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A prospective cohort study on the effect of lipid accumulation product index on the incidence of cardiovascular diseases

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Abstract

Background Cardiovascular disease (CVD) is a chronic disease with a serious prognosis, and obesity is a risk factor for CVD. Lipid accumulation product index (LAP) is a new indicator of obesity, waist circumference, and triglycerides were included in the formula, but its association with CVD is inconsistent. Therefore, this study researched the effect of LAP levels on CVD.

Methods This prospective cohort study was based on the Kailuan cohort. A total of 95,981 participants who completed the first physical examination in 2006 and had no history of CVD or LAP absence were included. The participants were divided into four groups according to the LAP quartile (Q1 - Q4). Up until December 31, 2022, incidence density was calculated for each group. The hazard ratio (HR) and 95% confidence interval (CI) of CVD in each group were calculated by the Cox proportional hazards model.

Results During a median follow-up period of 15.95 years, 9925 incident CVD events occurred (2123 myocardial infarction and 8096 stroke). There were differences in potential confounders among the four groups ($P < 0.001$). The incidence density and 95% CI of CVD in Q1-Q4 groups were 4.76(4.54, 5.00), 6 0.50(6.24, 6.77), 8.13(7.84, 8.44) and 9.34(9.02, 9.67), respectively. There were significant differences in the survival curves among the four groups by log-rank test ($P < 0.001$). After adjusting for potential confounders, Cox proportional hazards model results showed that compared with the Q1 group, the HR and 95% CI of CVD in the Q2, Q3, and Q4 groups were1.15(1.08, 1.23), 1.29(1.21, 1.38) and 1.39(1.30, 1.49), respectively. The HR and 95%CI of myocardial infarction were 1.28(1.10, 1.49), 1.71(1.47, 1.98) and 1.92(1.64, 2.23), respectively. The HR and 95%CI of stroke were 1.11 (1.03, 1.19), 1.20 (1.12, 1.29) and 1.28 (1.19, 1.38), respectively. After subgroup analysis by gender, there was no significant interaction ($P = 0.169$), and the relationship between LAP and CVD in different genders was consistent with the main results. After subgroup analysis by age, there was a significant interaction ($P = 0.007$), and the association between LAP and CVD in different age groups was consistent with the main results. After subgroup analysis by BMI, there was no significant interaction

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($P = 0.506$), and the association between LAP and CVD in different BMI groups was consistent with the main results. The results remained robust after sensitivity analyses. For each unit increase in ln(LAP), the HR and 95%CI of CVD were 4.07 (3.92, 4.23).

Conclusion This study demonstrated that the risk of CVD increased with the increase of LAP level. The risk of CVD in group Q2 - Q4 was 1.15, 1.29, and 1.39 times higher than that in group Q1, respectively.

Clinical trial registration number ChiCTR2000029767

Keywords Lipid accumulation product index, Cardiovascular disease, Cohort

Introduction

In 2022, the prevalence of cardiovascular diseases (CVD) in China reached 330 million individuals [1]. Among the primary risk factors for CVD, obesity has been particularly emphasized [2]. Chronic disease data from 2018 indicated that the rates of overweight and obesity among Chinese adults were 33.3% and 14.1%, respectively [3]. It is projected that by 2030, the prevalence of overweight and obesity will rise to 65.3%, affecting approximately 789.95 million individuals [3]. Since the World Health Organization (WHO) recommended the use of Body Mass Index (BMI) for the assessment of obesity due to its convenience and wide applicability, it has been extensively employed for evaluating the degree of obesity [4]. Data from 2021 attributed 1.95 million global cardiovascular deaths to high BMI [5]. However, given that BMI does not accurately assess body fat accumulation, research has suggested the importance of considering obesity in individuals with normal BMI [6]. In 2005, Kahn introduced the Lipid Accumulation Product (LAP) index, which includes waist circumference (WC) and triglycerides (TG), offering a better assessment of body fat accumulation [7]. Studies have demonstrated that LAP can predict the occurrence of various diseases, including CVD, metabolic syndrome, and hypertension [8–13]. A study in Greece indicated a positive correlation between LAP levels and the incidence of CVD over 10 years [14], whereas research in Iran showed no association [15]. To date, only one cohort study based on the Chinese population has investigated the relationship between LAP and CVD, finding no association [16]. Previous studies on the impact of LAP on CVD incidence yielded inconsistent results, and none considered the influence of time. Based on the Kailuan cohort, survival analysis was employed to investigate the effect of temporal changes in LAP levels on CVD incidence during long-term follow-up in a large and stable population. This study, based on the Kailuan cohort, aimed to investigate the relationship between the LAP index and the incidence of CVD in the Chinese population. Additionally, this study aimed to compare the predictive performance of LAP and BMI for CVD risk in this population, as assessed by the Harrell's C index.

Methods

Participants

The study population was from the Kailuan Study (Tangshan, China), which was a large population-based prospective cohort study in the Kailuan community. Kailuan Community is an energy-dominated community located in the North China Plain. In 2006, the cohort initially enrolled 101,510 participants, including all on-the-job workers and retirees. This project was completed jointly by Kailuan General Hospital and 10 affiliated hospitals. The detailed study design of the Kailuan study can be referred to in the literature published by our research group [17]. This study included all individuals aged 18 years or older who underwent health examinations and provided informed consent in 2006, totaling 101,510 participants. After excluding 2944 participants with LAP missing and 2585 participants with a history of CVD, 95,981 participants were included.

Human ethics and consent to participate declarations

The study procedures were by the principles of the Declaration of Helsinki and were approved by the Ethics Committee of Kailuan Pharmaceutical Group and Kailuan Group Company (approval No. 2006-05). All participants agreed to participate in the study and provided written informed consent.

Data collection

General information (including gender, smoking, drinking, physical activity, and medication) and anthropometric indicators (including height, weight, and blood pressure) were collected from the Kailuan Study and physical examination data in 2006. Among them, WC was collected as follows: the participants was asked to stand upright with feet together, arms naturally lowered, exposing the abdominal skin, and breathing gently during measurement. Measurements were made using a waistline, with the lower edge of the scale placed horizontally around 1 cm from the upper edge of the navel. The reading was recorded and the waist circumference was accurate to 0.1 cm.

Biochemical data

Study participants were required to avoid a high-fat diet within 24 h before their biochemical examination. On the morning of the examination, 5 ml of fasting venous blood was drawn from the elbow, and after centrifugation, the supernatant serum was collected for biochemical indicator testing using an automatic biochemical analyzer (Hitachi 7600). The indicators measured included triglycerides (TG), fasting blood glucose (FBG), creatinine, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and high-sensitivity C-reactive protein (hs-CRP), among others. All procedures were strictly performed by the instruction manual, and blood samples were collected and analyzed by professional medical personnel. Detailed information on the content and methods of data collection can be found in previously published articles by our research group [17].

