The correlation between lipoprotein associated phospholipase A$_2$ and central overweight status

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Abstract

Objective: Being overweight is associated with an increased risk of diabetes mellitus, hypertension, and cardiovascular disease. Lipoprotein-associated phospholipase A$_2$ (Lp-PLA$_2$) can independently predict the risk of cardiovascular disease. This study is aimed to investigate whether Lp-PLA$_2$ was associated with an overweight status. Methods: This was a cross-sectional study that enrolled 3760 Chinese adults (age, 18–50 years) who underwent medical examination department of Xiamen Chang-Gung Hospital (XCGH) from 2018 to 2020. To explore the distribution of overweight classifications in the Chinese population, we evaluated the correlation of the overweight status with Lp-PLA$_2$, after correcting for possible influencing factors. Results: The Lp-PLA$_2$ level was greater in male than in female subjects ($p < 0.001$). Subjects with a central overweight status had a greater Lp-PLA$_2$ level than those with normal weight and a peripheral overweight status, in both male and female cohorts. The Lp-PLA$_2$ level was significantly greater in those with additional comorbidities (namely diabetes mellitus (DM), hypertension (HTN), overweight, and metabolic syndrome (MetS)). The age-adjusted and LDL-adjusted Lp-PLA$_2$ level also was significantly higher in the DM (+) and HTN (−) subgroups than in the DM (−), HTN (−), DM (−), and HTN (+) subgroups. Conclusion: Lp-PLA$_2$ is associated with sex, central overweight status, diabetes, hypertension, and MetS in adults aged < 50 years and the age-adjusted and LDL-adjusted Lp-PLA$_2$ was significantly higher in the DM (+) and HTN (−) subgroups than in the DM (−) and HTN (−) and DM (−) and HTN (+) subgroups.

Introduction

Obesity is a chronic metabolic disease[1] that contributes to inflammatory response in the adipose tissue,[2] and its prevalence is also increasing worldwide.[3] Obesity is closely associated with cardiovascular diseases,[4] such as hypertension and hyperlipidemia.[5] Therefore, it is important to assess cardiovascular-predictive factors associated with obesity.

Lp-PLA$_2$ (lipoprotein-associated phospholipase A$_2$) catalyzes the hydrolysis of acetyl ester at the sn-2 position of platelet-activating factor (PAF),[6] also known as

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platelet-activating factor acetylhydrolase (PAF-AH). It is a calcium-independent serine lipase produced predominantly by the macrophages, monocytes, T lymphocyte, and mast cells, which circulates by binding mainly to apolipoprotein B (apo B),[7] with the low-density lipoprotein (LDL) (80%) and high-density lipoprotein (HDL) (20%),[8] could independently predict cardiovascular risk.[9] Since Lp-PLA$_2$ activity is positively associated with LDL and adiposity[10] that helps predict the risk of atherosclerosis and cardiovascular disease.[11] Lp-PLA$_2$ had significant positive correlation with systolic, diastolic, mean arterial pressure (MAP), total cholesterol, LDL, plasma glucose, and HbA1c[12] as well, so it may be a proper predictor for obesity.

LDL oxidation is associated with lipid peroxidation, an extensive hydrolysis, and releasing pro-inflammatory mediators like oxidized fatty acids (oxFA) and lysophosphatidylcholine (lysoPC).[13] The hydrolysis is mediated through a Lp-PLA$_2$ which is closely associated with LDL.[14] The study by Laura Jackisch et al. suggests that adipocytes viewed as an important contributing source of Lp-PLA$_2$ expression in adipocytes and adipose tissue. Also, a multiple-regression model found triacylglycerols as the key predictor of Lp-PLA$_2$,[15] so we may predict obesity by measuring Lp-PLA$_2$.

Lp-PLA$_2$ is a novel inflammatory biomarker of cardiovascular disorders in metabolic diseases[12] that can provide important information about plaque inflammation and stability[16] and is also the main cause of coronary artery disease. The United States Food and Drug Administration approved Lp-PLA$_2$ as a predictor of coronary artery disease using the PLAC Test ELISA kit on December 2014.[17] It may also be used to predict obesity as an independent risk factor. In summary, both an overweight status and increased Lp-PLA$_2$ activity can cause heart damage.

