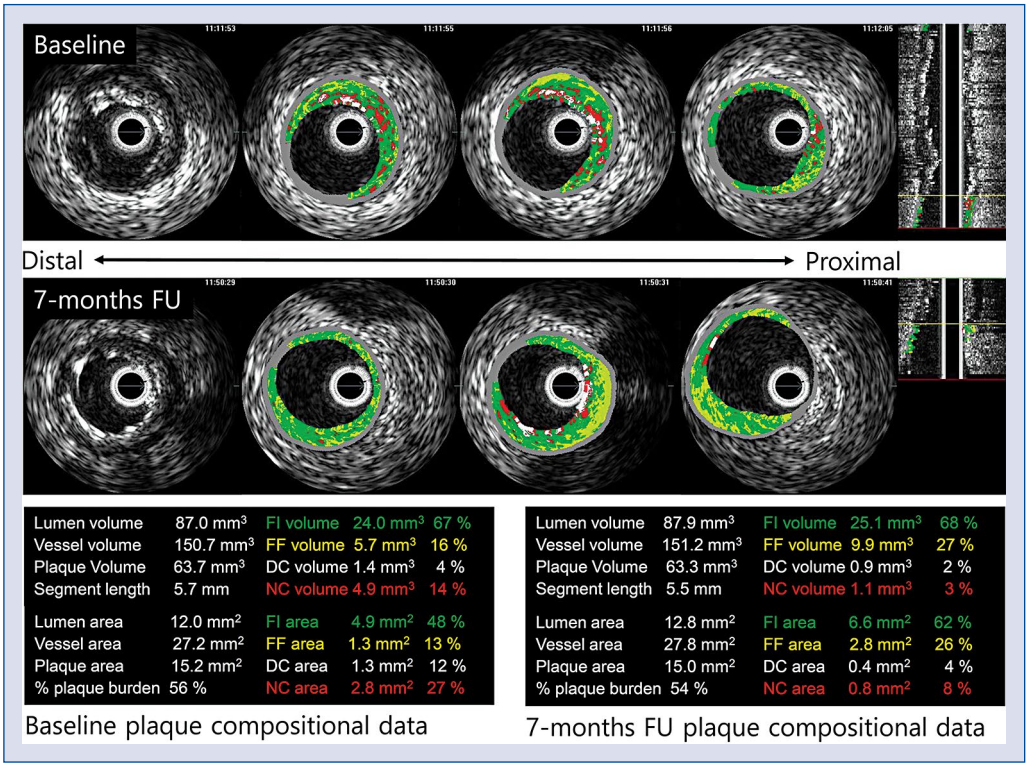

Figure 1. Virtual histology-intravascular ultrasound (VH-IVUS) findings of the analyzed segment in patient. Baseline and 7-months follow-up (FU) VH-IVUS images of the reference segment proximal to the stent in 73-year-old male. Images showed that necrotic core (NC) volume was decreased from 14% to 3% and NC area at minimal luminal area was also decreased from 27% to 8% whereas fibrofatty (FF) volume was increased from 16% to 27% and FF area was increased from 13% to 26%. He had atorvastatin daily 10 mg for 7-months FU period. Patient baseline low-density lipoprotein cholesterol level was decreased from 98 mg/dL to 68 mg/dL at 7-month FU period.

was calculated as the lesion EEM CSA divided by the average reference EEM CSA.

In this study, characteristics of culprit lesion were measured before PCI, the lesion but also proximal and distal reference segment to the stent after PCI were examined. The usual imaging studies comparing plaque composition with the F/U study which uses the side branch, vessel calcium, curvature, etc. However, it is very difficult to select the same segment of the F/U imaging with the baseline segment. So, the proximal and distal segment of the implanted stent was selected. F/U CAG and VH-IVUS examination was performed for comparison in same manner.

Spectral analysis of IVUS radiofrequency data

These analyses were done on the target lesion with customized software (IVUS Lab., Volcano Therapeutics, Rancho Cordova, CA, USA). For both lumen and media-adventitia interface, automatic border detection was done at the predefined lesion segment. Then, the border detection was manually corrected again in the lesion after automatic border detection. Manual analyzing of the image was performed by two cardiologists who were unaware of subject lipid profile, and third cardiologist, who was also blinded to lipid profile intervened when an opinion differed. After confirming border detection, the software automatically calculates and shows the results. For each frame, histologic findings were expressed in colors (green for fibrous, green-yellow for fibro-fatty, white for dense calcified, and red for necrotic core area). The area of each plaque component was analyzed at the minimal luminal area site and plaque volume over the culprit lesion as well as the reference segments which were used for comparison according to F/U examination at the proximal and the distal segment to the implanted stent (Fig. 1).

