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Association of the atherogenic index of plasma and modified triglyceride-glucose indices with digestive diseases among middle-aged and older population in China

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Abstract

Background Previous studies have shown that metabolic imbalances contribute to digestive diseases. This study aimed to investigate the relationship of the atherogenic index of plasma (AIP) and modified triglyceride-glucose (TyG) indices with digestive diseases.

Methods We recruited participants aged 45 years or older from the China Health and Retirement Longitudinal Study (CHARLS, 2011 – 2020). The indices assessed included AIP, TyG, triacylglycerol glucose-waist circumference (TyG-WC), the triacylglycerol glucose-waist-to-height ratio (TyG-WHtR), and the triacylglycerol glucose-body mass index (TyG-BMI). We used logistic regression and restricted cubic spline (RCS) analyses to examine the associations between these indices and the incidence of digestive diseases.

Results A total of 4,453 participants were included in our analysis, 53.3% of whom were female, with an average age of 60 years. The incidence of digestive diseases in middle-aged and older adults was 6.18%. Compared with those in the lowest tertile group, the odds ratios (ORs) with 95% confidence intervals (CIs) for digestive diseases in the highest tertile for AIP, TyG, TyG-WC, TyG-WHtR, and TyG-BMI were 1.452 (1.07–1.972), 1.193 (0.873–1.631), 1.349 (1.044–1.743), 1.5 (1.089–2.068), and 1.312 (0.956–1.799), respectively. Sensitivity analyses confirmed the robustness of the correlations between these indices and digestive diseases.

Conclusion Our study revealed that the AIP, TyG-WC, and TyG-WHtR were independently associated with the incidence of digestive diseases. These findings highlight the importance of considering and optimizing metabolic factors in management strategies for digestive diseases.

Keywords Digestive diseases, Metabolic, Atherogenic index of plasma, Modified triglyceride glucose indices, CHARLS

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Background

Digestive diseases have become a global health problem, with a rapidly rising incidence worldwide. The common cause of hospital admission globally is digestive diseases, which account for 13.5% of all hospitalizations [1]. Digestive diseases account for more than one-third of all diseases and approximately one-fifth of all new cases, highlighting the urgent need to address this public health issue. The prevalence of digestive diseases is even higher in the middle-aged and elderly population [2]. In addition, there is evidence that some nonneoplastic digestive disorders, such as *Helicobacter pylori* infection and chronic gastritis, are precursors to the development of digestive cancers [3, 4]. Therefore, the prevention of digestive diseases in middle-aged and elderly people may help mitigate the development of gastrointestinal tumours, decrease medical costs, and reduce the burden of public health care. Accordingly, it is crucial to identify risk factors for digestive diseases early and accurately and to take effective preventive measures.

Digestive diseases encompass a wide range of conditions, including gastroesophageal reflux disease (GERD), gastric ulcers, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), hepatitis, cirrhosis, and fatty liver disease. Studies have shown that atrophic gastritis, IBD and fatty liver disease are associated with dyslipidaemia [5–7]. The atherogenic index of plasma (AIP), an indicator of dyslipidaemia, is calculated from triglycerides and high-density lipoprotein (HDL) and can represent the level of small, dense low-density lipoprotein (LDL) particles [8]. Interestingly, the AIP also indicates the degree of insulin resistance (IR) in people [9]. A key factor in the pathophysiology of metabolic syndrome raises IR, a pathophysiological condition marked by abnormalities in the ability of insulin to control glucose metabolism in cells [10]. Research has demonstrated that metabolic syndrome increases the risk of reflux oesophagitis and could worsen enteric neuropathy [11, 12]. Although the gold standard for determining IR is the high insulin-normoglycaemic clamp, its labor-intensiveness and high cost render it unsuitable for general clinical use [13]. The triglyceride-glucose (TyG) index, which was created using fasting triglycerides and glucose, has been suggested as an easy-to-use and trustworthy proxy indicator of IR in epidemiological research [14]. Compared with the hyperinsulinaemic-euglycaemic clamp method, the TyG index is more practical and cost-effective for clinical applications. Modified TyG indices, such as the triacylglycerol glucose-waist circumference (TyG-WC), triacylglycerol glucose-waist-to-height ratio (TyG-WHtR), and triacylglycerol glucose-body mass index (TyG-BMI), combined with obesity-related metrics, including waist circumference (WC), the waist-to-height ratio (WHtR), and body mass index (BMI), could be used to assess IR better and monitor the likelihood of metabolic diseases [15, 16]. These indicators have been used in the assessment of colorectal neoplasms, hypertension, cardiovascular diseases and metabolic syndrome [17–20].

However, studies on the correlation of the AIP and TyG-related indices with digestive diseases are lacking. This study aims to investigate the association of the AIP and TyG-related indices with digestive diseases among individuals aged 45 years or older to provide more practical clinical indicators for assessing the risk of digestive diseases. Data for this study were obtained from the China Health and Retirement Longitudinal Study (CHARLS) database.

Methods

Study population

The China Health and Retirement Longitudinal Study (CHARLS) aims to examine the health, economic status, family status, and impact of ageing in the Chinese population, with a focus on individuals aged 45 years and older [21]. CHARLS covers both urban and rural areas nationwide and uses a multistage stratified probability proportional to the size sampling strategy. The initial survey in 2011 included approximately 17,000 participants, providing a representative sample. Thereafter, follow-up examinations were conducted every two years, in 2013, 2015, 2018, and 2020.

The goal of CHARLS is to interview each respondent face-to-face. Contact information for each respondent has been available at the time of the baseline survey, so the relocated sample could be quickly deployed to teams near their place of residence. When the respondent lived in a place that cannot be traced, the interviewer submitted a request to the project team. Upon approval, the interviewer usually completed the questionnaire interview by the agent or video. Mostly agents were relatives, such as spouses or children. The current response rate has remained above 86% in any round of follow-up surveys. The study followed the principles outlined in the Strengthening the Reporting of Observational Studies in Epidemiology, and detailed data are available from the official website (http://charls.pku.edu.cn/). The study received approval from the Peking University Biomedical Ethics Committee (approval number IRB00001052-11015). All participants provided written informed consent prior to their participation.

