Fasting Lipoprotein Lipase Protein Levels Can Predict a Postmeal Increment of Triglyceride Levels in Fasting Normohypertriglyceridemic Subjects

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Background: Although a postprandial increment in triglyceride (TG) levels is considered to be a risk factor for atherogenesis, tests (e.g., fat load) to assess postprandial changes in TG levels cannot be easily applied to clinical practice. Therefore, fasting markers that predict postprandial TG states are needed to be developed. One current candidate is lipoprotein lipase (LPL) protein, a molecule that hydrolyzes TGs. This study investigated whether fasting LPL levels could predict postprandial TG levels. **Methods:** A total of 17 subjects (11 men, 6 women, mean age 52 ± 11 years) with normotriglyceridemia during fasting underwent the meal test. Several fasting parameters, including LPL, were measured for the area under the

curve of postprandial TGs (AUC-TG). **Results:** The subjects' mean fasting TG level was 1.30 mmol/L, and their mean LPL level was 41.6 ng/mL. The subjects' TG levels increased after loading (they peaked after two postprandial hours). Stepwise multiple regression analysis demonstrated that fasting TG levels were a predictor of the AUC-TG. In addition, fasting LPL mass levels were found to be a predictor of the AUC-TG ($\beta = 0.65$, $P < 0.01$), and this relationship was independent of fasting TG levels. **Conclusion:** Fasting LPL levels may be useful to predict postprandial TG increment in this population. *J. Clin. Lab. Anal.* 30:404–407, 2016.

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Key words: cardiovascular disease; hypertriglyceridemia; lipoprotein lipase; meal test; postprandial

INTRODUCTION

Circulating triglyceride (TG) levels are known to be elevated after the meals, and postprandial hypertriglyceridemia has been identified as a risk factor for atherogenesis (1). However, difficulties have been reported with conducting such meal tests to assess postprandial hypertriglyceridemia in clinical practice. Therefore, fasting markers that can predict postprandial TG states are needed to be developed. Lipoprotein lipase (LPL) is a key enzyme that plays a key role in the metabolism of TGs (2,3). However, LPL activities are typically measured following heparin injection, which is often unfeasible in clinical practice.

Recently, it has become possible to measure plasma and serum LPL mass levels in the absence of heparin (preheparin LPL mass levels) (4,5). The development of this method has facilitated studies into TG-related

pathologies. In fact, several studies have examined the utility of measuring preheparin LPL mass levels as a way of elucidating the lipid metabolism profiles of patients with hyperchylomicronemia (6,7) or coronary heart disease (8), or examining TG catabolism in patients with hypertriglyceridemia (9). Although LPL mass levels are generally considered to be linked with TG levels (2,3), the changes seen in LPL mass and TG levels are not always consistent (10,11). Therefore, it would be useful to

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clarify the relationships between LPL markers and lipid metabolism. In particular, fasting LPL mass levels might be helpful for predicting the postprandial increase in TG levels. We here investigated the potential of fasting LPL mass levels to postprandial TG changes using the meal test.

MATERIALS AND METHODS

A total of 17 subjects with normotriglyceridemia with fasting (<1.68 mmol/l of TG levels) were enrolled in this study, which was approved by the Ethics Committee of the Kyoto Medical Center. All subjects gave informed consent. Subjects who had a history of cardiovascular disease or viral hepatitis were excluded. None of the subjects were taking medications that affected TG levels.

Blood was sampled after an overnight fast. Body mass index (BMI) and blood pressure were measured before the meal test. Serum total cholesterol, TG, and HDL-cholesterol levels (where HDL is high-density lipoprotein) were measured enzymatically (Kyowa Medex Co., Ltd., Tokyo, Japan). Plasma glucose levels were also measured enzymatically (Arkray, Inc., Kyoto, Japan). Sera were diluted at a 100-fold level and then, LPL mass levels were measured using a sandwich enzyme-linked immunosorbent assay (Immuno-Biological Laboratories Co., Ltd., Gunma, Japan). Current smokers were defined as those with a current smoking habit by a self-report.

Meal Test C® (Saraya Co., Ltd., Osaka, Japan; cookie test) was used for the meal test in the present study (12). This test used cookies, which consisted of 75 g carbohydrates (85% flour starch and 15% maltose), 28.5 g butter fat, and 8.0 g protein for a total of 592 kcal (one pack). Cookies were ingested with water, and blood samples were obtained 0, 1, 2, and 4 hr later. The area under the curve of postprandial TG levels (AUC-TG) was then calculated.

Initially, Kolmogorov–Smirnov test examined a normality of each parameter, and then all parameters were confirmed to be normally distributed. Differences between groups were analyzed by using unpaired *t*-test. Correlations between AUC-TG and other parameters were examined by using Pearson's correlation coefficient test and a stepwise multiple linear regression analysis (that considered age, gender, BMI, systolic blood pressure, fasting plasma glucose, total cholesterol, TG, HDL-cholesterol, LPL, and current smoking). $P < 0.05$ was accepted as significant.

RESULTS

Table 1 shows the clinical data of the study subjects. Current smokers were 12.2%. There were no significant differences in the LPL levels (men, 42.6 ± 26.8 vs. women, 39.9 ± 15.0 ng/ml; $P = 0.83$) and AUC-TG (men, 583 ± 220 vs.