Internationally, the most common parameters for measuring obesity are the waist-to-height ratio (WHtR) and body mass index (BMI), which evaluate the degree of obesity through weight, height, and waist circumference. Few studies have analyzed the correlation between Lp-PLA$_2$ and an overweight status in the Chinese population. Therefore, we aimed to analyze the correlation between the overweight type and Lp-PLA$_2$ level through physical health examinations and to better understand the difference sexes.

Methods

Subjects and data collection

This was a cross-sectional study that enrolled 3760 Chinese adults (age, 18–50 years) who underwent health examinations at the medical examination department of XCGH from 2018 to 2020. The study was approved by the Institutional Review Board of XCGH (XMCGIRB2020030) and was conducted in accordance with the Declaration of Helsinki in 2013. Trained nurses collected the data at the health examination by using a standardized questionnaire that contained all complete data, including past history, personal history, medication history, fasting time, and physical examination data, including weight, height blood pressure, and waist circumference. We excluded subjects (1) age younger than 18 years old or over 50 years old; (2) with pregnancy, which affects metabolic tests; (3) who were not fasting for more than 12 hours, which affects metabolic test values; (4) with chronic diseases that significantly affect metabolic function, such as abnormal thyroid function, status post thyroidectomy, chronic hepatitis, liver cirrhosis, pituitary gland disease, adrenal gland disease, and malignant tumors.

Laboratory measurements

The clinical chemistry workup included fasting blood glucose (FBG) measured by Hexokinase enzyme assay (Cobas Mira Chemistry System: Roche Diagnostic Systems, Montclair, NJ); total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG) measured by automatic biochemical analyzer (DxC 800, Beckman CoulterUniCel® DxC SYNCHRON®, Ireland). Glutamic pyruvic transaminase (GPT), creatinine, and lipoprotein-related phospholipase A$_2$ (Lp-PLA$_2$) with quantitative test measured by turbidimetric immunology (ABBOTT ARCHITECT c8000/c16000).

Body height and weight were measured using scales and calibrated meters, respectively. BMI was estimated using the following formula: body weight (kg)/[height (m)]^2, the cut-off point was 24 kg/m^2,[18] with normal BMI <24 kg/m^2 and overweight BMI ≥24 kg/m^2. Waist circumference was measured between the lowest rib and the midpoint of the iliac crest. The cut-off point of the waist-to-height ratio (WHtR) was 0.5, with peripheral overweight definition: WHtR < 0.5 and central overweight definition: WHtR ≥ 0.5.[19] Blood pressure was measured after a 15-min rest, and the subject was seated using an automated sphygmomanometer which is placed on the right arm. The mean arterial pressure was calculated using the following equation: (2/3) × diastolic pressure + (1/3) × systolic pressure.[20] Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg. Diabetes mellitus was defined as fasting glucose ≥ 7.0 mmol/L. Metabolic syndrome (MetS) was defined as subjects who had three or more of the following criteria: (1) waist circumference ≥ 90 cm in men and ≥ 80 cm in women; (2) hypertriglyceridemia: triglycerides (TG) ≥ 1.7 mmol/L (3) low HDL level < 1.03 mmol/L in men and < 1.29 mmol/L in women; (4) blood pressure ≥ 130/85 mmHg; and (5) fasting glucose ≥ 5.6 mmol/L.

Table 1. The basic characteristics of the study subjects by sex.