We used data from 2011–2020 to explore the associations of modified TyG indices and the AIP with digestive disorders. The 2011 survey served as the baseline, and participants were followed up four times: 2013, 2015, 2018, and 2020. We included patients aged ≥45 years, those with no digestive diseases in 2011, those with no missing values for the AIP or modified TyG indices

information, and those with no missed visits or missing follow-up data. Therefore, we excluded participants who were missing or who were diagnosed with digestive disorders (n=4217), individuals under 45 years of age (n=68), and individuals lost to follow-up or with missing data on digestive diseases (n=1987). We also excluded participants without complete data on TyG, TyG-WC, TyG-WHtR, TyG-BMI and AIP (n=6980). Our analysis ultimately included a total of 4453 eligible subjects (Fig. 1).

Digestive diseases

The digestive diseases were defined as self-reports of the doctor's diagnosis and self-reports of any treatment. Participants could report a diagnosis in response to the following question: "Have you been diagnosed with stomach or other digestive diseases (except for tumour or cancer) by a doctor?"; alternatively, the diagnosis may be deduced on the basis of the subject's recent treatment regimen in response to the following question: "Are you now taking any of the following treatments to treat digestive disease or its complications?". During follow-up, participants were asked to confirm the accuracy of their previously reported illness status. Adjustments were made to address potential recall bias.

Calculation of indices

The weights of the participants were measured using an Omron electronic scale model HN-286, and the heights were measured using a Seca Corporation 213 stadiometer while the participants wore light clothing and no shoes. The weights and heights of the participants were measured, with their backs resting on the vertical back plate of the metre, upper limbs naturally drooping, heels together against the vertical back plate, toes separated by 60°, and the head kept at the ear-eye level. WC was measured using a tape measure at the midpoint between the upper edge of the ilium and the lower edge of the 12th rib (the narrowest part of the waist), horizontally circling the abdomen.

The blood samples obtained from the participants were stored and measured according to the laboratory procedure manual of CHARLS. Venous blood samples were collected after an overnight fast by professional staff following standard procedures and analysed using a Hitachi 7180 chemistry analyser (Hitachi, Tokyo, Japan). The boronate affinity high-pressure liquid chromatography method was applied to detect glycosylated haemoglobin A1c (HbA1c). The enzymatic colorimetric test was applied to detect high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC) and glucose. Blood samples were collected by professionals from the Chinese Center for Disease Control and Prevention and stored at −80 °C. The laboratory used quality control (QC) samples daily during the testing of the CHARLS study samples. Two professional staff members checked the initial results on a weekly basis to ensure that the assays were within range, that values were appropriate, and that the QC samples indicated reliability in the

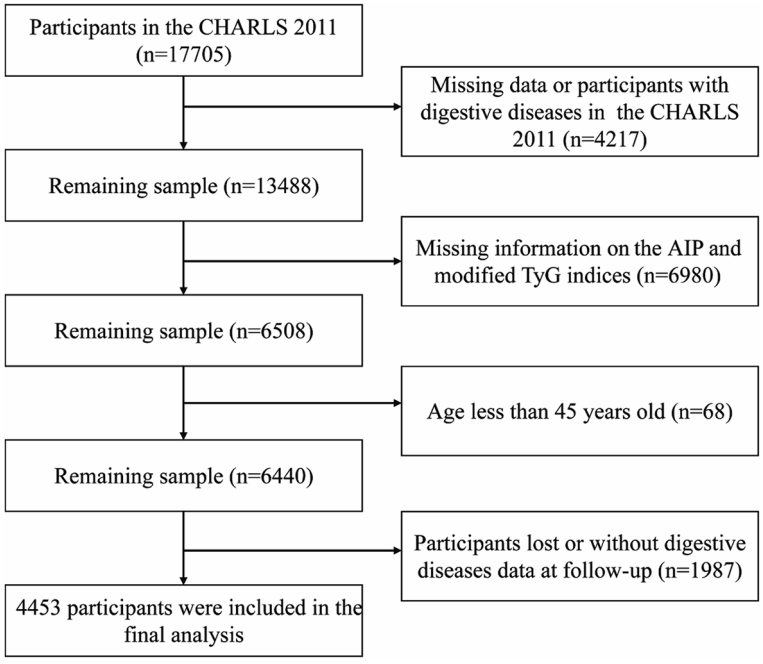

Fig. 1 Flow chart for selecting study population. CHARLS, China Health and Retirement Longitudinal Study; AIP, atherogenic index of plasma; TyG, triglyceride glucose.

process. Both the intra- and inter-assay coefficients of variation were maintained at a maximum of 1.5% and 2.1%, respectively.

The formulas and grouping information for the AIP and modified TyG indices are shown in Additional file 1 and 2.

Data collection

The study data that were collected included the following: (i) demographic data, including age (continuous variable), sex (male/female), education (below high school/above high school), place of residence (rural/urban), and marital status (married/unmarried); (ii) body measures, including the continuous variables body mass index (BMI), waist circumference, systolic blood pressure (SBP), and diastolic blood pressure (DBP); (iii) lifestyle data, such as smoking status, drinking status, and meal frequency (<3 or ≥3 meals per day); (iv) medical history, including cardiovascular illnesses, diabetes mellitus, hypertension, dyslipidaemia, liver diseases, and yes/no responses to tests for these conditions; (v) glycosylated haemoglobin (HbA1c), glucose, TG, TC, HDL-C, and LDL-C were all continuous variables examined in the laboratory investigations.

Weight (kg) divided by height (m^2) was used to compute BMI. Acquisition of the above indicators in the CHARLS database adheres to a strict operation process. When the interviewer enters a logical error or abnormal value, the system will deploy a pop-up box to remind the visitor. The interviewer used an OmronTM HEM-7112 Monitor, a digital sphygmomanometer, to measure the participants' blood pressure (BP). Before the blood pressure readings were collected, the participants were instructed to relax for at least five minutes. SBP and DBP had to be measured three times. We transformed data that did not cooperate with the measurement and could not be measured into null values; the remaining results were averaged to obtain the final SBP and DBP. We treated outliers in waist circumference and body mass index as null values. Cardiovascular diseases included stroke and heart condition. Disease status was determined based on a self-reported medical history or receipt of any specific treatment. More details of the definitions of diseases were in the Additional file 3. During follow-up, participants were asked to confirm the accuracy of their previously reported disease status to correct for potential recall bias.

