Predictive Value of Remnant-like Particle Cholesterol as an Indicator of Coronary Artery Stenosis in Patients with Normal Serum Triglyceride Levels

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Abstract

Objective We designed the present study to evaluate the association of various lipid and fibrinolytic components with coronary artery stenosis with respect to the triglyceride (TG) level.

Methods Levels of TG, remnant-like particle cholesterol (RLP-C), total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), lipoprotein-(a), uric acid, blood glucose, tissue plasminogen activator (t-PA), t-PA inhibitor type 1, anti-thrombin III, and protein C were measured in 208 patients who underwent diagnostic coronary angiograms.

Patients Of these 208 patients, 59 were hypertriglyceridemic (150 mg/dl or higher) and 149 were normotriglyceridemic.

Results Both LDL-C and HDL-C showed significant differences between patients with and those without coronary artery stenosis in both hypertriglyceridemic and normotriglyceridemic patient subgroups. However, RLP-C showed a significant difference in the normotriglyceridemic patient subgroup ($p=0.012$) but not in the hypertriglyceridemic patient subgroup ($p=0.736$).

Conclusion Our current retrospective study disclosed that RLP-C levels are closely associated with coronary artery stenosis in patients with normal TG levels. (Internal Medicine 39: 540–546, 2000)

Key words: RLP-C, coronary risk factor, hypertriglyceridemia, normotriglyceridemia

Introduction

Hypercholesterolemia has been recognized as a risk factor

for coronary artery disease (1, 2). The risk for atherosclerotic coronary artery disease is directly correlated with low-density lipoprotein cholesterol (LDL-C) level (3). However, the triglyceride (TG) concentration alone is not always a good marker of the atherogenic potential (4, 5). In fact, the incidence of coronary artery disease in patients with familial hypertriglyceridemia has been reported to be relatively low (6). TG concentration has been considered to be a more efficient marker for coronary artery disease in certain patient subgroups as compared with others (7). One limitation of using plasma TG concentration as a predictor for coronary artery disease is that it does not separate the less atherogenic TG-rich lipoproteins, such as chylomicrons and nascent very-low-density lipoproteins (VLDL) (8), from their potentially more atherogenic components, such as VLDL remnants. Unfortunately, limited information is available for clinical use as to which factor has an additional discriminating power for isolating coronary artery disease patients in combination with the TG level. Such being the case, we designed the current study to compare the association of various lipid and fibrinolytic components with coronary artery stenosis between hypertriglyceridemic and normotriglyceridemic subjects. We also evaluated the levels of remnant-like particle cholesterol (RLP-C). RLP-C is a recently established simple assay method that estimates at least a part of serum triglyceride-rich lipoprotein remnants (9).

Methods

The study population was composed of 300 consecutive patients who underwent diagnostic coronary angiograms for possible coronary artery diseases. Data from repeated angiograms for the same patient were excluded. Patients who had liver disease, renal disease, endocrinologic disorders, neoplasm, and acute inflammatory disease were excluded. Patients who had had acute myocardial infarction within the past 1 month were also excluded. Of the remaining patients, the study

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population was limited to 208 patients. Written informed consent was obtained from each of these 208 patients before the study. The study protocol was approved by the Ethics Committee of our hospital.

Coronary angiogram was carried out mainly through the percutaneous brachial approach and occasionally through the femoral approach using the standard Judkin's technique. At least 5 views of the left coronary artery and 3 of the right were obtained. Computer-assisted quantitative coronary angiography was carried out in all patients using a cardiovascular angiography analysis system (10, 11). According to the reporting system of the American Heart Association (12), narrowing of greater than 51% stenosis was considered significant.