Outcome event data

The cardiovascular laboratory staff of Kailuan General Hospital visited the 11 hospitals of Kailuan Group to collect the outcome events every six months. At the same time, since 2010, Kailuan Medical Insurance Center has collected the medical information of the participants outside the above-mentioned medical institutions, and the above-mentioned staff members have gone to the relevant medical institutions to collect the outcome events.

Definitions of covariates

BMI was calculated as weight (kg) divided by the square of height (m^2). Estimated Glomerular Filtration Rate (eGFR) was estimated using the Chronic Kidney Disease Epidemiology Collaboration formula [18]. Drinking was defined as an average consumption of at least 100 ml per day of spirits (with an alcohol content of 50% or higher) over the past year, for a duration of more than one year, without having quit [17]. Smoking was defined as having smoked at least one cigarette per day on average over the past year, for a duration of more than one year, without having quit [17]. Physical exercise was classified into three categories: regular, occasional, and never. "Regular" exercise was defined as sessions lasting at least 30 min each, occurring three or more times per week. "Occasional" exercise referred to activities that did not meet the criteria for "regular." "Never" was defined as participants who never engaged in exercise [17]. Educational level was classified into three categories: "Below high school," "High school," and "College or above." "Below high school" included categories for the illiterate, primary school, and junior high school. "High school" encompassed technical secondary school and high school. "College or above" referred to junior college, bachelor's degree, and graduate studies. Hypertension was defined as having either a systolic blood pressure (SBP) of 140 mmHg or higher, or a diastolic blood pressure (DBP) of 90 mmHg or higher; or having both SBP below 140 mmHg and DBP below 90 mmHg while currently taking antihypertensive medication [19]. Diabetes was defined as having a fasting blood glucose (FBG) level of 7.0 mmol/L or higher, or having an FBG level below 7.0 mmol/L while currently using antidiabetic medication [20].

Definition of group

The calculation formula for LAP is based on existing research [21]: For males, LAP = [WC−61.3] × TG, and for females, LAP = [WC−55.6] × TG. The participants were divided into four groups according to the quartile of LAP. Quartile 1 (Q1) includes males with LAP < 22.49 cm·mmol/L and females with LAP < 17.29 cm·mmol/L. Quartile 2 (Q2) includes males with 22.49 ≤ LAP < 36.95 cm·mmol/L and females with 17.29 ≤ LAP < 30.67 cm·mmol/L. Quartile 3 (Q3) includes males with 36.95 ≤ LAP < 63.17 cm·mmol/L and females with 30.67 ≤ LAP < 52.99 cm·mmol/L. Quartile 4 (Q4) includes males with LAP ≥ 63.17 cm·mmol/L and females with LAP ≥ 52.99 cm·mmol/L.

Follow-up and outcome events

The beginning point of follow-up was the first physical examination. The study outcome event was the first occurrence of CVD (including myocardial infarction and stroke) as the endpoint event. Loss to follow-up was defined as not being followed up once after the first physical examination. The follow-up period ended on December 31, 2022. CVD events were defined according to the International Classification of Diseases, 10th Revision, with I63 for hemorrhagic stroke, I60 and I61 for ischemic stroke, and I21 for myocardial infarction. During the follow-up period, the diagnostic criteria were all adopted by the World Health Organization criteria [22, 23], and the diagnoses were confirmed and recorded by professional physicians based on the inpatient medical records.

Statistical methods

SAS 9.4 software was used to analyze the data. *P*-value < 0.05 was considered statistically significant (two-sided).

Missing covariate data were assumed to be random, and complete conditional random imputation was used to handle missing covariate values. Imputation was performed with the use of discriminant analysis for categorical variables and regression modeling for continuous variables. The entire imputation process was performed 20 iterations and 1 independent imputation datasets were generated.

The continuous variables with a normal distribution are displayed as mean (standard deviation), continuous

variables with a skewed distribution are shown as median (interquartile range), and categorical variables are presented as frequency (percentage). Differences between groups were tested using the Analysis of Variance (ANOVA) for normally distributed variables, the Kruskal-Wallis test for skewed variables, and the $\chi 2$ test for categorical variables.

According to the time when the participants entered the cohort, the follow-up person-years of each group were calculated by the exact calculation method. The incidence density was calculated using the following formula: incidence density = (number of new cases/total Person-Years) × 1000. The Log-Log Survival (LLS) plot method was used to determine whether the assumptions of the Cox proportional hazards (PH) regression analysis were met. The hazard ratio (HR) and 95% confidence interval (CI) of the Cox proportional hazards model were used to evaluate the association between LAP and CVD.

CVD incidence and time were used as the dependent variables, with LAP as the independent variable, to assess the impact of LAP on CVD incidence while adjusting for potential confounders. Given the skewed distribution of the covariates hs-CRP and eGFR, logarithmic transformations were applied to these variables in the adjusted model.

A simple CVD risk prediction model based on the Framingham study was utilized [24]. Non-laboratory indicators not included in the initial model were then incorporated. Laboratory indicators were subsequently included to complete the analysis. Model 1: Adjusted for age, BMI, SBP, gender(male/female), smoking (current/never/former), diabetes(yes/no), use of antihypertensive medication (yes/no). Model 2: Expands on model 1 by further adjusting for drinking (current/never/former), educational level (below high school/high school/ college or above), physical exercise (never/occasional/regular), CVD family history (yes/no), use of antidiabetic medication (yes/no), and use of lipid-lowering medication (yes/no). Model 3: Expands on model 2 by further adjusting for LDL-C, HDL-C, ln(hs-CRP), and ln(eGFR).

Harrell's C index was used to evaluate the predictive ability of LAP, BMI, and the established model for CVD. Two models were established for each index, and the models' C indices along with their 95% CIs were calculated. Model 1: adjusted for LAP or BMI only. Model 2: adjusted for LAP or BMI, age, SBP, gender (male/female), smoking (current/never/former), diabetes (yes/no), use of antihypertensive medication (yes/no), drinking(current/never/former), educational level (below high school/high school/college or above), physical exercise (never/occasional/regular), CVD family history (yes/no), use of antidiabetic medication (yes/no), use of lipid-lowering medication (yes/no), LDL-C, HDL-C, ln(hs-CRP), and ln(eGFR).