Statistical analysis

Baseline characteristics were summarized according to the AIP index tertile groups. Normality was assessed using the Shapiro–Wilk test. Since all continuous variables did not follow a normal distribution, they are expressed as medians (interquartile ranges), and categorical variables are expressed as counts and percentages. Differences between groups were compared using the Kruskal–Wallis H test and Pearson chi-square test. We calculated the incidence of digestive diseases on the basis of the AIP and modified TyG indices. Even though the percentage of missing data was low, multiple imputation was used to account for missing variables to maximize the sample size. Additional file 4 describes the distribution of missing variables from the data. Logistic regression models were developed to estimate odds ratios (ORs) and 95% confidence intervals (CIs) to assess the relationships between the indices and digestive diseases. Three logistic regression models were constructed from a clinical specialty perspective. Using no adjustment as a reference, we first adjusted for demographic information, such as age and sex, and subsequently adjusted for lifestyle habits and medical history information. In Model I, we did not adjust for any covariates. In Model II, we adjusted for age and sex. In Model III, we further adjusted for age, sex, smoking status, drinking status, meal frequency, SBP, TC, and LDL-C. In the multicollinearity test, we determined the variance inflation factor [22] for each variable included in the analysis, and all the variables were less than 5. Additionally, restricted cubic spline (RCS) logistic regression analyses with four nodes (at the 5th, 35th, 65th, and 95th percentiles) were performed to test for linear relationships between indices and digestive diseases. To test the heterogeneity of the results, subgroup analyses were performed for sex, age (≤65 years vs. >65 years), residence, smoking status and drinking status. The findings were further validated through sensitivity analyses. We constructed a logistic regression model that excluded any participants with missing values to eliminate the potential impact of missing data on the main results. Additionally, propensity score matching was used to create a well-matched baseline cohort to assess whether the correlations between AIP, TyG-WC, and TyG-WHtR with digestive diseases were stable and reliable. Statistical analyses were performed using R software version 4.4.1 (http://www.R-project.org/). Statistical significance was defined as a *P* value of less than 0.05 (two-sided).

Results

Baseline characteristics of the participants

Fig. 1 shows a flowchart illustrating the screening of the study population. A total of 4,453 individuals participated in the baseline survey. The mean age of the entire group was approximately 60 years, and 53.3% were female. Table 1 lists the baseline characteristics of the participants by AIP tertiles. The mean AIP value for all participants was 0.36. Compared with those in the lowest tertile (Tertile 1), participants in the higher tertiles (Tertile 2 and Tertile 3) had higher proportions of females and

Table 1 Baseline characteristics of the participants according to AIP tertiles

AIP tertile		Tertile 1 (< 0.20)	Tertile 2 (0.20–0.47)	Tertile 3 (> 0.47)	*P*-value
Participants(n)		1524	1479	1450	
Age, years, (median [IQR])		60.00 [53.00, 66.00]	59.00 [53.00, 66.00]	59.00 [53.00, 65.00]	0.239
Sex (%)	Female	754 (49.5)	836 (56.5)	786 (54.2)	< 0.001
	Male	770 (50.5)	643 (43.5)	664 (45.8)	
Place (%)	Rural	1362 (89.4)	1279 (86.5)	1209 (83.4)	< 0.001
	Urban	162 (10.6)	200 (13.5)	241 (16.6)	
Marriage (%)	Married	1357 (89.0)	1319 (89.2)	1317 (90.8)	0.209
	Unmarried	167 (11.0)	160 (10.8)	133 (9.2)	
Education (%)	Below high school	1374 (90.2)	1328 (89.8)	1287 (88.8)	0.435
	High school or above	150 (9.8)	151 (10.2)	163 (11.2)	
Smoke (%)	No	907 (59.5)	962 (65.0)	893 (61.6)	0.007
	Yes	617 (40.5)	517 (35.0)	557 (38.4)	
Drink (%)	No	1033 (67.8)	1129 (76.3)	1103 (76.1)	< 0.001
	Yes	491 (32.2)	350 (23.7)	347 (23.9)	
Meal frequency (%)	< 3	202 (13.3)	193 (13.0)	171 (11.8)	0.436
	≥ 3	1322 (86.7)	1286 (87.0)	1279 (88.2)	
Liver diseases (%)	No	1498 (98.3)	1446 (97.8)	1419 (97.9)	0.551
	Yes	26 (1.7)	33 (2.2)	31 (2.1)	
Hypertension (%)	No	1257 (82.5)	1123 (75.9)	942 (65.0)	< 0.001
	Yes	267 (17.5)	356 (24.1)	508 (35.0)	
Diabetes (%)	No	1475 (96.8)	1406 (95.1)	1338 (92.3)	< 0.001
	Yes	49 (3.2)	73 (4.9)	112 (7.7)	
Dyslipidemia (%)	No	1463 (96.0)	1372 (92.8)	1229 (84.8)	< 0.001
	Yes	61 (4.0)	107 (7.2)	221 (15.2)	
Cardiovascular diseases (%)	No	1422 (93.3)	1343 (90.8)	1267 (87.4)	< 0.001
	Yes	102 (6.7)	136 (9.2)	183 (12.6)	
Digestive diseases (%)	No	1442 (94.6)	1396 (94.4)	1340 (92.4)	0.024
	Yes	82 (5.4)	83 (5.6)	110 (7.6)	
BMI, kg/m2 (median [IQR])		22.00 [20.18, 24.03]	23.40 [21.30, 26.11]	24.91 [22.70, 27.55]	< 0.001
Waist circumference, cm (median [IQR])		80.75 [76.00, 87.00]	85.60 [79.00, 92.20]	90.20 [83.60, 97.00]	< 0.001
SBP, mmHg (median [IQR])		124.67 [113.00, 138.67]	127.67 [114.83, 142.00]	130.33 [119.00, 145.33]	< 0.001
DBP, mmHg (median [IQR])		73.67 [66.00, 81.33]	75.33 [68.00, 84.00]	77.33 [69.67, 86.00]	< 0.001
Glucose, mg/dL (median [IQR])		99.54 [92.70, 107.28]	101.52 [93.96, 109.98]	107.19 [98.14, 120.96]	< 0.001
HbA1c, % (median [IQR])		5.10 [4.80, 5.30]	5.10 [4.90, 5.40]	5.20 [4.90, 5.50]	< 0.001
HDL-C, mg/dL (median [IQR])		61.86 [53.74, 71.13]	49.10 [43.69, 54.90]	37.89 [32.86, 43.69]	< 0.001
LDL-C, mg/dL (median [IQR])		111.73 [92.40, 131.93]	120.23 [98.97, 142.27]	115.59 [91.62, 139.56]	< 0.001
TC, mg/dL (median [IQR])		186.34 [166.24, 208.38]	190.21 [165.46, 214.37]	197.17 [173.97, 225.39]	< 0.001
TG, mg/dL (median [IQR])		66.38 [54.87, 77.88]	105.32 [92.04, 123.01]	185.85 [149.57, 245.15]	< 0.001
TyG (median [IQR])		8.11 [7.90, 8.29]	8.60 [8.43, 8.78]	9.21 [8.96, 9.63]	< 0.001
TyG-WC (median [IQR])		654.78 [608.57, 706.13]	736.89 [676.00, 800.12]	839.75 [766.64, 909.60]	< 0.001
TyG-WHtR (median [IQR])		4.12 [3.83, 4.51]	4.66 [4.28, 5.09]	5.27 [4.80, 5.77]	< 0.001
TyG-BMI (median [IQR])		177.39 [162.26, 195.56]	201.43 [183.05, 225.42]	233.30 [208.97, 258.90]	< 0.001

