# Impact of serum levels of lipoprotein lipase, hepatic lipase, and endothelial lipase on the progression of coronary artery disease

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## ABSTRACT

*Purpose:* The purpose of this study was to investigate the relationship between serum levels of lipoprotein lipase (LPL), hepatic lipase (HL), and endothelial lipase (EL) and the progression of coronary artery disease (CAD).
*Materials and methods:* According to the inclusion criteria, exclusion criteria, diagnostic criteria, angiography results, and the random matching scheme, the enrolled patients were divided into the following two groups: the progression-free group (n = 47) and the progression group (n = 15). The baseline characteristics and various biochemical parameters were obtained from the medical records and medical history. Serum LPL, HL, and EL levels were detected by ELISA. The correlation between serum LPL, HL, and EL levels and coronary lesions was statistically analyzed with SPSS software.
*Results:* Significant differences were observed in serum levels of HL and EL between the progression-free group and the progression group (HL, $75.5 \pm 39.2$ ng/mL vs. $125.1 \pm 42.1$ ng/mL, $P < 0.05$; EL, $139.2 \pm 59.6$ pg/mL vs. $175.1 \pm 40.1$ pg/mL, $P < 0.05$), while the difference in the LPL level was not significant ($P > 0.05$). Receiver operating characteristic curve (ROC) analysis showed that the area under the curve (AUC) values of LPL, HL, and EL were 0.506 (95% CI: 0.369–0.642, $P = 0.9470$), 0.792 (95% CI: 0.664–0.888, $P < 0.0001$), and 0.693 (95% CI: 0.553–0.811, $P = 0.0095$), respectively. Additionally, logistic regression analysis showed that the serum level of HL was an independent risk factor for coronary artery lesion progression.
*Conclusion:* Serum levels of EL and HL, but not the serum level of LPL, were positively correlated with the progression of CAD. The serum level of HL was an independent risk factor for the progression of CAD, while the serum level of EL or LPL was not an independent risk factor for the progression of CAD. For the diagnosis of CAD progression, the serum level of HL was better than the serum level of EL or LPL.

## 1. Introduction

Atherosclerosis (AS) is a key pathological characteristic of coronary artery disease (CAD). The link between disorder of lipid metabolism and atherosclerotic cardiovascular disease has been frequently established.[1–3] Accordingly, lipid lowering, especially decreasing the level of low-density lipoprotein (LDL), has become a cornerstone of treatment strategies for reducing the incidence of cardiovascular events. Despite the widespread use of these therapies, there remains a considerable residual risk of cardiovascular events.

Recent studies have shown that triglyceride-rich lipoproteins (TRLs), mainly including chylomicron (CM) and very low-density lipoprotein (VLDL), have pro-AS effects, but they failed to confirm that the elevated fasting or postprandial triglyceride (TG) level is an independent risk factor for CAD since TRL disorders were often accompanied by LDL and high-density lipoprotein (HDL) metabolic abnormalities.[4–6] Many patients suffered from residual risks although therapies for lowering LDL and/or increasing HDL were administered for the prevention of cardiovascular diseases. Additional treatment aimed at reducing the TG level could further reduce the risk of cardiovascular events.

Lipoprotein lipase (LPL), hepatic lipase (HL), and endothelial lipase (EL), members of the family of triglyceride lipases, are not only important catalytic enzymes in lipoprotein metabolism, but they also play a vital role in the regulation of vascular local immune inflammatory processes

deeply involved in AS progression.[7,8] The purpose of this study was to investigate the relationship between serum levels of LPL, HL, and EL and the progression of AS in patients suffering from CAD.

## 2. Methods

The study was conducted in accordance with the principles of the Declaration of Helsinki, and it was approved by the Ethics Review Committee of Rui Jin Hospital, Shanghai Jiao Tong University School of Medicine. Written informed consent was obtained from all of the subjects prior to their inclusion in the study.

