Relationship between lipid accumulation product index and arterial stiffness in the Chinese population with hypertension: a report from the China Hypertension Registry Study

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Abstract

Background: The relation of LAP index with baPWV have been evaluated in several previous studies and yield inconsistent results. The aim of the study was to investigate the association between the lipid accumulation product (LAP) index and arterial stiffness in the Chinese population with hypertension.

Methods: We conducted a cross-sectional analysis in 4926 participants chinese population with hypertension (aged 64.42 ± 9.44 years). The LAP was developed from population-based frequency plots of adult waist circumferences and circulating triglyceride concentrations. Arterial stiffness was determined by measuring brachial-ankle pulse wave velocity (baPWV).

Results: Multivariate linear regression analyses showed that LAP index was independently and positively associated with baPWV (β , 25.06 cm/s (95% confidence interval [CI]: 10.91, 39.22 cm/s). Consistently, Multiple logistic analyses showed a positive association between LAP index risk of elevated baPWV (>75th percentile) (odds ratio [OR], 1.24; 95% CI 1.09, 1.40). A restricted cubic spline showed that the significant linear association existed between LAP index and baPWV. Similar results were found in various subgroups.

Conclusion: LAP is a significant positive associated with with baPWV and elevated baPWV in Chinese hypertensive adults.

Background

The European Society of Hypertension/European Society of Cardiology Guidelines on Arterial Hypertension suggest that brachial–ankle pulse wave velocity (baPWV) measurement should be used as a tool to evaluate subclinical damage of target organs[1]. So, arterial stiffness can be evaluated non-invasively by measuring baPWV, which is the gold standard and widely used method. It is reported that metabolic syndrome[2], cardiovascular disease(CVD)[3], stroke[4], mortality[5], and kidney disease[6] are all related to elevated baPWV. In China, hypertension is not only a common health problem but also a major pathogenic factor of arterial stiffness, which can cause a high proportion of hypertension and cardiovascular disability[7, 8]. According to the latest national hypertension survey of 451,755 adults in China from 2012 to 2015, the prevalence rate of hypertension is 27.9%[9]. There are estimates suggesting that the total number of hypertension patients among Chinese adults is 244.5 million[10]. Therefore, a better understanding of the potential risk factors of increased arterial stiffness among hypertensive patients may help to prevent the onset of arterial stiffness and related cardiovascular diseases.

Lipid accumulation product (LAP) index, as a new index to predict cardiovascular diseases, has attracted the attention of many researchers. LAP was proposed as a better continuous marker/index to describe lipid over-accumulation in relationship to central obesity and metabolic risks[11], and was shown to outperform BMI in the identification of CVD risk[12] and diabetes[13]. The calculation method of LAP index varies with gender: males: $[(WC-65) * TG]$; women: $[(WC-58) * TG]$ [14]. There are only a few previous studies on LAP and arterial stiffness, but their conclusions are inconsistent[15–17]. Moreover, all the

above studies were carried out in healthy adults, and few people in hypertensive patients pay attention to the effect of LAP on arterial stiffness.

In order to fill the gap in the above research. This cross-sectional analysis uses the data of a Chinese hypertension registration study to evaluate the association between the LAP index and arterial stiffness in the Chinese population with hypertension.

Methods

Subject population and design

This study was based on the data collected by the China hypertension Registry Study (Registration number: ChiCTR1800017274); Briefly, the China Hypertension Registry Study is an ongoing, real-world, observational study conducted in Wuyuan, Jiangxi province of China. The full details regarding the design and rationale of the study were extensively described elsewhere[18]. Participants were recruited in 2018 were consecutively enrolled if they (1) were aged ≥ 18 years, (2) had hypertension, defined as seated resting blood pressure $\geq 140/90$ mmHg or self-reported use of antihypertensive medications. The participants were excluded when subjects with neurological abnormalities led to the inability to follow-up according to the study protocol. In accordance with the Declaration of Helsinki conducted the study. Approval of the study protocol was provided by the Ethics Committees of the Biomedical Institute of Anhui Medical University (Approved No. Of ethic committee: CH1059). Before each participant entered this study, they all signed informed consent.

