Characterization of LDL Particle Size Among Carriers of a Defective or a Null Mutation in the Lipoprotein Lipase Gene

The Québec LIPD Study

Isabelle L. Ruel, Daniel Gaudet, Patrice Perron, Jean Bergeron, Pierre Julien, Benoît Lamarche

Objective—The objective of the present study was to compare the impact of the null P207L and defective D9N mutations in the LPL gene on LDL particle size among heterozygous carriers.

Methods and Results—LDL particle size was measured on whole plasma by 2% to 16% non-denaturing polyacrylamide gradient gel electrophoresis in a cohort of 206 heterozygous carriers of either the P207L or the D9N mutation. The P207L carriers (N=88) presented with a more atherogenic lipoprotein-lipid profile compared with the D9N carriers (N=118). Accordingly, LDL particle size was smaller in the P207L carriers than in the D9N subjects (248.8±1.0 Å vs 254.5±1.0 Å, P<0.001), and the difference remained significant after adjustment for plasma triglyceride (TG) levels. The difference in LDL diameter between the P207L and the D9N carriers was 3-fold greater in individuals with plasma TG levels >3.5 mmol/L than in subjects with TG ≤3.5 mmol/L. The factors that statistically contributed to LDL particle size variation in multivariate analyses were plasma TG levels (11.6%) and age (6.4%) in subjects with TG levels ≤3.5 mmol/L and HDL cholesterol levels (15.5%) and the LPL gene mutation (null versus defective, 7.0%) in patients with TG levels >3.5 mmol/L.

Conclusions—These results suggest that the null P207L mutation in the LPL gene has a greater impact on LDL particle size than the defective D9N mutation and that this mutation-specific effect is amplified at greater plasma TG concentrations. (Arterioscler Thromb Vasc Biol. 2002;22:1181-1186.)

Key Words: lipoprotein lipase ■ gene ■ defects ■ LDL particle size ■ lipoproteins

The main cholesterol transporting particles in human plasma, LDLs are heterogeneous with respect to size, density, composition, and physicochemical properties.1 A number of cross-sectional and prospective case-control studies have examined the relationship between LDL heterogeneity and the risk of coronary heart disease (CHD).2–4 Results from these studies have demonstrated that small, dense LDL particles were more common in individuals with CHD than in control subjects. Population-based prospective data from the Québec Cardiovascular Study have recently confirmed that the presence of small, dense LDL particles predicted subsequent coronary disease events.5 Variations in LDL particle size are closely interrelated with concomitant variations in plasma triglyceride (TG) and HDL cholesterol levels.6–8 For that reason, it has been difficult to dissect the individual contribution of each of these metabolic risk factors to CHD risk. Nevertheless, results from the Québec Cardiovascular Study have indicated that the association between reduced LDL particle size and the risk of future cardiovascular events may be independent of variations in plasma TG and HDL cholesterol levels.5

It must be stressed that LDL particle size and plasma TG levels, although significantly correlated with one another, share a variance of less than 50%.9 Thus, as much as half of the variance in LDL particle size may be attributed to factors other than plasma TG concentrations, such as genetic or other metabolic parameters. Because of its pivotal role in intravascular lipoprotein and TG metabolism, LPL has been considered a potentially important candidate gene in the expression of the LDL particle size phenotype.10 The Saguenay-Lac-St-Jean region in the province of Québec in Canada is characterized by a particularly high frequency of familial LPL deficiency.11 The P207L mutation in the LPL gene has been referred to as a null mutation because of a complete loss of plasma postheparin LPL activity in the homozygous P207L carriers.12 Heterozygous carriers of the P207L mutation usually show a deteriorated lipid profile that includes elevated plasma TG levels and decreased HDL cholesterol concentrations.13 There are several other common structural variants in the LPL gene, which have been shown to have a more modest effect on LPL lipolytic function.14 One of these mutations, the D9N mutation, has been associated with a

Received March 21, 2002; revision accepted April 22, 2002.

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Arterioscler Thromb Vasc Biol is available at http://www.atvbaha.org

DOI: 10.1161/01.ATV.0000020677.33243.1C
marginal-to-substantial increase in plasma TG levels. Site-directed mutagenesis and expression studies demonstrated that the activity and mass in the media from cells transfected with LPL-N9 was approximately 20% to 30% less than that from LPL-D9-transfected cells. Thus, LPL is partially expressed in the homozygous carriers of the D9N mutation and, based on this, the D9N mutation is referred to as a defective mutation.

