The effect of low-density lipoprotein particle size change on the restenosis after coronary stent implantation

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The effect of low-density lipoprotein particle size change on the restenosis after coronary stent implantation

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감사의 글

먼저 본 연구가 나오기까지 모든 과정을 주관하신 하나님께 감사를 드립니다. 한 논문이 나오기까지 많은 노력과 인내가 필요함을 알게 되었고, 연구 과정에 있어 미숙한 점들이 떠올라 많은 아쉬움이 남지만, 모든 시행착오를 발판삼아 한 단계 더 올라가는 계기로 삼고자 합니다.

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늘 사랑과 기도로 격려를 아끼지 않았던 어머니, 동생 명욱과 논문 완성의 기쁨을 함께 하고 싶습니다.

끝으로 이 논문을 하늘나라로 가신 사랑하는 고 김종기 아버지께 바칩니다.

저자 씀

ABSTRACT

The effect of low-density lipoprotein particle size change on the restenosis after coronary stent implantation

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Small dense LDL (sd-LDL) has emerged as an important risk factor in coronary atherosclerosis, endothelial dysfunction and vascular inflammation, which is related with neointimal hyperplasia. Therefore, we investigated whether changes in LDL particle size after percutaneous coronary intervention (PCI) are related to the development of in-stent restenosis (ISR).

A total of 412 stents (Bare metal stent: 278 lesions, Drug eluting stent: 134 lesions) in 274 patients who underwent coronary angiography (CAG) were evaluated. The particle size and fraction of LDL, hsCRP and lipid profiles were measured at both the baseline and follow-up CAG. The development of ISR was evaluated at six to nine months after PCI.

ISR occurred in 80 lesions (19 %). ISR was lower in the patients with increase of LDL particle size (Group 1) than those with no change or decrease (Group 2) (14 % vs. 26 %, p = 0.004). Logistic multivariate analysis revealed that stent length (≥ 24 mm) (OR = 2.035, p = 0.019), post minimal luminal diameter (≥ 3 mm) (OR = 0.538, p = 0.041), acute

coronary syndrome (OR = 2.244, p = 0.009), decrement in HDL cholesterol (OR = 1.029, p = 0.047) and increase in LDL particle size (OR = 0.502, p = 0.030) were independent predictors of ISR.

In the present study, increase in LDL particle size between baseline and follow-up CAG was associated with reducing the ISR. Therefore, modification of LDL particle size may have a beneficial effect on reduction of the ISR.

Key words : small dense low-density lipoprotein, coronary stent, restenosis

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I. INTRODUCTION

Although coronary stent implantation reduced the restenosis rate, compared to balloon angioplasty, in stent restenosis(ISR) has remained a serious problem[1]. Several previous studies have shown that neointimal proliferation plays the most important role in restenosis after stent implantation[2, 3]. Neointimal hyperplasia is related to both insulin resistance and endothelial dysfunction, which decrease nitric oxide (NO) and decrease the migration and proliferation

of vascular smooth muscle cells, thus interfering with the attenuation of binding of inflammatory cells to the vascular wall[4-7].

Low-density lipoprotein (LDL) has been recognized as an atherogenic lipoprotein and lowering LDL has been shown to improve endothelial function and reduce the risk of cardiovascular events[8-12]. Among LDL fractions of particles, small dense LDL (sd-LDL) is particularly important in the development of endothelial dysfunction and atherosclerosis[13-15]. Several large prospective studies showed that coronary artery disease (CAD) risk increased significantly when sd-LDL was the predominant LDL subclass present[13, 16, 17]. Previous angiographic clinical trials have also indicated that treatment benefit was related to a decrease in sd-LDL particles[18, 19].

Although sd-LDL, which is oxidized to LDL within atherosclerotic plaque itself, has been known to induce the formation of vulnerable plaques and resulting in acute coronary events, the precise relationship between the particle size of a lipoprotein molecules and ISR after coronary stent implantation remains unclear. Therefore, we investigated whether a change in LDL particle size influences the ISR following coronary stent implantation.

