Higher oxidized high-density lipoprotein to apolipoprotein A-I ratio is associated with high-risk coronary plaque characteristics determined by CT angiography

Kazuki Suruga, MD[a], Toru Miyoshi, MD, PhD [a], Kazuhiko Kotani, MD, PhD [b], Keishi Ichikawa, MD[b], Takashi Miki, MD, PhD [a], Kazuhiro Osawa, MD, PhD [c], Kentaro Ejiri, MD, PhD[a], Hironobu Toda, MD, PhD [a], Kazufumi Nakamura, MD, PhD [a], Hiroshi Morita, MD, PhD [d], Hiroshi Ito, MD, PhD [a]

[a]Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

[b]Division of Community and Family Medicine, Jichi Medical University, Shimotsuke, Tochigi, Japan

[c]Department of Cardiology, Okayama Red Cross Hospital, Okayama, Japan

[d]Department of Cardiovascular Therapeutics, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan.

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Number of figures: 1, **number of tables:** 3

Address for correspondence: Toru Miyoshi, MD

Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan.

2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan

Phone: (81) 86-235-7351 Fax: (81) 86-235-7353

E-mail: miyoshit@cc.okayama-u.ac.jp

Acknowledgement

This study was supported by the Grant-in-Aid for Scientific Research(C) (18K08758)

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

Key words: high-density lipoprotein; coronary artery disease; high-risk plaque; oxidized lipoprotein; computed tomography

Abstract

Background: Oxidized high-density lipoprotein (oxHDL), unlike native HDL, is characterized by reduced cholesterol efflux capability and anti-inflammatory properties. The ratio of oxHDL to apolipoprotein A-I (oxHDL/apoAI) is a possible marker of dysfunctional HDL. The aim of this study was to evaluate the association between oxHDL/apoAI and coronary plaque characteristics that increase the likelihood of cardiovascular events as determined by coronary computed tomography (CT) angiography.

Methods: A total of 297 patients (mean age; 67 years, men; 63 %) who underwent coronary CT angiography for suspected stable 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%. Serum concentrations of oxHDL were measured using an enzyme-linked immunosorbent assay.

Results: Patients with higher oxHDL/ApoAI showed significantly greater prevalence of HRP ($p = 0.03$) and significant stenosis ($p < 0.01$) compared with patients with low oxHDL/ ApoAI. The multivariate logistic analysis demonstrated that oxHDL/ApoAI significantly associated with the presence of HRP and significant coronary stenosis ($p = 0.01$ and < 0.01). In the follow-up study including 243 patients for a median period of 1.8 years, univariate cox regression analysis showed that oxHDL/ApoAI, HRP and significant stenosis were significant predictors of cardiovascular events.

Conclusions: A high oxHDL/apoAI was associated with the presence of HRP and significant stenosis determined by coronary CT angiography, which can lead to cardiovascular events in patients with suspected stable CAD.

1. Introduction

The progression of atherosclerosis and coronary artery disease (CAD) is associated with lipid abnormalities such as increased low-density lipoprotein cholesterol (LDL-C) and decreased high-density lipoprotein cholesterol (HDL-C) [1, 2]. Decreased HDL-C is reported to be an independent risk factor for CAD [3]. However, previous clinical studies have shown that cholesteryl ester transfer protein inhibitors significantly increased HDL-C levels but failed to reduce cardiovascular events [4, 5]. Therefore, factors beyond the HDL level alone may be responsible for the increased risk of cardiovascular (CV) events. Recent studies have focused more on HDL function than on HDL levels. The HDL are constantly remodeled and can undergo a variety of modifications including oxidation and transforming into proatherogenic properties that are dysfunctional [6]. Oxidized HDL (oxHDL) was inferior to native HDL in cholesterol efflux capabilities and anti-inflammatory properties [7], Our report also demonstrates that the decrease in oxHDL is associated with slowed coronary artery calcification [8]. Meanwhile, the level of oxHDL is affected by the HDL level. In patients with high-risk CV events, the higher oxHDL level and lower HDL level are anticipated compared to patients with low-risk CV events. Therefore, to assess the clinical relevance of oxHDL, the ratio of oxHDL to apolipoprotein A-I (oxHDL/apoAI) was is a possible marker of dysfunctional HDL. However, the association between oxHDL and coronary plaque characteristics remains unknown.

