

## 관동맥질환에서 저밀도 지단백 입자 크기의 분포

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## Low-Density Lipoprotein Particle Size Distribution in Subjects with Coronary Artery Disease

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## ABSTRACT

**Background :** Low-density lipoprotein (LDL) cholesterol has been shown to be a major risk factor for coronary artery disease (CAD) in animal studies, clinical trials, and observational epidemiologic studies. It has a hydrated density of 1.019 to 1.063 kg/L, a diameter of 20 to 30 nm, and displays -mobility on paper or agarose gel electrophoresis. With technique such as density gradient ultracentrifugation and gel electrophoresis, it is possible to separate lipoproteins accurately on the basis of their density, charge, and particle size. Further, it has been shown that a smaller LDL is associated with an increased risk of coronary artery disease, even when total cholesterol level is only slightly raised. The aim of this study was to analyze LDL particle size distribution in patients with angiographically confirmed coronary artery disease and in control subjects, using nondenaturing gradient polyacrylamide gel electrophoresis, and to investigate the relationship between LDL particle size and the other traditional coronary risk factors. **Methods :** Baseline characteristics such as age, sex, body mass index, history of hypertension or NIDDM, smoking habits, and plasma lipoprotein profiles were obtained in 33 and 27 subjects with and without CAD angiographically confirmed, respectively. We determined LDL peak particle diameter (LDL-PPD) using nondenaturing gradient polyacrylamide gel electrophoresis in CAD and control group. 4% to 12% polyacrylamide gradient gels were used for this assay, and the diameters of LDL subclass peaks were calculated by comparison with a standard calibration curve. This procedure permits the assignment according to distribution of particle diameters as exhibiting pattern A, B, or INT. **Results :** Traditional coronary risk factors (age, sex, body mass index, history of hypertension or NIDDM, smoking habits, plasma triglyceride, HDL-cholesterol, and total to HDL-cholesterol ratio) were found to be significantly different between two groups, except the plasma total cholesterol and LDL-cholesterol. The mean value of LDL-PPD in patients with CAD was significantly lower than that in control subjects (26.110.4 nm versus 27.011.9 nm,  $p = 0.006$ ). LDL-PPD showed relatively strong associations with plasma triglyceride ( $r = -0.536$ ,  $p < 0.01$ ), HDL-cholesterol ( $r = 0.497$ ,  $p < 0.01$ ), and total to HDL-cholesterol ratio ( $r = -0.516$ ,  $p < 0.01$ ), but showed no relation to total cholesterol ( $r = -0.168$ ) or LDL-cholesterol ( $r = -$

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0.028). **Conclusion** : These results suggest an association between small LDL and the presence of CAD and also suggest that LDL-PPD may be associated with the plasma lipid levels. (**Korean Circulation J 1998;28(8):1253-1259**)

**KEY WORDS** : Low-density lipoprotein peak particle diameter (LDL-PPD) · Coronary artery disease.

## 서 론

(low - density lipoprotein, LDL) 1.019

~1.063 kg/L hydrated density 20~30 nm 환 자 1997 5 7

1) , , 60

가 , 2)3) LDL su -

bclass small LDL( dense LDL) 50%

4 - 6) (33 ), (27 )

LDL 가

가 , Austin gradient gel electrophore -

sis , LDL major peak가 25.5 nm 방 법

LDL secondary peak

pattern A, major peak가 25.5 nm 가

secondary peak patt - 95

ern B LDL 2)4)7) McN - mmHg ,

amara LDL 140 mg/dl

(scoring) 8)9) 가 , 10

sm -

all, dense LDL (BMI, body mass index, kg/height<sup>2</sup>) (kg)

9 - 11) (m<sup>2</sup>)

Small LDL -

triglyceride apo B 가, HDL - cholesterol

- , Seldinger sheath

가 , 3,000 heparin

가 small sheath 6 French(F)

LDL

8 - 11) American Co -

lege of Cardiology/American Heart Association (ACC/AHA) 12)

(LDL peak

particle diameter, LDL - PPD)