### 2.1. Study population

This was a cross-sectional study that consecutively enrolled a total of 184 patients with CAD confirmed by selective coronary angiography (CAG) at the coronary intervention center of Rui Jin Hospital, Shanghai Jiao Tong University School of Medicine. The group consisted of patients who fulfilled the following criteria: age ≥18 years, two or more CAGs within 12–24 months, and comprehensive clinical data. Patients with coronary artery bypass grafting (CABG), valvulopathy, idiopathic cardiomyopathy, or significant concomitant diseases (cancer, infections, severe hepatic or renal insufficiency, type 1 diabetes, thyroid disorders, disturbance of consciousness, and autoimmune diseases) were excluded.

According to CAG results, a total of 20 patients were diagnosed with in situ coronary plaque progression. Among these 20 patients, serum samples were obtained from 15 cases; and these 15 cases were enrolled in the progression group. On the basis of propensity score matching (1:3), a total of 47 patients were included in the progression-free group.

### 2.2. Coronary angiography

Selective coronary angiography was performed through the radial or femoral artery approach, and the findings were interpreted by at least two experienced cardiologists blinded to the study protocol.

On comparing CAG examinations, in situ coronary atherosclerotic plaque progression was diagnosed if the results fulfilled one of the following criteria: (1) if a major epicardial coronary artery showed luminal diameter narrowing ≥ 50%, and a further narrowing ≥ 10% was noted, (2) if a major epicardial coronary artery showed luminal diameter narrowing ≤ 50%, and a further narrowing ≥ 30% was noted, (3) newly emerging major epicardial coronary artery narrowing ≥ 30% was noted, and (4) complete occlusion of a major epicardial coronary artery with luminal diameter narrowing was noted.

### 2.3. Biochemical investigation

From each enrolled subject, blood samples were collected after overnight fasting. All of the samples were analyzed by the laboratory department of Rui Jin Hospital to determine the biochemical profile. Specifically, the levels of serum glucose, TG, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein-cholesterol (LDL-c), HbA1c, serum creatinine (SCr), and uric acid (UA) were measured by a Hitachi 912 Analyzer (Roche Diagnostics, Germany). The remaining samples were centrifuged at 2000 rpm for 20 min to collect the serum samples, which were then stored at −80 °C until further analysis.

### 2.4. Measurement of LPL, HL, and EL

Serum concentrations of LPL, HL, and EL were measured using commercially available human ELISA kits (LPL ELISA Kit, Cat. No.: STA-611, Cell Biolabs Inc., USA; HTGL Serum ELISA Kit, Cat. No.: 27180, IBL International, Japan; EL ELISA Kit, Cat. No.: 27182, IBL International, Japan). Both the intra-batch and inter-batch coefficients of variation were less than 5%. No significant cross-reactivity or interference between these isozymes was observed. LPL, HL, and EL measurements were

performed by an experienced investigator blinded to subjects' clinical information and status.

### 2.5. Statistical analysis

Analysis was carried out with SPSS software (V.19.0, SPSS Inc., USA). Continuous variables are described as mean ± SD for normally distributed data or medians with interquartile ranges (IQR) for non-normally distributed data, as appropriate. Categorical data are summarized as frequencies or percentages. Differences in quantitative parameters between groups were assessed by $t$-test (for normally distributed data) or a non-parametric test (for non-normally distributed data). Logistic regression models were used to determine the factors associated with the presence of in situ coronary atherosclerotic plaque progression. All of the analyses were performed using 2-sided tests, and a P value of <0.05 was considered to be statistically significant.