Recent advances in coronary computed tomography (CT) angiography have allowed for the identification of high-risk coronary plaque characteristics as well as coronary atherosclerotic burden both of which are involved in acute coronary syndrome. [9-12] A previous study showed that the presence of low attenuation plaques, positive remodeling, and spotty calcification were predictors of acute coronary syndrome [9]. In addition, quantitative analysis of coronary plaque trees revealed that the prevalence of elevated non-calcified plaque volume is associated with

cardiovascular events [13]. Thus, the presence of high-risk plaque features and severe coronary stenosis determined by coronary CT angiography are promising for assessing risk for coronary artery disease.

The aim of this study was to evaluate the association between the oxHDL/apoAI and coronary plaque characteristics that increase the likelihood of acute coronary events in patients with suspected stable CAD.

2. Materials and Methods

2.1 Study protocol and patients

Patients with suspected stable CAD that were undergoing coronary CT angiography in the Okayama University Hospital (Okayama, Japan) and agreed to have their serum stored were eligible for this study. Exclusion criteria were prior percutaneous coronary intervention, or coronary bypass surgery graft, severe heart failure (New York Heart Association classification ≥ 3, and allergy to iodinated contrast agent, and known severe renal failure (estimated glomerular filtration rate < 30 $mL^{-1}min^{-1}1.73$ m^2). From November 2016 to April 2019, 297 patients were enrolled in this study. The primary aim of this study was to determine the association between the oxHDL and the oxHDL/apoAI with plaque characteristics as determined by coronary CT angiography. A secondary goal was to correlate any associations between the oxHDL/apoAI and plaque characteristics with the prognosis of these patients. Follow-up clinical information was obtained from a review of the medical records or through telephone interviews conducted by attending physicians. For the analysis of secondary outcomes, 243 patients had clinical follow up. CV events were defined as CV death, acute coronary syndrome, or late coronary revascularization over 60 days after the indexed CT acquisition due to suspected stable CAD.

This prospective study was approved by the Ethics Committee of Okayama University

Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences (Protocol Number 1508-009). This study was conducted according to the principles expressed in the Declaration of Helsinki. All patients provided written informed consent prior to being included in the study.

2.2 CT image acquisition

CT scans were performed using a 128-slice CT scanner (SOMATOM Definition Flash; Siemens Medical Solutions, Erlangen, Germany) as described previously [14]. 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, followed by a second bolus consisting of 80 % of the initial volume of contrast medium diluted to 50 % with normal saline and then a compensatory 20 % bolus of normal saline. 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.

2.3 Coronary CT angiography analysis

Coronary artery stenosis and plaques were evaluated with axial and curved multiplanar reformatted images using commercially available cardiac reconstruction software (Virtual Place, Raijin; AZE Inc., Tokyo, Japan) [14]. One experienced senior cardiologist and one senior CT technologist who were blinded to clinical data performed the analyses. Significant coronary artery stenosis was defined as a luminal narrowing of > 70 %. Plaques were categorized as “calcified” (when the number of Hounsfield Units (HU) was > 130), “non-calcified” (HU < 130), or “low-density” (HU < 50). The vascular remodeling index was calculated by dividing the cross-sectional lesion vessel area by the proximal reference vessel area. Positive remodeling was defined as a

remodeling index > 1.05. High-risk plaques were defined by low-density plaques with positive remodeling. Spotty calcification was defined as having a length (longitudinal direction of the vessel) and width (perpendicular to the longitudinal direction of the vessel) of calcification that was < 3/2 and < 2/3 of the vessel diameter, respectively. 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 [15].