A venous blood sample was taken with minimal venostasis from an antecubital vein for the determination of each factor as follows: total cholesterol (automated enzymatic methods), high-density lipoprotein cholesterol (HDL-C; selective inhibition assay), LDL-C [Friedewald's equation (13) : LDL-C = total cholesterol - HDL-C - TG/5], TG (automated enzymatic methods), lipoprotein-(a) [Lp(a); latex immunoassay with a rabbit monoclonal anti-human Lp(a) antibody. This method is based on the latex-enhanced particle agglutination technology. A more detailed characterization has been given elsewhere (14)], RLP-C (immunoabsorption assay using mouse monoclonal anti-human apo B-100 and anti-human apo A-I immunoaffinity mixed gels. Briefly, the standard assay contains 5µl of serum and 50 µl of mixed gel, which adsorbs lipoproteins containing apo A-I as well as most of the lipoproteins containing apo B-100. After 60 minutes of gentle shaking, unbound cholesterol present in the supernatant are measured enzymatically.), as well as uric acid (automated enzymatic methods), blood glucose (automated enzymatic methods), tissue plasminogen activator antigen [t-PA; enzyme-linked immunosorbent assay using monoclonal antibodies (15)], and t-PA inhibitor type 1 antigen [PAI-1; enzyme-linked immunosorbent assay (16). This procedure measured the total quantity of PAI-1 present, free or complexed with t-PA and in active or in inactive form], antithrombin III activity (AT III; chromogenic substrate assay), protein C activity (latex photometric immunoassay). Venous blood samples were collected before the catheterization and after the subjects had fasted for 12 hours. All lipid-lowering drugs were withdrawn >7 days before the study. The calculated values of LDL-C in 3 subjects with TG levels of >400 mg/dl were excluded from the analyses concerning LDL-C.

The 4 conventional coronary risk factors were determined in each patient as follows: hypertension (systolic pressure >160 mmHg or diastolic pressure >95 mmHg, or a satisfactory prior diagnosis), smoking habit (current smoker or former smoker with >10 cigarettes per day), diabetes mellitus (overt diabetes necessitating treatment or abnormal oral glucose tolerance test), obesity [body mass index (BMI) >26]. Each variable was examined when each patient underwent coronary angiogram. Blood pressure (BP) was measured by nurses in a standardized clinical setting with a mercury sphygmomanometer in the supine position after at least 10 minutes of rest. BP measure-

ments were repeated at least three times in a blind fashion, and the mean values of repeated measurements represented the BP value. BMI was calculated from weight (kg) divided by height (m) squared.

For statistical analysis, Student's unpaired 2-tailed *t* test was used for comparisons between two groups. Mann-Whitney's *U* test was performed if data sets were not normally distributed. Discrete data were analyzed by use of the chi-square test. A *p* value of less than 0.05 was considered significant in each test. Multivariate logistic regression analysis was performed to determine the association of each parameter. It remains undetermined whether RLP-C is an independent covariate in relation to the various lipid and fibrinolytic variables. Thus, multivariate statistical analyses were carried out to assess the independent correlations between RLP-C level and levels of the other variables. Values of RLP-C, TG, Lp(a), glucose, t-PA, and PAI-1 were transformed into natural logarithms in these multivariate statistical analyses.

Results

Patient characteristics

The mean age of the 208 patients studied was 63.8±8.7 years (mean±SD) and ranged from 39 to 83 years. There were 149 males and 59 females. Of the patients, 56 (26.9%) had no significant coronary artery stenosis or occlusion, whereas 152 (73.1%) had significant organic stenosis. We defined the former 56 cases as group N (the group of patients who had no stenosis) and the latter 152 cases as group S (the group of patients who had at least one stenosis or occlusion). The number of patients found to have 1-, 2-, or 3-vessel and left main disease in group S was 71, 47, 25, and 9, respectively. Patient characteristics were compared between group S and group N, as shown in Table 1. The mean age and male-female ratio were higher in group S. No significant differences were observed in the prevalence of conventional risk factors between groups S and N.