A total of 5233 subjects had baPWV measurements taken at baseline. After excluding those with ankle-brachial systolic blood pressure indexes (ABI) < 0.90 ($n = 133$), or using lipid-lowering medications ($n = 174$), Finally, 4926 patients were selected for the study (Figure S1).

Data Collection

Standardized questionnaires were used to obtain information about demographic factors, lifestyle behaviours (smoking and alcohol consumption), disease history, family history of diseases, and medication use at baseline. At the same time, we also collected the anthropometric indices included weight, height, waist circumference (WC), hip circumference (HC) of all participants. The body mass index (BMI) was calculated as the body weight in kilograms / square of the height in meters (kg/m^2). Blood pressure (BP) was measured in the sitting position using an electronic sphygmomanometers (Omron; Dalian, China). After a 10-minute rest period, BP was measured three times, and the average of the three measurements was used for final analyses.

BaPWV measurements

The baPWV (cm/s) and ankle-brachial index (ABI) was automatically measured simultaneously in the supine position after having rested for more than 10 minutes, using automatic waveform analyzer (BP-203RPE III device; Omron Health Care, Kyoto, Japan). The specific measurement method is as follows: blood pressure cuff is wrapped on arms and ankles, the lower edge of the armband is located 2–3 cm above the cubital fossa transverse stripes, while the lower edge of the ankle band is located 1–2 cm above the medial malleolus. And the baPWV value was calculated as the ratio of transmission distance from the brachium to ankle divided by the transit time. L_b and L_a refer to the path length from suprasternal incision to brachial muscle and from suprasternal incision to ankle (L_a), respectively. ΔT_{ba} is the ankle-brachial artery pressure wave foot time difference. baPWV was measured twice automatically and the higher value of the the left and right side was used in the final analysis.

Laboratory Tests

After an 8-10-hour fasting period, all blood samples were taken from the cubital vein and delivered to the BiaoJia Biotechnology Laboratory, Shenzhen, China. Automatic clinical analyzers (Beckman Coulter) were used to measure biochemical included creatinine, uric acid, plasma homocysteine (Hcy), fasting total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C), and fasting plasma glucose (FPG). LAP was determined from WC (cm) plus TG (mmol/L) for men $[(WC-65) * TG]$ and women $[(WC-58) * TG]$ [19]; To prevent non-positive values for LAP, any male WC values of 65 cm or less were revised upward to 66.0 cm, and any female WC values of 58 cm or less were revised upward to 59 cm[12]. The estimated glomerular filtration rate (eGFR) was calculated by the chronic kidney disease (CKD) epidemiology collaboration formula[20].

Statistical Analysis

Based on quartiles of LAP levels, the study population was divided into four groups. The characteristics were presented as mean (SD), and categorical variables were expressed as count (percentage). We compared baseline characteristics on participants quartiles of LAP levels by one-way analysis of variance (ANOVA) for continuous variables and chi-square or Fisher's exact test for categorical variables, as appropriate. The distribution of serum concentrations of TBIl was strongly skewed toward the left. Thus, we performed the ln-transformed (ln LAP) before analysis.

Because the predictive value of baPWV in cardiovascular events is unavailable. In this study, elevated baPWV is defined as a value greater than 75% of baPWV value and greater than 20.59 cm/s. Beta coefficient (β) and 95% confidence interval (CI) used to investigate the association between LAP and baPWV were calculated using multivariate linear regression; Odds ratios (OR) and 95%CI used to investigate the association between LAP and elevated baPWV in hypertensive participants were calculated using multivariate logistic regression for three models. These three models are as follows: model1 adjusted only for age, sex; model 2 adjusted for prior covariates and BMI, SBP, DBP, pulse, smoking status, drinking status, model 3 adjusted for these prior covariates plus FBG, TC, HDL, LDL-C, Hcy, uric acid, eGFR, diabetes mellitus, antihypertensive drugs, antiplatelet drugs. Variables known as traditional risk factors for stroke and the potential confounders were selected if the effect estimates

individually changed by at least 10%[21]. To characterize the shape of the dose-response relationship of LAP index with baPWV and elevated baPWV, we performed a generalized additive model (GAM) and a fitted smoothing curve (penalized spline method). As additional exploratory analyses, possible modifications of the association between LAP index and baPWV were also evaluated for variables including sex (male vs. Female), age (< 65 vs. ≥65 years), BMI (< 25 vs. ≥25 kg/m²), current smoking (no vs. yes), current drinking (no vs. yes), SBP (< 140, 140–159, ≥ 160mmHg), DBP (< 90, 90–99, ≥ 100mmHg), Diabetes mellitus (no vs. yes, and eGFR (< 60 vs. ≥60 mL/min/1.73 m²).