2.4 Risk factors and laboratory analysis

Information on demographics, smoking status, and medications for each participant were collected. Hypertension was defined as systolic blood pressure (BP) ≥140 mmHg or diastolic BP ≥90 mmHg, and/or the use of anti-hypertensive medication. Dyslipidemia was defined as one or more of the following factors: low-density lipoprotein cholesterol levels ≥140 mg/dL, fasting triglyceride levels ≥150 mg/dL, high-density lipoprotein cholesterol levels <40 mg/dL, or taking anti-dyslipidemic medication. Smoking was defined as a self-reported history of current smoking. Laboratory values including triglycerides, low-density lipoprotein cholesterol (LDL-C), HDL-C, apoAI and hemoglobinA1c were determined at the central laboratory in our hospital. Residual serum was separated and stored at −80 °. Serum concentrations of oxHDL were measured once a year using an enzyme-linked immunosorbent assay (Ikagaku Corp., Kyoto, Japan) as previously described [8].

2.5 Follow-up methods

The patients were followed up prospectively from the date of undergoing CT. Follow-up clinical information was obtained from review of the medical records or telephone interviews by attending physicians. CV events was defined as CV death, acute coronary syndrome, or late coronary revascularization over 60 days after the indexed CT acquisition. Patients who underwent scheduled

revascularization within 60 days after the indexed CT were censored at the time of the first revascularization.

2.6 Statistical Analysis

Categorical variables are presented as number of patients (percentage) and continuous variables as mean ± standard deviation or median (interquartile range). Differences between any two groups were evaluated using the chi-square test for categorical variables or the Mann–Whitney U test for continuous variables. Associations of variables were assessed by Pearson's correlation coefficient. The independent associations of HRP and significant stenosis with other parameters were assessed by univariate and multivariate logistic regression analyses. The multivariate analyses included age, male sex, hypertension, diabetes mellitus, statin use, LDL-C, and one of the following factors; log-transformed oxHDL, apoAI, HDL-C, and log-transformed oxHDL/apoAI. Univariate and multivariate Cox proportional hazards regression analyses were performed to identify factors associated with CV events. A p value of < 0.05 was considered significant. All statistical analyses were performed using SPSS 25.0 (IBM, Armonk, NY, USA).

3. Results

3.1 Patients' characteristics

The baseline characteristics of the patients are summarized in Table 1. The mean age of all patients was 69 years old, and 63% of patients were male; 35% of patients had diabetes mellitus and 56% had dyslipidemia. The median serum oxHDL concentration was 122 U/mL. HDL-C level was significantly correlated with apoAI level ($r = 0.86$, $p < 0.01$), log-transformed oxHDL ($r = 0.24$, $p < 0.01$), but not log-transformed oxHDL/apoAI ($r = -0.08$, $p = 0.16$).

3.2 Plaque characteristics and oxHDL/apoAI

Among all patients, the prevalence of HRP and significant stenosis presented in 39 patients (13%) and 57 patients (19%), respectively. The plaque characteristics stratified by the median values of oxHDL (122 U/mL) and oxHDL/apoAI (0.80) were evaluated. As shown in Figure 1A, patients with high oxHDL had a significantly greater prevalence of significant stenosis compared to patients with low oxHDL (24% and 14%, $p = 0.03$). However, no difference in calcified plaques (81% and 80%, $p = 0.78$), non-calcified plaques (54% and 45%, $p = 0.09$), positive remodeling (52% and 59%, $p= 0.24$), low density plaque (42% and 49%, $p = 0.22$), spotty calcification (38% and 30%, $p = 0.15$), or HRP (13% and 13%, $p = 0.88$) were found between the high and low oxHDL groups. Meanwhile, as shown in Figure 1B, patients with high oxHDL/apoAI had a significantly greater prevalence of non-calcified plaques (58% and 41%, $p < 0.01$), positive remodeling (62% and 49%, $p=0.02$), spotty calcification (42% and 25%, $p < 0.01$), HRP (17% and 9%, $p = 0.03$), and significant stenosis (28% and 10%, $p < 0.01$). No difference in calcified plaques (84% and 77%, $p = 0.14$) and low-density plaques (50 % and 42 %, $p = 0.18$) were found between the high and low oxHDL/apoAI groups.