Preliminary data from one family have indicated that LPL heterozygosity may be associated with small LDL particles and that mutations in the LPL gene may be a relatively prevalent cause of the small, dense LDL particle phenotype. The aim of the present study was therefore to examine and compare the impact of the null P207L and defective D9N mutation in the LPL gene on LDL particle size by using a large sample of heterozygous LPL-deficient French Canadians. The concomitant contribution of plasma TG in modulating LDL particle size among carriers of different LPL mutations was also of particular interest.

Methods

Description of the Subjects
A sample of 206 unrelated patients (109 men and 97 women) bearing a defect in the LPL gene was recruited from a pool of patients referred to the Chicoutimi Hospital Lipid Clinic for dyslipidemia. All patients were participants in the Quebec LIPD (Lipoprotein Lipase Deficiency) Study and were from the Saguenay-Lac-St-Jean region, located in the northeastern part of the province of Quebec, Canada. These subjects were heterozygous carriers for either the null P207L (N=88) or the defective D9N (N=118) mutations in the LPL gene. Participants had to be off lipid-lowering therapy for a minimum of 6 weeks before evaluation. All participants gave their written consent to participate in this study, which received the approval from local ethics committees.

Clinical Data
Medical and nutritional histories in carriers of the D9N and P207L mutations in the LPL gene were obtained through questionnaires. Physical exams were performed at the Chicoutimi Hospital Lipid Clinic by trained nurses and physicians. Body mass index (BMI) and waist circumference were measured by using standardized procedures. Postmenopausal status was assigned to women who did not have menses during the year that preceded the study. Among postmenopausal women under hormonal replacement therapy, approximately 89% were taking oral estrogen, 10% as patch, and ~1% as gel. Subjects were considered to have type 2 diabetes if a diagnosis of diabetes had been previously established or if two fasting glucose values >7.8 mmol/L or a glycemia >11.1 mmol/L 2 hours after a standardized 75-g oral glucose tolerance test had been recorded in the medical chart. Medication use refers to the use of diuretics and β-blockers because all subjects were not using hypolipidemic medication at time of evaluation. Smoking habits were categorized into two groups: 1) patients who had never smoked and 2) smokers or ex-smokers.

Mutations in the LPL Gene
Subjects were screened for the presence of mutations in the LPL gene after their informed, written consent had been obtained. The P207L mutation in the LPL gene was detected by a mismatch-Polymerase chain reaction (PCR)-based approach followed by digestion with the restriction enzyme DdeI. The D9N mutation in the LPL gene was detected by standard PCR followed by digestion with the enzyme TaqI, as previously described. The detection of the −93T/G mutation was performed as previously described.

Results

Table 1 compares the characteristics of carriers of the null P207L and defective D9N mutations. D9N carriers were older than subjects bearing the P207L mutation (P=0.003), while body weight, BMI, and waist circumference were comparable between the two groups. Smoking habits and the prevalence of type 2 diabetes and apoE genotype were also similar between the two groups. Among heterozygous carriers of the D9N mutation, 92.2% were also carriers of the −93T/G mutation in the LPL gene, whereas only 1 heterozygote for the P207L mutation had the −93T/G mutation (1.1%, P=0.001). There were more women in proportion among carriers of the P207L mutation although this difference did not reach statistical significance (P=0.12). Carriers of the P207L mutation tended to have a more atherogenic lipoprotein lipid profile compared with carriers of the D9N mutation.

Statistical Analyses

Unless otherwise specified, variables with a skewed distribution were presented as geometric means ± SD and were log-transformed for analysis. Age, weight, BMI, waist girth, and all lipid variables in carriers of both mutations were treated as continuous variables and compared with the Student t test. Nonparametric variables were compared with the χ² test. The Spearman rank test was used for univariate correlation analyses. Multivariate analyses were conducted to identify the determinants of LDL particle size by using general linear model analysis. A subanalysis was conducted in a sample of 60 carriers of the P207L mutation individually matched one to one with 60 carriers of the D9N mutation on the basis of their maximal within-pair difference in plasma TG levels was ±0.3 mmol/L, ensuring a similar distribution of plasma TG levels within the two groups. Statistical analyses were performed with the SAS package from SAS Institute.