Data were analyzed using the Empower (R;www.empowerstats.com; X&Y Solutions, Inc, Boston, MA, USA) and the statistical package (R) (<http://www.R-project.org>, The R Foundation). Effects that met the 5% significance level were considered statistically significant, with all tests were two-sided.

Results

Baseline characteristics

A representative sample of 4926 participants of the China Hypertension Registry study was eligible and enrolled in the analysis. From the study population, the mean age of those participants was 64.42 ± 9.44 years old, and 2440 (49.53%) people were men. The overall mean baseline LAP index was 40.65, ranging from 0.14 to 514.60. And mean baPWV was 1855.27 (414.58) cm/s. The baseline clinical characteristics of participants according to the quartile of in LAP index are presented in Table 1. Compared with participants in the lowest quartile group, participants with a higher LAP index tended to be younger, women, and have diabetes mellitus and higher BMI, and have a low prevalence of current smokers and drinkers, and have lower values of HDL, Hcy. Likewise, significant differences in biological parameters were observed among the groups. DBP, pulse, FBG, TC, LDL, eGFR and uric acid of the participants in the highest LAP index quartile were significantly higher than those in the first quartile. Moreover, the high LAP index groups had a higher use of antihypertensive drugs, antiplatelet drugs glucose-lowering drugs (all $P < 0.05$).

Table 1
Clinical characteristics of the study population according to LAP

Variable	In LAP				P value
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
LAP range	0.14 to ≤14.75	14.75 to ≤29.79	29.79 to ≤52.83	52.83 to ≤514.60	< 0.001
Participants	1230	1233	1231	1232	
Males, N	865 (70.33%)	620 (50.28%)	501 (40.70%)	454 (36.85%)	< 0.001
Age, year	67.47 ± 8.81	65.25 ± 9.53	63.85 ± 9.20	61.10 ± 9.07	< 0.001
BMI, kg/m ²	19.91 ± 2.24	22.60 ± 2.35	24.50 ± 2.71	26.12 ± 3.08	< 0.001
Smoking status, N (%)	539 (43.82%)	331 (26.85%)	256 (20.80%)	262 (21.27%)	< 0.001
Drinking status, N (%)	393 (31.95%)	294 (23.84%)	263 (21.36%)	266 (21.59%)	< 0.001
SBP, mmHg	147.01 ± 19.08	147.22 ± 17.56	146.97 ± 16.25	147.54 ± 17.18	0.850
DBP, mmHg	86.43 ± 11.22	88.86 ± 10.99	89.17 ± 10.59	91.15 ± 10.43	< 0.001
pulse, bpm	74.00 ± 15.98	75.44 ± 14.85	75.74 ± 13.52	78.49 ± 13.92	< 0.001
Hcy, μmol/L	19.55 ± 11.63	19.05 ± 12.77	17.90 ± 11.00	17.41 ± 10.77	< 0.001
FBG, mmol/L	5.69 ± 1.06	5.91 ± 1.13	6.17 ± 1.69	6.72 ± 2.11	< 0.001
TC, mmol/L	4.79 ± 1.00	5.02 ± 1.02	5.28 ± 1.06	5.48 ± 1.19	< 0.001
HDL-C, mmol/L	1.71 ± 0.44	1.53 ± 0.37	1.43 ± 0.33	1.31 ± 0.33	< 0.001
LDL-C, mmol/L	2.50 ± 0.65	2.83 ± 0.70	3.13 ± 0.74	3.31 ± 0.81	< 0.001

Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CHD, coronary heart disease; FBG: fasting blood glucose; Hcy, homocysteine; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate.