II. METHODS

1. Subjects

This study enrolled 274 consecutive patients who underwent coronary angiography at Yongdong Severance Hospital, Yonsei University, Seoul, South Korea, from October 2003 through November 2006, after excluding patients with chronic renal failure or end stage renal disease, hepatic failure or liver cirrhosis, apparent thyroid disease, infectious or inflammatory disease, or malignancy.

The diagnosis of hypertension was based on a known history of hypertension and a systolic blood pressure over 140 mmHg or a diastolic blood pressure over 90 mmHg. The diagnosis of diabetes mellitus was based on a fasting serum glucose level over 126 mg/dL or a history of treatment with either oral hypoglycemic agents or insulin. Height and weight were recorded in all subjects, and body mass index (BMI) was calculated as weight (kg)/height^2 (m^2).

The diagnoses of myocardial infarction and angina pectoris were based on clinical symptoms, EKG changes, and biochemical markers. Significant CAD on coronary angiogram was defined as a stenosis of ≥ 50% of the luminal

diameter in ≥1 branch of the coronary arteries. Study subjects were divided into two groups; Group 1 was the patients with increase of LDL particle size between baseline and follow-up angiography and Group 2 was the patients with no change or decrease of LDL particle size between baseline and follow-up angiography.

2. Coronary angiographic analysis and percutaneous coronary intervention (PCI) procedure

Significant CAD on coronary angiogram was defined as a stenosis of ≥ 50% of the luminal diameter in ≥ 1 branch of the coronary arteries. Therefore, the patients with significant luminal stenosis and the evidence of ischemia were indicated to PCI procedure.

All patients were treated with oral aspirin (200 mg), clopidogrel (75-300 mg according to previous medication status) or ticlopidine (500 mg), and intravenous heparin 100 IU/kg prior to the procedure. The target-activated clotting time was 250 to 300 s. Coronary angiography (CAG) was performed via a 6.5 F vascular sheath in the femoral artery, according to standard techniques. The culprit artery was intubated with a 6F guiding catheter and wired with an 0.014-inch guiding wire. In all patients, the culprit lesions were pre-dilated with a slightly undersized balloon. The procedure was considered to be successful if the quantitative coronary angiography (QCA) estimated a residual stenosis < 30 % and TIMI 3 flow was observed after coronary stent implantation. Follow-up CAG was performed within 9 months following the coronary stent implantation

3. Baseline and follow-up quantitative angiographic analysis

The lesion morphology was classified according to the American College of Cardiology/ American Heart Association grading system as type A, B1, B2, or C. QCA was performed using an off-line quantitative coronary angiographic system (CMS, Medis Medical Imaging System, Nuenen, Netherlands) by a single individual who was blinded to the patient's treatment assignment. A contrast-filled non-tapered catheter tip was used for calibration. Baseline coronary angiography was performed in multiple projections. The minimal luminal diameter (MLD) of the treated coronary segments, the reference diameter, the percent diameter stenosis and the lesion length on the baseline angiogram were determined in the view that demonstrated the lesion to be the most severe and not foreshortened. Baseline and follow-up angiograms were evaluated in the same view. We defined ISR as a diameter stenosis >50% at the time of follow-up angiography at 6-9 months.

4. Analysis of lipoprotein and metabolic parameters

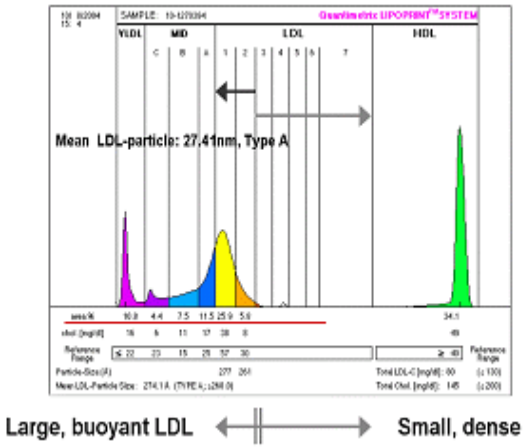
Fasting blood samples were obtained by venipuncture on both the day of the PCI and the day of the follow-up CAG. Total cholesterol, high-density lipoprotein (HDL) cholesterol, and LDL cholesterol were measured by a direct enzymatic method (Daiicgi, Tokyo, Japan). Triglycerides were measured using the glycerophosphate oxidase with glycerol blanking method (Asan, Seoul, Korea). The fasting serum insulin level was measured with an immunoradiometric assay and a gamma counter (Hewlett-Packard, USA).