LDL Particle Size Characterization
Non-denaturing 2% to 16% polyacrylamide gradient gels (8×8 cm) prepared in batches in our laboratory were used to determine LDL particle size by using a modification of a procedure described previously. Briefly, aliquots of 3.0 μL of whole plasma samples were mixed 1:1 with a sampling buffer containing 20% sucrose and 0.25% bromophenol blue. A 15-minute pre-run at 75V preceded the electrophoresis of plasma samples at 150V for 3 hours. Gels were stained with 0.07% Sudan black for 1 hour and stored in a 0.81% acetic acid, 4% methanol solution until analysis. Gels were analyzed using the Imagemaster 1-D Prime computer software (Pharmacia LKB), and LDL particle size was computed based on the relative migration of plasma standards of known diameter. A mean LDL particle size was obtained by integrating the relative contribution of each subclass of LDL for a given subject. Analysis of pooled plasma standards revealed that measurement of LDL particle size was highly reproducible with an interassay coefficient of variation <1%.

Plasma Lipid-Lipoprotein Measurements
Blood was drawn in tubes containing 0.15% EDTA after a 12-hour fast, and plasma was isolated by centrifugation (2500 rpm at 4°C for 15 minutes). Cholesterol and TG levels in plasma as well as in lipoprotein fractions isolated by sequential ultracentrifugation (subgroup of subjects only) were analyzed by standard enzymatic methods. HDL cholesterol was measured in the supernatant fraction after precipitation of apolipoprotein (apo) B-containing lipoproteins with dextran sulfate and magnesium chloride. Plasma LDL cholesterol levels were estimated with the Friedewald formula when TG levels were <4.5 mmol/L. Plasma apoB levels were measured by the rocket immunoelectrophoresis method of Laurell as reported. The apoE genotype was determined by using the procedure described by Hixson and Vernier.

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TABLE 1. Characteristics of Heterozygous Carriers of the P207L or D9N Mutations in the LPL Gene

<table>
<thead>
<tr>
<th>Mutations in the LPL Gene</th>
<th>P207L (N=88)</th>
<th>D9N (N=118)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>46.4±12.6</td>
<td>51.4±10.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>72.3±13.3</td>
<td>73.8±14.4</td>
<td>0.46</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.4±3.6</td>
<td>27.5±4.8</td>
<td>0.93</td>
</tr>
<tr>
<td>Waist circumference, cm²</td>
<td>89.6±1.1</td>
<td>91.4±1.1</td>
<td>0.24</td>
</tr>
<tr>
<td>Smokers and ex-smokers, %</td>
<td>64.1%</td>
<td>69.2%</td>
<td>0.45</td>
</tr>
<tr>
<td>Type II diabetes, %</td>
<td>16.3%</td>
<td>16.9%</td>
<td>0.90</td>
</tr>
<tr>
<td>%APOE Genotype*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x2</td>
<td>31.3%</td>
<td>25.7%</td>
<td></td>
</tr>
<tr>
<td>x3</td>
<td>43.4%</td>
<td>56.9%</td>
<td>0.16</td>
</tr>
<tr>
<td>x4</td>
<td>25.3%</td>
<td>17.4%</td>
<td></td>
</tr>
<tr>
<td>−93T/G mutation carriers, †%</td>
<td>1.1%</td>
<td>92.2%</td>
<td>0.001</td>
</tr>
<tr>
<td>Menopausal women, %</td>
<td>63.8%</td>
<td>76.0%</td>
<td>0.19</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>41/47</td>
<td>68/50</td>
<td>0.12</td>
</tr>
<tr>
<td>Hormonal therapy, †%</td>
<td>83.3%</td>
<td>65.8%</td>
<td>0.10</td>
</tr>
<tr>
<td>Plasma cholesterol, mmol/L</td>
<td>7.0±1.4</td>
<td>6.3±1.3</td>
<td>0.04</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L§</td>
<td>3.0±1.3</td>
<td>3.7±1.1</td>
<td>0.004</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>0.77±1.47</td>
<td>0.96±1.56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Plasma TG, mmol/L</td>
<td>5.8±2.7</td>
<td>2.9±2.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL TG, mmol/L§</td>
<td>0.49±1.62</td>
<td>0.42±1.56</td>
<td>0.06</td>
</tr>
<tr>
<td>LDL apoB, g/L¶</td>
<td>0.86±1.32</td>
<td>0.95±1.31</td>
<td>0.03</td>
</tr>
<tr>
<td>LDL TG/LDL apoB, g/L¶</td>
<td>0.58±1.65</td>
<td>0.44±1.47</td>
<td>0.001</td>
</tr>
<tr>
<td>Plasma apoB, g/L¶</td>
<td>1.18±1.28</td>
<td>1.18±1.28</td>
<td>0.92</td>
</tr>
<tr>
<td>HDL particle size, Å²</td>
<td>81.8±1.0</td>
<td>82.6±1.0</td>
<td>0.19</td>
</tr>
<tr>
<td>LDL particle size, Å²</td>
<td>248.8±1.0</td>
<td>254.5±1.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are expressed as means±SD. *Values are expressed as geometrical means±SD.