TABLE 1. Clinical Data of the Study Subjects

	Data
Age (years)	52 ± 11
BMI (kg/m^2)	24.8 ± 2.8
Men/women (number)	11/6
Smoking (%)	12.0
Systolic blood pressure (mmHg)	137 ± 13
Fasting plasma glucose (mmol/l)	6.1 ± 1.2
Total cholesterol (mmol/l)	5.33 ± 1.47
TG (mmol/l)	1.30 ± 0.30
HDL-cholesterol (mmol/l)	1.47 ± 0.41
LPL (ng/ml)	41.6 ± 22.8
AUC-TG	607 ± 191

Values are number, percentage, or means $\pm$ standard deviation.

Fig. 1. Reaction curve of serum triglyceride levels after postprandial state.

women, 650 ± 126 ; $P = 0.51$) between genders. Women (1.50 ± 0.20 mmol/l) exhibited significantly higher TG levels than the men (1.17 ± 0.30 mmol/l; $P = 0.01$). As shown in Figure 1, the subjects' postprandial TG levels increased over time and peaked at two postprandial hours (2 hr, 2.14 ± 0.66 mmol/l; 4 hr, 2.12 ± 0.96 mmol/l).

As shown in Table 2, the subjects' systolic blood pressure levels and fasting TG and HDL-cholesterol levels were significantly correlated with their AUC-TG. In addition, a weak inverse correlation was detected between the subjects' fasting TG and LPL mass levels ($r = -0.13$, $P = 0.63$), although it was not significant.

As shown in Table 3, fasting TG levels and smoking were found to be predictors of the AUC-TG in a stepwise multiple regression analysis. Furthermore, fasting LPL mass levels were demonstrated to be a predictor of the AUC-TG, and this relationship was independent of fasting TG levels.

TABLE 2. Pearson's Correlation Coefficients of Fasting Values of the Measured Parameters With AUC-TG

Parameters	<i>r</i>	<i>P</i>
Age (years)	0.35	0.17
Gender (men)	-0.23	0.38
BMI (kg/m ²)	0.11	0.69
Smoking (current habit)	0.373	0.14
Systolic blood pressure (mmHg)	0.55	0.02*
Fasting plasma glucose (mmHg)	0.10	0.71
Total cholesterol (mmol/l)	0.27	0.30
TG (mmol/l)	0.62	0.01*
HDL-cholesterol (mmol/l)	-0.40	0.11
LPL (ng/ml)	0.51	0.04*

P, probability value.

*P < 0.05.

TABLE 3. A Stepwise Multiple Regression Analysis for the Area Under the Curve of Postprandial Triglyceride Levels

Independent parameters	β	<i>P</i>
TG	0.71	<0.01**
LPL	0.65	<0.01**
Smoking	0.34	0.01*

β , standardized regression coefficient; *P*, probability value.

The following parameters were used: age, sex, systolic blood pressure, BMI, fasting plasma glucose, total cholesterol, TG, HDL-cholesterol, LPL, smoking.

*P < 0.05; **P < 0.01.

DISCUSSION

Fasting LPL levels, in addition to fasting TG levels and current smoking, were independently, significantly, and positively predictive of postprandial TG increment among fasting normotriglyceridemic subjects. Cardiovascular events are associated with postprandial TG increment (1, 13–17), while postprandial hypertriglyceridemia is not easily detectable in daily practice (15, 16). Fasting TG levels have been shown to predict postprandial hypertriglyceridemia (16), and this is supported by the results of the present study. Existing smoking habits have also been found to predict postprandial hypertriglyceridemia (18–21), which is consistent with the results of the present study. So, smoking can contribute to TG-rich lipoproteins formation and release from the liver, and thus provide a metabolic mechanism for atherogenesis (18).

Simple markers (i.e., those obtained during fasting) that can be used to predict postprandial hypertriglyceridemia are required, as the postprandial TG state is clinically important, but it is difficult to conduct examinations involving meal loading and frequent blood tests. Thus, it is important to elucidate the clinical significance of the one-time measurement of fasting LPL mass levels as a simple marker.

LPL activities promote TG clearance in the circulation and are regulated during fasting at the posttranslational levels via a shift in extracellular LPL toward an inactive form (22). We speculated that low LPL mass levels might predict large increases in postprandial TG levels, but no evidence of this was obtained in the present study. Instead, our findings (opposite to the speculation) suggest that LPL levels might be increased during fasting as a compensatory mechanism in individuals that tend to exhibit increased postprandial TG levels or disturbed LPL levels. Fasting LPL mass levels are also known to be controlled by several LPL-related molecules, such as angiopoietin-like protein 4 (23–25). The mechanistic issues merit further investigations.

The present study had some limitations. First, we only examined a small number of subjects. In addition, this study did not assess the levels of other TG-related markers (e.g., free fatty acids) or cardiovascular parameters. Thus, the present study is only preliminary, and its limitations should be addressed in future.

In summary, fasting LPL mass levels may be useful as a predictor of postprandial TG increment in fasting normotriglyceridemic subjects, and fasting LPL mass is a simply easy-to-use marker that can be applied to clinical practice. However, further studies, especially of the mechanisms responsible for the positive association between fasting LPL mass levels and the postprandial TG levels, are required to confirm the results of this study.

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