P values were calculated by Kruskal-Wallis rank sum test or Pearson's Chi-squared test. Values were represented by median (IQR) for continuous variables and frequency (percentage) for categorical variables

AIP, atherogenic index of plasma; IQR, interquartile range; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI: body mass index; HbA1c, glycated hemoglobin; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride glucose; TyG-BMI, triglyceride glucose-body mass index; TyG-WC, triglyceride glucose-waist circumference; TyG-WHtR triglyceride glucose-waist-to-height ratio

Table 2 Incidence rate of digestive diseases

Index	Participants (*n*)	Digestive diseases events(*n*)	Incidence rate (95% CI) (%)
Total	4453	275	6.18(5.47–6.88)
TyG			
Tertile 1(< 8.35)	1506	91	6.042(4.839–7.246)
Tertile 2(8.35–8.86)	1464	77	5.26(4.116–6.403)
Tertile 3(> 8.86)	1483	107	7.215(5.898–8.532)
TyG-WC			
Median 1(≤ 734.19)	2227	118	5.299(4.368–6.229)
Median 2(> 734.19)	2226	157	7.053(5.989–8.117)
TyG-WHtR			
Tertile 1(< 4.32)	1494	82	5.49(4.33–6.64)
Tertile 2(4.32–5.01)	1484	76	5.12(4.00-6.24)
Tertile 3(> 5.01)	1475	117	7.93(6.55–9.31)
TyG-BMI			
Tertile 1(< 185.51)	1485	81	5.455(4.3–6.61)
Tertile 2 (185.51-219.96)	1484	86	5.795(4.606–6.984)
Tertile 3(> 219.96)	1484	108	7.278(5.956–8.599)
AIP			
Tertile 1(< 0.20)	1524	82	5.381(4.248–6.513)
Tertile 2(0.20–0.47)	1479	83	5.612(4.439–6.785)
Tertile 3(> 0.47)	1450	110	7.586(6.223–8.949)

TyG, triglyceride glucose; TyG-BMI, triglyceride glucose-body mass index; TyG-WC, triglyceride glucose-waist circumference; TyG-WHtR triglyceride glucose-waist-to-height ratio; AIP, atherogenic index of plasma; CI confidence

urban dwellers. They also presented a significantly higher BMI, WC, SBP, and DBP and glucose, TC, and LDL-C levels. Additionally, the TyG, TyG-WC, TyG-WHtR, and TyG-BMI values were elevated (all *P* values < 0.05). Furthermore, individuals in the higher AIP tertiles had higher frequencies of hypertension, dyslipidaemia, diabetes, cardiovascular diseases, and digestive diseases (all *P* values < 0.001).

The incidence rate of digestive diseases

In total, 275 participants developed digestive diseases during follow-up, and the overall incidence of digestive diseases was 6.18%. As shown in Table 2, the incidence of digestive diseases gradually increased in the tertiles of TyG-BMI and AIP (from Tertile 1 to Tertile 3). The incidence for each AIP tertile was as follows: Tertile 1: 5.381%; Tertile 2: 5.612%; Tertile 3: 7.586%. The incidence for each TyG-BMI tertile was as follows: Tertile 1: 5.455%; Tertile 2: 5.795%; Tertile 3: 7.278%. The incidence of digestive diseases was greater in Tertile 3 than in Tertile 1 for both TyG and TyG-WHtR. The numbers of digestive disorders in the Median 1 group and Median 2 group of TyG-WC patients were 118 (5.299%) and 157 (7.053%), respectively. Regardless of age, the incidence of digestive diseases was greater in females when they were stratified by age. Furthermore, the findings indicated a slight decline in incidence with increasing age in both males and females (Fig. 2).

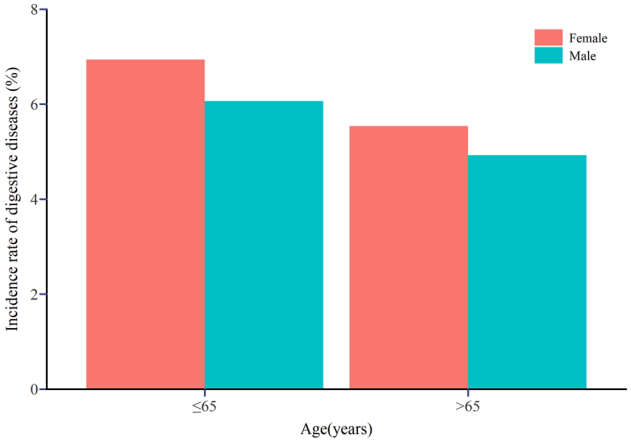

Fig. 2 Comparative chart showed the incidence rates of digestive categorized by age groups and sex.