The clinical diagnoses confirmed following coronary angiography were as follows: myocardial infarction in 61 cases,

Table 1. Comparison of Baseline Characteristics between Patients with (Group S) and Those without (Group N) Angiographically Determined Coronary Artery Stenosis

	Group S (n=152)	Group N (n=56)	Test for trend
Age (yr)	64.8±8.1	61.0±9.8	p=0.021
Male gender (%)	74.3	64.3	p=0.040
Coronary risk factors (%)			
Hypertension	44.1	41.1	NS
Diabetes mellitus	23.7	19.6	NS
Smoking	49.3	42.9	NS
Obesity	21.7	25.0	NS

Data presented are mean±SD or percent of patients. NS: not statistically significant.

angina pectoris in 97 cases, silent myocardial ischemia in 7 cases, positive stress test in 18 cases, neurocirculatory asthenia in 21 cases, cardiomyopathy in 2 cases, aortic disease in 2 cases.

Monovariate analysis

Mean levels of lipid and fibrinolytic components in group S and group N of the total patients studied are presented in Table 2. HDL-C was significantly lower in Group S. LDL-C, TG, and RLP-C were significantly higher in group S. Protein C tended to be lower in group S but the difference did not reach statistical significance.

We divided the patients into 2 subgroups according to the TG levels. Patients with a TG level of 150 mg/dl (1.69 mmol/l) or higher were classified as the hypertriglyceridemic subgroup; 59 of the patients fell into this category. Patients with values lower than 150 mg/dl were classified as the normotriglyceridemic subgroup. This subgroup consisted of 149 patients. The two subgroups were similar with respect to clinical characteristics. Levels of TG, HDL-C, and RLP-C showed highly significant differences between normotriglyceridemic and hypertriglyceridemic patient subgroups, as shown in Table 3. Levels of total cholesterol, t-PA, glucose, BMI, and diastolic BP also reached significant differences between normotriglyceridemic and hypertriglyceridemic patient subgroups (Table 3).

We investigated whether differences exist in the association

of the levels of various factors with coronary artery stenosis between hypertriglyceridemic and normotriglyceridemic patient subgroups. The mean levels of the various variables in groups S and N of the hypertriglyceridemic patient subgroup are presented in Table 4; those of the normotriglyceridemic patient subgroup are presented in Table 5. An appropriate *p*

Table 3. Comparison of the Lipid and Fibrinolytic Parameters between Normotriglyceridemic and Hypertriglyceridemic Patient Subgroups

	Normo-TG	Hyper-TG	<i>p</i> Value
T. Chol. (mg/dl)	193.1±31.9	206.9±39.1	0.045
LDL-C (mg/dl)	127.3±33.0	127.9±42.3	0.935
HDL-C (mg/dl)	45.27±14.13	36.47±12.43	0.002
TG (mg/dl)	102.9±27.3	212.8±58.1	<0.0001
Lp (a) (mg/dl)	23.40±21.11	18.88±16.12	0.261
RLP-C (mg/dl)	4.94±4.77	9.01±5.25	<0.0001
uric acid (mg/dl)	5.61±1.62	6.14±1.79	0.113
glucose (mg/dl)	103.7±28.7	121.9±37.7	0.024
t-PA (ng/ml)	9.08±4.21	11.86±5.48	0.013
PAI-1 (ng/ml)	30.39±24.35	38.70±34.40	0.134
AT III (%)	99.43±15.02	97.06±13.85	0.830
protein C (%)	99.63±23.04	102.34±21.92	0.551
BMI (kg/m ²)	23.6±3.3	25.1±3.5	0.033
systolic BP (mmHg)	120.9±16.2	123.9±16.1	0.366
diastolic BP (mmHg)	68.9±10.1	73.2±9.6	0.035

Data presented are mean±SD. Normo-TG: normotriglyceridemic patient subgroup, Hyper-TG: hypertriglyceridemic patient subgroup. Other abbreviations as in Table 2.