Next, factors associated with HRP and significant stenosis were evaluated using logistic regression models (Table 3 and 4). As shown in Table 3, in the univariate analysis, HRP was significantly associated with male sex ($p = 0.01$), apoAI ($p < 0.01$), HDL-C ($p < 0.01$), and oxHDL/apoAI ($p < 0.01$). The multivariate analysis showed that HRP was independently associated with apoAI ($p = 0.03$), HDL-C ($p = 0.02$), and oxHDL/apoAI ($p = 0.01$), respectively. As shown in Table 4, in the univariate analysis, significant stenosis was significantly associated with male sex ($p = 0.01$), oxHDL ($p = 0.02$), apoAI ($p < 0.01$), HDL-C ($p = 0.03$), and oxHDL/apoAI ($p < 0.01$). The multivariate analysis showed that significant stenosis was independently associated with oxHDL ($p < 0.01$) and oxHDL/apoAI ($p < 0.01$), respectively.

3.3 Predictors of cardiovascular events

Among the 297 patients in the cross-sectional cohort, 243 (82 %) patients were followed throughout the study period. During the median follow-up period of 1.8 years, 24 CV events (no CV death, 2 acute coronary syndromes, 22 late coronary revascularizations) occurred in study patients. The univariate Cox analysis showed that log-transformed oxHDL/apoAI (HR, 2.58, 95% CI, 1.38 to 4.80, $p < 0.01$), HRP (HR, 5.17; 95% CI, 2.28 to 11.71, $p < 0.01$) and significant stenosis (HR, 6.64; 95% CI, 2.96 to 14.89, $p < 0.01$) were significant risk factors associated with CV events. In the multivariate Cox analysis including oxHDL/apoAI, HRP, and significant stenosis, HRP (HR, 2.70; 95% CI, 1.09 to 6.69, $p = 0.03$) and significant stenosis (HR, 4.22; 95% CI, 1.70 to 10.46, $p < 0.01$) were significant risk factors associated with CV events, while oxHDL/apoAI was not (HR, 1.44; 95%CI, 0.77 to 2.67, $p = 0.25$).

4. Discussion

The major finding of this study is that high oxHDL/ApoAI was significantly associated with the presence of HRP and significant stenosis as determined by coronary CTA. To our knowledge, this is the first detailed study to evaluate the association between oxHDL/ApoAI and coronary plaque characteristics in patients with suspected stable CAD.

This study shows that oxHDL/apoAI, rather than oxHDL, identified patients with HRP and significant stenosis. A previous study reported that the elevated level of oxHDL in patients with psoriasis was associated with non-calcified plaque burden as determined by CT [16]. Thus, increased oxHDL could play a role in the development of coronary atherosclerosis. However, as oxHDL levels were positively correlated with HDL-C level, the interpretation of increased oxHDL should be done with caution. In this study, logistic univariate regression analysis showed that the oxHDL and oxHDL/apoAI were associated with the presence of HRP. However, multivariate analyses identified oxHDL/apoAI, not oxHDL, as a significant factor associated with HRP. Thus,

oxHDL/apoAI may be a useful index to evaluate HRP that increase the likelihood of CV events.

Our results indicate that dysfunctional HDL plays an important role in changes to coronary plaque characteristics which predispose to CV events. Previous studies reported that CT-verified HRP is associated with several CV risk factors such as increased age, male sex, and the occurrence of hypertension, diabetes, dyslipidemia, and smoking behavior [15, 17], which are pro-oxidative conditions. The results of our study demonstrate that oxHDL/apoAI could be a more direct marker associated with coronary plaque characteristics that were evaluated by CT.