The LDL subfraction was analyzed by polyacrylamide tube gel electrophoresis (Quantimetrix Lipoprint^{TM} LDL system, Redondo Beach, CA, USA)[20]. It was categorized as pattern A or B according to the mean LDL particle size and the fraction of sd-LDL (subtypes 3-7 of LDL) was measured (Figure 1).

$$\text{sd-LDL fraction(\%)} = \frac{\text{LDL3+LDL4+LDL5+LDL6+LDL7}}{\text{LDL1+LDL2+LDL3+LDL4+LDL5+LDL6+LDL7}} \times 100(\%)$$

LDL subtype 1~2 was large, buoyant LDL and subtype 3~7 was small, dense LDL (It was defined that the pattern of mean LDL particle size over 26.5 nm was large, buoyant dominant ‘pattern A’. In contrast, the particle size below 26.5 nm was small, dense LDL dominant ‘pattern B’)[21].

(a)



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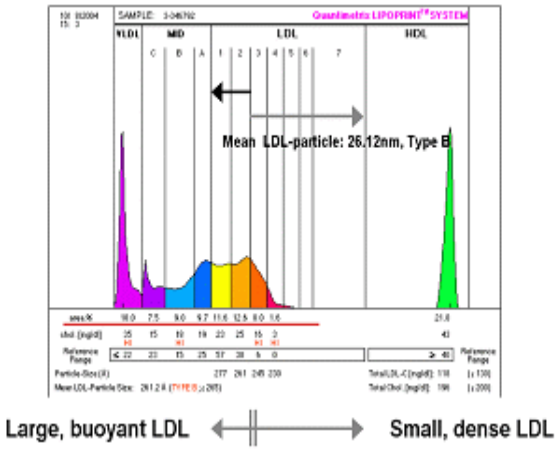

Figure 1. Densitometric scans of LDL subfraction. LDL subtype 1, 2 represents large, buoyant LDL, and LDL subtype 3~7 represents small, dense LDL. Areas under the curve for each fraction were measured, and the fraction of small, dense LDL was calculated. (a) Large, buoyant LDL dominant pattern A which has mean LDL particle size greater than 26.5nm (b) Small, dense LDL dominant pattern B which has mean LDL particle size smaller than 26.5nm[21].

5. Statistical Analysis

In this study, we categorized all cases into two groups according to the presence of change in LDL particle size**.** Results are expressed as a mean ± S.D. Comparisons of discrete variables were made using the Chi-square method and the student's *t*-test was used to compare continuous variables. If the distribution was skewed, a non-parametric test was used. Independent predictors of restenosis after coronary stent implantation were determined using a multiple logistic regression analysis. In multiple logistic regression analysis, the variables were chosen such that $p < 0.1$, based on a simple linear regression analysis, was considered to be significantly associated with atherosclerosis or restenosis after coronary stent implantation. All statistical analysis was performed with SPSS 13.0 (SPSS Inc., Chicago, IL, USA). P values <0.05 were considered to be statistically significant.