## 3. Results

### 3.1. Baseline clinical characteristics

Baseline characteristics of the subjects with or without plaque

**Table 1**

**Baseline characteristics of patients in the progression-free and progression groups.** Data are expressed as mean ± SD or frequency counts (percentages), as appropriate. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; HbA1c, glycated hemoglobin; TG, total triglycerides; TC, total cholesterol; HDL-c, high-density lipoprotein-cholesterol; LDL-c, low-density lipoprotein-cholesterol; SCr, serum creatinine; UA, uric acid.

| Variables | Progression-free group (n = 47) | Progression group (n = 15) | P value |
|---|---|---|---|
| Male/Female | 44/3 | 15/0 | NS |
| Age (years) | 61.6 ± 9.34 | 60.3 ± 10.0 | NS |
| BMI (kg/m²) | 25.0 ± 2.9 | 27.0 ± 1.6 | <0.05 |
| Smoking, n (%) | 23 (48.9%) | 10 (66.7%) | NS |
| Hypertension, n (%) | 21 (44.7%) | 13 (86.7%) | <0.05 |
| SBP (mmHg) | 130.0 ± 18.8 | 129.2 ± 16.8 | NS |
| DBP (mmHg) | 74.6 ± 10.0 | 75.9 ± 11.6 | NS |
| Diabetes, n (%) | 26 (55.3%) | 6 (40.0%) | <0.05 |
| FBG (mmol/L) | 5.5 ± 1.3 | 5.9 ± 1.5 | NS |
| HbA1c (%) | 6.3 ± 1.2 | 7.0 ± 1.7 | NS |
| TG (mmol/L) | 1.9 ± 1.4 | 1.8 ± 0.6 | NS |
| TC (mmol/L) | 4.2 ± 0.9 | 4.2 ± 0.9 | NS |
| HDL-c (mmol/L) | 1.0 ± 0.3 | 1.0 ± 0.2 | NS |
| LDL-c (mmol/L) | 2.5 ± 0.8 | 2.5 ± 0.8 | NS |
| SCr (μmol/L) | 89.5 ± 19.0 | 88.4 ± 14.1 | NS |
| UA (μmol/L) | 357.9 ± 67.0 | 392.3 ± 65.1 | NS |

**Table 2**

**Biochemical indexes before the last CAG of patients in the progression-free and progression groups.** Data are expressed as mean ± SD. FBG, fasting blood glucose; HbA1c, glycated hemoglobin; TG, total triglycerides; TC, total cholesterol; HDL-c, high-density lipoprotein-cholesterol; LDL-c, low-density lipoprotein-cholesterol.

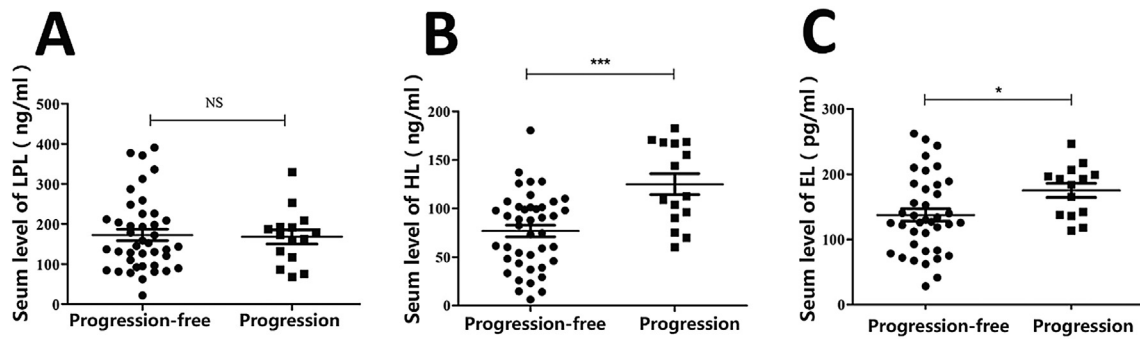| Variables | Progression-free group (n = 47) | Progression group (n = 15) | P value |
|---|---|---|---|
| FBG (mmol/L) | 5.4 ± 1.3 | 6.6 ± 3.2 | <0.05 |
| HbA1c (%) | 6.07 ± 0.68 | 7.25 ± 2.39 | <0.05 |
| TG (mmol/L) | 1.5 ± 1.1 | 1.5 ± 0.7 | NS |
| TC (mmol/L) | 3.5 ± 0.8 | 3.5 ± 0.5 | NS |
| HDL-c (mmol/L) | 1.1 ± 0.3 | 1.1 ± 0.2 | NS |
| LDL-c (mmol/L) | 1.9 ± 0.7 | 1.9 ± 0.7 | NS |
| SCr (μmol/L) | 88.9 ± 13.7 | 89.4 ± 18.3 | NS |
| UA (μmol/L) | 377.6 ± 77.7 | 357.3 ± 68.7 | NS |