Due to the skewed distribution of LAP among study participants, LAP was log-transformed and included as a continuous variable in the Cox model. LAP was treated as a time-dependent variable, changing over time. The area under the curve (AUC) of LAP values from 2006 to 2018 was calculated and adjusted as a covariate in the model. Missing LAP values during the follow-up period were imputed using the mean of the adjacent two years. The change in CVD risk associated with each unit increase in the natural logarithm of LAP (Ln(LAP)) was calculated for different gender groups. The adjusted model, in addition to including the AUC for LAP and time, retained all other covariates consistent with the three models previously mentioned.

To ensure the robustness of the results, the following sensitivity analyses were conducted based on Model 3: (1) Excluding participants with missing covariate data that was not imputed at baseline. (2) Excluding participants who were on antihypertensive, antidiabetic, and lipid-lowering medications at baseline. (3) Excluding participants lost to follow-up after baseline. (4) Excluding participants lost to follow-up after baseline. (4) Excluding participants with a follow-up time of less than three years. The main analysis included the above four conditions that excluding participants.

Due to multiple analyses conducted on the same dataset, the *P*-values were adjusted using the Bonferroni method. Since four repeated analyses were performed in the primary analysis, the two-sided *P*-value was adjusted to 0.013.

Results

According to the inclusion and exclusion criteria, 95,981 participants were finally included. In a study population comprising 95,981 participants with an average age of 51.45±12.49 years, 76,448 were male (79.65%). The participants were divided into four quartiles: Q1 with 24,001, Q2 with 23,970, Q3 with 24,001, and Q4 with 23,999 individuals. Differences in gender, age, education level, drinking, smoking, physical exercise, BMI, SBP, DBP, WC, TG, LDL-C, HDL-C, hs-CRP, eGFR, hypertension, diabetes, and the use of antihypertensive, antidiabetic, and lipid-lowering medications were statistically significant across the quartiles ($P<0.001$), as shown in Table 1. The baseline characteristics of included and excluded study participants were compared, as shown in Supplementary Table 1.

The Harrell's C index and its 95% confidence interval for Model 1 were 0.583 (0.577, 0.588) for LAP and 0.556 (0.550, 0.561) for BMI. For Model 2, the Harrell's C index and its 95% confidence interval were 0.721 (0.716, 0.725) for LAP and 0.720 (0.715, 0.724) for BMI.

The association between LAP and the incidence of CVD was examined over a total follow-up duration of

Table 1 Basic characteristics of different groups of population

Variables	Q1 *N* = 24,001	Q2 *N* = 23,970	Q3 *N* = 24,001	Q4 *N* = 23,999	*P*
Male (%)	19,120 (79.66)	19,089 (79.64)	19,125 (79.65)	19,114 (79.64)	< 0.001
Age (years)	49.08 ± 13.65	51.47 ± 12.40	52.82 ± 11.98	52.43 ± 11.48	< 0.001
Educational level (%)					< 0.001
below high school	17,714 (73.81)	19,626 (81.88)	19,569 (81.50)	19,555 (81.48)	
high school	3800(15.83)	2847 (11.88)	2895 (12.06)	2977 (12.40)	
college or above	2487 (10.36)	1497 (6.25)	1547 (6.44)	1467 (6.11)	
Drinking (%)	9732 (40.55)	8219 (34.29)	8701 (36.24)	9179 (38.25)	< 0.001
Smoking (%)	8920 (37.17)	7603 (31.72)	7848 (32.69)	8479 (35.33)	< 0.001
Physical exercise (%)					< 0.001
never	2495 (10.40)	2024 (8.44)	2061 (8.58)	2054 (8.56)	
occasional	17,616 (73.40)	18,402 (76.77)	18,156 (75.62)	18,390 (76.63)	
regular	3890 (16.21)	3544 (14.79)	3794 (15.80)	3555 (14.81)	
BMI (kg/m^2)	22.57 ± 2.62	24.56 ± 2.76	25.86 ± 2.92	27.04 ± 3.13	< 0.001
SBP (mm Hg)	124.01 ± 18.39	129.60 ± 19.23	132.80 ± 19.47	136.05 ± 19.47	< 0.001
DBP (mm Hg)	79.46 ± 10.24	82.75 ± 10.63	84.48 ± 10.69	86.53 ± 10.79	< 0.001
WC (cm)	77.95 ± 7.37	85.54 ± 7.07	90.09 ± 7.63	94.25 ± 8.68	< 0.001
TG (mmol/L)	0.77 ± 0.27	1.10 ± 0.31	1.56 ± 0.46	3.24 ± 1.76	< 0.001
LDL-C (mmol/L)	2.30 ± 0.80	2.37 ± 0.81	2.39 ± 0.84	2.28 ± 0.88	< 0.001
HDL-C (mmol/L)	1.57 ± 0.37	1.56 ± 0.36	1.53 ± 0.36	1.51 ± 0.38	< 0.001
FBG (mmol/L)	5.14 ± 1.06	5.29 ± 1.25	5.47 ± 1.44	5.74 ± 1.74	< 0.001
hs-CRP (mg/L)	0.50 (0.20, 1.41)	0.70 (0.28, 1.90)	0.90 (0.34, 2.30)	1.14 (0.45, 2.93)	< 0.001
eGFR (mL/min/1.73 m^2)	85.49 (72.38, 98.71)	80.38 (67.18, 94.83)	79.63 (66.93, 94.14)	78.90 (65.75, 93.77)	< 0.001
Hypertension (%)	6670 (27.79)	9821 (40.97)	11,724 (48.83)	13,611 (56.71)	< 0.001
Diabetes (%)	992 (4.13)	1568 (6.54)	2472 (10.30)	3728 (15.53)	< 0.001
Taking antihypertensive medication (%)	1205 (5.02)	1916 (7.99)	2893 (12.05)	3769 (15.70)	< 0.001
Taking antidiabetic medication (%)	278 (1.16)	412 (1.72)	626 (2.61)	841 (3.50)	< 0.001
Taking lipid-lowering medication (%)	137 (0.57)	233 (0.97)	365 (1.52)	662 (2.76)	< 0.001

Body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBG), high sensitivity C-reactive protein (hs-CRP), and estimated glomerular filtration rate (eGFR). The continuous variables with a normal distribution are displayed as mean (standard deviation), continuous variables with a skewed distribution are shown as median (interquartile range), and categorical variables are presented as frequency (percentage). Differences between groups were tested using the Analysis of Variance (ANOVA) for normally distributed variables, the Kruskal-Wallis test for skewed variables, and the χ2 test for categorical variables

Quartile 1 (Q1) includes males with LAP < 22.49 cm·mmol/L and females with LAP < 17.29 cm·mmol/L.