III. RESULTS

1. Clinical Characteristics between group 1 and group 2

Baseline characteristics were similar between two groups (Table 1). Total cholesterol, LDL-cholesterol and triglyceride were significantly higher in group 1 at stent implantation (183.4 ± 36.6 vs. 165.3 ± 29.0 mg/dl, $p < 0.001$, 110.1 ± 32.5 vs. 95.5 ± 24.7 mg/dl, $p < 0.001$, 146.6 ± 70.2 vs. 118.0 ± 61.5 mg/dl, $p < 0.001$). HDL-cholesterol and fraction of small dense LDL at stent implantation was lower (42.3 ± 10.3 vs. 44.9 ± 9.6 mg/dl, $p = 0.040$, 22.9 ± 20.2 vs. 6.1 ± 8.0 mg/dl, $p < 0.001$) and LDL size was smaller in group 1 (26.1 ± 1.2 vs. 27.0 ± 0.4 nm, $p < 0.001$). LDL size was larger and fraction of small dense LDL was smaller in group 1 on follow-up angiography (26.9 ± 0.4 vs. 26.7 ± 0.6 nm, $p = 0.007$ and 7.9 ± 9.4 vs. 11.8 ± 13.5 mg/dl, $p = 0.006$). The decrement of total cholesterol, LDL-cholesterol and triglyceride was larger (28.22 ± 35.07 vs. 2.90 ± 37.39, $p < 0.001$, 21.90 ± 31.99 vs. 3.97 ± 33.40, $p < 0.001$, 30.00 ± 58.44 vs. -10.04 ± 63.52, $p < 0.001$) in group 1 (Table 2). Statin use was similar between two groups (Table 1). The change in mean LDL particle size between baseline

and follow-up CAG was 0.75 ± 0.99 nm in group 1 and -0.28 ± 0.41 nm in group 2 ($p < 0.001$) (Figure 2).

Table 1. Baseline characteristics between group1 (Increase of LDL particle size) and group 2 (No change or decrease of LDL particle size) by patient

	Group 1 (N = 152)	**Group 2 (N =122)**	**P-value**
Age (years)	59.8 ± 10.3	60.4 ± 9.7	0.596
Male (%)	89 (58.9 %)	62 (61.2 %)	0.711
BMI (kg/m2)	25.3 ± 2.6	25.5 ± 3.2	0.626
DM (%)	37 (24.5 %)	29 (24.0 %)	0.918
Hypertension (%)	96 (63.6 %)	74 (61.2 %)	0.682
Smoking (%)	72 (45.0 %)	55 (45.5 %)	0.773
ACS (%)	65 (43.0 %)	43 (35.5 %)	0.208
Muti-vessel disease (%)	107 (70.9 %)	77 (63.6 %)	0.206
Insulin (mU/L)	10.4 ± 9.4	10.9 ± 9.4	0.792
hsCRP (mg/l)	3.9 ± 8.8	7.7 ± 22.7	0.098
Statin (%)	128 (84.8 %)	97 (80.2 %)	0.318

Values are presented as n (%) or mean ± SD; BMI, body mass index; DM, diabetes mellitus; ACS, acute coronary syndrome; hs CRP, high sensitivity C-reactive protein.

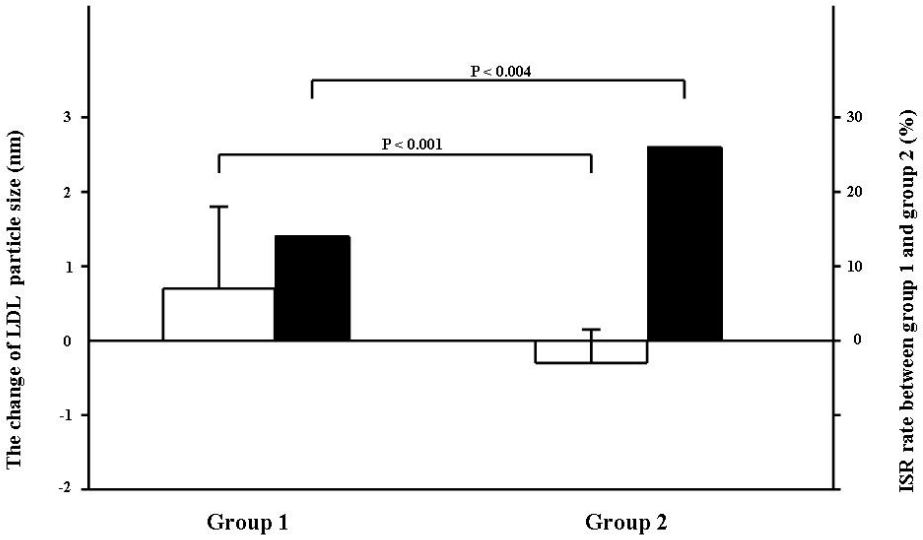

Figure 2. The change in LDL particle size in group 1 (patients with increase of LDL particle size between baseline and follow-up angiography) and group 2 (patients with no increase or decrease of LDL size between baseline and follow-up angiography). ISR(black bar) was lower in group 1 than group 2 (14% vs. 26%, p=0.004); LDL, low-density lipoprotein.