Variable	Total (n = 3760)	Men (n = 2292)	Women (n = 1468)	p Value
Age (year)	41.0 ± 5.9	41.1 ± 5.8	40.9 ± 6.0	0.409
Waist circumstance (cm)	82.2 ± 10.4	87.2 ± 9.0	74.5 ± 7.2	<0.001
Waist-to-height ratio	0.50 ± 0.05	0.51 ± 0.05	0.47 ± 0.05	<0.001
SBP (mmHg)	118.3 ± 17.4	124.1 ± 16.0	109.2 ± 15.4	<0.001
DBP (mmHg)	73.2 ± 12.9	77.7 ± 12.0	66.2 ± 10.9	<0.001
MAP (mmHg)	88.2 ± 13.9	93.2 ± 12.8	80.5 ± 11.9	<0.001
Fasting glucose (mmol/L)	5.1 ± 1.2	5.2 ± 1.4	4.9 ± 0.6	<0.001
Total cholesterol (mmol/L)	5.05 ± 0.97	5.18 ± 1.01	4.84 ± 0.86	<0.001
Triglycerides (mmol/L)	1.6 ± 1.8	2.0 ± 2.1	1.1 ± 0.8	<0.001
LDL cholesterol (mmol/L)	3.4 ± 0.8	3.6 ± 0.8	3.1 ± 0.8	<0.001
HDL cholesterol (mmol/L)	1.3 ± 0.3	1.2 ± 0.3	1.5 ± 0.3	<0.001
TG/HDL cholesterol	1.4 ± 2.6	1.8 ± 3.2	0.8 ± 1.1	<0.001
GPT (μ/L)	27.1 ± 30.3	34.0 ± 35.8	16.2 ± 12.3	<0.001
Creatinine (umol/L)	73.5 ± 17.9	81.4 ± 18.5	61.3 ± 6.6	<0.001
$Lp\text{-}PLA_2$ (IU/L)	587 ± 149	621 ± 149	534 ± 131	<0.001
Hypertension, n (%)	519 (13.8)	444 (19.4)	75 (5.1)	<0.001
Diabetes, n (%)	105 (2.8)	93 (4.1)	12 (0.8)	<0.001
Metabolic syndrome, n (%)	751 (20.0)	631 (27.5)	120 (8.2)	<0.001
Overweight status, n (%)				<0.001
Normal	1900 (50.5)	837 (36.5)	1063 (72.4)	
Peripheral type	306 (8.1)	190 (8.3)	116 (7.9)	
Central type	1554 (41.3)	1265 (55.2)	289 (19.7)	

SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglycerides; GPT: glutamic pyruvic transaminase; $Lp\text{-}PLA_2$: lipoprotein-associated phospholipase A_2.
Data are shown as mean ± standard deviation or frequency (percentage).

Statistic analysis

According to a previous study investigating the relationship between LDL and $Lp\text{-}PLA_2$ level in type 2 diabetic patients, the standardized regression coefficient of LDL was 0.11. Given the effect size, a minimum sample size of 1966 was required to achieve a type I error of 1% and power of 99%.[12] The basic characteristics of male and female subjects were compared using an independent sample t-test for continuous variables or the chi-square test for categorical variables. We further compared the $Lp\text{-}PLA_2$ level of subjects according to the presence or absence of comorbidities (hypertension, diabetes, MetS, and weight status) using an independent sample t-test in the whole cohort and after stratifying by sex. The basic characteristics of the subjects among different overweight types (normal weight, peripheral overweight, and central overweight) were compared using one-way analysis of variance for continuous variables or chi-square test for categorical variables. A pairwise comparison was performed using the Bonferroni adjustment when the overall test was significant. Finally, the $Lp\text{-}PLA_2$ levels of subjects were compared according to the combination of hypertension and diabetes mellitus using a general linear model in which age was adjusted. In an alternative model, LDL-adjusted $Lp\text{-}PLA_2$ levels were compared among the subgroups. All tests were two-tailed, and statistical significance was set at $p < 0.05$. Data analyses were conducted using SPSS 25 (IBM SPSS Inc., Chicago, IL, USA).

Results

A total of 3760 subjects were included in the study, of whom 2292 (60.9%) were men. The mean age was 41 years (standard deviation [SD] = 5.9 years). The average $Lp\text{-}PLA_2$ level was 587 IU/L (SD = 149 IU/L). Irrespective of sex, 50.5% of the subjects were classified as normal weight, 41.3% as central overweight, and 8.1% as peripheral overweight. The level of GPT, $Lp\text{-}PLA_2$ was greater in male subjects than in female subjects (34.0 ± 35.8 μ/L vs. 16.2 ± 12.3 μ/L, $p < 0.001$), (621 ± 149 IU/L vs. 534 ± 131 IU/L, $p < 0.001$). The prevalence of overweight status (any type) was substantially higher in men than in women (63.5% vs. 27.6%), which was mainly attributed to the central type of overweight status (55.2% vs. 19.7%, $p < 0.001$) (Table 1).