Quartile 2 (Q2) includes males with 22.49 ≤ LAP < 36.95 cm·mmol/L and females with 17.29 ≤ LAP < 30.67 cm·mmol/L.

Quartile 3 (Q3) includes males with 36.95 ≤ LAP < 63.17 cm·mmol/L and females with 30.67 ≤ LAP < 52.99 cm·mmol/L.

Quartile 4 (Q4) includes males with LAP ≥ 63.17 cm·mmol/L and females with LAP ≥ 52.99 cm·mmol/L.

1,385,995.63 person-years, with a median follow-up time of 15.95 years. A total of 9925 CVD events occurred during the follow-up period (2123 myocardial infarction events, 8096 stroke events, 294 both events). In the study, a total of 3333 participants lost to follow-up had neither follow-up information nor outcome information. The baseline characteristics of participants lost to follow-up and those who were followed up were compared, as shown in Supplementary Table 2. The incidence density per quartile was 4.53 (95% CI: 4.31, 4.77) for Q1, 6.19 (95% CI: 5.93, 6.46) for Q2, 7.77 (95% CI: 7.47, 8.07) for Q3, and 8.89 (95% CI: 8.57, 9.22) for Q4, as presented in Table 2. The survival curves of different LAP groups were significantly different after a log-rank test ($P < 0.001$), as illustrated in Fig. 1. The LLS plot showed that there was crossover between groups, indicating that the PH assumption is not satisfied. However, after truncating the follow-up time to 3 years, the PH assumption was satisfied for the population with a follow-up time of more than 3 years.

The missing data for incorporated in the analysis of covariate were as follows: education level 352(0.37%), smoking 145(0.15%), drinking 158(0.16%), physical exercise 342(0.36%), hs-CRP 477(0.50%), SBP 1988(2.07%), HDL-C 970(1.01%), LDL-C 983(1.02%), BMI 1008(1.05%), eGFR 990(1.03%). Multivariate Cox regression analysis of model 3 showed that compared with the Q1 group, the HR and 95%CI of CVD in the Q2 group, Q3 group, and Q4 group were 1.15(1.08, 1.23), 1.29(1.21, 1.38) and 1.39(1.30, 1.49), respectively (Table 2). The

Table 2 LAP levels with the risk of CVD (HR and 95%CI)

	Q1	Q2	Q3	Q4	*P*-trend
Case/Participants (n/N)	1685/24,001	2260/23,970	2795/24,011	3185/23,999	
Incidence rate (1,000 person-years)	4.76(4.54, 5.00)	6.50(6.24, 6.77)	8.13(7.84, 8.44)	9.34(9.02, 9.67)	< 0.001
Non-adjusted Model	1.00	1.37 (1.28, 1.46)	1.71(1.61, 1.82)	1.97(1.86, 2.09)	< 0.001
Multivariate adjusted model 1	1.00	1.17(1.09, 1.24)	1.30(1.22, 1.39)	1.41(1.31, 1.50)	< 0.001
Multivariate adjusted model 2	1.00	1.15(1.08, 1.23)	1.30(1.22, 1.38)	1.40(1.31, 1.50)	< 0.001
Multivariate adjusted model 3	1.00	1.15(1.08, 1.23)	1.29(1.21, 1.38)	1.39(1.30, 1.49)	< 0.001

Lipid accumulation product index (LAP), cardiovascular disease (CVD), hazard Ratio (HR), confidence interval (CI).

Model 1: Adjusted for age, BMI, SBP, gender(male/female), smoking (current/never/former), diabetes(yes/no), use of antihypertensive medication (yes/no)

Model 2: Expands on model 1 by further adjusting for drinking (current/never/former), educational level (below high school/high school/ college or above), physical exercise (never/occasional/regular), CVD family history (yes/no), use of antidiabetic medication (yes/no), and use of lipid-lowering medication (yes/no)

Model 3: Expands on model 2 by further adjusting for LDL-C, HDL-C, ln(hs-CRP), and ln(eGFR).

Cochran-Armitage trend test was used for incidence, and the variables of the four groups were put into the model as continuous variables for linear trend test

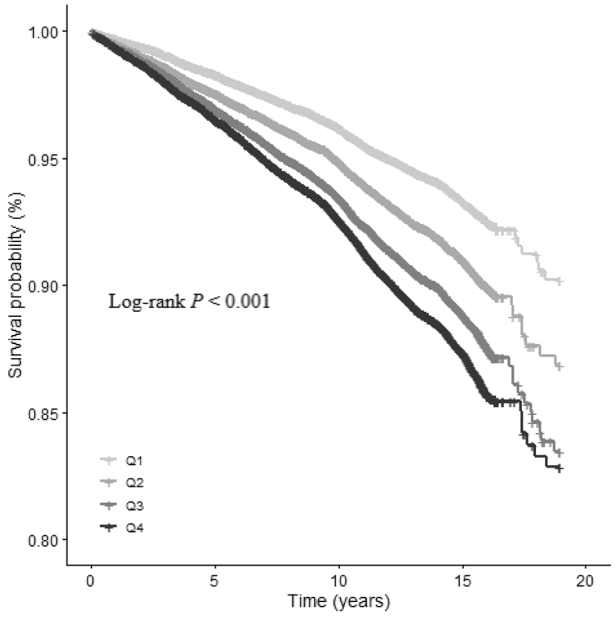

Fig. 1 Survival curves for different LAP levels groups

HR and 95%CI of myocardial infarction were 1.28(1.10, 1.49), 1.71(1.47, 1.98) and 1.92(1.64, 2.23), respectively (Table 3). The HR and 95%CI for stroke were 1.11 (1.03, 1.19), 1.20 (1.12, 1.29) and 1.28 (1.19, 1.38), respectively (Table 3).

After stratification by gender, there was no statistically significant difference in the interaction effect between gender and group (P=0.169), as shown in Table 4. In males, multivariate Cox regression analysis of multivariate adjust model showed that compared with the Q1 group, the HR and 95%CI of CVD in the Q2, Q3, and Q4 groups were 1.15(1.07, 1.23), 1.29(1.20, 1.38) and 1.38(1.28, 1.48), respectively. In female, compared with the Q1 group, the HR and 95%CI of CVD in the Q2 group, Q3 group and Q4 group were 1.28(1.01, 1.63), 1.43(1.13, 1.80) and 1.57(1.25, 1.98), respectively.