2. Angiographic findings

ISR had developed in 80 lesions (19 %) at the time of follow-up coronary angiography. ISR was lower in the patient with group 1 than group 2(14% vs. 26%, p=0.04, Figure 2). Follow-up MLD (2.59 ± 0.89 vs. 2.38 ± 1.00, p = 0.024) was significant larger in group 1. Stent diameter (3.28 ± 0.38 vs. 3.25 ± 0.40, p = 0.375), reference diameter (3.30 ± 0.39 vs. 3.25 ± 0.39, p = 0.164), pre-PCI MLD (0.81 ± 0.35 vs. 0.79 ± 0.35, p = 0.554) and post-PCI MLD (3.30 ± 0.39 vs. 3.24 ± 0.40, p = 0.118) were similar between two groups (Table 3). Also, there was no difference in the distribution of target vessels and the frequency of drug-eluting stent use (Table 3).

Table 2. Lipid profiles between baseline and at follow-up after coronary stent implantation in group 1 (Increase of LDL particle size) and group 2 (No change or decrease of LDL particle size) by patient

		Group 1 (N = 152)	Group 2 (N = 122)	p-value
T. chol (mg/dl)	**Baseline**	183.4 ± 36.6	165.3 ± 29.0	< 0.001
	Follow-up	155.1 ± 34.4	162.4 ± 33.4	0.081
	Delta	28.22 ± 35.07	2.90 ± 37.39	< 0.001
HDL (mg/dl)	**Baseline**	42.3 ± 10.3	44.9 ± 9.6	0.040
	Follow-up	42.8 ± 9.8	44.6 ± 10.9	0.170
	Delta	-0.46 ± 10.18	0.31 ± 9.27	0.514
LDL (mg/dl)	**Baseline**	110.1 ± 32.5	95.5 ± 24.7	< 0.001
	Follow-up	87.9 ± 25.5	91.5 ± 27.3	0.263
	Delta	21.90 ± 31.99	3.97 ± 33.40	< 0.001
TG (mg/dl)	**Baseline**	146.6 ± 70.2	118.0 ± 61.5	< 0.001
	Follow-up	116.6 ± 55.9	128.0 ± 68.1	0.130
	Delta	30.00 ± 58.44	-10.04 ± 63.52	< 0.001
LDL size (nm)	**Baseline**	26.1 ± 1.2	27.0 ± 0.4	< 0.001
	Follow-up	26.9 ± 0.4	26.7 ± 0.6	0.007
sd LDL (%)	**Baseline**	22.9 ± 20.2	6.1 ± 8.0	< 0.001
	Follow-up	7.9 ± 9.4	11.8 ± 13.5	0.006

Values are presented as n (%) or mean ± SD; T. chol, Total cholesterol; HDL, high-density lipoprotein; TG, Triglyceride; LDL, low-density lipoprotein; sd LDL, small dense low-density lipoprotein. Delta stands for the subtraction of follow-up value from baseline value.

* LDL size: mean particle size of small dense LDL.

Table 3. Angiographic findings between baseline and at follow-up after stent implantation in group 1 (Increase of LDL particle size) and group 2 (No change or decrease of LDL particle size) by lesion

	Group 1 (N =226)	**Group 2 (N =186)**	**P-value**
Target vessel			0.495
LAD	100 (44.2 %)	88 (47.3 %)	
LCx	56 (24.8 %)	37 (19.9 %)	
RCA	70 (31.0 %)	61 (32.8 %)	
B2 or C lesion	208 (92.0 %)	162 (87.1 %)	0.138
Lesion length (mm)	19.9 ± 7.5	19.4 ± 6.1	0.389
Drug-eluting stent	64 (28.3 %)	70 (37.6 %)	0.057
Stent diameter (mm)	3.28 ± 0.38	3.25 ± 0.40	0.375
RD (mm)	3.30 ± 0.39	3.25 ± 0.39	0.164
Pre-PCI MLD (mm)	0.81 ± 0.35	0.79 ± 0.35	0.554
Post-PCI MLD (mm)	3.30 ± 0.39	3.24 ± 0.40	0.118
Follow-up MLD	2.59 ± 0.89	2.38 ± 1.00	0.024
In-stent restenosis	32 (14%)	48 (26%)	0.004

Values are presented as n (%) or mean ± SD; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; RD, reference diameter; PCI, percutaneous coronary intervention; MLD, minimal luminal diameter.