We further compared the $Lp\text{-}PLA_2$ levels of subjects with hypertension, diabetes mellitus, MetS, and weight status (Table 2). In the whole cohort, the $Lp\text{-}PLA_2$ level was significantly greater in those with each condition (namely, DM, HTN, overweight and MetS). After separating by sex, no difference in the $Lp\text{-}PLA_2$ levels was

Table 2. The Lp-PLA$_2$ level (IU/L) according to comorbidity, metabolic syndrome, and weight status in the whole cohort and after stratification by sex.

Condition/Population	With condition		Without condition		
	Number	Mean ± SD	Number	Mean ± SD	p Value
Hypertension					
Total	519	615 ± 164	3241	583 ± 146	<0.001
Men	444	626 ± 158	1848	620 ± 147	0.432
Women	75	549 ± 183	1393	534 ± 128	0.307
Diabetes					
Total	105	669 ± 157	3655	585 ± 148	<0.001
Men	93	674 ± 159	2199	619 ± 149	0.001
Women	12	633 ± 137	1456	534 ± 131	0.009
Metabolic syndrome					
Total	751	624 ± 157	3009	578 ± 145	<0.001
Men	631	634 ± 153	1661	616 ± 148	0.010
Women	120	570 ± 164	1348	531 ± 127	0.002
Weight status					
Total	1860	610 ± 151	1900	565 ± 143	<0.001
Men	1455	630 ± 151	837	607 ± 146	0.001
Women	405	541 ± 130	1063	532 ± 132	0.209

Lp-PLA$_2$: lipoprotein-associated phospholipase A$_2$; SD: standard deviation.

observed between those with hypertension and those without, which was possibly due to the small sample size. However, the Lp-PLA$_2$ level was significantly higher in men ($p = 0.001$), but not in women ($p = 0.209$).

The basic participant characteristics according to overweight type and age, with respect to male and female subjects, are shown in Table 3. The results demonstrate that ALT and Lp-PLA$_2$ levels significantly differed among the overweight group in the male and female cohorts ($p < 0.001$), ($p < 0.001$ and $p = 0.002$, respectively). Subjects with the central overweight status had a greater Lp-PLA$_2$ level than those with normal weight and peripheral overweight status in both the male and female cohorts. The detailed results of the other basic characteristics are also provided (Table 3).

We further evaluated the level of age-adjusted and LDL-adjusted Lp-PLA$_2$ levels according to the combination of hypertension and diabetes mellitus. The results showed that the age-adjusted and LDL-adjusted Lp-PLA$_2$ levels were both was significantly higher in the DM (+) and HTN (−) subgroups than in the DM (−) and HTN (−) and DM (−) and HTN (+) subgroups ($p < 0.05$). However, the age-adjusted and LDL-adjusted Lp-PLA$_2$ level were not significantly greater in the DM (+) and HTN (+) subgroups than in the other groups, which was possibly due to the small sample size of this subgroup (Table 4).

Discussion

This cross-sectional study investigated the association between overweight status and Lp-PLA$_2$ in a population of 2292 men and 1468 women. We evaluated the correlation between Lp-PLA$_2$ levels and risk factors of overweight status, such as hypertension, diabetes mellitus, and MetS, in a Chinese population. The age-adjusted and LDL-adjusted Lp-PLA$_2$ level was significantly higher in the DM (+) and HTN (−) subgroups than in the DM (−), HTN (−), DM (−), and HTN (+) subgroups.