Relationships of indices with digestive diseases

The dose–response associations between the indices and digestive diseases were evaluated, and their patterns were elucidated using the RCS, as shown in Fig. 3. The results revealed that the AIP ($P=0.6011$), TyG ($P=0.6899$) and TyG-BMI ($P=0.3044$) were linearly related to digestive disorders, whereas TyG-WC ($P=0.0421$) and TyG-WHtR ($P=0.0025$) were nonlinearly related to digestive disorders. The logistic regression analyses of the relationships between the different indices and digestive diseases are presented in Table 3. We constructed three covariate models with varying adjustments to accurately capture this relationship. According to the uncorrected logistic regression model, the risk of digestive disease was significantly greater in the highest tertile of the AIP and TyG-WHtR groups than in the lowest tertile, with ORs (95% CIs) of 1.444 (1.074 − 1.94) and 1.484 (1.108 − 1.987), respectively ($P<0.05$). Compared with that in the Median 1 group, the risk of digestive disease gradually increased with increasing TyG-WC ($P=0.015$). Adjusting for potential confounders such as age, sex, smoking status, drinking status, meal frequency, SBP, TC, and LDL-C levels revealed that the OR for participants in Tertile 3, compared with those in Tertile 1 based on AIP, was 1.452 (1.07 − 1.972) ($P=0.017$). Similarly, for TyG-WHtR, the OR (95% CI) for Tertile 3 was 1.5 (1.089–2.068) ($P=0.011$). For TyG-WC, after adjusting for confounders, the OR (95% CI) for TyG-WC in the Median 2 group was 1.349 (1.044 − 1.743) ($P=0.022$). As shown in Table 3, there was still a significant positive association (Model III: OR = 1.525, 95% CI 1.009 − 2.30) between the AIP and the incidence of digestive diseases when the AIP was considered a continuous variable. TyG-WC and TyG-WHtR, as continuous variables, were not associated with

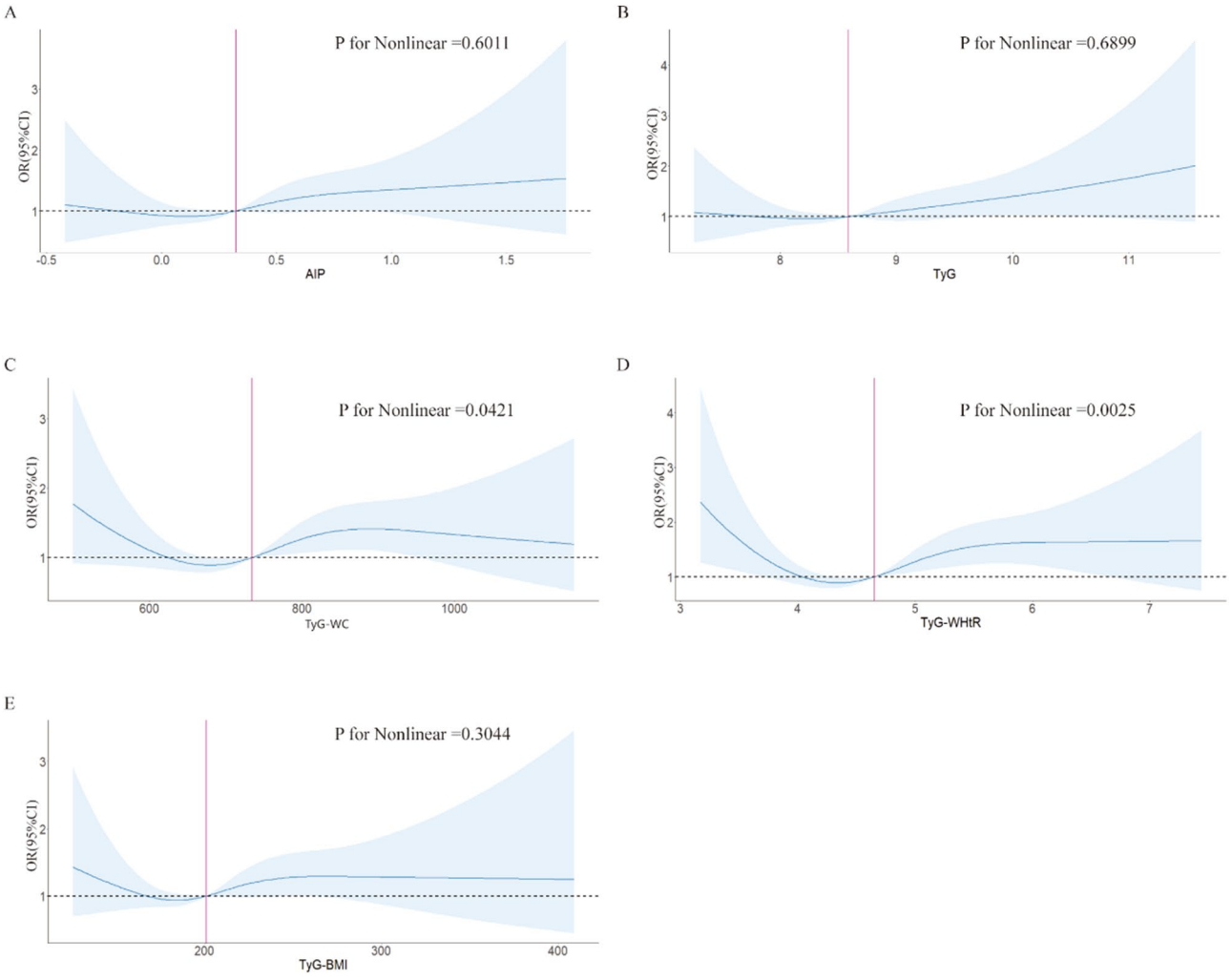

Fig. 3 Association of the indices with the incidence of digestive diseases. AIP, atherogenic index of plasma; TyG, triglyceride glucose index; TyG-BMI, triglyceride glucose-body mass index; TyG-WC, triglyceride glucose-waist circumference; TyG-WHtR triglyceride glucose-waist-to-height ratio; OR, odds ratio; CI, confidence interval.