Table 2. Comparison of the Lipid and Fibrinolytic Parameters between Patients with (Group S) and Those without (Group N) Angiographically Determined Coronary Artery Stenosis

	Group S	Group N	<i>p</i> Value
T. Chol.(mg/dl)	200.7±35.2	188.2±31.4	0.082
LDL-C (mg/dl)	133.3±35.9	113.7±31.6	0.010
HDL-C (mg/dl)	38.09±10.98	52.63±13.58	0.002
TG (mg/dl)	145.2±66.4	107.6±43.4	0.011
Lp (a) (mg/dl)	24.78±22.05	21.14±18.89	0.136
RLP-C (mg/dl)	6.84±5.63	3.84±2.57	0.0004
uric acid (mg/dl)	5.93±1.57	5.34±1.88	0.092
glucose (mg/dl)	115.2±36.1	99.9±23.3	0.085
t-PA (ng/ml)	10.05±4.60	8.91±4.59	0.077
PAI-1 (ng/ml)	32.93±27.67	31.57±24.36	0.625
AT III (%)	95.90±14.17	98.13±13.50	0.364
protein C (%)	98.20±21.82	106.22±22.35	0.060
BMI (kg/m ²)	24.5±3.2	23.6±3.8	0.189
systolic BP (mmHg)	121.9±15.8	122.5±17.0	0.861
diastolic BP (mmHg)	70.6±9.8	70.8±10.6	0.911

Data presented are mean±SD. T. Chol.: total cholesterol, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, TG: triglyceride, Lp(a): lipoprotein-(a), RLP-C: remnant-like particle cholesterol, t-PA: tissue plasminogen activator, PAI-1: t-PA inhibitor type 1, AT III: antithrombin III, BMI: body mass index, BP: blood pressure.

Table 4. Comparison of the Lipid and Fibrinolytic Parameters between Patients with (Group S) and Those without (Group N) Angiographically Determined Coronary Artery Stenosis Assessed in the Hypertriglyceridemic Patient Subgroup

	Group S	Group N	<i>p</i> Value
T. Chol.(mg/dl)	210.4±38.2	180.0±40.4	0.130
LDL-C (mg/dl)	132.7±40.5	90.7±41.6	0.038
HDL-C (mg/dl)	34.65±11.63	50.65±9.81	0.010
TG (mg/dl)	215.3±60.0	193.5±41.0	0.404
Lp (a) (mg/dl)	19.80±16.49	12.00±12.57	0.273
RLP-C (mg/dl)	9.15±5.49	7.98±3.12	0.736
uric acid (mg/dl)	6.37±1.73	4.30±1.28	0.039
glucose (mg/dl)	122.5±38.7	118.8±36.4	0.743
t-PA (ng/ml)	11.40±5.17	13.48±7.28	0.223
PAI-1 (ng/ml)	37.23±32.42	40.10±42.06	0.489
AT III (%)	96.74±14.63	99.50±8.20	0.714
protein C (%)	101.68±22.74	107.50±15.26	0.624
BMI (kg/m ²)	25.4±3.6	24.3±3.2	0.366
systolic BP (mmHg)	123.3±15.1	125.1±18.1	0.647
diastolic BP (mmHg)	73.1±10.4	73.1±9.5	0.993

Data presented are mean±SD. Abbreviations as in Table 2.

Table 5. Comparison of the Lipid and Fibrinolytic Parameters between Patients with (Group S) and Those without (Group N) Angiographically Determined Coronary Artery Stenosis Assessed in the Normotriglyceridemic Patient Subgroup

	Group S	Group N	<i>p</i> Value
T. Chol.(mg/dl)	195.4±32.5	189.2±30.8	0.396
LDL-C (mg/dl)	133.7±33.4	116.4±29.8	0.033
HDL-C (mg/dl)	40.50±11.23	53.35±15.01	<00001
TG (mg/dl)	106.3±24.9	97.2±30.5	0.162
Lp (a) (mg/dl)	22.75±20.08	23.21±22.78	0.721
RPL-C (mg/dl)	5.85±5.61	3.39±2.18	0.012
uric acid (mg/dl)	5.69±1.43	5.47±1.91	0.073
glucose (mg/dl)	108.7±32.9	95.2±17.5	0.047
t-PA (ng/ml)	9.46±4.29	8.46±4.05	0.207
PAI-1 (ng/ml)	31.36±26.14	28.77±21.33	0.632
AT III (%)	95.16±15.04	98.58±14.98	0.303
protein C (%)	93.98±20.78	109.03±23.86	0.003
BMI (kg/m ²)	23.8±3.1	23.3±4.2	0.571
systolic BP (mmHg)	120.9±16.8	120.7±16.0	0.975
diastolic BP (mmHg)	68.1±8.9	69.9±11.9	0.523