After age stratification, a significant interaction effect was observed (P=0.007), as shown in Table 4. In the age < 60 years, multivariate Cox regression analysis of multivariate adjust model showed that compared with the Q1 group, the HR and 95%CI of CVD in the Q2 group, Q3 group, and Q4 group were 1.20(1.11, 1.30), 1.33(1.23, 1.45) and 1.43(1.32, 1.56), respectively. In the age ≥ 60 years, compared with the Q1 group, the HR and 95%CI of CVD in the Q2 group, Q3 group and Q4 group were 1.06(0.96, 1.18), 1.17(1.06, 1.31) and 1.24(1.11, 1.39), respectively.

After stratification by BMI, there was no statistically significant difference in the interaction effect between BMI and group (P=0.506), as shown in Table 4. In BMI < 25 kg/m^2 population, multivariate Cox regression analysis of multivariate adjust model showed that compared with the Q1 group, the HR and 95%CI of CVD in the Q2, Q3, and Q4 groups were 1.17(1.08, 1.27), 1.30(1.19, 1.42) and 1.42(1.29, 1.56), respectively. In BMI ≥ 25 kg/m^2 population, compared with the Q1 group, the HR and 95%CI of CVD in the Q2 group, Q3 group and Q4 group were 1.07(0.95, 1.21), 1.21(1.08, 1.36) and 1.31(1.16, 1.47), respectively.

After several sensitivity analyses in this study, it was found that the results remained robust and the trend was consistent with the main results, as shown in Table 5.

The ln(LAP) was used as a continuous variable in the Cox regression analysis. And the results of multivariate adjusted model 3 after adjusting for variables showed that for every unit increase in ln(LAP), the HR and 95%CI of CVD in the total population were 4.07 (3.92, 4.23). The HR and 95%CI for CVD were 3.95 (3.79, 4.11) in the male and 4.41 (3.93, 4.95) in the female. The results are shown in Table 6.

Discussion

Utilizing data from the Kailuan cohort study, this research has demonstrated that the risk of CVD incidence escalates progressively with increasing levels of

Table 3 LAP levels with the risk of myocardial infarction and stroke (HR and 95%CI)

	Q1	Q2	Q3	Q4	*P*-trend
Myocardial Infarction					
Case/Participants (n/N)	292/24,001	437/23,970	640/24,011	754/23,999	
Incidence rate (1000 person-years)	0.81(0.72, 0.91)	1.22(1.11, 1.34)	1.80(1.67, 1.94)	2.13(1.98, 2.29)	< 0.001
Non-adjusted Model	1.00	1.51(1.30, 1.75)	2.23(1.94, 2.56)	2.63(2.30, 3.01)	< 0.001
Multivariate adjusted Model 1	1.00	1.32(1.13, 1.53)	1.74(1.50, 2.02)	1.96(1.69, 2.29)	< 0.001
Multivariate adjusted Model 2	1.00	1.30(1.12, 1.52)	1.74(1.50, 2.02)	1.96(1.69, 2.29)	< 0.001
Multivariate adjusted Model 3	1.00	1.28(1.10, 1.49)	1.71(1.47, 1.98)	1.92(1.64, 2.23)	< 0.001
Stroke					
Case/Participants (n/N)	1439/24,001	1865/23,970	2242/24,011	2550/23,999	
Incidence rate (1000 person-years)	4.05(3.85, 4.27)	5.33(5.09, 5.58)	6.46(6.20, 6.73)	7.39(7.11, 7.68)	< 0.001
Non-adjusted Model	1.00	1.32 (1.23, 1.41)	1.60 (1.50, 1.71)	1.83 (1.72, 1.96)	< 0.001
Multivariate adjusted Model 1	1.00	1.12 (1.04, 1.20)	1.20 (1.12, 1.29)	1.29 (1.20, 1.39)	< 0.001
Multivariate adjusted Model 2	1.00	1.11 (1.03, 1.19)	1.20 (1.12, 1.29)	1.28 (1.19, 1.38)	< 0.001
Multivariate adjusted Model 3	1.00	1.11 (1.03, 1.19)	1.20 (1.12, 1.29)	1.28 (1.19, 1.38)	< 0.001

Lipid accumulation product index (LAP), cardiovascular disease (CVD), hazard ratio (HR), confidence interval (CI).

Model 1: Adjusted for age, BMI, SBP, gender(male/female), smoking (current/never/former), diabetes(yes/no), use of antihypertensive medication (yes/no)

Model 2: Expands on model 1 by further adjusting for drinking (current/never/former), educational level (below high school/high school/ college or above), physical exercise (never/occasional/regular), CVD family history (yes/no), use of antidiabetic medication (yes/no), and use of lipid-lowering medication (yes/no)

Model 3: Expands on model 2 by further adjusting for LDL-C, HDL-C, ln(hs-CRP), and ln(eGFR).

Cochran-Armitage trend test was used for incidence, and the variables of the four groups were put into the model as continuous variables for linear trend test

LAP. LAP was superior to BMI in predicting CVD. Compared to Q1, the risk of developing CVD in the second to fourth quartiles (Q2 - Q4) was 1.15, 1.29, and 1.39 times higher, respectively. This trend was consistent for both stroke and myocardial infarction, with a more pronounced effect of LAP on CVD incidence in the age<60 years.

A cohort study in Greece involving 3042 participants over a 10-year follow-up for CVD events corroborated a positive correlation between LAP and a 10-year incidence rate of CVD, aligning with our findings [14]. When comparing LAP with other anthropometric indicators such as BMI, WC, and waist-to-hip ratio, LAP emerged as the optimal predictor after adjusting for relevant covariates. However, our study is limited to comparisons with BMI only, which is a shortcoming. Yet, compared to the Greek cohort, our study boasts advantages such as a different ethnicity, a larger population, and a longer follow-up period. Another study in Iran in 2014, involving 2378 individuals of normal weight over a 10-year follow-up, identified LAP as a predictive marker for CVD, consistent with our results [25]. However, that study did not account for gender or the impact of antihypertensive and lipid-lowering medications, aspects that were addressed in our research. Bozorgmanesh et al. found that LAP was associated with an increased risk of CVD in female, but no independent association was found in male. This was consistent with our study, where LAP can assess the risk of CVD incidence in female. In our study, a larger male sample size allowed us to observe this association in male as well [11]. Jafari et al. [26] suggested that using the combined lipid indices of LAP, Triglyceride-Glucose Index, and Visceral Adiposity Index may be more reliable in predicting the 5-year and 10-year CVD risk compared to simple lipid measurements. Among these indices, LAP performed the best, making it a stronger indicator for predicting CVD risk. This is consistent with our research, which found that, without adjusting for covariates, the C-index of LAP is superior to that of BMI, indicating better predictive ability. However, it is still recommended to use LAP as a supplementary index in combination with other predictors for assessing CVD risk.