Table 3 Relationship of modified TyG indices and AIP with the risk of digestive in different models

Index	Model I (OR, 95%CI)	*P*	Model II (OR, 95%CI)	*P*	Model III (OR, 95%CI)	*P*
TyG-WC						
Median 1	Ref		Ref		Ref	
Median 2	1.356(1.06–1.735)	0.015	1.347(1.053–1.724)	0.018	1.349(1.044–1.743)	0.022
TyG-WHtR						
Tertile 1	Ref		Ref		Ref	
Tertile 2	0.929(0.674–1.281)	0.655	0.923(0.668–1.276)	0.627	0.925(0.668–1.283)	0.642
Tertile 3	1.484(1.108–1.987)	0.008	1.471(1.087–1.99)	0.013	1.5(1.089–2.068)	0.011
AIP						
as continuous variable	1.426(1.005–2.024)	0.047	1.404(0.989–1.995)	0.058	1.525(1.009–2.306)	0.045
Tertile 1	Ref		Ref		Ref	
Tertile 2	1.046(0.764–1.431)	0.781	1.029(0.751–1.409)	0.86	1.029(0.749–1.414)	0.858
Tertile 3	1.444(1.074–1.94)	0.015	1.423(1.058–1.913)	0.02	1.452(1.07–1.972)	0.017

Model I was unadjusted

Model II adjusted age, sex

Model III further adjusted age, sex, smoke, drink, meal frequency, SBP, TC, LDL-C

OR, odds ratio; Ref, reference; CI, confidence; TyG-WC, triglyceride glucose-waist circumference; TyG-WHtR, triglyceride glucose-waist-to-height ratio; AIP, atherogenic index of plasma

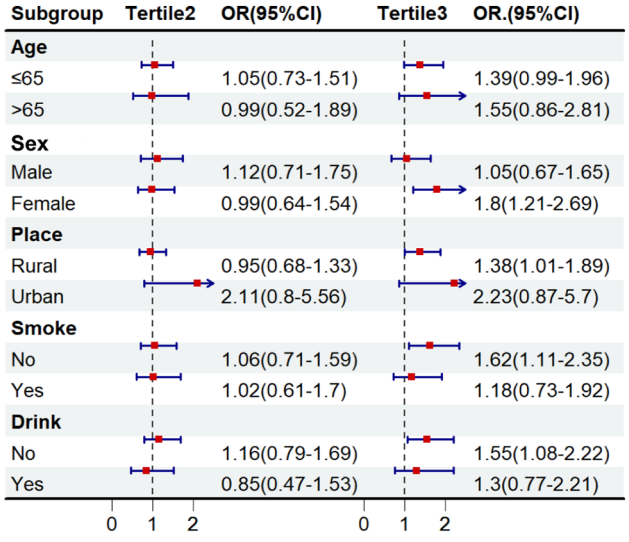

Fig. 4 Subgroup analyses of the associations between AIP groups and digestive diseases incidence. AIP was divided into tertile1, tertile2, and tertile3. AIP, atherogenic index of plasma; OR, odds ratio; CI, confidence interval.

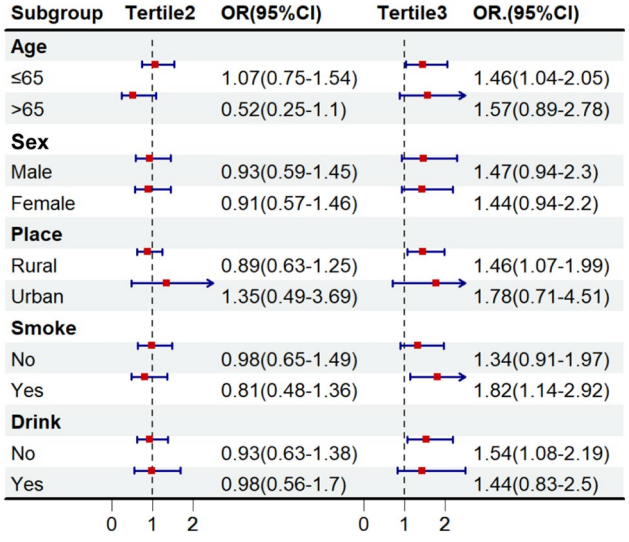

Fig. 5 Subgroup analyses of the associations between TyG-WHtR groups and digestive diseases incidence. TyG-WHtR was divided into tertile1, tertile2, and tertile3. TyG-WHtR triglyceride glucose-waist-to-height ratio; OR, odds ratio; CI, confidence interval.

digestive diseases (Additional file 5). After adjusting for age, sex, smoking status, drinking status, meal frequency, cardiovascular diseases, diabetes, and hypertension, we obtained results that were similar to those of Model III. Compared to individuals in the lowest group, those in the highest group had a higher incidence of digestive diseases for AIP, TyG-WC and TyG-WHtR (Additional file 9). There was no significant association between TyG or TyG-BMI and the incidence of diseases, and the ORs (95% CI) were 1.193 (0.873–1.631) and 1.312 (0.956–1.799), respectively (Additional file 5).

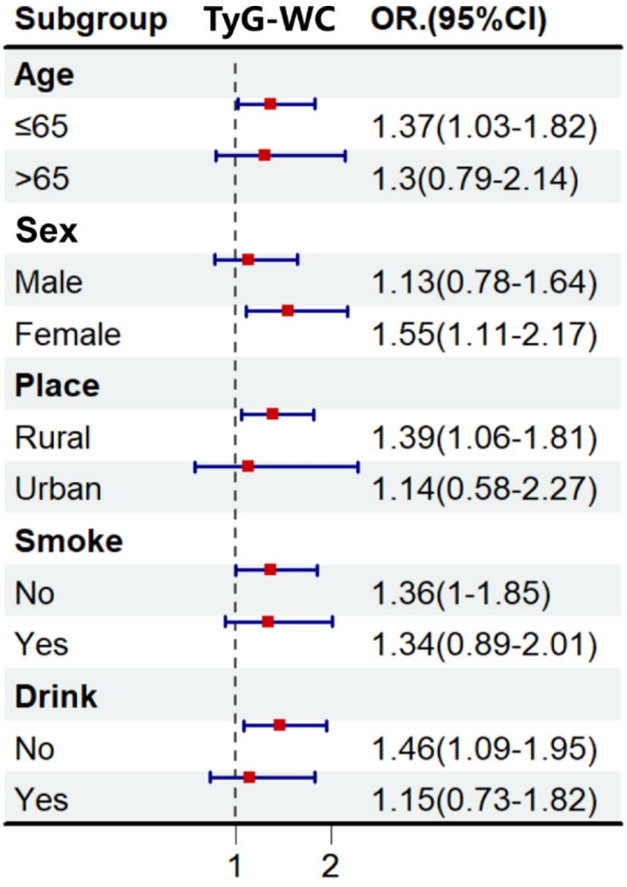

Fig. 6 Subgroup analyses of the associations between TyG-WC and digestive diseases incidence. TyG-WC, triglyceride glucose-waist circumference; OR, odds ratio; CI, confidence interval.