\$diabetes mellitus was defined as self-reported physician diagnosis of diabetes or FBG concentration ≥ 7.0 mmol/L or use of glucose-lowering drugs.

Variable	ln LAP				P value
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Uric acid, mmol/L	416.46 ± 115.47	416.62 ± 116.96	430.02 ± 120.91	463.09 ± 124.52	< 0.001
eGFR, mL/min/1.73 m ²	83.93 ± 19.91	85.24 ± 19.73	87.37 ± 18.68	88.55 ± 19.24	< 0.001
Diabetes mellitus [§]	108 (8.78%)	175 (14.19%)	236 (19.17%)	376 (30.52%)	< 0.001
Antihypertensive drugs	678 (55.12%)	743 (60.26%)	763 (61.98%)	787 (63.88%)	< 0.001
Antiplatelet drugs	16 (1.30%)	35 (2.84%)	33 (2.68%)	24 (1.95%)	0.034
Glucose-lowering drugs	22 (1.79%)	40 (3.24%)	58 (4.71%)	81 (6.57%)	< 0.001
Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CHD, coronary heart disease; FBG: fasting blood glucose; Hcy, homocysteine; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate.					
[§] diabetes mellitus was defined as self-reported physician diagnosis of diabetes or FBG concentration ≥ 7.0 mmol/L or use of glucose-lowering drugs.					

Association of LAP index with baPWV and elevated baPWV

Overall, the LAP index was found to be positive associated with baPWV in models 1–3. Values are the regression coefficients (β) of association, with model 1 adjusted for age, sex; model 2 adjusted for age, sex, BMI, SBP, DBP, pulse, smoking status, and drinking status; model 3 adjusted for age, sex, BMI, SBP, DBP, pulse, smoking status, drinking status. FBG, TC, HDL, LDL-C, Hcy, uric acid, eGFR, diabetes mellitus, antihypertensive drugs, and antiplatelet drugs. In models 1–3, according to the β coefficients, for every 1-unit increase in ln LAP, the increases in baPWV were 19.81 cm/s (95%CI: 9.51, 30.11 cm/s), 42.39 cm/s (95%CI: 30.56, 54.22 cm/s) and 25.06 cm/s (95%CI: 10.91, 39.22 cm/s), respectively. As possible confounding factors were removed the association became greater. We also converted ln LAP from a continuous variable to a quartiles variable (Table 2). Compared with participants in the first quartile group, participants in quartile 2, quartile 3, and quartile 4 of the LAP index tended to have increased β coefficients of baPWV (all P-trend < 0.001).

Table 2
The association between LAP and baPWV in different models

LAP Index	BaPWV, cm/s, β (95%CI)		
	Model 1	Model 2	Model 3
Per 1 unit increase	19.81 (9.51, 30.11)	42.39 (30.56, 54.22)	25.06 (10.91, 39.22)
Quartiles			
Q1 (0.14 to ≤14.75)	0	0	0
Q2 (14.75 to ≤29.79)	46.38 (16.63, 76.14)	81.62 (54.37, 108.86)	70.29 (42.00, 98.59)
Q3 (29.79 to ≤52.83)	29.99 (-0.35, 60.33)	103.14 (72.52, 133.76)	84.00 (50.29, 117.72)
Q4 (52.83 to ≤ 514.60)	75.90 (44.75, 107.04)	150.06 (115.80, 184.32)	109.96 (69.73, 150.18)
P for trend	< 0.001	< 0.001	< 0.001
Model 1 was adjusted for age, sex.			
Model 2 was adjusted for age, sex, BMI, SBP, DBP, pulse, smoking status, drinking status.			
Model 3 was adjusted for age, sex, BMI, SBP, DBP, pulse, smoking status, drinking status. FBG, TC, HDL, LDL-C, Hcy, uric acid, eGFR, diabetes mellitus, antihypertensive drugs, antiplatelet drugs.			