* x2 corresponds to homozygous or heterozygous carriers of the x2 allele; x3 corresponds to homozygous or x3/x3; x4 corresponds to homozygous or heterozygous carriers of the x4 allele (N=83 in the P207L group and N=109 in the D9N subjects).
†N=88 (P207L) and 115 (D9N).
‡This percentage is function of the number of menopausal women in each group.
§N=47 (P207L) and N=95 (D9N). †N=61 (P207L) and N=75 (D9N).
¶N=59 (P207L) and N=74 (D9N); ‡N=77 (P207L) and N=91 (D9N).

in the LPL gene. Accordingly, LDL particle size was significantly smaller in the P207L carriers than in the D9N subjects (248.8±1.0 vs 254.5±1.0 Å, P<0.001), and the difference remained highly significant (P=0.0001) after a correction for age and sex (not shown).

Table 2 presents the results of univariate correlations between LDL particle size and other variables among the P207L and D9N mutation carriers. With the exception of plasma LDL TG levels, the associations between LDL particle size and other metabolic variables tended to be similar between the two groups. Plasma TG and HDL cholesterol levels were the best univariate correlates of LDL particle size, in both the P207L and the D9N heterozygous carriers. In a multivariate stepwise regression model that included age and log₁₀-transformed waist girth, LDL particle size, and plasma cholesterol, TG, and HDL cholesterol levels as independent variables, plasma TG (P207L, 7.8%; D9N, 3.5%; P<0.05) and HDL cholesterol levels (P207L, 26.1%; D9N, 16.5%; P<0.001) were the only significant multivariate correlates of LDL particle size among the P207L carriers as well as among the D9N group (not shown).

Because, as in other populations, plasma TG levels were a strong correlate of LDL particle size in this LPL deficiency cohort, and because plasma TG levels were significantly different between carriers of the P207L and D9N mutation in the LPL gene, the impact of each mutation on LDL particle size was investigated while controlling for variations in TG by using different analytical approaches. First, the P207L and D9N carriers were categorized into two subgroups (Figure) by using an arbitrary TG cutpoint of 3.5 mmol/L, which corresponded to the median of the TG level distribution in the entire study group. The difference in mean LDL particle size between the D9N and the P207L carriers was 3-fold greater in subjects with plasma TG concentrations >3.5 mmol/L compared with the difference among those having TG levels

![LDL particle size as a function of plasma TG levels](https://example.com/ldl-tg.png)
The mean TG concentration was similar between the D9N and P207L carriers among subjects with TG levels ≤3.5 mmol/L (1.9±0.1 mmol/L for both groups, P=0.9) as well as among subjects with TG levels >3.5 mmol/L (10.7±2.0 and 12.6±1.4 mmol/L, respectively, P=0.4). Thus, the difference in LDL particle size between the P207L and D9N carriers with TG levels >3.5 mmol/L could not be explained by differences in plasma TG levels. A subanalysis (N=18 for the P207L carriers and N=43 for the D9N carriers) was performed to compare LDL particle size between carriers of the D9N and P207L mutations among individuals within normal TG limits (≤2 mmol/L). LDL particle size remained significantly lower among the P207L carriers compared with the D9N carriers (255.1±1.0 vs 259.3±1.0 Å, P=0.02), and this difference remained significant even after further adjustment for plasma TG levels (data not shown). Multivariate analyses were also conducted to identify the correlates of LDL particle size among all subjects presenting TG levels below and above 3.5 mmol/L (Table 3). In subjects with TG levels below 3.5 mmol/L, age (P=0.05) and plasma TG levels (P=0.01) were significant multivariate correlates of LDL particle size. The multivariate determinants of LDL particle size in subjects with plasma TG levels >3.5 mmol/L were HDL cholesterol levels (P=0.002) as well as the LPL gene mutation (P207L or D9N, P=0.03).