Insulin resistance, a reduction in the rate of glucose disposal caused by a given insulin concentration, often occurs in individuals with obesity or diabetes mellitus, and may develop with aging.[21] This means that the elderly are prone to be more insulin resistance and that Lp-PLA$_2$ levels increase with age. This age-related phenomenon is due to the unavoidable natural aging process and often clusters in certain individuals during aging,[22] which compactible to our results aims at adults less than 50 years of age.

Lp-PLA$_2$ was recently found to be a novel inflammatory biomarker that correlates with several components that contributes to MetS. Since Lp-PLA$_2$ is a vascular-specific inflammation biomarker, measuring Lp-PLA$_2$ levels may be useful for complete evaluation of atherosclerosis in patients with MetS.[23] The adipose tissue located in visceral or intra-abdominal cavities is likely to be infiltrated by macrophages, and this is an important cause of chronic low-grade inflammation with MetS and abdominal obesity.[24] Chronic low-grade inflammation displayed higher Lp-PLA$_2$ activity was observed in patients with MetS.[25] Thus, the presence of elevated Lp-PLA$_2$ activity and MetS may identify high-risk individuals.[26] The results in the study by Noto H et al. suggest that central obesity may

Table 3. The basic participant characteristics according to overweight type in male and female subjects.

Population/Variable	Normal (n = 1900)	Peripheral (n = 306)	Central (n = 1554)	p Value
Men (n = 2292)				
Age (year)	40.5 ± 6.1	39.9 ± 6.3	41.7 ± 5.5[ab]	<0.001
Waist circumference (cm)	79.1 ± 6.0	83.6 ± 3.4[a]	93.0 ± 6.5[ab]	<0.001
Waist-to-height ratio	0.47 ± 0.04	0.48 ± 0.01[a]	0.55 ± 0.04[ab]	<0.001
SBP (mmHg)	117.2 ± 14.6	123.2 ± 13.5[a]	128.9 ± 15.5[ab]	<0.001
DBP (mmHg)	72.6 ± 10.5	75.7 ± 9.7[a]	81.4 ± 12.0[ab]	<0.001
MAP (mmHg)	87.5 ± 11.3	91.5 ± 10.4[a]	97.2 ± 12.6[ab]	<0.001
Fasting glucose (mmol/L)	5.0 ± 1.4	5.0 ± 0.9	5.4 ± 1.5[ab]	<0.001
Total cholesterol (mmol/L)	5.03 ± 0.98	5.06 ± 0.83	5.30 ± 1.03[ab]	<0.001
Triglycerides (mmol/L)	1.6 ± 2.1	1.7 ± 1.1	2.3 ± 2.2[ab]	<0.001
LDL cholesterol (mmol/L)	3.4 ± 0.8	3.5 ± 0.8	3.7 ± 0.8[ab]	<0.001
HDL cholesterol (mmol/L)	1.32 ± 0.29	1.24 ± 0.25[a]	1.15 ± 0.23[ab]	<0.001
TG/HDL-C	1.3 ± 2.8	1.5 ± 1.2	2.2 ± 3.5[ab]	<0.001
GPT (μ/L)	27.7 ± 40.6	30.7 ± 51.1	38.7 ± 28.2[ab]	<0.001
Creatinine (umol/L)	80.7 ± 15.5	83.2 ± 10.2	81.6 ± 21.0	0.219
Lp-PLA$_2$ (IU/L)	607 ± 146	604 ± 156	633 ± 149[ab]	<0.001
Female (n = 1468)				
Age (year)	40.3 ± 6.1	42.1 ± 5.9[a]	42.9 ± 5.1[a]	<0.001
Waist circumference (cm)	71.5 ± 5.2	76.9 ± 3.3[a]	84.5 ± 5.2[ab]	<0.001
Waist-to-height ratio	0.45 ± 0.03	0.48 ± 0.01[a]	0.54 ± 0.03[ab]	<0.001
SBP (mmHg)	105.5 ± 12.8	114.7 ± 15.4[a]	120.4 ± 17.9[ab]	<0.001
DBP (mmHg)	64.1 ± 9.3	69.4 ± 11.6[a]	72.5 ± 12.8[ab]	<0.001
MAP (mmHg)	77.9 ± 10.0	84.5 ± 12.4[a]	88.5 ± 13.9[ab]	<0.001
Fasting glucose (mmol/L)	4.8 ± 0.4	4.9 ± 0.5[a]	5.2 ± 1.0[ab]	<0.001
Total cholesterol (mmol/L)	4.79 ± 0.83	4.84 ± 0.98	5.01 ± 0.89[a]	0.001
Triglycerides (mmol/L)	0.9 ± 0.6	1.1 ± 0.8[a]	1.5 ± 1.2[ab]	<0.001
LDL cholesterol (mmol/L)	3.1 ± 0.7	3.2 ± 0.9	3.4 ± 0.8[a]	<0.001
HDL cholesterol (mmol/L)	1.54 ± 0.30	1.42 ± 0.32[a]	1.35 ± 0.29[a]	<0.001
TG/HDL-C	0.7 ± 0.7	0.9 ± 1.0	1.3 ± 2.0[ab]	<0.001
GPT (μ/L)	15.0 ± 12.1	16.7 ± 9.6	20.4 ± 12.8[ab]	<0.001
Creatinine (umol/L)	61.3 ± 6.2	61.8 ± 7.5	61.1 ± 7.3	0.667
Lp-PLA$_2$ (IU/L)	532 ± 132	507 ± 117	555 ± 132[ab]	0.002

SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglycerides; GPT: glutamic pyruvic transaminase; Lp-PLA$_2$: lipoprotein-associated phospholipase A$_2$.
Data are shown as mean ± standard deviation; "a" and "b" indicate a significant difference in the central overweight group compared to the normal group and peripheral overweight group, respectively, in the Bonferroni multiple comparison test.

Table 4. The age-adjusted and LDL-adjusted Lp-PLA$_2$ level (IU/L) according to the comorbidity combination in the whole cohort, after excluding subjects with peripheral overweight and normal weight.

Lp-PLA$_2$ level (IU/L)	DM (−), HTN (−) (n = 1129)	DM (+), HTN (−) (n = 38)	DM (−), HTN (+) (n = 348)	DM (+), HTN (+) (n = 39)	p Value
Age-adjusted	611 ± 4	710 ± 26[a]	629 ± 9[b]	661 ± 22	<0.001
LDL-adjusted	615 ± 4	697 ± 23[a]	622 ± 8[b]	636 ± 22	0.004

Data are shown as the estimated marginal mean ± standard error derived from the general linear model.
"a," "b" indicate a significant difference between the DM (−), HTN (−) group and DM (+), HTN (−) group, respectively, in the Bonferroni multiple comparison. Lp-PLA$_2$, Lipoprotein-associated phospholipase A$_2$.

contribute to changes in Lp-PLA$_2$ activity in patients with MetS.[27] Lp-PLA$_2$ activity and MetS have shown that abdominal obesity may have been independently responsible for the changes in Lp-PLA$_2$ observed in the study by Gong et al.[28]. However, in our study, we used Lp-PLA$_2$ mass which had stable results and good repeatability rather than Lp-PLA$_2$ activity mentioned above. Since Lp-PLA$_2$ mass concentrations measured by quantitative

SISCAPA-mass spectrometry were substantially higher than activity concentrations measured by immunoassay and showed an improved consistency. Lp-PLA$_2$ quantitatively detected by immunoassay appears to be strongly inhibited by interaction of Lp-PLA$_2$ with lipoprotein,[29] which had low sensitivity and easy to be interfered by various components in blood like bilirubin, hemoglobin, chylomicron, fibrinogen, and other lipoproteins. Therefore, we only detect Lp-PLA$_2$ mass by turbidimetric immunology quantitative test in this study.