As shown in Table 3, in a fully adjusted model, a positive association between the LAP and the risk of elevated baPWV was still exists. For every 1-unit increase in lnLAP, the adjusted ORs of elevated baPWV for participants in models 1–3 were 1.17 (95% CI: 1.09, 1.25), 1.42 (95% CI: 1.28, 1.58) and 1.24 (95% CI: 1.09, 1.40), respectively. When we converted ln LAP from a continuous variable to a quartiles variable, the adjusted OR of elevated baPWV for participants in quartile2- 4 was 1.51 (95% CI:1.18, 1.93), 1.80 (95% CI: 1.33, 2.44), and 2.24 (95% CI:1.56, 3.21) compared with participants in quartile 1 (P -trend < 0.001). A generalized additive model and penalized spline method was used further analyses the dose–response relation between lnLAP and baPWV and elevated baPWV (Fig. 1A-1B), showing that there were significant positive linear association of LAP index with baPWV and elevated baPWV.

Table 3
The association between LAP and elevated baPWV in different models

LAP Index	Elevated baPWV, OR (95%CI)		
	Model1	Model 2	Model 3
Per 1 unit increase	1.17 (1.09, 1.25)	1.42 (1.28, 1.58)	1.24 (1.09, 1.40)
Quartiles			
Q1 (0.14 to ≤14.75)	1	1	1
Q2 (14.75 to ≤29.79)	1.27 (1.04, 1.55)	1.66 (1.31, 2.10)	1.51 (1.18, 1.93)
Q3 (29.79 to ≤52.83)	1.26 (1.02, 1.54)	2.16 (1.65, 2.83)	1.80 (1.33, 2.44)
Q4 (52.83 to ≤ 514.60)	1.71 (1.38, 2.11)	3.14 (2.32, 4.26)	2.24 (1.56, 3.21) 1
P for trend	< 0.001	< 0.001	< 0.001
Model 1 was adjusted for age, sex.			
Model 2 was adjusted for age, sex, BMI, SBP, DBP, pulse, smoking status, drinking status.			
Model 3 was adjusted for age, sex, BMI, SBP, DBP, pulse, smoking status, drinking status. FBG, TC, HDL, LDL-C, Hcy, uric acid, eGFR, diabetes mellitus, antihypertensive drugs, antiplatelet drugs.			

Subgroup analyses by potential effect modifiers

To assess the relationship between ln LAP (per 1 unit increment) and baPWV in various groups, we performed exploratory subgroup analyses (Fig. 2). There were no significant interactions in the following of the subgroup variables included sex (male vs. Female; P -interaction = 0.808), age (< 65 vs. ≥65 years; P -interaction = 0.587), BMI (< 25 vs. ≥25 kg/m²; P -interaction = 0.568), current smoking (no vs. yes; P -interaction = 0.061), current drinking (no vs. yes; P -interaction = 0.861), SBP (< 140, 140–159, ≥ 160mmHg; P -interaction = 0.283), DBP (< 90, 90–99, ≥ 100mmHg; P -interaction = 0.550), Diabetes mellitus (no vs. yes; P -interaction = 0.894), and eGFR (< 60 vs. ≥60 mL/min/1.73 m²; P -interaction = 0.366). After adjustment for age, sex, BMI, SBP, DBP, pulse, smoking status, drinking status. FBG, TC, HDL, LDL-C, Hcy, uric acid, eGFR, diabetes mellitus, antihypertensive drugs, antiplatelet drugs, except for the stratifying variables (all P for interactions > 0.05).

Discussion

The current study includes 4926 participants, which is the largest number of research on the same subject so far. In this relatively large-scale cross-sectional study, we found for the first time that LAP index is independently positively correlated with baPWV and elevated baPWV in Chinese hypertensive patients, and no significant interaction was found in other subgroups.