In experimental studies regarding the underlying mechanisms between oxHDL and the development of coronary atherosclerosis, Sharma et al. showed that oxHDL had reduced cholesterol efflux capabilities, pro-oxidative properties of LDL, and proinflammatory effects on monocytes [18, 19]. OxHDL induces the dysfunction of endothelial cell and endothelial progenitor cells and promotes apoptosis in monocytes/macrophages [20, 21]. OxHDL, unlike native HDL, can be taken up by macrophages and may contribute to foam cell formation [22]. Therefore, several lines of experimental data suggest that oxHDL is involved in pathophysiology of human arteriosclerosis. To clarify whether oxHDL/apoAI is as a predictor for progression of CV events in patients with stable CAD, a large prospective study with long term follow-up is required.

Recent research demonstrated that the elevation of HDL-C concentration by medications in patients did not cause a reduction in the incidence of CV events [4, 5]. In patients with metabolic disorders or manifestations of CV disease, the cholesterol efflux properties and anti-inflammatory effects of HDL are not always reflected by HDL concentrations, but rather depend on the protein and lipid composition of HDL particles. Recently, we reported that the decreases in oxHDL as well as oxHDL/apoAI were associated with the slowed progression of coronary artery calcification as determined by CT [8]. However, it remains unclear whether the increase in oxHDL reflects the biological dysfunction of HDL. Future studies are required to identify a medical therapy that

reduces oxHDL, will improve the anti-atherosclerotic function of HDL, and leads to the regression and stabilization of coronary artery plaques.

Our study has several limitations. First, this is a retrospective single center study with a small number of patients. Patient selection may have been biased and a prospective study would be preferable. Second, we included only Japanese patients with suspected stable CAD; the results cannot be applied to other ethnic groups and the general population. Third, follow-up study was relatively short and small number of CV events were documented. To determine the impact of oxHDL/apoAI on CV death and acute coronary syndrome, a large long-term study is warranted.

In conclusion, this study demonstrated that an increase in the oxHDL/apoAI was significantly associated with the presence of HRP and significant stenosis determined by coronary CT angiography in patients with suspected stable CAD. The oxHDL/apoAI may be a potential biomarker to assess CV risk. Further studies are required to identify the best method with which to improve HDL functions for protection against CV events.

Conflicts of interest

All authors have no conflicts of interest in relation to the materials presented in this article.

Financial support

This study was funded by the Grant-in-Aid for Scientific Research(C) (18K08758)

References

[1] Prospective Studies C, Lewington S, Whitlock G, Clarke R, Sherliker P, Emberson J, et al. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. Lancet. 2007;370:1829-39.

[2] Boekholdt SM, Arsenault BJ, Mora S, Pedersen TR, LaRosa JC, Nestel PJ, et al. Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins: a meta-analysis. Jama. 2012;307:1302-9.

[3] Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology. 2014;63:2889-934.

[4] Schwartz GG, Olsson AG, Abt M, Ballantyne CM, Barter PJ, Brumm J, et al. Effects of dalcetrapib in patients with a recent acute coronary syndrome. The New England journal of medicine. 2012;367:2089-99.

[5] Barter PJ, Caulfield M, Eriksson M, Grundy SM, Kastelein JJ, Komajda M, et al. Effects of torcetrapib in patients at high risk for coronary events. The New England journal of medicine. 2007;357:2109-22.

[6] Navab M, Reddy ST, Van Lenten BJ, Fogelman AM. HDL and cardiovascular disease: atherogenic and atheroprotective mechanisms. Nature reviews Cardiology. 2011;8:222-32.

[7] Srivastava RAK. Dysfunctional HDL in diabetes mellitus and its role in the pathogenesis of cardiovascular disease. Molecular and cellular biochemistry. 2018;440:167-87.

[8] Miki T, Miyoshi T, Kotani K, Kohno K, Asonuma H, Sakuragi S, et al. Decrease in oxidized high-density lipoprotein is associated with slowed progression of coronary artery calcification:

Subanalysis of a prospective multicenter study. Atherosclerosis. 2019;283:1-6.

[9] Motoyama S, Sarai M, Harigaya H, Anno H, Inoue K, Hara T, et al. Computed tomographic angiography characteristics of atherosclerotic plaques subsequently resulting in acute coronary syndrome. Journal of the American College of Cardiology. 2009;54:49-57.