3. Multivariate analysis of in-stent restenosis after coronary stent implantation

Logistic multivariate analysis showed that stent length (≥ 24 mm) (OR = 2.035, p = 0.019), post minimal luminal diameter (≥ 3 mm) (OR = 0.538, p = 0.041), acute coronary syndrome on initial admission (OR = 2.244, p = 0.009), decrement in HDL cholesterol (OR = 1.029, p = 0.047) and increase in LDL particle size (OR = 0.502, p = 0.030) were independent predictors of ISR in all lesions.

However, differences of lipid profiles such as LDL cholesterol and triglyceride between baseline and follow up and drug-eluting stent use were not significant predictors (OR = 0.584, p = 0.099) (Table 4) (Figure 3).

Table 4. Multiple logistic regression analysis for independent determinants of restenosis after coronary stent implantation

	Odds ratio	95 % C.I.	p-value
Male gender	1.408	0.625-3.169	0.409
Age (≥ 55 years)	1.015	0.982-1.049	0.384
BMI (> 25 kg/m^2)	0.846	0.474-1.505	0.569
Hypertension	1.262	0.701-2.272	0.438
DM	0.682	0.352-1.321	0.256
Smoking	1.125	0.563-2.248	0.738
ACS	2.244	1.219-4.131	0.009
Delta LDL-chol	0.992	0.983-1.001	0.066
Delta HDL-chol	1.029	1.000-1.058	0.047
Delta TG	1.000	0.996-1.005	0.842
hsCRP	0.998	0.984-1.013	0.811
***Increase in LDL size**	0.502	0.270-0.936	0.030
Drug-eluting stent	0.584	0.308-1.107	0.099
Stent length (≥ 24 mm)	2.035	1.124-3.684	0.019
Post MLD (≥ 3.0 mm)	0.538	0.297-0.974	0.041

Table 4. BMI, body mass index; DM, diabetes mellitus; ACS, acute coronary syndrome; hs CRP, high sensitivity C-reactive protein; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; MLD, minimal luminal diameter.

*Increase in LDL size, Increase in LDL particle size between that measured initially and at follow-up angiography