Statistical analysis

All analyses were performed with SPSS (version 18.0; SPSS Inc., Chicago, Illinois). Continuous variables were analyzed using the Student t-test or Mann-Whitney test and categorical data were compared by χ^2 test or Fisher exact test. Comparison between the three groups was performed using analysis of variance or Kruskal-Wallis test. Univariate binary logistic regression analysis was done to see the relationship between regression of NCV ≥ 10% and F/U lipid level. Criteria of F/U lipid level were chosen based on established value in the guidelines. Multivariable logistic regression analysis was done to find independent factors for regression of NCV ≥ 10%. All factors revealing p-value < 0.1 in baseline findings and univariate analysis were entered into the multivariable analysis as variables. Dyslipidemia and baseline TC were not co-entered into the multivariable analysis because of its overlapping definition. A p-value < 0.05 was considered statistically significant.

Results

Patient demographics

Follow-up LDL-C level < 70 mg/dL was achieved in 10 patients (Group 1, mean F/U LDL-C 56.9 ± 16.8 mg/dL) out of 61 patients and the remaining 51 patients showed F/U LDL-C ≥ 70 mg/dL (Group 2, mean F/U LDL-C 96.3 ± 23.6 mg/dL). Table 1 showed that group 1 had a lower body mass index (23.4 ± 2.9 vs. 26.3 ± 3.7, p = 0.021), lower prevalence of dyslipidemia (10% vs. 48%, p = 0.035), lower level of baseline TC (168.1 ± ± 41.5 mg/dL vs. 195.8 ± 35.8 mg/dL, p = 0.033) and lower level of baseline LDL-C (105.1 ± 26.3 mg/dL vs. 130.0 ± 28.7 mg/dL, p = 0.014) compared to the group 2. F/U lipid values also showed similar significant differences between the two groups. But, changes of each lipid value during the F/U period showed no significant differences between the two groups. Other demographics such as kind of statin, medications, ejection fraction (EF) and diagnosis revealed no significant differences between the two groups. Angiographic and VH-IVUS findings of the culprit lesion (n = 61), which was a stented lesion and was not used for comparison between baseline and F/U examination, also showed no significant differences between the two groups (Table 2).

Coronary plaque composition according to the LDL-C level

When the plaque composition of analyzed segments between the two groups according to the F/U LDL-C level < 70 mg/dL was compared, there were no significant differences in terms of baseline and F/U plaque composition (Table 3). The changes of plaque composition were not significantly different between the two groups during the F/U period. There were also no significant differences in segment length, plaque burden and imaged vessel of analyzed segments.

However, as shown in Table 4, F/U high--density lipoprotein cholesterol (HDL-C) (odds ratio [OR] 1.06, 95% confidence interval [CI] 1.00–1.11, p = 0.054) and F/U LDL-C < 70 mg/dL (OR 3.43, 95% CI 0.97–12.17, p = 0.056) showed a strong tendency of regression of NCV ≥ 10%. Multivariable logistic regression analysis with variables of BMI, baseline TC, baseline LDL-C, EF, remodeling index, stent length, F/U HDL-C and F/U LDL-C < 70 mg/dL was performed to find independent factors for regression of NCV ≥ 10%. F/U HDL-C (OR 1.07, 95% CI 1.01––1.14, p = 0.020) and F/U LDL-C < 70 mg/dL (OR 8.02, 95% CI 1.58–40.68, p = 0.012) were the independent factors for regression of NCV ≥ 10% and other variables did not show statistical significance in multivariable analysis (Table 5). Coronary plaque compositional changes according to statin type used show no significant differences (Table 6).

Discussion

Necrotic core, one of the coronary plaque compositions, is a most important feature of vulnerable plaque. It is associated with no-reflow phenomenon during PCI [10], positive coronary artery remodeling [11], clinical presentation feature such as acute coronary syndrome [12], high strain site [13] and localized endothelial dysfunction [14]. All of the above features are associated with worse clinical presentation or prognosis in patients with CAD. Necrotic core of more than 10% of coronary plaque composition is an important factor in determining coronary lesion classification such as thin-cap fibroatheroma, fibrotic plaque, fibrocalcific atheroma and pathological intimal thickening [15].

