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Relationship between serum preheparin lipoprotein lipase mass, plasma glucose and metabolic syndrome in older subjects

SIR—The biomarkers regarding the pathophysiology of metabolic syndrome (MetS), a risk factor for atherosclerosis, remain to be explored. Recently, low serum levels of preheparin lipoprotein lipase mass (preLPL) in MetS have been reported in a wide range of ages. Although the associations between MetS, metabolic measures including MetS components and preLPL among older people can differ from younger adults, the specific correlations in older individuals have not been examined. In the present study, 125 Japanese subjects (37 men and 88 women, mean 76.9 years) were investigated to observe the association between preLPL, MetS and metabolic measures, such as body mass index, blood pressure, lipid panels and plasma glucose (PG). In simple correlation and multiple regression analysis, among metabolic measures, only PG was significantly and inversely correlated to preLPL. Additionally, MetS subjects showed significantly lower preLPL levels than non-MetS subjects, even after adjustments for age and sex. These results suggest that the significant correlation of PG to preLPL might be reflective of age-related metabolic features, and that preLPL might be a biomarker connected with the pathophysiology of MetS, even in older subjects.

Introduction

Recently, obesity/obesity-based disorders and ageing have become two overlapping and mounting public health problems. In particular, MetS, a cluster of metabolic
abnormalities, such as obesity, dyslipidaemia, hypertension and hyperglycaemia with an underlying condition of insulin resistance, has drawn much attention [1, 2]. MetS is considered a risk factor for atherosclerosis and its sequelae, such as cardiovascular and cerebrovascular diseases [1, 2]. Biological markers regarding MetS pathophysiology, e.g. high-sensitive C-reactive protein and adiponectin [3], have been explored, but presently, the biomarkers of MetS remain to be further elucidated.

Lipoprotein lipase (LPL) is a lipolytic enzyme involved in catalysing the hydrolysis of triglycerides (TG) in chylomicrons and very low-density lipoprotein particles. LPL is produced mainly in adipocytes or skeletal muscle cells [4]. A small quantity of LPL protein, preLPL, is measured in serum, and it has been reported that preLPL is related negatively to TG or visceral adiposity, and positively to HDL-cholesterol [5–7]. Also, preLPL is significantly lower in type 2 diabetes mellitus [4]. A small quantity of LPL protein, preLPL, is measured in serum, and it has been reported that preLPL is related negatively to TG or visceral adiposity, and positively to HDL-cholesterol [5–7]. Furthermore, a recent study over a wide range of ages reported a low preLPL level in MetS, proposing preLPL may be a biomarker of MetS [7].

We have recognised changes in body composition and fat distribution with advancing age, resulting in visceral obesity and insulin resistance development in older adults [8, 9]. Ageing also promotes increases in the occurrence of MetS and abnormalities of metabolic measures such as components used in the definition of MetS [10]. Thus, due to age-related complex pathophysiological mechanisms, the associations between preLPL, metabolic measures including MetS components and MetS among older people can differ from younger adults; however, the specific correlations in older individuals have not been examined. In a prior report examining preLPL in MetS, including older individuals, the subjects’ mean age was 55.6 years (≥20 years younger than in the present study). This study was aimed at describing the associations among preLPL, metabolic measures and MetS in a restricted population of ≥70 years.

**Subjects and methods**

In total, 125 Japanese subjects (37 men and 88 women), aged 70–95 [mean 76.9 ± 6.4 (SD)] years, participated in this cross-sectional study, approved by the Institutional Ethics Committee of Kyoto Medical Center. All subjects were consecutively recruited from outpatient and community-living volunteers, and gave informed consent. Eligible subjects were in a subjectively asymptomatic state without any clinical features of ischaemic heart, cerebrovascular, kidney, liver and cognitive diseases. All subjects had a similar lifestyle: non-smoking and non-sedentary/non-athletic. Subjects currently taking drugs known to affect blood pressure (BP) and lipid/glucose metabolism were excluded. In each subject, the following metabolic measures were determined after an overnight fast: seated systolic blood pressure (SBP) and diastolic blood pressure (DBP) (by a standard sphygmomanometer), PG, serum total cholesterol (TC), TG (by standard methods, respectively) and high-density lipoprotein-cholesterol (HDL-C) (by a homogeneous method). PreLPL was determined by an enzyme-linked immunosorbent assay [11]. The within-run coefficient variation (CV) was 2.8% and between-day CV was 4.3%. According to the NCEP-ATP III report [12] with a minor modification of obesity for Japanese [13], MetS was defined as the presence of at least three of the following five conditions: (i) obesity (identified by body mass index (BMI) of ≥25 kg/m²), (ii) elevated BP (identified by SBP of ≥130 and/or DBP of ≥85 mmHg), (iii) hypertriglyceridaemia (identified by TG of 1.69 mmol/l), (iv) low HDL cholesterol (identified by HDL-C of <1.04 in men and <1.29 mmol/l in women) and (v) elevated glucose (identified by PG of ≥6.1 mmol/l).