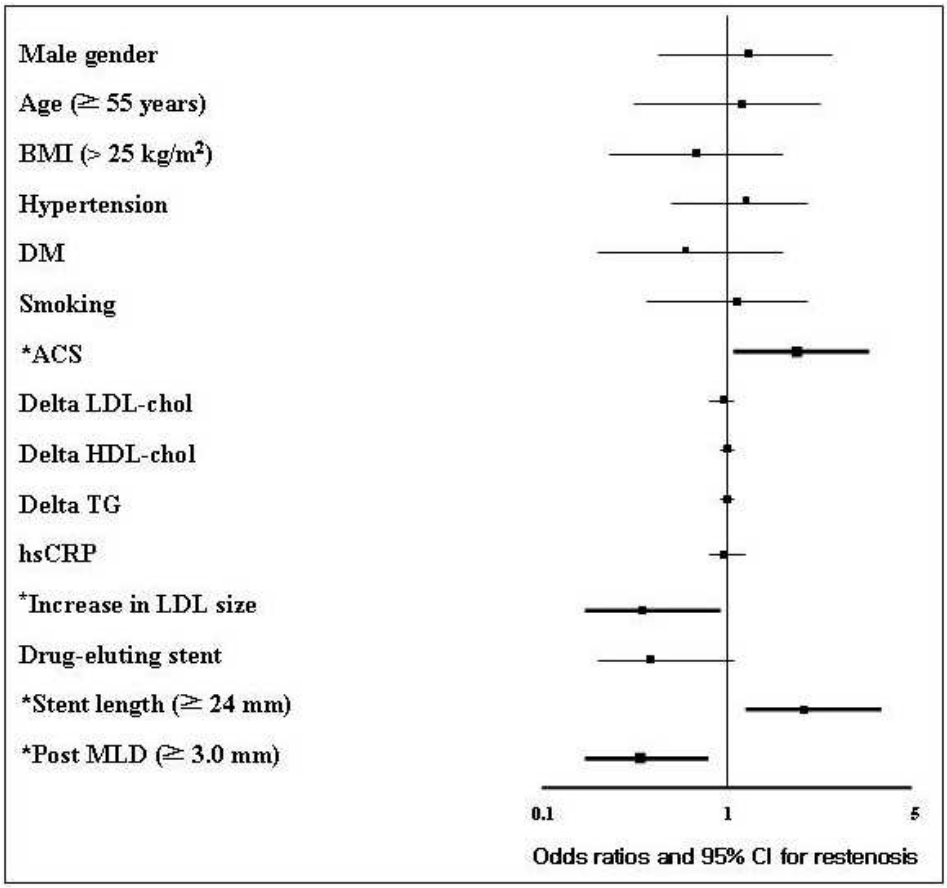

Figure 3. Multiple logistic regression analysis for independent determinants of restenosis after coronary stent implantation. The odds ratio are shown on a logarithimic scale with their 95% CIs

IV. DISCUSSION

In the present study, a change in LDL particle size was associated with in-stent restenosis. The sd-LDL is well-known as an atherogenic LDL particle[22, 23]. A potential mechanism for this atherogenicity involves its relatively lower affinity for the LDL receptor, while it binds avidly to the scavenger receptor. Another explanation cites that sd-LDL is more susceptible to oxidation and, thus, may increase susceptibility to oxidative stress, enhance inflow into the arterial wall, and increase binding to the glycosaminoglycans in the arterial wall[24-28]. Several large prospective studies have suggested that LDL particle size and amount can be risk factors, adding to other lipid variables for CAD[13, 19, 23]. Also, previous study from our lab. showed that sd-LDL was independently associated with the incidence and extent of CAD in a Korean population[21, 29].

A high carbohydrate intake in the Korean population causes the synthesis of free fatty acids in the liver, which, in turn, may stimulate the production of large, triglyceride-rich VLDL and is also associated with increased levels of sd-LDL. Therefore, sd-LDL might play a relatively more important role in the development or progression of CAD in a Korean population, considering that

Koreans have a relatively lower overall LDL concentration than do Western populations.

Recently, the drug-eluting stent was introduced and significantly reduced in-stent restenosis (ISR) after stent implantation. However, ISR remains a serious medical problem, the main mechanism of which is thought to be neointimal hyperplasia, which is related to endothelial dysfunction and vascular inflammation[2, 3]. Because sd-LDL is also related to vascular inflammation, endothelial dysfunction, and the progression of CAD, we evaluated the rate of ISR according to changes in LDL particle size between baseline and six-to-nine month follow-up angiography. According to our results, angiographic ISR rate on follow-up were angiogram higher in group 2 (patients with no change or decrease of LDL particle size), even after controlling for other angiographic parameters and CAD conventional risk factors. Consistent with previous studies, we found that angiographic parameters, such as stent length and post minimal luminal diameter, were the most significant predictors of ISR. Howerer, implantation of DES was not a significant predictors of ISR (OR = 0.584, p = 0.099). It may be due to the fact that DES was implanted at longer (22.29 ± 8.35 vs. 18.49 ± 5.64, p < 0.001) and/ or smaller lesion (3.11 ± 0.33 vs. 3.34 ± 0.39, p = 0.004).