The main finding of this study was that the target level of LDL-C < 70 mg/dL is very important in regression of percent NCV ≥ 10% in patients with CAD. And this study also showed other significant findings as follows: 1) Decreasing the LDL-C level under 70 mg/dL was more important than increasing the HDL-C level for reducing NCV more than 10%; 2) Coronary plaque compositional changes showed no significant differences among the statin types in conventional dosage.

Table 1. Baseline clinical characteristics of the patients.

Variables	Total (n = 61)	Group 1 (n = 10) F/U LDL-C < 70 mg/dL	Group 2 (n = 51) F/U LDL-C ≥ 70 mg/dL	P
Age [years]	59.9 ± 11.4	60.1 ± 9.2	60.0 ± 11.9	0.972
Male gender	45 (73.8%)	8 (80.0%)	37 (72.5%)	1.000
Weight [kg]	68.9 ± 11.9	65.4 ± 11.9	69.6 ± 11.9	0.321
BMI [kg/m^2]	25.8 ± 3.7	23.4 ± 2.9	26.3 ± 3.7	0.021
Smoking	30 (49.2%)	7 (70.0%)	23 (45.1%)	0.182
Comorbidities:				
Hypertension	34 (55.7%)	5 (50.0%)	29 (56.9%)	0.738
DM	15 (24.6%)	3 (30.0%)	12 (23.5%)	0.696
History of MI	0 (0%)	0 (0%)	0 (0%)	
Dyslipidemia	25 (41.7%)	1 (10.0%)	24 (47.1%)	0.035
Baseline lipid level [mg/dL]:				
TC	191.3 ± 37.9	168.1 ± 41.5	195.8 ± 35.8	0.033
TG	164.9 ± 102.1	211.9 ± 177.0	154.5 ± 79.0	0.351*
HDL-C	43.3 ± 9.3	39.0 ± 7.1	44.2 ± 9.5	0.107
LDL-C	125.7 ± 29.6	105.1 ± 26.3	130.0 ± 28.7	0.014
F/U lipid level [mg/dL]:				
TC	150.7 ± 34.3	113.6 ± 20.3	158.2 ± 31.6	< 0.001
TG	154.2 ± 86.8	161.8 ± 121.9	152.7 ± 79.7	0.764
HDL-C	44.9 ± 10.5	42.9 ± 9.93	45.3 ± 10.7	0.530
LDL-C	89.9 ± 26.9	56.9 ± 16.8	96.3 ± 23.6	< 0.001*
Changes of lipid level [mg/dL]:				
ΔTC	–41.4 ± 45.2	–54.5 ± 30.5	–38.8 ± 47.4	0.377*
ΔTG	–11.5 ± 95.3	–50.1 ± 131.2	–3.8 ± 86.1	0.346*
ΔHDL-C	1.5 ± 10.5	4.0 ± 13.2	1.0 ± 10.0	0.413
ΔLDL-C	–34.8 ± 30.8	–41.2 ± 22.7	–33.5 ± 32.2	0.477
Medication:				1.000
ACEI	46 (75.4%)	8 (80.0%)	38 (74.5%)	1.000
ARB	7 (11.5%)	1 (10.0%)	6 (11.8%)	0.147
BB	39 (63.9%)	4 (40.0%)	35 (68.6%)	1.000
CCB	9 (14.8%)	1 (10.0%)	8 (15.7%)	1.000
ASA	58 (95.1%)	10 (100.0%)	48 (94.1%)	1.000
Insulin	1 (1.6%)	0 (%)	1 (2.0%)	1.000
OHA	12 (19.7%)	2 (20.0%)	10 (19.6%)	0.322
Lipid lowering agent	54 (88.5%)	8 (80.0%)	46 (90.2%)	0.082
EF [%]	63.7 ± 8.7	68.1 ± 6.0	62.9 ± 8.9	0.678
Diagnosis:	28/7/6/20	5/2/0/3	23/5/6/17	0.203
SAP/UA/ /NSTEMI/STEMI	(45.9%/11.5%/ /9.8%/32.8%)	(50.0%/20.0%/ /0/80.0%)	(45.1%/9.8%/ /11.8%/33.3%)	
Prescribed statin:				
Atorvastatin	31 (50.8%)	5 (50.0%)	26 (51.0%)	
Rosuvastatin	13 (21.3%)	4 (40.0%)	9 (17.6%)	
Pitavastatin	17 (27.9%)	1 (10.0%)	16 (31.4%)	