**Fig. 1.** **Serum levels of LPL, HL, and EL in the progression-free and progression groups.** Data are expressed as mean ± SD. LPL, lipoprotein lipase; HL, hepatic lipase; EL, endothelial lipase; NS, no significance; ***P < 0.001; *P < 0.05.

progression are presented in Table 1. Compared with the patients in the progression-free group, patients in the progression group had higher BMI, higher frequency of hypertension, and lower frequency of diabetes. Before the first CAG, all of the patients had started the necessary therapies, including anti-platelet, lipid-lowering, and blood pressure control treatments. Therefore, no significant differences were observed in blood pressure, fasting blood glucose, HbA1c, lipid profile, and renal function between the two groups.

### 3.2. Biochemical indexes before the last CAG

Compared with the patients in the progression-free group, patients in the progression group had higher levels of fasting blood glucose and HbA1c. There was no significant difference in LDL-c, HDL-c, TC, TG, SCr, and UA. Relevant data are summarized in Table 2.

### 3.3. Association between serum LPL, HL, and EL levels and plaque progression

The serum LPL level was lower in the progression group (172.9 ± 60.1 ng/mL) than in the progression-free group (176.9 ± 79.8 ng/mL), but there was no significant difference (P > 0.05;

Fig. 1A). Notably, patients in the progression group had higher HL and EL levels compared with those in the progression-free group (HL: 125.1 ± 42.1 ng/mL vs. 75.5 ± 39.2 ng/mL; EL: 175.1 ± 40.1 pg/mL vs. 139.2 ± 59.6 pg/mL; both P < 0.05; Fig. 1B and C).

To establish whether the LPL, HL, or EL serum level was an independent factor for predicting the progression of an atherosclerotic plaque, we performed univariate (entry) and multivariate (forward) logistic regression analyses. The multivariate model indicated that HL was still an independent factor for the progression of an atherosclerotic plaque, while LPL or EL was not an independent factor for the progression of an atherosclerotic plaque (Table 3). Further analysis revealed that when the level of HL was >101.8 ng/mL, the odds ratios were as high as 6.400 (univariate analysis, P = 0.005) and 7.799 (multivariate analysis, P = 0.011) (Table 4).

### 3.4. ROC analysis

The ROC analysis showed that HL was the best factor to indicate the presence of plaque progression in CAD patients among the three triglyceride lipases. The area under the curve (AUC) reached 0.792 (95% CI: 0.664–0.888, P < 0.0001), which was better than that of EL [0.693 (95% CI: 0.553–0.811, P = 0.0095)] or LPL [0.506 (95% CI: 0.369–0.642, P = 0.9470)] (Fig. 2). Further analysis revealed that the

**Table 3**
**Logistic regression analysis for the presence of in situ coronary atherosclerotic plaque progression (Model 1).** BMI, body mass index; FBG, fasting blood glucose; HbA1c, glycated hemoglobin; TG, total triglycerides; TC, total cholesterol; HDL-c, high-density lipoprotein-cholesterol; LDL-c, low-density lipoprotein-cholesterol; SCr, serum creatinine; UA, uric acid; LPL, lipoprotein lipase; EL, endothelial lipase; HL, hepatic lipase.

| | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | P | OR | 95% CI | P |
| Sex | 0.000 | 0.000 | 0.999 | – | | |
| Age | 0.985 | 0.924 - 1.049 | 0.633 | – | | |
| BMI | 1.312 | 1.028 - 1.674 | 0.029 | 1.816 | 1.124 - 2.934 | 0.015 |
| Smoking | 0.568 | 0.168 - 1.918 | 0.363 | – | | |
| Hypertension | 0.298 | 0.060 - 1.486 | 0.140 | – | | |
| Diabetes | 0.774 | 0.234 - 2.561 | 0.675 | – | | |
| FBG | 1.303 | 0.982 - 1.730 | 0.067 | – | | |
| HbA1c | 1.750 | 1.109 - 2.762 | 0.016 | – | | |
| TG | 1.004 | 0.552 - 1.828 | 0.989 | – | | |
| TC | 0.920 | 0.447 - 1.893 | 0.820 | – | | |
| HDL-c | 0.973 | 0.085 - 11.080 | 0.982 | – | | |
| LDL-c | 0.869 | 0.347 - 2.177 | 0.765 | – | | |
| SCr | 0.985 | 0.951 - 1.021 | 0.421 | – | | |
| UA | 1.003 | 0.995 - 1.011 | 0.506 | – | | |
| LPL | 0.999 | 0.991 - 1.007 | 0.856 | – | | |
| EL | 1.013 | 1.001–1.025 | 0.039 | – | | |
| HL | 1.030 | 1.012 - 1.049 | 0.001 | 1.037 | 1.011 - 1.064 | 0.006 |

**Table 4**
**Logistic regression analysis for the presence of in situ coronary atherosclerotic plaque progression (Model 2).** BMI, body mass index; FBG, fasting blood glucose; HbA1c, glycated hemoglobin; TG, total triglycerides; TC, total cholesterol; HDL-c, high-density lipoprotein-cholesterol; LDL-c, low-density lipoprotein-cholesterol; SCr, serum creatinine; UA, uric acid; LPL, lipoprotein lipase; EL, endothelial lipase; HL, hepatic lipase.

| | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | P | OR | 95% CI | P |
| Sex | 0.000 | 0.000 | 0.999 | – | | |
| Age | 0.985 | 0.924 - 1.049 | 0.633 | – | | |
| BMI | 1.312 | 1.028 - 1.674 | 0.029 | 1.666 | 1.115 - 2.489 | 0.013 |
| Smoking | 0.568 | 0.168 - 1.918 | 0.363 | – | | |
| Hypertension | 0.298 | 0.060 - 1.486 | 0.140 | – | | |
| Diabetes | 0.774 | 0.234 - 2.561 | 0.675 | – | | |
| FBG | 1.303 | 0.982 - 1.730 | 0.067 | – | | |
| HbA1c | 1.750 | 1.109 - 2.762 | 0.016 | – | | |
| TG | 1.004 | 0.552 - 1.828 | 0.989 | – | | |
| TC | 0.920 | 0.447 - 1.893 | 0.820 | – | | |
| HDL-c | 0.973 | 0.085 - 11.080 | 0.982 | – | | |
| LDL-c | 0.869 | 0.347 - 2.177 | 0.765 | – | | |
| SCr | 0.985 | 0.951 - 1.021 | 0.421 | – | | |
| UA | 1.003 | 0.995 - 1.011 | 0.506 | – | | |
| LPL | 0.999 | 0.991 - 1.007 | 0.856 | – | | |
| EL | 1.013 | 1.001–1.025 | 0.039 | – | | |
| HL > 101.8 | 6.400 | 1.767 - 23.183 | 0.005 | 7.799 | 1.593 - 38.184 | 0.011 |
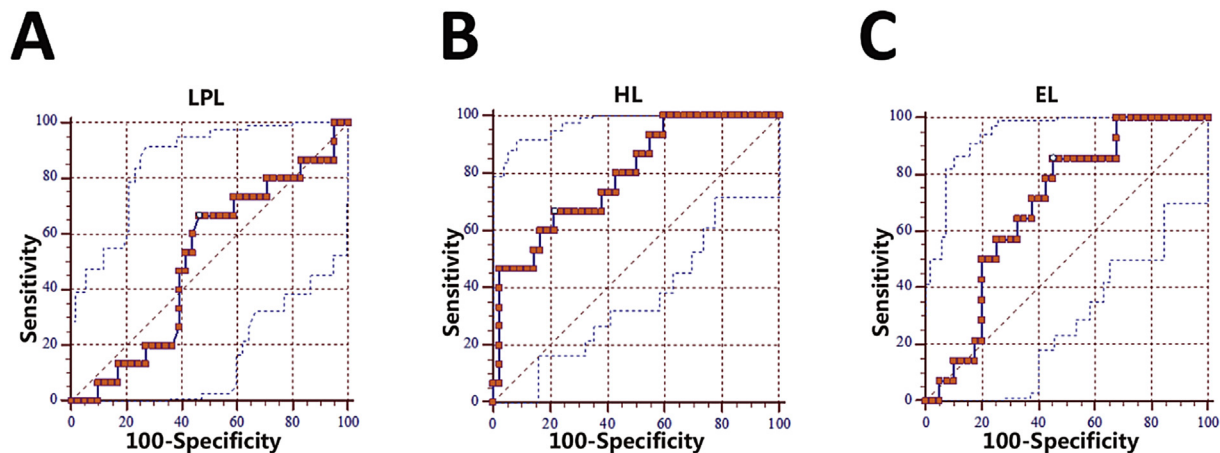
**Fig. 2. ROC analysis of serum LPL, HL, and EL in the progression-free and progression groups.** LPL, lipoprotein lipase; HL, hepatic lipase; EL, endothelial lipase.