The impact of the null and defective mutations on LDL particle size was also investigated after matching 60 carriers of the P207L mutation and 60 D9N heterozygotes for plasma TG levels (Table 4). Body weight and waist circumference were higher among the D9N heterozygous carriers than the TG-matched subjects bearing the P207L mutation (P=0.04 and P=0.02, respectively). The difference in the proportion of women among carriers of the P207L and D9N mutations was not significant (P=0.2). The lipoprotein lipid profile, including plasma apoB levels (P=0.30), was similar between TG-matched carriers of the P207L and D9N mutations in the LPL gene. However, pairing for plasma TG levels did not eliminate the difference in LDL particle size between the P207L and D9N carriers (251.2±1.0 vs 253.9±1.0 Å, respectively, P=0.04). Further adjustment for sex had no significant impact on this TG-adjusted difference in LDL particle size (P=0.04).

Discussion
To the best of our knowledge, this is the first study to have investigated and compared the impact of a variant in the LPL gene (P207L) versus one not causing (D9N) a complete loss of plasma postheparin LPL activity in the homozygous state on LDL particle size. The presence of the P207L null mutation in the LPL gene was associated with a greater reduction in LDL particle size compared with the D9N defective mutation. These data are consistent with data obtained from Hokanson et al17 who showed evidence of genetic linkage of small LDL particles to LPL gene in heterozygous lipase deficiency. Plasma TG levels has been identified as the single best metabolic correlate of LDL particle size in several populations.4,6–8 In the present study, LDL particle sizes averaged 251.7 Å, a value that was markedly lower when compared with the mean LDL size of 2536 individuals without primary dyslipidemia who were investigated as part of other research projects conducted in our laboratory (mean LDL size, 257.3±4.7 Å, with values ranging from 239.8 to 274.7 Å). This is not a surprising observation because plasma TG levels were markedly elevated in these LPL-deficient individuals. As shown in previous studies, we found a strong linkage disequilibrium between the LPL D9N variant and the LPL −93 variant suggesting the possibility that elevated plasma TG levels and LDL particle size associated with the D9N mutation may have been attributed to some extent to the functional effect of the −93 polymorphism.21 In fact, whether it is the D9N

<table>
<thead>
<tr>
<th>Variables</th>
<th>Plasma TG</th>
<th>% Variance</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3.5 mmol/L (N=103)</td>
<td>11.6%</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>6.4%</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>&gt;3.5 mmol/L (N=103)</td>
<td>15.5%</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>LPL gene mutation (P207L vs D9N)</td>
<td>7.0%</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

The model included the following variables at entry: sex; LPL gene mutation; age; and log10-transformed plasma cholesterol, TG, and HDL cholesterol levels, HDL particle size, and waist girth.

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mutation, the −93T/G mutation, or the combination of the 2 that contributes to the increased plasma TG levels among D9N carriers remains unsettled.27

Our data also suggested that the correlates of LDL particle size were similar between carriers of the P207L and D9N mutations, plasma TG, and HDL cholesterol levels showing the strongest and most significant univariate correlations with LDL particle size in the two groups of subjects. These data suggest that the strongest metabolic correlates of LDL particle size among heterozygous carriers of mutations in the LPL gene are the same as those generally observed among noncarriers of LPL mutations.4,6,8 Among subjects within normal TG level limits, carriers of the null P207L mutation still presented smaller LDL particle size than carriers of the defective D9N mutation. However, the LPL mutation–specific impact on LDL particle size appeared to be amplified among subjects characterized by a marked increase in plasma TG levels. Indeed, the P207L mutation was associated with an even greater reduction in LDL particle size compared with the D9N mutation among individuals with plasma TG values >3.5 mmol/L. Consequently, the nature of the LPL defect (null versus defective) was an important predictor of LDL particle size among individuals characterized by a marked hypertriglyceridemia, independent of plasma TG levels and HDL metabolism. Because plasma TG levels were higher among the P207L heterozygous carriers compared with the D9N heterozygous carriers, we have investigated further whether the nature of the mutation in the LPL gene could still modulate LDL particle size after adjustment for plasma TG levels. LDL particle size remained significantly smaller in the P207L carriers compared with the D9N subjects after matching for plasma TG levels. These results suggested that the LPL mutation–specific effect on LDL diameter was independent of concomitant variations in plasma TG levels. Taken together, results from the present study suggest that there is a LDL mutation–specific impact on LDL particle size, the null mutation resulting in smaller LDL particles than the defective mutation.