*Mann-Whitney test; n — number; F/U — follow-up; LDL-C — low-density lipoprotein cholesterol; BMI — body mass index; DM — diabetes mellitus; MI — myocardial infarction; TC — total cholesterol; TG — triglyceride; HDL-C — high-density lipoprotein cholesterol; ACE — angiotensin converting enzyme inhibitor; ARB — angiotensin receptor blocker; BB — beta-blocker; CCB — calcium channel blocker; ASA — acetylsalicylic acid; OHA — oral hypoglycemic agent; EF — ejection fraction; SAP — stable angina pectoris; UA — unstable angina; NSTEMI — non ST-segment elevation myocardial infarction; STEMI — ST-segment elevation myocardial infarction

Table 2. Angiographic and virtual histology-intravascular ultrasound findings of culprit lesions.

Variables	Total (n = 61)	Group 1 (n = 10) F/U LDL-C < 70 mg/dL	Group 2 (n = 51) F/U LDL-C ≥ 70 mg/dL	P
Lesion length [mm]	19.5 ± 7.8	18.6 ± 7.6	19.7 ± 7.9	0.678
Plaque volume [mm^3]	26.0 ± 21.5	42.1 ± 29.7	35.0 ± 19.8	0.256
Remodeling index	1.00 ± 0.19	1.11 ± 0.25	0.98 ± 0.17	0.052
Lesion characteristics [%]:				
Fibrous area	58.6 ± 14.1	62.5 ± 9.5	57.8 ± 14.8	0.337
Fibrofatty area	13.9 ± 12.2	12.9 ± 9.2	14.1 ± 12.7	0.691*
Dense-calcium area	8.7 ± 10.4	6.3 ± 4.6	9.2 ± 11.2	0.424
Necrotic core area	19.1 ± 11.0	19.4 ± 8.8	19.0 ± 11.4	0.903
Kinds of stents:	52/13/5/23	8/4/0/2	44/9/5/21	0.328
Cypher/Taxus/ /Endeavor/Pico	(55.9%/14.0%/ /5.4%/24.7%)	(57.1%/28.6%/ /0%/14.3%)	(55.7%/11.4%/ /6.3%/26.6%)	
Stent length [mm]	22.4 ± 4.6	20.4 ± 2.8	22.7 ± 4.7	0.082
Stent diameter [mm]	3.3 ± 0.4	3.1 ± 0.3	3.3 ± 0.4	0.210

*Mann-Whitney test; n — number, F/U — follow-up, LDL-C — low-density lipoprotein cholesterol

Table 3. Comparison of baseline and follow-up (F/U) virtual histology-intravascular ultrasound findings of analyzed segment.