cutoff value of HL level was 101.8 ng/mL.

## 4. Discussion

Accumulating evidence suggests that triglyceride lipases affect the occurrence and progression of AS.[9–11] Lipolysis not only regulates the lipoprotein level and lipid profile in circulation, but it also generates lipolytic products that can induce inflammation in vascular cells. Besides, these enzymes might exert a direct influence on an atherosclerotic plaque and its local microenvironment. This is the first clinical study to explore the association between triglyceride lipase family members and the presence of in situ coronary plaque progression determined by CAG.

### 4.1. LPL and AS

The physiological function of LPL is to catalyze the hydrolysis of triglycerides in plasma TRLs on the capillary endothelial cell surface, providing free fatty acids and glycerol for tissue utilization.[12] However, LPL likely contributes to lipid accumulation in macrophages and smooth muscle cells since it is also present in the vessel wall.[7,13]

Previous studies have suggested that the role of LPL during the development of AS depends on its origin and distribution. Serum LPL, which is mainly derived from the adipose tissue and muscle tissue and binds to endothelial cells, plays a role in anti-AS, while macrophage-derived LPL, which is located in vessel walls, facilitates the development of AS.[14–17] According to our data, the serum level of LPL was lower in the progression group than in the progression-free group, but the difference was not statistically significant. Besides, decreased serum LPL concentration was not proved to be an independent risk factor. To some extent, the results seemed inconsistent with those of previous studies. The reason might be attributed to the fact that a large part of serum LPL was bound to endothelial cells by heparan sulfate proteoglycan (HSPG) and glycosylphosphatidylinositol anchored high density lipoprotein binding protein 1 (GPIHBP1).

### 4.2. HL and AS

HL possesses both triglyceride lipase and phospholipase A1 activities.[18] Together with LPL, HL also acts as a lipase of the vascular compartment.[19] Generally, the serum level of HL is extremely low, since most HLs are combined with HSPG on the surface of hepatocytes. Previous studies have drawn some controversial conclusions on the relationship between serum HL and coronary heart disease.[8,20,21] In the present study, ROC analysis revealed that HL had the best diagnostic value among these three triglyceride lipases. Logistic regression analysis confirmed that serum HL level was an independent risk factor for the

progression of coronary artery lesions; and when the HL level was >101.8 ng/mL, its OR reached as high as 7.799. Therefore, detection of the serum HL level in patients with coronary heart disease offers great clinical value for predicting the progress of lesions, and reduction of the serum HL level can be very beneficial for the prevention and treatment of AS.