Data presented are mean±SD. Abbreviations as in Table 2.

value by unpaired two-tailed *t* test or Mann-Whitney's *U* test is presented for each variable. Both LDL-C and HDL-C levels were significantly different between groups S and N in the overall population (Table 2), in the hypertriglyceridemic patient subgroup (Table 4), and in the normotriglyceridemic patient subgroup (Table 5). While the RPL-C level was not significantly different in the hypertriglyceridemic patient subgroup (Table 4, *p*=0.736), it was significantly different in the normotriglyceridemic patient subgroup (Table 5, *p*=0.012). The protein C level showed a significant difference between groups S and N only in the normotriglyceridemic patient subgroup. The uric acid level showed a significant difference only in the hypertriglyceridemic patient subgroup. These differences persisted after adjustment for age and gender between groups S and N.

Multivariate analysis

Multivariate statistical analyses were carried out to assess the independent correlations between the RPL-C level and the levels of the other variables, as can be seen in Table 6. The association of RPL-C level with the presence of coronary artery stenosis showed a marked difference between hypertriglyceridemic and normotriglyceridemic patient subgroups. Therefore, we evaluated whether the relationship among RPL-C and the other variables differed between hypertriglyceridemic and normotriglyceridemic patient subgroups. Multivariate analysis showed that the TG level was the only independent factor associated with RPL-C level when assessed in both overall patients and the hypertriglyceridemic patient subgroup. However, it showed that the levels of glucose and Lp(a) were independent factors associated with the RPL-C level

Table 6. Multivariate Statistical Analyses for Correlations of RPL-C Level with Levels of Various Lipid and Fibrinolytic Parameters

	Total patients		Normo-TG		Hyper-TG	
<i>r</i> ²	0.489		0.587		0.557	
	<i>b</i>	<i>p</i>	<i>b</i>	<i>p</i>	<i>b</i>	<i>p</i>
LDL-C	−0.041	0.701	0.259	0.079	−0.136	0.522
HDL-C	−0.110	0.362	0.125	0.434	−0.160	0.557
TG	0.429	0.001	0.220	0.143	0.407	0.050
Lp (a)	−0.106	0.295	−0.385	0.015	−0.042	0.841
uric acid	0.062	0.618	0.084	0.623	0.112	0.649
glucose	0.160	0.133	0.640	0.0001	−0.044	0.831
t-PA	0.059	0.583	−0.066	0.638	0.149	0.482
PAI-1	−0.046	0.648	0.035	0.808	−0.021	0.923
AT III	0.133	0.223	−0.036	0.795	0.380	0.091
protein C	0.180	0.109	0.117	0.440	0.034	0.864

Normo-TG: TG, normotriglyceridemic patient subgroup, Hyper-TG: hypertriglyceridemic patient subgroup, *b*: coefficient, *p*, *p* value. Other abbreviations as in Table 2.

and the TG level was not associated when assessed in the normotriglyceridemic patient subgroup.

Multivariate statistical analyses that took into account the values of BMI, systolic BP, and diastolic BP as well as the lipid and fibrinolytic parameters were also performed. Each coefficient value of BMI, systolic BP, and diastolic BP was between 0.1 and −0.1 in overall, hypertriglyceridemic, and normotriglyceridemic patients, suggesting that the RPL-C level was little influenced by these 3 parameters. Each *p* value for these 3 parameters was more than 0.2 in each patient subgroup.