[10] Puchner SB, Liu T, Mayrhofer T, Truong QA, Lee H, Fleg JL, et al. High-risk plaque detected on coronary CT angiography predicts acute coronary syndromes independent of significant stenosis in acute chest pain: results from the ROMICAT-II trial. Journal of the American College of Cardiology. 2014;64:684-92.

[11] Hecht HS, Achenbach S, Kondo T, Narula J. High-Risk Plaque Features on Coronary CT Angiography. JACC Cardiovascular imaging. 2015;8:1336-9.

[12] Miyoshi T, Osawa K, Ichikawa K, Suruga K, Miki T, Yoshida M, et al. Emerging Role of Coronary Computed Tomography Angiography in Lipid-Lowering Therapy: a Bridge to Image-Guided Personalized Medicine. Current cardiology reports. 2019;21:72.

[13] Andreini D, Magnoni M, Conte E, Masson S, Mushtaq S, Berti S, et al. Coronary Plaque Features on CTA Can Identify Patients at Increased Risk of Cardiovascular Events. JACC Cardiovascular imaging. 2019.

[14] Osawa K, Miyoshi T, Miki T, Koide Y, Kawai Y, Ejiri K, et al. Coronary lesion characteristics with mismatch between fractional flow reserve derived from CT and invasive catheterization in clinical practice. Heart and vessels. 2017;32:390-8.

[15] Osawa K, Miyoshi T, Yamauchi K, Koyama Y, Nakamura K, Sato S, et al. Nonalcoholic Hepatic Steatosis Is a Strong Predictor of High-Risk Coronary-Artery Plaques as Determined by Multidetector CT. PloS one. 2015;10:e0131138.

[16] Sorokin AV, Kotani K, Elnabawi YA, Dey AK, Sajja AP, Yamada S, et al. Association Between Oxidation-Modified Lipoproteins and Coronary Plaque in Psoriasis. Circ Res. 2018;123:1244-54.

[17] Ferencik M, Mayrhofer T, Bittner DO, Emami H, Puchner SB, Lu MT, et al. Use of High-Risk Coronary Atherosclerotic Plaque Detection for Risk Stratification of Patients With Stable Chest Pain: A Secondary Analysis of the PROMISE Randomized Clinical Trial. JAMA cardiology. 2018;3:144-52.

[18] Sharma N, Desigan B, Ghosh S, Sanyal SN, Ganguly NK, Majumdar S. The role of oxidized HDL in monocyte/macrophage functions in the pathogenesis of atherosclerosis in Rhesus monkeys. Scandinavian journal of clinical and laboratory investigation. 1999;59:215-25.

[19] Yao S, Tian H, Zhao L, Li J, Yang L, Yue F, et al. Oxidized high density lipoprotein induces macrophage apoptosis via toll-like receptor 4-dependent CHOP pathway. Journal of lipid research. 2017;58:164-77.

[20] Nakajima T, Origuchi N, Matsunaga T, Kawai S, Hokari S, Nakamura H, et al. Localization of oxidized HDL in atheromatous plaques and oxidized HDL binding sites on human aortic endothelial cells. Annals of clinical biochemistry. 2000;37 (Pt 2):179-86.

[21] Matsunaga T, Hokari S, Koyama I, Harada T, Komoda T. NF-kappa B activation in endothelial cells treated with oxidized high-density lipoprotein. Biochemical and biophysical research communications. 2003;303:313-9.

[22] Thorne RF, Mhaidat NM, Ralston KJ, Burns GF. CD36 is a receptor for oxidized high density lipoprotein: implications for the development of atherosclerosis. FEBS letters. 2007;581:1227-32.

Figure Legends

Figure 1 The prevalence of coronary plaque characteristics according to the oxHDL and oxHDL/apoAI

(A) Patients were divided into two groups based on the median value of oxHDL. (B) Patients were divided into two groups based on the median value of oxHDL/apoAI.