Data are expressed as the mean ± SD. To compare differences among groups, the unpaired t-test, χ²-test or analysis of variance followed by Tukey’s post hoc test was used as appropriate. To observe the correlations between preLPL and metabolic measures, we used Pearson’s rank coefficient test as well as multiple regression analysis adjusted for values in all metabolic measures. In these correlation analyses, TG had a skewed distribution, so TG was logarithmically transformed. In addition, a general linear model was made to determine the relationship between preLPL (as a dependent variable) and the MetS category (as a fixed variable), with adjustments for age and sex (as covariates). P < 0.05 was considered significant.

**Results**

In the whole study population, mean levels of the respective measures were as follows: BMI, 21.9 ± 3.3 kg/m² (range, 15.0–34.6); SBP, 144.1 ± 16.3 mmHg (93–190); DBP, 79.3 ± 7.7 mmHg (60–108); TC, 5.03 ± 0.78 mmol/l (3.06–7.67); TG, 1.24 ± 0.63 mmol/l (0.37–3.53); HDL-C, 1.49 ± 0.45 mmol/l (0.65–2.67); PG, 5.56 ± 0.93 mmol/l (3.89–8.88); preLPL, 35.8 ± 7.3 ng/ml (21.0–57.3). No significant differences in preLPL levels between men and women was observed (35.7 ± 8.0 vs. 35.8 ± 7.0 ng/ml, P > 0.05).

In the simple correlation test for preLPL, only PG was significantly and inversely correlated to preLPL among metabolic measures (Table 1). Other measures did not show any relative significance. In multiple regression analysis (Table 1), PG remained significantly and inversely correlated to preLPL.

Among all subjects, 23 subjects with MetS (8 men and 15 women; age: 75.0 ± 4.3 years) and 102 without MetS (29 men and 73 women; age: 77.4 ± 6.7 years) were detected, without significant differences in the mean age and number distribution by sex (P > 0.05 in all). Subjects with MetS showed a significant lower preLPL level than those without MetS (31.7 ± 6.2 vs. 36.7 ± 7.3 ng/ml, P = 0.003). In a general linear model adjusted for age and sex, this difference remained significant (F = 7.9, P = 0.006).
According to the number of components used in the definition of MetS, the study subjects were grouped into the following three categories: category 0, no components; category 1, 1–2 components and category 3, ≥3 components. Category 3 showed a significant lower preLPL level (n = 23; 31.7 ± 6.2 ng/ml) than category 0 (n = 11; 34.7 ± 8.0 ng/ml, P > 0.05) or category 1 without MetS (n = 91; 36.9 ± 7.2 ng/ml, P = 0.007). In a general linear model adjusted for age and sex, this difference remained significant (β = 4.6, P = 0.012).

### Discussion

Our study found that PG showed the best correlation to preLPL among all metabolic measures. This association has already been shown in a prior study [7], and can be supported by the observation that LPL expression and production in adipocytes are controlled by insulin [14, 15]; however, we confirmed that there was no significant association between preLPL and other metabolic measures relevant to lipid panels and body weight, although the previous report indicated that preLPL was associated with not only PG but also lipid metabolism and body weight [7]. An inconsistency might just reflect an age-related metabolic feature. A progressive increase of glucose intolerance with ageing [16] and change in lipid metabolism, that is, lipid levels decline after reaching a peak level in middle- and early older-aged individuals, has been documented [17]. In addition, body weight-related measures, especially BMI, are claimed to become a poor measure of obesity in older people [18, 19]. These age-dependent changes, in contrast to younger adults, can attenuate the correlations between preLPL, lipids and BMI.

Our study further disclosed lower preLPL levels in MetS compared to non-MetS, even in an older population. Our data are noteworthy in expanding on the prior result of a significant association between MetS and preLPL [7] in older people. Accordingly, in older as well as in younger adults, preLPL might be a biomarker of MetS. Although the detailed mechanism of the low preLPL level in MetS remains to be clarified, low preLPL may reportedly reflect insulin resistance [5–7], which underlies MetS. It is also known that older people generally become more insulin resistant with age [20], which is thought reasonable to partly explain the results.

In this study, there were potential limitations, such as a cross-sectional design and a relatively small sample size. Further studies with a prospective design and larger sample size are needed to clarify our theory.

In summary, this study showed that PG was the only significant measure correlated to preLPL among various metabolic measures, maybe reflecting metabolism on lipid and obesity in older subjects. We also disclosed lower preLPL levels in MetS than non-MetS, suggesting that preLPL might be a biomarker connected with the pathophysiology of MetS, even in an older population. This knowledge will help us to better understand the relationships between MetS and atherosclerotic diseases in older people.

### Key points

- Plasma glucose is only one significant correlate of serum preheparin lipoprotein lipase mass among various metabolic measures, and this might be a feature reflective of metabolism on lipid and obesity in older subjects.
- Lower levels of serum preheparin lipoprotein lipase mass in metabolic syndrome suggest that it might be a biomarker connected with the pathophysiology of metabolic syndrome, even in an older population.

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### Conflicts of interest

None declared.

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