Subgroup analysis

Subgroup analyses revealed that the associations of the AIP, TyG-WC and TyG-WHtR with digestive diseases were heterogeneous across age, sex, residence, smoking status, and drinking status. Specifically, in the age-stratified subgroups, changes in TyG-WC were significant in the age≤65 years subgroup in Median 2 compared with Median 1 (OR 1.37, 95% CI 1.03−1.82, $P=0.028$) (Fig. 6 and Additional file 8). Participants in Tertile 3 demonstrated a greater risk of digestive diseases in rural areas for AIP and TyG-WHtR based on Tertile 1 data (Figs. 4 and 5). Moreover, participants from rural areas in the Median 2 were also more likely to have digestive diseases than those in the Median 1 for the TyG-WC. Females in the AIP Tertile 3 group and in the TyG-WC Median 2 group were more likely to suffer from digestive diseases. Compared with the AIP Tertile 1 group, nonsmokers in the AIP Tertile 3 group were linked to digestive diseases. However, smokers in the TyG-WHtR Tertile 3 group were associated with more digestive disorders in comparison to the TyG-WHtR Tertile 1 group. Nondrinkers in Tertile 3 demonstrated a greater risk of digestive

diseases for AIP and TyG-WHtR based on the Tertile 1 data. Moreover, TyG-WC was associated with digestive diseases in nondrinkers. Furthermore, there was no interaction between the above indices and any of the subgroup variables (*P* values for interactions were all >0.05) (Additional files 6–8).

Sensitivity analysis

Consistent results were observed when various methods were used to verify the stability of the main findings of the study. The main result of the investigation remained unaffected even after eliminating subjects whose covariate data were missing in the fully adjusted model. Compared with those in the Tertile 1 group, the AIP (OR 1.40, 95% CI 1.03–1.88, *P*=0.029) and TyG-WHtR (OR 1.46, 95% CI 1.08–1.98, *P*=0.015) were associated with digestive diseases (Table 4). TyG-WC was also associated with digestive disease (OR 1.33, 95% CI 1.04–1.71; *P*=0.023). We then used a propensity score matching approach to match the baseline data. The results of multifactorial logistic regression after PSM still suggested a significant association of the AIP and TyG-WHtR with digestive diseases when comparing Tertile 3 and Tertile 1 (AIP: OR 1.452, 95% CI 1.07–1.972, *P*=0.017; TyG-WHtR: OR 1.50, 95% CI 1.089–2.068, *P*=0.013). There was a substantial association between the incidence of digestive diseases and TyG-WC (OR 1.349, 95% CI 1.044–1.743; *P*=0.022). With these sensitivity analyses, we could confidently assert that the findings of this study were robust.

Discussion

In this study, we explored the longitudinal associations of the AIP and modified TyG indices with digestive diseases in middle-aged and elderly Chinese individuals based on a nationally representative survey. To our knowledge, this is the first study to examine these associations in a Chinese population. We found significant associations between AIP, TyG-WC, and TyG-WHtR and the incidence of digestive diseases. Additionally, RCS regression suggested a positive linear relationship between the AIP score and the incidence of digestive diseases. Our research may offer new perspectives for improving methods for preventing digestive diseases.

Table 4 Relationship between modified TyG and AIP with the risk of digestive diseases in different sensitivity analyses

Index	Model Excluding Any Variables with Missing Values		Model After Propensity Score Matching	
	OR (95% CI)	*P*	OR (95% CI)	*P*
TyG-WC				
Median 1	Ref		Ref	
Median 2	1.33 (1.04–1.71)	0.023	1.349(1.044–1.743)	0.022
TyG-WHtR				
Tertile 1	Ref		Ref	
Tertile 2	0.92 (0.66–1.27)	0.61	0.925(0.668–1.283)	0.642
Tertile 3	1.46 (1.08–1.98)	0.015	1.500(1.089–2.068)	0.013
AIP				
Tertile 1	Ref		Ref	
Tertile 2	1.04 (0.76–1.43)	0.799	1.029(0.749–1.414)	0.858
Tertile 3	1.40 (1.03–1.88)	0.029	1.452(1.07–1.972)	0.017

OR, odds ratio; Ref, reference; CI, confidence; TyG-WC, triglyceride glucose-waist circumference; TyG-WHtR, triglyceride glucose-waist-to-height ratio; AIP, atherogenic index of plasma

Digestive diseases are a common set of illnesses worldwide that can increase the risk of death and generate significant health care costs [23]. Studies have demonstrated a significant positive global genetic correlation between metabolic syndrome and conditions such as gastritis, gastric ulcers, and gastroesophageal reflux disease [24]. Researchers are increasingly focusing on the AIP and TyG indices, which are markers of glucose and lipid metabolism disorders. The AIP has been shown to be an excellent biomarker for prognostic predictions of cardiovascular events, and it is the best predictor of hypertension [25–27]. Bregenzer et al. reported that the traditional insulin resistance index, HOMA-IR, is associated with Crohn's disease [28]. Given that insulin levels are not widely measured, the TyG index has been recognized as a simple and useful alternative indicator of IR in the clinical setting. In addition, the TyG index has good predictive power for the incidence of metabolic syndrome in different countries or ethnicities [29, 30]. BMI, WC and WHtR were found to be reliable indicators of obesity. The modified TyG indices, which integrate basic indicators of the human body, comprehensively evaluate the metabolic state of an organism, significantly improving the usefulness and accuracy of the assessment. Kityo et al. reported that the TyG-BMI was superior to the TyG in predicting all-cause mortality in a Korean population [31]. BMI was less effective than WC and WHtR for differentiating overweight and obese individuals in the abdomen [32, 33]. Li et al. concluded that TyG-WC and TyG-WHtR performed better in predicting MetS than the TyG [30]. However, the relationships of the AIP and modified TyG indices with digestive diseases has remained largely unexplored. The findings of this large population-based cohort study provide the first evidence of the associations of AIP, TyG-WC, and TyG-WHtR with digestive diseases.