Variables	Total (n = 93)	Group 1 (n = 14) F/U LDL-C < 70 mg/dL	Group 2 (n = 79) F/U LDL-C ≥ 70 mg/dL	P
Analyzed segment:				0.511
Proximal to the stent	17 (18.3%)	3 (21.4%)	14 (17.7%)	
Distal to the stent	12 (12.9%)	3 (21.4%)	9 (11.4%)	
Both side	64 (68.8%)	8 (57.1%)	56 (70.9%)	
Segment length [mm]	5.1 ± 2.2	5.8 ± 2.4	5.0 ± 2.1	0.175
Plaque burden [%]	50.1 ± 10.1	49.2 ± 12.4	50.23 ± 9.69	0.731
Imaged vessel	54/11/25/3	11/0/2/1	43/11/23/2	0.154
LAD/LCX/ /RCA/LM	(58%/12%/ /275/35)	(79%/0%/ /14%/7%)	(54%/14%/ /29%/3%)	
Baseline				
Fibrous volume [mm^3]	10.9 ± 9.4	11.8 ± 13.0	10.7 ± 8.7	0.419*
Fibrofatty volume [mm^3]	2.7 ± 3.5	3.2 ± 5.0	2.6 ± 3.2	0.444*
Dense calcium volume [mm^3]	1.3 ± 1.6	1.5 ± 2.3	1.3 ± 1.5	0.440*
Necrotic core volume [mm^3]	2.7 ± 3.2	3.3 ± 4.4	2.6 ± 3.0	0.364*
Fibrous volume [%]	62.1 ± 11.2	61.6 ± 9.4	62.2 ± 11.5	0.856
Fibrofatty volume [%]	14.3 ± 10.2	14.5 ± 9.4	14.2 ± 10.4	0.924
Dense calcium volume [%]	8.4 ± 8.3	7.9 ± 5.3	8.5 ± 8.7	0.827
Necrotic core volume [%]	15.0 ± 10.2	16.1 ± 9.7	14.8 ± 10.3	0.677
F/U:				
Fibrous volume [mm^3]	10.8 ± 9.6	12.8 ± 14.0	10.5 ± 8.7	0.427*
Fibrofatty volume [mm^3]	2.5 ± 2.5	2.8 ± 1.9	2.4 ± 2.6	0.083*
Dense calcium volume [mm^3]	1.5 ± 2.2	2.0 ± 3.8	1.4 ± 1.8	0.221*
Necrotic core volume [mm^3]	2.7 ± 3.8	3.8 ± 7.8	2.5 ± 2.6	0.198*
Fibrous volume [%]	61.5 ± 12.8	62.1 ± 9.5	61.3 ± 13.3	0.845
Fibrofatty volume [%]	15.3 ± 11.0	21.2 ± 15.1	14.2 ± 9.9	0.115
Dense calcium volume [%]	10.1 ± 13.0	6.1 ± 6.4	10.8 ± 13.7	0.219
Necrotic core volume [%]	13.9 ± 9.5	10.7 ± 8.7	14.5 ± 9.5	0.174

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Table 3. (cont.). Comparison of baseline and follow-up (F/U) virtual histology-intravascular ultrasound findings of analyzed segment.

Variables	Total (n = 93)	Group 1 (n = 14) F/U LDL-C < 70 mg/dL	Group 2 (n = 79) F/U LDL-C ≥ 70 mg/dL	P
Change of plaque composition [mm^3]:				
Fibrous volume	–0.1 ± 3.8	1.0 ± 3.1	–0.3 ± 3.9	0.615*
Fibrofatty volume	–0.2 ± 2.8	–0.4 ± 4.4	–0.2 ± 2.5	0.185*
Dense calcium volume	0.2 ± 1.4	0.4 ± 1.7	0.2 ± 1.4	0.410*
Necrotic core volume	0.0 ± 2.6	1.0 ± 4.0	–0.1 ± 2.4	0.243*
Change of % plaque composition [%]:				
Fibrous volume	–0.6 ± 11.2	1.0 ± 15.1	–0.8 ± 10.4	0.685
Fibrofatty volume	1.0 ± 12.1	6.7 ± 17.5	0.0 ± 10.7	0.372*
Dense calcium volume	1.7 ± 9.9	–1.8 ± 6.8	2.3 ± 10.2	0.191*
Necrotic core volume	–1.1 ± 9.3	–5.4 ± 12.3	–0.4 ± 8.6	0.167

*Mann-Whitney test; n — number; LDL-C — low-density lipoprotein cholesterol; LAD — left anterior descending artery; LCX — left circumflex artery; RCA — right coronary artery; LM — left main

Table 4. Univariate analysis for regression of percent necrotic core volume.

Variables	OR	95% CI	P
F/U TC < 200 mg/dL	1.10	0.12–9.90	0.933
F/U TG < 150 mg/dL	0.66	0.22–1.96	0.450
F/U HDL-C [mg/dL]	1.06	1.00–1.11	0.054
F/U LDL-C < 70 mg/dL	3.43	0.97–12.17	0.056

OR — odds ratio; CI — confidence interval; F/U — follow-up; TC — total cholesterol; TG — triglyceride; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol

Table 5. Independent factors for regression of percent necrotic core volume using multivariable logistic regression analysis.

Variables	OR	95% CI	P
Body mass index		N/S	
Baseline TC		N/S	
Baseline LDL-C		N/S	
Ejection fraction		N/S	
Remodeling index		N/S	
Stent length		N/S	
F/U HDL-C	1.07	1.01–1.14	0.020
F/U LDL-C < 70 mg/dL	8.02	1.58–40.68	0.012

Abbreviations — see Table 4

Table 6. Change of virtual histology-intravascular ultrasound findings according to the statins.