가 , 12

30 3,000 rpm, LDL  
 4 15 total ch - LDL major peak가 25.5 nm  
 olesterol, triglyceride, HDL - cholesterol secondary peak pattern A,  
 . Hitachi 747 (Hitachi, Japan) major peak가 25.5 nm seco -  
 total cholesterol , trigl - ndary peak pattern B .  
 yceride glycerol - 3 - phosphate ,  
 HDL - cholesterol dextran sulfate - MgCl 2  
 wald , Friede -  
 LDL - cholesterol .  
 LDL Hatch Lees <sup>13)</sup> differential ultracentrifuga -  
 tion LDL . ,  
 LDL 1 mM EDTA 0.01%  
 Na azide 가 , Potassium bromide(KBr)  
 1.09~1.10 kg/L SW Ti50.1  
 Rotor(Beckman, Palo alto, CA) 42,000 rpm, 20  
 24  
 LDL tube  
 , micropipet  
 LDL - PPD gradient polyacrylamide  
 gel electrophoresis .  
 LDL - PPD <sup>14)15)</sup>  
 4~12% nondenaturing gradient gel(NOVEX,  
 San diego, CA) tank buffer(0.025 M tris pH 8.3,  
 0.192 M glycine) 30 mV 20 prerunning  
 , 10 lane 8 2 sample buffer  
 (0.0125 M Tris - Cl pH 6.8, 20% glycerol, 0.2%  
 Bromophenol Blue) 10 l PBS (1 : 5)  
 LDL 10 l 10 µl , 2 lane  
 high molecular weight standards (Phar -  
 macia, Uppsala, Sweden) quality control sample  
 , 70 mV 12 running , 0.125% Co -  
 massie blue solution , 50% me -  
 thanol/10% acetic acid solution .  
 gel densitometry (Stratagene, La Jolla,  
 CA) - thy -  
 roglobulin 17 nm, ferritin 12.2 nm -  
 , LDL

<sup>2)4)7)</sup>  
 LDL  
 LDL major peak가 25.5 nm  
 secondary peak pattern A,  
 major peak가 25.5 nm seco -  
 ndary peak pattern B .  
 통계분석  
 ± ,  
 WIN SPSS PC+ categorical  
 variables <sup>2</sup> - test , continuous variable unp -  
 aired ' t ' - test p 0.05  
 가  
 . LDL - PPD  
 Person correlation coefficient 가 .

## 결 과

### 관동맥질환 위험 인자의 비교

, , , ,  
 (Table 1). , 61 ± 10  
 52 ± 12 (p =  
 0.005), 가  
 24/33 (72.7%), 9/27  
 (33.3%)  
 (p = 0.002).  
 25.2 ± 3.3 kg/m 2 23.0 ± 3.2 kg/m 2  
 (p = 0.011),  
 39.4%, 45.5% 14.8%,  
 3.7% (p =  
 0.036, p < 0.001).

**Table 1.** Baseline characteristics in subjects with or without coronary artery disease

	CAD (n = 33)	Controls (n = 27)	p value
Age (years)	61 ± 10	52 ± 12	0.005
Sex			
Male	24 (72.7%)	9 (33.3%)	0.002
Female	9 (27.3%)	18 (66.7%)	
BMI (kg/m <sup>2</sup> )	25.2 ± 3.3	23.0 ± 3.2	0.011
NIDDM	13 (39.4%)	4 (14.8%)	0.036
Hypertension	16 (48.5%)	8 (29.6%)	0.138
Smoking	15 (45.5%)	1 ( 3.7%)	< 0.001

**Table 2.** Plasma lipid profiles in subjects with or without coronary artery disease

	CAD (n = 33)	Control (n = 27)	p value
Total cholesterol (mg/dl)	197.5 ± 28.5	190.6 ± 33.8	0.405
Triglyceride (mg/dl)	166.3 ± 98.2	115.1 ± 76.5	0.027
HDL-cholesterol (mg/dl)	39.3 ± 9.7	47.0 ± 11.4	0.008
LDL-cholesterol (mg/dl)	124.9 ± 30.2	120.6 ± 30.0	0.579
T-chol/HDL-chol ratio	5.3 ± 1.3	4.3 ± 1.2	0.003

**Table 3.** Mean value of LDL-PPD and frequency of LDL subclass phenotype

	CAD (n = 33)	Control (n = 27)	p value
LDL-PPD(nm)	26.1 ± 10.4	27.0 ± 11.9	0.006
LDL subclass			0.296
Pattern A	26(78.8%)	24(88.9%)	
Pattern B	7(21.2%)	3(11.1%)	

16/33 (48.5%)                      8/27(29.6%)  
(p=0.138).

### 혈청 지질 농도의 비교

Total cholesterol      LDL - cholesterol

(197.5 ± 28.5 mg/dl VS 190.6 ± 33.8 mg/dl, p = 0.405, 124.9 ± 30.2 mg/dl VS 120.6 ± 30.0 mg/dl, p = 0.579).      , triglyceride

HDL - cholesterol      166.3 ± 98.2 mg/dl VS 115.1 ± 76.5 mg/dl (p = 0.027), 39.3 ± 9.7 mg/dl VS 47.0 ± 11.4 mg/dl (p = 0.008)

    , total/HDL - cholesterol ratio      5.3 ± 1.3 VS 4.3 ± 1.2 (p = 0.003)

(Table 2).