A previous study reported that an increase in LDL size was noted with colespitol/ lovastatin therapy and that a decrease in LDL size was strongly associated with angiographic regression[30]. In the diabetes atherosclerosis intervention study (DAIS), a decrease in LDL size after treatment with fenofibrate was associated with CAD regression[19]. However, in most studies, triglyceride (TG) and HDL-cholesterol were strong confounders and obscured any independent relationship between a change in sd-LDL and CAD regression. However, this present study demonstrated that a decrease in LDL size was associated with in-stent restenosis after controlling for TG and HDL-cholesterol by reducing LDL-cholesterol to less than 100 mg/dl. This result suggests that the quality, as well as quantity, of LDL-cholesterol might be important in CAD. Although statin therapy did not significantly reduce rates of ISR, the therapy may not have been sufficient to affect the quality of LDL-cholesterol. Other TG-lowering or HDL-cholesterol-raising agents might be helpful, in conjunction with LDL-cholesterol lowering therapy, in reducing rates of ISR.

Some limitations of the present study need to be addressed. This study was not randomized according to the statin or other lipid lowering drugs, therefore it is difficult to evaluate the effect to the statin dose or type. Even so, this study is the first to significantly demonstrate the effect of LDL particle size change on

the ISR.

In conclusion, the present study suggests that a change in LDL particle size between baseline and follow-up angiography was associated with in-stent restenosis, even after controlling for Lipid levels, hsCRP, and angiographic parameters. Therefore, modification of LDL particle size may additionally reduce ISR in combination with previously proven treatment. A large randomized trial will be needed to validate our study.

V. CONCLUSIONS

Low-density lipoprotein (LDL) has been recognized as an atherogenic lipoprotein. Among LDL fractions of particles, small dense LDL (sd-LDL) is particularly important in the development of endothelial dysfunction and atherosclerosis. This study demonstrates than whether a change in LDL particle size influences the ISR following stent implantation.

This study suggests that increase in LDL particle size between baseline and follow-up angiography was associated with reducing the ISR. Therefore, modification of LDL particle size may have a beneficial effect for decreasing the ISR.

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ABSTRACT (IN KOREAN)

관상동맥 내 스텐트 삽입술 후 저밀도 지질단백의 입자
크기 변화가 관상동맥 재협착률에 미치는 영향

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김명현

미세입자 저밀도 지질단백(sd-LDL)은 관상동맥 동맥경화의 발생과 진행에 중요한 위험 인자로 알려져 있으며, 초기 동맥경화 발생의 혈관내피세포 기능 장애 및 혈관 내막 증식증과 관련이 있다. 따라서, 저자는 관상동맥 내 스텐트 삽입술 후 저밀도 지질단백의 입자 크기 변화가 관상동맥 내 스텐트 재협착률에 미치는 영향에 대해 연구하고자 하였다.

관상동맥 내 스텐트 삽입술을 시행받은 272 명의 환자에서 412 개의 관상동맥 내 병변(금속스텐트: 278 개, 약물 용출 스텐트: 134 개)을 대상으로 하였다. 스텐트 삽입시와 추적 관상동맥 조영술 시에 저밀도 지질단백의 크기와 분율, 고감도 C 반응단백(hs-CRP) 및 지질계수(lipid profile)를 측정하였고, 스텐트 내 재협착(ISR)은 관상동맥 중재술 시행 후 6 개월에서 9 개월 사이에 측정하였다.

스텐트 재협착은 19%인 80 개의 병변에서 나타났다. 스텐트 재협착은 지질단백의 크기가 증가한 군(1 군)에서 지질단백의 크기가 증가하거나 또는 감소한 군(2 군)에 비해 낮았다(14% 대 26%, p = 0.004). 다중회귀분석에서 스텐트 길이가 24mm 이상인 경우(OR = 2.035, p = 0.019), 술후 최소내경이 3mm 이상인 경우(OR = 0.538,

p = 0.041), 급성 관상동맥 증후군(OR = 2.244, p = 0.009) 그리고 지질단백의 크기가 증가한 경우(OR = 0.502, p = 0.030)가 스텐트 재협착의 독립적인 예측인자였다.

이상의 연구결과에서, 관상동맥 스텐트 삽입술 전후 지질단백 입자 크기의 증가가 혈관 내 재협착의 감소와 관련이 있음을 알 수 있었다. 이로써, 지질 단백 입자 크기의 개선을 통해 혈관 내 재협착을 줄이는 데에 효과를 거둘 수 있을 것이라 생각한다.

핵심되는 말 : 미세입자 저밀도 지질단백, 관상동맥 스텐트, 재협착