Although previous studies have not directly explored the associations of the AIP and modified TyG indices with digestive diseases, several studies have investigated the relationships between metabolic abnormalities and digestive diseases. Research has shown that patients with inflammatory bowel disease have higher triglyceride and lower HDL-C levels than healthy individuals [34, 35]. The associations of dysglycaemia with irritable bowel syndrome and gastrointestinal polyps may also be related to insulin resistance [36, 37]. These studies suggest that

metabolic abnormalities can increase the risk of digestive diseases. Glucose–lipid metabolism abnormalities are influenced by various factors, such as age, sex, smoking, and drinking [38–45]. Furthermore, a national survey of elderly people revealed that health demand and utilization were lower in underdeveloped rural areas due to limited access to health services [46]. Therefore, the AIP and TyG-related indices may be affected by these factors, resulting in different associations between indices and digestive diseases in subgroup analyses. In addition, the limited number of cases of digestive disorders may have affected our ability to observe this association. Thus, more large-sample studies are needed to analyse different subgroups in the future.

The mechanism underlying the associations of the AIP, TyG-WC, and TyG-WHtR indices with digestive diseases may be related to the following factors. These indices reflect physical glycolipid metabolism and are associated with obesity. An organism that is frequently metabolically unbalanced could be in a state of immunological dysfunction, inflammation, and gut microbiome dysbiosis. First, patients with digestive disorders are also in a state of chronic inflammation. Various cytokines and chemokines, including tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6), have been evaluated as predictors of inflammatory bowel disease [47, 48]. Research has shown that the levels of proinflammatory factors involved in glycolipid metabolism, such as TNF-α and IL-6, increase and play important roles in pathophysiological processes [49]. Microoxidized low-density lipoprotein stimulates macrophages to produce reactive oxygen species by activating NOX2 [50]. In atrophic gastritis, NOX2 activation by the stomach mucosa triggers an inflammatory response [51]. Second, metabolic imbalance is characterized by an immune response with an increase in the total number of macrophages, a shift in the M1/M2 macrophage ratio, and a decrease in regulatory T cells [30, 52]. The development of digestive diseases involves dysregulation of the immune response and abnormal activation of various immune cells, including macrophages and lymphocytes [53–55]. Obesity leads to imbalances in cellular metabolic homeostasis and promotes macrophage activation [56]. In colitis, macrophages are the first to be activated, which is key to disease initiation, and they are the most important immune cells that amplify the inflammatory cascade [57]. Macrophage polarization is controlled by both NF-κB and MAPK signalling, which contribute to sustained inflammation [58]. Finally, abnormalities in glycolipid metabolism can occur with much higher frequencies of Proteobacteria and Firmicutes and lower frequencies of Bacteroidetes and Verrucomicrobia [59, 60]. Short-chain fatty acids, metabolites produced by reduced microbes, can lower the intestinal pH, inhibit pathogens, and modulate the intestinal mucosal barrier function [61]. Patients with digestive diseases have reduced levels of SCFAs in their faeces. The administration of treatments that increase SCFA levels can inhibit the NF-κB pathway, reduce proinflammatory factor levels, promote intestinal homeostasis, and maintain intestinal health [62–65].

One of the strengths of our study was that our data were derived from CHARLS, which provides reliable medical and long-term follow-up data, ensuring a high level of evidence. Additionally, we controlled for covariates and performed sensitivity analyses to increase the stability and robustness of our results. More importantly, our study was the first to compare the relationships of the AIP and modified TyG indices with the incidence of digestive diseases. These findings provide new insights for the early detection of digestive diseases in middle-aged and older adults living in communities. More effective endoscopic prioritization of patients with high AIP, TyG-WC, and TyG-WHtR indices may also reduce the economic and clinical burden of current screening methods.

Nonetheless, our study has several limitations. First, inferring a causal relationship between AIP, TyG-WC and TyG-WHtR with digestive diseases requires more robust studies, such as Mendelian randomization. Other studies are needed in the future to enhance the causal effect of the above results. Second, we relied on self-reported digestive diseases. Although participants were instructed to report information based on a previous physician's diagnosis, the possibility of bias was undeniable. Owing to the data limitations of the CHARLS, we used the same digestive disease assessment method as described in earlier research [66, 67]. Additionally, although we adjusted for multiple covariates, the potential impact of all confounding factors could not be fully mitigated. Third, we did not collect data on subtypes of digestive diseases, such as peptic ulcers and inflammatory bowel disease, and such associations among different subtypes need to be further explored in the future.

Conclusions

Our findings revealed that the incidence of digestive diseases was associated with TyG-WC, TyG-WHtR, and AIP among middle-aged and older Chinese individuals. Given their ease of measurement and acceptance, these indicators could be used as a routine examination to provide more personalized prevention or treatment for digestive diseases.

Abbreviations

AIP	Atherogenic index of plasma
TyG	Triglyceride-glucose
TyG-WC	Triacylglycerol glucose-waist circumference
TyG-WHtR	Triacylglycerol glucose-waist-to-height ratio
TyG-BMI	Triacylglycerol glucose-body mass index
RCS	Restricted cubic spline

OR	Odds ratio
CI	Confidence intervals
GERD	Gastroesophageal reflux disease
IBS	Irritable bowel syndrome
IBD	Inflammatory bowel disease
IR	Insulin resistance
WC	Waist circumference
WHtR	Waist-to-height ratio
BMI	Body mass index
CHARLS	China health and retirement longitudinal study
FBG	Fasting blood glucose
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
HbA1c	Glycosylated hemoglobin
TG	Triglycerides
TC	Total cholesterol
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
TNF-α	Tumor necrosis factor-α
IL-6	Interleukin-6

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02321-8.

Supplementary Material 1

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Author contributions
TTG, MDR and YF: conceptualization and design of the study. TTG and YRL: data extraction and organization. TTG and XZ: statistical analyses and interpretations. TTG: draft of the manuscript and literature search. YRL and XZ: revision of manuscript. SXH: supervised the entire study and provided critical review. All authors reviewed and approved the submitted manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Consent for publication
All the authors gave their consent to publication.

Competing interests
The authors declare no competing interests.

Ethical approval
The CHARLS has been approved by Biomedical Ethical Review Committee of Peking University. At the time of enrollment, each subject gave written agreement that was informed, and the protocol was carried out in accordance with the Declaration of Helsinki's guidelines.

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