Conversely, a 13-year-long cohort study in Iran with 4353 participants found no association between LAP levels and CVD incidence, diverging from our findings [15]. This discrepancy could stem from cultural and geographical differences between the Iranian and Chinese populations. Additionally, the validation of the LAP-CVD relationship may necessitate a larger sample size, a gap our study has filled. The Iranian cohort used specific

Table 4 Stratification analysis of LAP levels and the risk of CVD (HR and 95%CI)

	Q1	Q2	Q3	Q4	*P*-interaction
Gender					0.169
Male[a]					
Case/Participants (n/N)	1581/19,120	2043/19,089	2450/19,125	2691/19,114	
Incidence rate (1000 person-years)	5.70(5.43, 5.99)	7.50(7.18, 7.83)	9.09(8.73, 9.45)	10.01(9.64,10.39)	
Multivariate adjusted model	1.00	1.15(1.07, 1.23)	1.29(1.20, 1.38)	1.38(1.28, 1.48)	
Female[a]					
Case/Participants (n/N)	104/4881	217/4881	345/4886	494/4885	
Incidence rate (1000 person-years)	1.36(1.12, 1.65)	2.89(2.53, 3.30)	4.66(4.19, 5.18)	6.85(6.27, 7.48)	
Multivariate adjusted Model	1.00	1.23(0.97, 1.56)	1.31(1.04, 1.67)	1.40(1.09, 1.79)	
Age					0.007
< 60 years[b]					
Case/Participants (n/N)	1020/19,296	1448/18,793	1757/18,173	2141/18,604	
Incidence rate (1000 person-years)	3.45(3.25, 3.67)	5.10(4.85, 5.37)	6.46(6.17, 6.77)	7.78(7.46, 8.12)	
Multivariate adjusted model	1.00	1.20(1.11, 1.30)	1.33(1.23, 1.45)	1.43(1.32, 1.56)	
≥ 60 years[b]					
Case/Participants (n/N)	665/4705	812/5177	1038/5838	1044/5395	
Incidence rate (1000 person-years)	11.40(10.57,12.30)	12.70(11.86,13.61)	14.46(13.61,15.37)	15.84(14.91,16.83)	
Multivariate adjusted Model	1.00	1.06(0.96, 1.18)	1.17(1.06, 1.31)	1.24(1.11, 1.39)	
BMI					0.506
< 25 kg/m^2[b]					
Case/Participants (n/N)	1338/19,960	1263/14,086	1017/9453	751/6289	
Incidence rate (1000 person-years)	4.54(4.31, 4.79)	6.19(5.85, 6.54)	7.53(7.08, 8.01)	8.41(7.83, 9.03)	
Multivariate adjusted model	1.00	1.17(1.08, 1.27)	1.30(1.19, 1.42)	1.42(1.29, 1.56)	
≥ 25 kg/m^2[b]					
Case/Participants (n/N)	347/4041	997/9884	1778/14,558	2434/17,710	
Incidence rate (1000 person-years)	5.86(5.28, 6.52)	6.95(6.53, 7.39)	8.52(8.14, 8.93)	9.67(9.29,10.06)	
Multivariate adjusted model	1.00	1.07(0.95, 1.21)	1.21(1.08, 1.36)	1.31(1.16, 1.47)	

Lipid accumulation product index (LAP), cardiovascular disease (CVD), hazard ratio (HR), confidence interval (CI).

Multivariate adjusted Model: Adjusted for age, BMI, SBP, gender(male/female), smoking (current/never/former), diabetes(yes/no), use of antihypertensive medication (yes/no), drinking (current/never/former), educational level (below high school/high school/ college or above), physical exercise (never/occasional/regular), CVD family history (yes/no), use of antidiabetic medication (yes/no), and use of lipid-lowering medication (yes/no), LDL-C, HDL-C, ln(hs-CRP), and ln(eGFR).

[a] All covariates in the multivariate adjusted model except gender were included

[b] All covariates in the multivariate adjusted model

cutoff values for LAP grouping, which had a predictive performance area under the curve of only 0.55, indicating insufficient predictive power. Our study, however, employed quartiles for LAP grouping and conducted trend tests for a more nuanced analysis. In contrast to another study within China that found no association between LAP levels and CVD incidence regardless of gender, our findings suggest otherwise [16]. This discrepancy may be due to the previous study's sampling method, which did not account for dietary and lifestyle variations among different regional populations. Our research, based on the stable and relatively homogenous Kailuan community population, represents a strength in this aspect.

After stratifying by gender and adjusting for relevant covariates, the results of this study indicate no interaction effect between gender and groups (P=0.169). Compared to the Q1 group, both males and females in the Q4 group exhibited a higher risk of disease incidence. The absence of gender differences in this study may be attributed to the distinct distribution of adipose tissue between genders; men tend to accumulate fat in the abdominal region, while women accumulate it in the gluteal-femoral areas [27]. Despite having a higher total fat mass, women generally possess a lower volume of visceral fat compared to men [28]. Increased visceral fat is independently associated with an elevated risk of metabolic abnormalities in the heart. Women have higher TG levels compared to

Table 5 Sensitivity analysis of LAP and CVD risk (HR and 95%CI)

	Q1	Q2	Q3	Q4	*P*-trend
Sensitive analysis 1[a]					
Case/Participants (n/N)	1545/22,042	2065/22,342	2528/22,324	2809/21,812	
Incidence rate (1000 person-years)	4.74(4.51, 4.99)	6.34(6.08, 6.62)	7.87(7.57, 8.18)	9.00(8.67, 9.34)	
Multivariate adjusted Model	1.00	1.13(1.06, 1.21)	1.26(1.18, 1.35)	1.36(1.27, 1.46)	< 0.001
Sensitive analysis 2[b]					
Case/Participants (n/N)	1449/22,508	1850/21,679	2193/20,593	2380/19,501	
Incidence rate (1000 person-years)	4.34(4.12, 4.56)	5.83(5.57, 6.10)	7.35(7.05, 7.66)	8.46(8.13, 8.81)	
Multivariate adjusted Model	1.00	1.14(1.07, 1.23)	1.31(1.22, 1.40)	1.44(1.33, 1.55)	< 0.001
Sensitive analysis 3[c]					
Case/Participants (n/N)	1685/23,109	2260/23,143	2795/23,185	3185/23,211	
Incidence rate (1000 person-years)	4.97(4.74, 5.21)	6.76(6.49, 7.04)	8.46(8.15, 8.78)	9.70(9.37,10.05)	
Multivariate adjusted Model	1.00	1.15(1.07, 1.22)	1.28(1.20, 1.37)	1.39(1.30, 1.48)	< 0.001
Sensitive analysis 3[d]					
Case/Participants (n/N)	1461/23,557	1928/23,404	2389/23,381	2707/23,309	
Incidence rate (1000 person-years)	4.14(3.39,4.36)	5.56(5.32,5.81)	6.97(6.70,7.26)	7.96(7.67,8.27)	
Multivariate adjusted Model	1.00	1.15(1.07, 1.23)	1.29(1.20, 1.39)	1.39(1.29, 1.50)	< 0.001

Lipid accumulation product index (LAP), cardiovascular disease (CVD), hazard ratio (HR), confidence interval (CI).