### LDL-PPD부포의 비교

LDL - PPD 26.1 ± 10.4  
nm 27.0 ± 11.9 nm  
(p = 0.006), LDL B  
7/33 (21.2%), 3/27 (11.1%)  
(Table 3).

## LDL-PPD와 혈청 지질 농도의 관련성

LDL - PPD triglyceride( $r = -0.536, p < 0.01$ ),

**Table 4.** Person correlation coefficient between LDL-PPD and plasma lipid profiles

	LDL-PPD	p value
Total - cholesterol	- 0.168	NS
Triglyceride	- 0.536	<0.01
HDL-cholesterol	0.497	<0.01
LDL-cholesterol	- 0.028	NS
Total-chol/HDL-chol ratio	- 0.516	<0.01

**Table 5.** Classification of LDL particle by Musliner and Krauss<sup>22)</sup>

Class	Subfraction density (g/ml)	Particle diameter (nm)
LDL I	1.025 - 1.035	26 - 27
LDL II	1.032 - 1.038	25.5 - 26
LDL III A	1.038 - 1.050	24.7 - 25.6
LDL III B		24.2 - 24.6
LDL IV A	1.048 - 1.065	23.3 - 24.2
LDL IV B		21.8 - 23.2

HDL - cholesterol ( $r = 0.497$ ,  $p < 0.01$ ), total/HDL - cholesterol ratio ( $r = -0.516$ ,  $p < 0.01$ ), total cholesterol, LDL - cholesterol ( $r = -0.168$ ,  $r = -0.028$ ).

고 안

LDL 가

. LDL ,

LDL 가

16)17)

가 18)

. 가 LDL 가

<sup>19)</sup> 30~50% 가 가 , LDL  
 가 가 LDL  
 LDL 가 가 freeradical oxidation 가  
<sup>20)</sup> <sup>26)</sup> small LDL  
<sup>27)</sup> density gradient ultracentrifugation ,  
 1.019~1.063 LDL(oxidized - LDL) scavenger  
 g/ml 50% , 25% , 20% foam cell  
 , 5% , LDL <sup>28)</sup> , sialic acid  
 95% apolipoprotein B - 100 proteoglycan ,  
<sup>21)</sup> density gradient ultracentrifugation <sup>29)</sup> ,  
 gel electrophoresis  
 가 가 <sup>2)14)</sup> LDL 가  
 LDL 2~12 <sup>8)14)</sup> 가 ,  
 Krauss <sup>22)</sup> 가 가  
 LDL 4 , gradient gel electrophoresis  
 (Table 5). Austin <sup>4)</sup> LDL  
 A B 가  
 LDL 가 ,  
<sup>4-8)23)24)</sup> 가 가  
 Lamarche <sup>6)</sup> 가  
 LDL - PPD가 가 ,  
 small LDL(LDL - PPD25.64 nm) 가  
 가 3.6~5.1 LDL  
 가 multivariate logi - 가  
 stic regression analysis , small LDL  
 가  
 . Coresh <sup>23)</sup> 가  
 98 100 ,  
 LDL <sup>30)31)</sup> <sup>32)</sup>  
 , LDL 가 , , , <sup>33)</sup>  
 LDL - cholesterol, HDL - cholesterol 가  
 triglyceride . 요 약  
 Small, dense LDL . 연구배경 :  
 LDL

1.019~1.063 kg/L hydrated density 20~30  
nm  
mobility  
subclass small LDL

PPD

방 법 :

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60

50%  
(33 ), (27 )  
12  
LDL  
4~12% nondenaturing gradient gel  
electrophoresis  
- thyroglobulin 17 nm, ferritin 12.2 nm -  
LDL

결 과 :

Total cholesterol LDL - cholesterol  
triglyceride HDL - chol -  
esterol 166.3 ± 98.2 mg/dl VS 115.1  
± 76.5 mg/dl (p = 0.027), 39.3 ± 9.7 mg/dl VS 47.0  
± 11.4 mg/dl (p = 0.008)  
total/HDL - cholesterol ratio 5.3 ± 1.3 VS  
4.3 ± 1.2 (p = 0.003)  
LDL - PPD  
26.1 ± 10.4 nm 27.0 ± 11.9  
nm (p = 0.006), LDL  
B  
7/33 (21.2%), 3/27  
(11.1%)  
LDL - PPD tri -  
glyceride (r = - 0.536, p < 0.01), HDL - cholesterol (r

= 0.497, p < 0.01), total/HDL - cholesterol ratio (r  
= - 0.516, p < 0.01)  
cholesterol, LDL - cholesterol  
(r = - 0.168, r = - 0.028).

결 론 :

중심 단어 : LDL - PPD

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