Influence of diabetes mellitus

RPL-C level may be influenced by the glucose level according to our multivariable analysis. Among the patients studied, 36 cases in group S and 11 cases in group N were diagnosed as having diabetes mellitus. Thus, we performed the second analysis among the subjects excluding these 47 diabetic patients (Table 7). In this additional analysis among the 161 non-diabetic patients analyzed, RPL-C showed a significant difference in the normotriglyceridemic subgroup but not in the hypertriglyceridemic subgroup.

Effect of lipid lowering medicine

Some drugs can affect lipoprotein profiles. Among the patients studied, 17 were taking statin, 8 were taking other lipid lowering medicine such as Niacin or Clofibrate, and 2 were taking both. Of these 27 patients, 20 were classified as group S and 7 were group N. The ratio of subjects who were on these lipid lowering drugs showed no significant difference between groups S and N. We performed the third analysis among the subjects excluding these 27 patients who were on the lipid lowering drugs. In this third analysis among the 181 patients ana-

Table 7. Comparison of the Lipid Parameters between Non-diabetic Patients with (Group S) and Those without (Group N) Angiographically Determined Coronary Artery Stenosis

Panel A: Comparison assessed in the hypertriglyceridemic patient subgroup

	Group S	Group N	<i>p</i> Value
TG (mg/dl)	216.6±66.3	168.5±63.6	0.274
RLP-C (mg/dl)	9.20±5.45	6.90±2.26	0.457
glucose (mg/dl)	102.8±14.5	91.0±11.1	0.279

Panel B: Comparison assessed in the normotriglyceridemic patient subgroup

	Group S	Group N	<i>p</i> Value
TG (mg/dl)	105.5±25.0	98.1±30.4	0.225
RLP-C (mg/dl)	5.48±4.81	3.44±2.20	0.021
glucose (mg/dl)	100.6±13.2	93.2±11.4	0.049

Data presented are mean±SD. Abbreviations as in Table 2.

lyzed, RLP-C also showed a significant difference in the normotriglyceridemic subgroup but not in the hypertriglyceridemic subgroup. Multivariate statistical analyses to assess the independent correlations between RLP-C level and levels of the other variables were also performed in these 181 patients. They showed the same tendency as the original ones; TG level was the only independent factor associated with RLP-C level when assessed in both overall patients and the hypertriglyceridemic patient subgroup but the levels of glucose and Lp (a) were independent factors associated with the RLP-C level, and the TG level was not associated when assessed in the normotriglyceridemic patient subgroup.

Discussion

Hypertriglyceridemia has been reported to be a powerful coronary risk factor when it coincides with a high LDL-C level (17, 18) or a low HDL-C level (19). However, the association of neither LDL-C level nor HDL-C level with the presence of angiographically determined coronary artery stenosis showed different tendencies between hypertriglyceridemic and normotriglyceridemic patient subgroups in the present study. In contrast, a significant difference was observed in RLP-C level between groups S and N in the normotriglyceridemic patient subgroup whereas no difference in RLP-C level was found in the hypertriglyceridemic patient subgroup, suggesting that a higher level of RLP-C is associated with an increased risk for coronary artery stenosis predominantly in the normotriglyceridemic subjects.

VLDL secreted by the liver is not considered to be atherogenic in normal individuals (8). VLDL is hydrolyzed gradually into smaller particles by the action of LPL, and produces remnants which are subsequently converted to LDL by hepatic

lipase. In the early studies of Gofman et al (20), VLDL remnants were suggested to be more atherogenic than LDL. It has been recently accepted that the levels of these TG-rich lipoprotein remnants may be as important as the LDL-C levels (21). But reports on the association between remnants of TG-rich lipoproteins and coronary artery disease are still limited, because the previous methods used to quantify TG-rich lipoprotein remnants were complex and did not lead to routine clinical use.