### 4.3. EL and AS

EL is mainly expressed in vascular endothelial cells, and to a lesser extent, in macrophages, hepatocytes, and myocytes; however, the functional significance of EL expression in these cell types has not been fully understood.[22] EL primarily has phospholipase activity and relatively less triglyceride lipase activity (activity ratio 1: 0.65), and it exhibits preferential substrate specificity for phospholipids of HDL.[23–26] HDL has been widely accepted as a protective factor against AS, but the effect of EL during the progression of AS remains not fully understood.

The results of this study showed that there was a correlation between the serum level of EL and the progression of an in situ coronary atherosclerotic plaque within 12–24 months. Specifically, the serum level of EL was higher in patients with lesion progression, reaching 175.1 + 40.1 pg/mL, which was statistically different from that in the progression-free group (139.2 + 59.6 pg/mL; P < 0.05). Further analysis showed that the cutoff value for predicting the progression was 133.8 pg/mL (P < 0.05), but it was not an independent risk factor. Therefore, its clinical value was inferior to that of serum HL. Considering that there was no significant difference in HDL levels between the progression-free and progression groups, there might be certain pro-AS mechanisms other than those regulating the metabolism of circulating HDL.

In conclusion, the present study assessed the potential of serum LPL, HL, and EL for predicting the progression of coronary plaque lesions in CAD patients. Among these three triglyceride lipases, a higher serum level of EL or HL was a risk factor for plaque progression, while serum LPL was a protective factor. In terms of diagnostic efficiency, HL was superior to LPL and EL. Besides, HL was also an independent risk factor for the progression of an in situ coronary atherosclerotic plaque.

## Conflicts of interest

The authors declare that they have no conflicts of interest to disclose.