Variables	Atorvastatin (n = 49)	Rosuvastatin (n = 19)	Pitavastatin (n = 25)	P
Change of plaque composition [mm^3]:				
Fibrous volume	0.7 ± 3.4	–1.0 ± 3.0	–0.9 ± 4.8	0.346*
Fibrofatty volume	0.0 ± 3.2	–0.6 ± 2.8	–0.3 ± 1.9	0.700*
Dense calcium volume	0.1 ± 1.2	0.5 ± 2.2	0.3 ± 1.1	0.467*
Necrotic core volume	0.0 ± 2.5	–0.3 ± 2.7	0.0 ± 2.6	0.161*
Change of % plaque composition [%]:				
Fibrous volume	–0.4 ± 13.4	1.1 ± 7.6	–2.4 ± 8.2	0.576
Fibrofatty volume	2.3 ± 14.4	–0.2 ± 10.6	–0.7 ± 7.5	0.712*
Dense calcium volume	0.6 ± 8.4	0.9 ± 7.8	4.4 ± 13.2	0.437*
Necrotic core volume	–2.0 ± 10.2	–2.0 ± 9.4	1.2 ± 7.4	0.362

*Kruskal-Wallis test; n — number

The YELLOW (Reduction in Yellow Plaque by Aggressive Lipid-Lowering Therapy) study showed that intensive statin therapy was more effective in reducing lipid core compared with standard statin therapy [16]. And there were many other studies showing the relationship between statin and plaque composition by using VH-IVUS. However, these studies did not show consistent results. For example, STABLE study [8] compared the effect of moderate intensity rosuvastatin (10 mg) with high intensity rosuvastatin (40 mg) on coronary plaque composition and it showed that both dosages reduced NCV and plaque volume but showed no differences between two groups. On the other hand, Matsushita et al. [17] showed moderate intensity statin therapy (atorvastatin 20 mg or pitavastatin 4 mg) resulted in more favorable outcome than low intensity statin therapy (pravastatin 10 mg or fluvastatin 30 mg). These inconsistent results with statin effects on coronary plaque composition could have resulted from different types and dosages of statins.

The other issue in this study was the coronary segment for analysis. All other studies analyzed the intermediate lesion for study. However, it was thought to be a limitation for the F/U study, because it was sometimes difficult to findan exactly identical lesion site with the baseline analyzed segment. Furthermore, VH-IVUS capture frames at the end-diastole, thus it can cause analysis of different frames, even though the examiner defines the same segment for F/U examination. This is a reason why the proximal or distal segment was selected for analysis in this F/U study.

Limitations of the study

This study has several limitations. First, this study was single center, retrospective study and consisted of small number of subjects. Because of the small number of subjects, regardless of same medical advice, patient compliance could be different and it might have influenced the results. Second, the number of patients with F/U LDL-C < 70 mg/dL was small (14 segments in 10 patients) and their baseline TC and LDL-C levels were lower, this may affect the results in this study. Third, group 1 had a tendency of positive remodeling compared to group 2. This did not, however, show statistical significance between the two groups. Furthermore, it was an analysis of the culprit lesion, not the analyzed segment for the F/U examination. And fourth, inaccuracy of detecting the necrotic core by VH-IVUS [18] may have presented results showing a decreasing tendency of NCV in group 1. However, those tendencies were not seen in group 2, so it was thought that this change of plaque composition by groups can be the F/U LDL-C effects.

This study found that the statin types used in conventional dosage were not important in changing the percent NCV, but the target LDL-C < 70 mg/dL was important, although it is well known that a high dose of stain can draw lower LDL-C level and a specific statin can decrease more LDL-C than others. This study in line with the previous studies suggests that F/U LDL-C is an important factor in determining coronary plaque composition and the statin type used is not so important. LDL-C and HDL-C were important in decreasing the percent NCV and this finding suggests that at least LDL-C < 70 mg/dL with any statin is important rather than doses or types of statin.

Conclusions

In conclusion, F/U LDL-C level < 70 mg/dL with any type of statin is associated with regression of NCV ≥ 10% in patients with CAD. This result supports the rationale of lowering LDL-C < 70 mg/dL suggested in several guidelines.

Conflict of interest: None declared

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