The relation of LAP index with baPWV have been evaluated in several previous studies and yield inconsistent results. Previous study has reported that LAP index in relation with the risk of arterial stiffness[15, 17].whereas some studies suggested that there was no association between LAP index and arterial stiffness[16]. Cicero et al.[15]conducted a study using the Brisighella Heart Study Database; A total of 1731 healthy adults were included in this study, The mean age was 58.7 ± 15.8 years and 58.4 ± 15.5 years for men and women, respectively ($p = 0.777$). And the results showed that LAP was significantly correlated with the increase of bapWV (RR = 0.014, 95%CI 0.008–0.020, $p < 0.001$). A Japanese study explored the relationship between surrogate markers of insulin resistance including LAP and arteriosclerosis risk, including 1720 male (the mean age: 38.8 ± 10.1 years) and 1098 female (the mean age: 39.1 ± 9.4 years) healthy adults.The results show that LAP is superior to other insulin resistance indexes including TyG, and LAP index is positively correlated with the elevated bapwv, which is more significant in women[17]. Wakabayashi et al[16]. included 954 Japanese health examination subjects aged 39–64, and found that LAP index was not related to the increased risk of arterial stiffness.The reasons for the inconsistency of the above research results may be related to the characteristics of the study population, the size of the sample and the definition of arterial stiffness.This study included 4926 participants with an average age of 64.42 ± 9.44 years, the results indicated that LAP index is positively correlated with bapwv and elevated baPWV, and there is no interaction between LAP index and baPWV in gender subgroup. Sex and menopause-related changes in body composition and lipid metabolism[22, 23], which may lead to differences in the significance of surrogate markers of insulin resistance related to gender and menopause may explain this finding. The women in this study population are basically in postmenopausal state, so the prediction ability of LAP index of women may decrease under estrogen level, which is similar to that of men. However, further research is needed to solve this hypothesis.

The exact mechanism of LAP index and arterial stiffness, especially in populations with hypertension, remains unclear. Studies have shown that LAP has a good correlation with insulin resistance and is considered as a surrogate marker of insulin resistance (IR)[24, 25]. IR is closely related to the occurrence and development of atherosclerotic and is a risk factor of CVD[26]. The specific pathological mechanism is as follows: it is generally believed that plasma insulin has a beneficial effect on vascular endothelial function[27], and vasodilation is induced by nitric oxide production accelerated by insulin receptor through phosphatidylinositol 3- kinase (PI3k)/Akt insulin signaling pathway[28]. On the contrary, insulin resistance leads to the decrease of NO production by impairing PI3K/Akt signaling pathway[29], which is consistent with previous research results, which shows that insulin resistance is related to vascular dysfunction[30]. The effect of insulin resistance on arterial stiffness include that increase of sympathetic activity and the activation of renin-angiotensin-aldosterone system. IR can make the body in subclinical stress state, start the immune system slowly and slightly, and induce sustained and slight chronic inflammation, which leads to arterial stiffness[31, 32].

In order to better interpret the results of this study, we should include the limitations. First of all, this study is an cross-sectional study, so the causal relationship between LAP and baPWV cannot be obtained. Second, other confounding variables may affect our results, but regression analysis has adjusted a large

number of main parameters, so we are trustful in our observation. Finally, the population of this study is the relatively old hypertensive population in China, so it is limited to generalizability the results of this study to other populations.

Conclusions

In summary, this large-scale cross-sectional study indicated that a significant positive association between LAP index and baPWV was found in Chinese adults with hypertension. In daily clinical practice, monitoring the LAP index deserves more attention for the early prevention of arterial stiffness progression in hypertensive patients.

Declarations

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Conflict of Interests

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were following the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Authors' contributions

YMS participated in the literature search, data analysis, and data interpretation. YMS wrote the manuscript. LHH extracted and collected data. LHH, MHL, WZ, TW, LJZ HHB conceived of the study and participated in its design and coordination. LP and XSC participated in the study design and provided critical revision. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Consent for publication

Not applicable.

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Figures

Figure 1

Association of LAP index with baPWV and elevated baPWV. A linear association between LAP index and baPWV and elevated baPWV was found ($P < 0.05$). The solid line and dashed line represent the estimated values and their corresponding 95% confidence interval. Adjustment factors included age, sex, BMI, SBP, DBP, pulse, smoking status, drinking status, FBG, TC, HDL, LDL-C, Hcy, uric acid, eGFR, diabetes mellitus, antihypertensive drugs, antiplatelet drugs.

Figure 2

Subgroup analyses by potential effect modifiers. *Each subgroup analysis adjusted for age, sex, BMI, SBP, DBP, pulse, smoking status, drinking status. FBG, TC, HDL, LDL-C, Hcy, uric acid, eGFR, diabetes mellitus, antihypertensive drugs, antiplatelet drugs. except for the stratifying variable.

Supplementary Files

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