Multivariate adjusted Model: Adjusted for age, BMI, SBP, gender(male/female), smoking (current/never/former), diabetes(yes/no), use of antihypertensive medication (yes/no), drinking (current/never/former), educational level (below high school/high school/ college or above), physical exercise (never/occasional/regular), CVD family history (yes/no), use of antidiabetic medication (yes/no), and use of lipid-lowering medication (yes/no), LDL-C, HDL-C, ln(hs-CRP), and ln(eGFR).

[a] This includes all covariates from the multivariable adjustment model, but missing covariate data were not imputed (n = 9396)

[b] This includes all covariates from the multivariable adjustment model, except for population who took antihypertensive, antidiabetic and lipid-lowering medication (n = 11,700)

[c] This includes all covariates from the multivariable adjustment model and the study population that was not followed up once after the baseline survey was excluded (n = 3333)

[d] This includes all covariates from the multivariable adjustment model and the study population that was followed up less than 3 years was excluded (n = 2330)

Table 6 Risk of CVD per unit increase in ln(LAP) (HR and 95%CI)

	Total Population	Male	Female
Case/Participants (n/N)	9925/95,981	8765/76,448	1160/19,533
Incidence rate (1000 person-years)	7.16(7.02, 7.30)	8.05(7.89, 8.22)	3.90(3.68, 4.13)
Multivariate adjusted model 1	5.13(4.96, 5.31)	4.75(4.58, 4.93)	7.02(6.37, 7.73)
Multivariate adjusted model 2	4.06 (3.91, 4.22)	3.93 (3.77, 4.09)	4.61 (4.11, 5.16)
Multivariate adjusted model 3	4.02 (3.87, 4.18)	3.91 (3.75, 4.07)	4.47 (3.99, 5.01)
Multivariate adjusted model 4	4.07 (3.92, 4.23)	3.95 (3.79, 4.11)	4.41 (3.93, 4.95)

Lipid Accumulation Product Index (LAP), cardiovascular disease (CVD), hazard Ratio (HR), confidence interval (CI).

Multivariate adjusted Model 1: Adjusted for AUC.

Multivariate adjusted Model 2: Expands on model 1 by further adjusting for age, BMI, SBP, gender(male/female), smoking (current/never/former), diabetes(yes/no), use of antihypertensive medication (yes/no)

Multivariate adjusted Model 3: Expands on model 2 by further adjusting for drinking (current/never/former), educational level (below high school/high school/ college or above), physical exercise (never/occasional/regular), CVD family history (yes/no), use of antidiabetic medication (yes/no), and use of lipid-lowering medication (yes/no)

Multivariate adjusted Model 4: Expands on model 3 by further adjusting for LDL-C, HDL-C, ln(hs-CRP), and ln(eGFR).

men; however, after adjusting for the amount of visceral fat by gender, no difference in TG levels was observed [28].

Following stratification by age and adjustment for relevant covariates, an interaction effect between age and groups was observed (P = 0.007). Both individuals aged ≥ 60 years and those < 60 years exhibited a higher risk of disease incidence in the Q4 group compared to the Q1 group. Moreover, the impact of LAP on the incidence of CVD was greater in individuals aged < 60 years than in those aged ≥ 60 years. Considering age as a significant risk factor for CVD, the influence of LAP appeared to diminish in the ≥ 60 years cohort after stratification and adjustment for age-related covariates [29]. This reduction

may be due to the prevalence of comorbidities, including CVD, in over half of the elderly population, diminishing the isolated impact of visceral fat accumulation. However, as age increases, fat distribution shifts from peripheral to more central visceral accumulation [30], implying that LAP still negatively affects the occurrence of CVD in individuals aged ≥ 60 years.

No significant interaction was observed between BMI and groups ($P=0.632$). Compared to the Q1 group, both the BMI < 25 kg/m^2 and the BMI ≥ 25 kg/m^2 in the Q4 group exhibited a higher risk of disease incidence. BMI and LAP are the same indicators of obesity, but the calculation methods are completely different. There was no evidence that people with low BMI had lower WC and TG levels, so LAP can be considered as a supplementary indicator of obesity.

The mechanisms by which the LAP influences the onset of CVD may include: Firstly, from the perspective of obesity and inflammation, preadipocytes and macrophages within adipose tissue produce pro-inflammatory cytokines. Excessive visceral fat can lead to dysfunction in subcutaneous adipose tissue, diminishing its capacity to store fat and thereby inflicting metabolic damage (such as insulin resistance and endothelial dysfunction), which in turn can trigger the development of CVD [31]. Secondly, from the standpoint of TG, while TG can be degraded by cells, cholesterol cannot, leading to the occurrence of diseases through the hydrolysis of TG and the accumulation of cholesterol in arterial wall foam cells mediated by TG and TG-rich lipoproteins (remnant cholesterol) [32].

In comparison with previous studies, this research employed a prospective cohort design, conducting long-term follow-up on a stable population with a large total sample size, which enhances its representativeness. However, some limitations are present in the study. Firstly, the proportion of male significantly outweighs that of females, potentially introducing a selection bias. Stratified analysis was utilized to further investigate the relationship between LAP levels and CVD incidence among male and female. Secondly, our study did not consider the window period for CVD, and a short follow-up time might result in the occurrence of diseases due to other reasons, which would not meet the PH assumption. Therefore, in the sensitivity analysis, we excluded participants with a short follow-up time and repeated the main analysis. Lastly, discrepancies between unadjusted models and the final model were observed, necessitating further application of epidemiological causal analysis methods to consider the differences after adjusting for variables.

In the data analysis section, we imputed missing covariates only once. While this retained more data, it also introduced the effects of imputation. Therefore, we conducted a sensitivity analysis on the non-imputed data to ensure the robustness of the results.

Conclusion

The findings of this study demonstrate that with each unit increase in ln(LAP) rises the risk of CVD by 4.07 times under long-term influence. LAP can serve as an alternative indicator to BMI within the general population for predicting the risk of CVD onset. Therefore, in the early prevention of CVD, LAP should be considered as a supplementary assessment indicator for obesity, monitoring visceral fat accumulation, and facilitating timely management of body fat, increased physical activity, and controlled dietary health to prevent the onset of CVD at an early stage.