The mechanisms leading to these differences in LDL size among heterozygous carriers of null and defective mutations in the LPL gene have yet to be identified. The cholesteryl ester transfer protein (CETP)-mediated exchange of TG from VLDL for cholesteryl esters from LDL and the hydrolysis of the resulting TG-enriched LDL by hepatic lipase (HL) are two of the key pathways through which the size and density of LDL particles are modulated. Results obtained by Bijvoet et al28 demonstrated that even with an increased number of VLDL and LDL particles, heterozygous carriers of the P207L mutation had near normal CETP activity. However, the magnitude of the hypertriglyceridemia has been identified as an important determinant of the rate of lipid transfer among lipoproteins through the action of CETP.29,30 Results from the present study are consistent with these observations. Indeed, subanalysis in a restricted number of subjects (N = 136) indicated that plasma LDL TG levels were 17% higher in heterozygotes for the null P207L mutation in the LPL gene than in carriers of the defective D9N mutation (P = 0.06). This increased LDL TG concentration among P207L carriers could not be attributed to an increase in the number of LDL particles because the LDL TG/LDL apoB ratio was significantly higher in this group than among the D9N carriers (P = 0.001). However, as shown above, the difference in LDL particle size between carriers of the null and defective mutations was independent of variations in plasma TG levels. This led us to hypothesize that variation in HL activity among the two groups of LPL mutation carriers may have played a key role in modulating LDL particle size in these individuals. We have recently observed an inverse and highly significant correlation (r = −0.43, P < 0.001) between postheparin LPL and HDL activity in a sample of 504 white males and females (C. Couillard, PhD, unpublished data, 2001). The P207L mutation affects the catalytic triad of the LPL, and in vitro studies have demonstrated the loss of catalytic activity associated with this mutation.12 In contrast, site-directed mutagenesis and expression studies demonstrated that the mutant D9N protein exhibited 20% to 30% less hydrolytic activity and dimeric mass compared with wild-type LPL.15 Thus, the lower LPL activity attributable to the P207L mutation compared with the D9N mutation may have been compensated by an increased HL activity. This metabolic adaptation, combined with an enrichment of LDL with TG, may have been responsible to a large extent for the increased susceptibility of carriers of the P207 mutation to having small dense LDL particles compared with D9N carriers, particularly at very high plasma TG concentrations. Further investigations are clearly warranted to validate these hypotheses. The nonlipolytic roles of LPL, such as that of a ligand,31 should also be considered in the study of the metabolic pathways leading to variations in LDL particle size among carriers of different mutations in the LPL gene.

Results of the present study indicated that the metabolic correlates of LDL particle size were similar between carriers of the null P207L and defective mutations in the LPL gene. However, heterozygous carriers of the P207L mutation were characterized by smaller particles than heterozygous carriers of the D9N mutation, and LDL particle size remained significantly smaller in the P207L carriers than in the D9N subjects after adjustment for plasma TG levels. These results suggest that a null mutation in the LPL gene had a greater impact on LDL particle size than a defective mutation, independent of TG levels. The impact of these observations on the risk of CHD among carriers of different mutations in the LPL gene remains to be established.

Acknowledgments

L.L. Ruel is a recipient of a partnership training award from the HFSC/CHHR. B. Lamarche is the recipient of the Canada Research Chair in Nutrition, Functional Foods and Cardiovascular Health. D. Gaudet is the holder of the Canada Research Chair in Preventive Genetics and Community Genomics. This research was supported in part by the Fonds de la Recherche en Santé du Québec (FRSQ) and Hydro-Québec.

References


Characterization of LDL Particle Size Among Carriers of a Defective or a Null Mutation in the Lipoprotein Lipase Gene: The Québec LIPD Study
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Arterioscler Thromb Vasc Biol. 2002;22:1181-1186; originally published online May 2, 2002;
doi: 10.1161/01.ATV.0000020677.33243.1C

Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1079-5642. Online ISSN: 1524-4636

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