Lp-PLA$_2$ and its isoforms appear to be heavily influenced by metabolic status, weight, and circulating lipid levels. Patients with type 2 diabetes mellitus who were observed an increase in Lp-PLA$_2$, which appear to be associated with an upregulation in systemic lipids.[15] Moreover, Lp-PLA$_2$ is associated with an unfavorable circulating lipid profile, including increased triacylglycerol and oxidized LDL, which is exacerbated in type 2 diabetes mellitus[30] and produces strong oxidative and inflammatory mediators.[31] In summary, each member of the PLA$_2$ family of enzymes plays a distinct role in generating active lipid metabolites that promote inflammatory metabolic diseases, including oxidative atherosclerosis, hyperlipidemia, diabetes mellitus, and obesity.[32]

A total of 3760 subjects were included in the study, of whom 2292 (60.9%) were men. The level of Lp-PLA$_2$ was greater in the male subjects than in female subjects, and Feng et al. reported that the Lp-PLA$_2$ levels showed a statistically significant difference between females and males (t = 4.866, *p < 0.001*). The reference intervals of serum Lp-PLA$_2$ were 194–640 U/L (18–49 years) and 208–698 U/L (50–88 years) for women and 230–728 U/L for men.[33] In addition, the median Lp-PLA$_2$ levels in men and women in the study by Winkler et al.[34] were 504 U/L and 446 U/L, respectively. The low Lp-PLA$_2$ levels observed in females may result from estrogen secretion, as Lp-PLA$_2$ levels in premenopausal women were lower than those in menopausal women. This estrogen effect was also suggested in a study by Yoshimura et al.[35] which showed a 26% reduction in Lp-PLA$_2$ levels in menopausal females 2 weeks after receiving estrogen replacement therapy. Subjects with central overweight status had a higher Lp-PLA$_2$ level than those with normal weight and peripheral overweight status, in both male and female cohorts. Another prior study of the impact of obesity on Lp-PLA$_2$ found that enzyme activity was positively associated with BMI and that Lp-PLA$_2$ function changes with adolescent obesity.[36] In addition, Lp-PLA$_2$ activity was discovered to be positively associated with BMI ($p = 0.004$) in the study by Seyfarth et al.[37]. We further evaluated the level of age-adjusted and LDL-adjusted Lp-PLA$_2$ levels according to the combination of hypertension and diabetes mellitus. Our results showed that the age-adjusted and LDL-adjusted Lp-PLA$_2$ level was significantly higher in the DM (+) and

HTN (−) subgroups and in those with each condition (namely, DM, HTN, overweight and MetS).

The present study has some limitations. First, this was a cross-sectional study based on routine health examinations of a general population; thus, the results cannot prove a causal relationship between Lp-PLA$_2$ and overweight status. Second, only body weight was measured, and no lean mass body fat percentage, or metabolically healthy obesity were assessed, all of which reflect obese lean mass. Third, our study focused on a physical examination population and may have selection errors due to the inclusion of patients with serious health issues, and thus, may not represent the general population. Last but not least, we used we used Lp-PLA$_2$ mass which had stable results and good repeatability rather than Lp-PLA$_2$ activity. In conclusion, our findings suggest that Lp-PLA$_2$ is associated with central overweight status, diabetes mellitus, hypertension, and MetS in adults less than 50 years of age.

Conclusion

Lp-PLA$_2$ is associated with sex, central overweight status, diabetes mellitus, hypertension, and MetS in adults less than 50 years of age and the age-adjusted and LDL-adjusted Lp-PLA$_2$ was significantly higher in the DM (+) and HTN (−) subgroups than in the DM (−) and HTN (−) and DM (−) and HTN (+) subgroups.

Author Contributions

Y.-H.C. and W.-C.L. analyzed and interpreted the patient data and were major contributors in writing the manuscript. Y.-C.C and W.-C.Y. interpreted the analyzed data. W.Y., H.-Y.H., and X.-X.J. assisted with data collection. Project administration: J.-Y.C., Supervision: J.-Y.C.; Y.-H.C. and W.-C.L. had equal contribution to the present study as co-first authors. J.-Y.C. as corresponding author. All authors read and approved the final paper.

and was conducted in accordance with the guidelines laid down in the Declaration of Helsinki in 2013.

Informed consent

The study was approved by Institutional Review Board of Chang-Gung Memorial Hospital (XMCGIRB2020030), so informed consent was not sought for the present study.

Trial registration

The authors declare that no funding was received, so it is not applicable.

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