Supplementary Information

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Supplementary Material 1

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Author contributions

TAN YZ collected data and drafted the manuscript. WU YT contributed to the design of the study. TAN YZ and WU YT contributed equally to this work. DING X analyzed data. LIANG XY collected data. ZHAO WL contributed to the discussion. LIU CM contributed to the discussion. LU XF supervised the revision of the manuscript and statistical refinement. WU SL critically revised the manuscript for intellectual content. ZHAO DD interpreted the data. LI Y designed the study and provided expertise support for the whole study.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

Data and resource availability

Data generated or analyzed during this study are not publicly available due to confidentiality agreements with research collaborators but are available from the corresponding author upon reasonable request.

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References

1. The Writing Committee of the Report on. Cardiovascular Health diseases in China, Summary of the China Cardiovascular Health and Disease Report 2022. Chin J Circulation. 2023;38(06):583–612.
2. Zhang, Haiyu, et al. Study on the Burden of Cardiovascular diseases and Risk factors in China in 1990 and 2019. Adv Mod Biomed. 2022;22(16):3070–5.
3. The Obesity Prevention and Control Branch of the Chinese Nutrition Society. Expert Consensus on the Prevention and Control of Obesity among Chinese residents. Chin J Prev Med. 2022;23(05):321–39.
4. Weisell RC. Body mass index as an indicator of obesity. Asia Pac J Clin Nutr. 2002;11:S681–4.
5. Vaduganathan M, et al. The global burden of cardiovascular diseases and risk: a compass for future health. Washington DC: American College of Cardiology Foundation; 2022. pp. 2361–71.
6. Wijayatunga NN, Dhurandhar EJ. Normal weight obesity and unaddressed cardiometabolic health risk—a narrative review. Int J Obes. 2021;45(10):2141–55.
7. Kahn HS. The lipid accumulation product performs better than the body mass index for recognizing cardiovascular risk: a population-based comparison. BMC Cardiovasc Disord. 2005;5(1):26.
8. Chen J, et al. Lipid Accumulation Product Combined with urine glucose excretion improves the efficiency of diabetes screening in Chinese adults. Front Endocrinol (Lausanne). 2021;12:691849.
9. He Ping, et al. The relationship between lipid Accumulation Index and Hypertension and diabetes in adults. Chin J Hypertens. 2021;29(11):1113–7.
10. Maturana MA, Moreira RM, Spritzer PM. Lipid accumulation product (LAP) is related to androgenicity and cardiovascular risk factors in postmenopausal women. Maturitas. 2011;70(4):395–9.
11. Bozorgmanesh M, Hadaegh F, Azizi F. Predictive performances of lipid accumulation product vs. adiposity measures for cardiovascular diseases and all-cause mortality, 8.6-year follow-up: Tehran lipid and glucose study. LIPIDS IN HEALTH AND DISEASE; 2010. p. 9.
12. Wiltgen D, et al. Lipid accumulation product index: a reliable marker of cardiovascular risk in polycystic ovary syndrome. Hum Reprod. 2009;24(7):1726–31.
13. Xia C, et al. Lipid accumulation product is a powerful index for recognizing insulin resistance in non-diabetic individuals. Eur J Clin Nutr. 2012;66(9):1035–8.
14. Kyrou I, et al. Lipid accumulation product in relation to 10-year cardiovascular disease incidence in caucasian adults: the ATTICA study. Atherosclerosis. 2018;279:10–6.
15. Fakhrolmobasheri M, et al. Lipid accumulation product and visceral adiposity index for incidence of cardiovascular diseases and mortality; results from 13 years follow-up in Isfahan cohort study. Obesity Science & Practice; 2023.
16. Wang Y, et al. Visceral adiposity measures are strongly associated with cardiovascular disease among female participants in Southwest China: a population-based prospective study. Front Endocrinol. 2022;13:969753.
17. Wu S, et al. Prevalence of Ideal Cardiovascular Health and its relationship with the 4-Year Cardiovascular events in a Northern Chinese Industrial City. Volume 5. Circulation: Cardiovascular Quality and Outcomes; 2012. pp. 1–8.
18. Levey AS, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604–12.
19. The Hypertension Prevention and Control Guidelines Revision Committee of China. 2018 Revised Version of the Chinese Hypertension Prevention and Control Guidelines. Prevention and Treatment of Cardio-Cerebrovascular Diseases, 2019. 19(01): pp. 1–44.
20. The Chinese Diabetes Society of the Chinese Medical Association. Guidelines for the Prevention and Treatment of type 2 diabetes in China (2017 Edition). Chin J Practical Intern Med. 2018;38(04):292–344.
21. Shen, Yuanyuan. The relationship between lipid Accumulation Product Index and Hypertension, Diabetes, and Cardiovascular diseases in Chinese adults. Peking Union Medical College; 2017. p. 69.
22. Tunstall-Pedoe H, et al. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. Circulation. 1994;90(1):583–612.
23. Aho K, et al. Cerebrovascular disease in the community: results of a WHO collaborative study. Bull World Health Organ. 1980;58(1):113.
24. D'Agostino RB Sr, et al. General cardiovascular risk profile for use in primary care: the. Framingham Heart Study Circulation. 2008;117(6):743–53.
25. Hosseinpanah F, et al. Lipid accumulation product and incident cardiovascular events in a normal weight population: Tehran lipid and glucose study. Eur J Prev Cardiol. 2016;23(2):187–93.
26. Jafari A, et al. Evaluation of the novel three lipid indices for predicting five- and ten-year incidence of cardiovascular disease: findings from Kerman coronary artery disease risk factors study (KERCADRS). Lipids Health Dis. 2023;22(1):169.
27. Camilleri G, et al. Genetics of fat deposition. Volume 25. European Review for Medical & Pharmacological Sciences; 2021. 1.
28. Lemieux S, et al. Are gender differences in cardiovascular disease risk factors explained by the level of visceral adipose tissue? Diabetologia. 1994;37:757–64.
29. Zhou M, et al. Aging and Cardiovascular Disease: current Status and challenges. Rev Cardiovasc Med. 2022;23(4):135.
30. Hunter GR, Gower BA, Kane BL. Age related shift in visceral fat. Int J body Composition Res. 2010;8(3):103.
31. Després J-P. Body fat distribution and risk of cardiovascular disease: an update. Circulation. 2012;126(10):1301–13.
32. Battineni G et al. Impact of obesity-Induced inflammation on Cardiovascular diseases (CVD). Int J Mol Sci, 2021. 22(9).

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