# References

1. Takarada S, Imanishi T, Ishibashi K, et al. The effect of lipid and inflammatory profiles on the morphological changes of lipid-rich plaques in patients with non-ST-segment elevated acute coronary syndrome: follow-up study by optical coherence tomography and intravascular ultrasound. *JACC Cardiovasc Interv*. 2010;3(7):766–772.
2. Pedicino D, Giglio AF, Galiffa VA, et al. Infections, immunity and atherosclerosis: pathogenic mechanisms and unsolved questions. *Int J Cardiol*. 2013;166(3):572–583.
3. Tall AR. Increasing lipolysis and reducing atherosclerosis. *N Engl J Med*. 2017;377(3):280–283.
4. Sarwar N, Sandhu MS, Ricketts SL, et al. Triglyceride-mediated pathways and coronary disease: collaborative analysis of 101 studies. *Lancet (London, England)*. 2010;375(9726):1634–1639.
5. Davignon J, Cohn JS. Triglycerides: a risk factor for coronary heart disease. *Atherosclerosis*. 1996;124(Suppl):S57–S64.
6. Sampson UK, Fazio S, Linton MF. Residual cardiovascular risk despite optimal LDL cholesterol reduction with statins: the evidence, etiology, and therapeutic challenges. *Curr Atheroscler Rep*. 2012;14(1):1–10.
7. Li Y, He PP, Zhang DW, et al. Lipoprotein lipase: from gene to atherosclerosis. *Atherosclerosis*. 2014;237(2):597–608.
8. Goldberg IJ. *Fat in the Blood, Fat in the Artery, Fat in the Heart: Triglyceride in Physiology and Disease. Arteriosclerosis, Thrombosis, and Vascular Biology*. 2018.
9. Yasuda T, Ishida T, Rader DJ. Update on the role of endothelial lipase in high-density lipoprotein metabolism, reverse cholesterol transport, and atherosclerosis. *Circ J : Off J Jpn Circ Soc*. 2010;74(11):2263–2270.
10. Muraba Y, Koga T, Shimomura Y, et al. The role of plasma lipoprotein lipase, hepatic lipase and GPIHBP1 in the metabolism of remnant lipoproteins and small dense LDL in patients with coronary artery disease. *Clinica chimica acta; international journal of clinical chemistry*. 2018;476:146–153.
11. He PP, Jiang T, OuYang XP, et al. Lipoprotein lipase: biosynthesis, regulatory factors, and its role in atherosclerosis and other diseases. *Clinica chimica acta; international journal of clinical chemistry*. 2018;480:126–137.
12. Trent CM, Yu S, Hu Y, et al. Lipoprotein lipase activity is required for cardiac lipid droplet production. *J Lipid Res*. 2014;55(4):645–658.
13. Yla-Herttuala S, Lipton BA, Rosenfeld ME, Goldberg IJ, Steinberg D, Witztum JL. Macrophages and smooth muscle cells express lipoprotein lipase in human and rabbit atherosclerotic lesions. *Proc Natl Acad Sci U S A*. 1991;88(22):10143–10147.
14. Yin W, Liao D, Wang Z, et al. NO-1886 inhibits size of adipocytes, suppresses plasma levels of tumor necrosis factor-alpha and free fatty acids, improves glucose metabolism in high-fat/high-sucrose-fed miniature pigs. *Pharmacol Res*. 2004;49(3):199–206.
15. Yin W, Yuan Z, Tsutsumi K, et al. A lipoprotein lipase-promoting agent, NO-1886, improves glucose and lipid metabolism in high fat, high sucrose-fed New Zealand white rabbits. *Int J Exp Diabetes Res*. 2003;4(1):27–34.
16. Mamputu JC, Desfaits AC, Renier G. Lipoprotein lipase enhances human monocyte adhesion to aortic endothelial cells. *J Lipid Res*. 1997;38(9):1722–1729.
17. Obunike JC, Paka S, Pillarisetti S, Goldberg IJ. Lipoprotein lipase can function as a monocyte adhesion protein. *Arterioscler Thromb Vasc Biol*. 1997;17(7):1414–1420.
18. Ruel IL, Couture P, Cohn JS, Lamarche B. Plasma metabolism of apoB-containing lipoproteins in patients with hepatic lipase deficiency. *Atherosclerosis*. 2005;180(2):355–366.
19. Kobayashi J, Miyashita K, Nakajima K, Mabuchi H. Hepatic lipase: a comprehensive view of its role on plasma lipid and lipoprotein metabolism. *J Atheroscler Thromb*. 2015;22(10):1001–1011.
20. Katzel LI, Coon PJ, Busby MJ, Gottlieb SO, Krauss RM, Goldberg AP. Reduced HDL2 cholesterol subspecies and elevated postheparin hepatic lipase activity in older men with abdominal obesity and asymptomatic myocardial ischemia. *Arterioscler Thromb : J Vasc Biol*. 1992;12(7):814–823.
21. Dugi KA, Feuerstein IM, Hill S, et al. Lipoprotein lipase correlates positively and hepatic lipase inversely with calcific atherosclerosis in homozygous familial hypercholesterolemia. *Arterioscler Thromb Vasc Biol*. 1997;17(2):354–364.
22. Azumi H, Hirata K, Ishida T, et al. Immunohistochemical localization of endothelial cell-derived lipase in atherosclerotic human coronary arteries. *Cardiovasc Res*. 2003;58(3):647–654.
23. Nakajima H, Ishida T, Satomi-Kobayashi S, et al. Endothelial lipase modulates pressure overload-induced heart failure through alternative pathway for fatty acid uptake. *Hypertension*. 2013;61(5):1002–1007.
24. Tatematsu S, Francis SA, Natarajan P, et al. Endothelial lipase is a critical determinant of high-density lipoprotein-stimulated sphingosine 1-phosphate-dependent signaling in vascular endothelium. *Arterioscler Thromb Vasc Biol*. 2013;33(8):1788–1794.
25. Dalan AB, Toptas B, Bugra Z, et al. The effects of endothelial lipase gene (LIPG) variants on inflammation marker levels and atherosclerosis development. *Mol Biol Rep*. 2013;40(8):5143–5149.
26. McCoy MG, Sun GS, Marchadier D, Maugeais C, Glick JM, Rader DJ. Characterization of the lipolytic activity of endothelial lipase. *J Lipid Res*. 2002;43(6):921–929.