A simple and reliable method to measure the presence of remnant lipoproteins has been developed recently in Japan (9). This method uses an immunoaffinity gel mixture of anti apo B-100 and anti apo A-I monoclonal antibodies coupled to Sepharose 4B. A subpopulation of TG-rich particles is separated in the unbound fraction enriched in apo E. It was demonstrated that this subpopulation mainly consisted of chylomicron remnants and VLDL remnants (9). RLP-C is the level of this subpopulation quantified by the assay of cholesterol. A more detailed characterization has been given elsewhere (9). Although there are some reports on the levels of VLDL remnants or intermediate-density lipoproteins (IDL) in patients with coronary artery stenosis (22), reports on the levels of RLP-C in patients with coronary artery stenosis are few (9, 23). Associations of RLP-C levels with coronary events have recently been reported (24, 25). We have previously reported that RLP-C levels are markedly high in patients who have established coronary artery stenosis (26). In the current study, we have demonstrated that the association of RLP-C level with the presence of coronary artery stenosis is high, especially in the normotriglyceridemic patients. A higher level of serum concentration of RLP-C appears to be a risk for the presence of coronary artery stenosis even when the serum TG level is not elevated. The present observations support for the first time

the importance of the RLP-C assay as a possible means of isolating the patients with coronary artery stenosis from normotriglyceridemic subjects. To our knowledge, there have been no similar reports discussing IDL level nor VLDL remnant level.

In the current study, RLP-C was correlated with coronary artery stenosis in the normotriglyceridemic patient subgroup but not in the hypertriglyceridemic patient subgroup. It is unclear why there was no significant difference in the levels of RLP-C between groups S and N in the hypertriglyceridemic patient subgroup. RLP-C has been reported to be highly correlated with the plasma triglyceride level (9). In the hypertriglyceridemic patient subgroup, RLP-C levels were relatively high even in group N, which is perhaps affected by higher TG levels (Table 4). In fact, both the TG level and RLP-C level in group N of the hypertriglyceridemic patient subgroup (Table 4) was higher than that in group S of the normotriglyceridemic patient subgroup (Table 5). Thus, the association between the RLP-C level and coronary artery stenosis in the hypertriglyceridemic patient subgroup might be expected to underestimate the real effects of RLP-C. The negative results obtained here with regard to the association of the RLP-C level and coronary artery stenosis in the hypertriglyceridemic patient subgroup should not be taken to imply a lack of involvement in coronary atherosclerosis, but only an indeterminacy of the analysis.

The independent association of uric acid with coronary artery disease is less certain as compared with other conventional coronary risk factors (27). The existence of correlations between the uric acid level and lipid parameters or obesity results in an underestimation of the association between uric acid and coronary artery disease in multivariate analyses (27). Our observation that a higher level of uric acid is associated with coronary artery stenosis only in the hypertriglyceridemic patients is in line with previous reports.

A positive correlation between the TG level and PAI-1 level has been previously reported (28, 29). In the current study, the PAI-1 level tended to be higher in the hypertriglyceridemic patient subgroup than in the normotriglyceridemic patient subgroup but this difference did not reach a statistical significance (Table 3). The level of t-PA was significantly high in the hypertriglyceridemic patient subgroup. With regard to the difference of the association with coronary artery stenosis between hypertriglyceridemic and normotriglyceridemic patient subgroups, neither the t-PA level nor PAI-1 level showed different tendencies between the two subgroups (Tables 4 and 5). On the contrary, protein C showed a significant difference between groups S and N in the normotriglyceridemic patient subgroup but not in the hypertriglyceridemic patient subgroup. However, there are few reports concerning the protein C level and coronary artery stenosis (30). It remains undetermined whether the difference of the association of protein C with coronary artery stenosis between hypertriglyceridemic and normotriglyceridemic patient subgroups is meaningful or not. The current study was not able to answer this question.

With regard to the study limitations, this is an observational retrospective association study of a selected population of pa-

tients. Thus, the findings will require confirmation in a prospective study. In conclusion, the current study found that RLP-C levels are strongly associated with coronary artery stenosis, especially in patients with normal TG levels. The RLP-C assay may provide a possible means of differentiating the patients with coronary artery stenosis from among the normotriglyceridemic subjects.

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