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Lipid accumulation product and type 2 diabetes risk: a population-based study

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Abstract

Background The Lipid Accumulation Product (LAP) is a measure that indicates excessive fat accumulation in the body. LAP has been the focus of research in epidemiological studies aimed at forecasting chronic and metabolic diseases. This study aimed to evaluate the association between LAP and type 2 diabetes mellitus (T2DM) among adults in western Iran.

Methods The study involved 9,065 adults who participated in the initial phase of the Ravansar non-communicable diseases study (RaNCD) cohort. To investigate the association between LAP and T2DM, multiple logistic regressions were employed. Additionally, the receiver operating characteristic (ROC) curve was used to evaluate LAP's predictive ability concerning T2DM.

Results The participants had an average age of 47.24 ± 8.27 years, comprising 49.30% men and 50.70% women. The mean LAP was 53.10 ± 36.60 for the healthy group and 75.51 ± 51.34 for the diabetic group ($P < 0.001$). The multiple regression analysis revealed that the odds of T2DM in the second quartile of LAP were 1.69 (95% CI: 1.25, 2.29) times greater than in the first quartile. Furthermore, the odds in the third and fourth quartiles were 2.67 (95% CI: 2.01, 3.55) and 3.73 (95% CI: 2.83, 4.92) times higher, respectively. The ROC analysis for predicting T2DM showed that the LAP index had an area under the curve (AUC) of 0.66 (95% CI: 0.64, 0.68).

Conclusion A strong association was identified between elevated LAP levels and T2DM in the adult population of western Iran. LAP is recommended as a potential tool for screening diabetes susceptibility.

Keywords Type 2 diabetes, Lipid accumulation product, Waist circumference, Triglyceride

Introduction

The World Health Organization (WHO) states that non-communicable diseases (NCDs) are the main cause of global mortality [1]. Type 2 diabetes mellitus (T2DM) is a significant NCD, contributing to 2.74% of all deaths worldwide. In Iran, T2DM is linked to 3% of total fatalities [2]. The age-standardized mortality rate for T2DM in Iran has been consistently rising since 2015 and is projected to increase slightly by 2030 [3]. Diabetes is a chronic condition that may lead to microvascular and microvascular complications, including cardiovascular disease (CVD) and diabetic nephropathy. Additionally, T2DM can cause disability and reduce quality of life [4].

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Early stages of T2DM often present no specific symptoms, making it easily overlooked [5].

Early diagnosis of T2DM is crucial as it allows for timely intervention, which can help reduce or prevent complications related to diabetes. This can ultimately lessen the burden of the disease for individuals and healthcare systems [5]. Obesity, particularly abdominal obesity, is a significant risk factor for T2DM, resulting from fat accumulation in the central body area [6–8]. Metabolic disorders in adipose tissue directly impact lipid and glucose balance [9]. It is proposed that T2DM may stem from complex metabolic disturbances caused by excessive abnormal lipid or liver fat accumulation [10–12]. Additionally, research shows that waist circumference (WC), a common measure of abdominal obesity, and elevated triglyceride (TG) levels are linked to a higher risk of developing T2DM [13–16].

New indicators that combine anthropometric measurements with blood lipid levels and liver enzyme values have been developed for the early detection of metabolic disorders. These indicators are simple, cost-effective, and suitable for large population studies [17–19]. One such indicator is the lipid accumulation product (LAP) index, which assesses visceral fat by combining WC and TG levels. Research in various populations indicates that the LAP index is a reliable predictor of chronic conditions like metabolic syndrome, CVD, hypertension, and T2DM [20–23].

However, there has not been a comprehensive study in Iran to evaluate LAP's effectiveness in predicting T2DM. If LAP proves to be a good predictor in Iranian populations, it could serve as a simple and accurate tool for T2DM screening. Establishing an appropriate cut-off point for LAP in this population could significantly aid in the early diagnosis of diabetes, allowing for timely preventive and control strategies. Given the high prevalence of obesity (27%) and overweight (42%) in the studied population, this research is particularly important. Thus, the present study aims to investigate the association between LAP and T2DM in a large adult population in western Iran.

Methods

Study design and participants

The current study is a cross-sectional analysis based on data from the baseline phase of the Ravansar non-communicable diseases (RaNCD) cohort study [24], which is part of the PERSIAN (Prospective Epidemiological Research Studies in Iran) studies [25]. Pregnant women and cancer patients were excluded due to significant physical and physiological changes, such as weight gain, hormonal fluctuations, and lifestyle alterations. To minimize potential biases, any missing data was removed before analysis. Individuals with liver conditions were also excluded, as they might affect triglyceride synthesis. Ultimately, the study included 9,065 participants (Fig. 1).

Data collection and measurements

All data was gathered at the RaNCD cohort center in accordance with the standard protocol of Persian studies [24]. The socioeconomic status (SES) was assessed through principal component analysis (PCA), considering factors like education level, welfare facilities and wealth [26].

Anthropometric indices were measured using a Bio-Impedance Analyzer BIA (Inbody 770, Inbody Co, Seoul, Korea). In addition, WC was measured using a flexible measuring tape at a point midway between the lower rib margin and the iliac crest, with measurements recorded to the nearest 0.5 cm. The study evaluated various biomarkers from fasting blood samples, including glucose, liver enzymes, and lipid profile.

Diabetic patients in the study were considered as individuals with a Fasting Blood Sugar (FBS) level of 126 mg/dL and/or a history of using medication to manage T2DM [24]. The LAP was calculated using the following formula: [waist circumference (cm) − 65] × Triglyceride concentration (mmol/L) for men, and [waist circumference (cm) − 58] × Triglyceride concentration (mmol/L) for women [27]. Additionally, participants' blood pressure and physical activity levels were assessed according to the RaNCD study protocol [24, 28].

Statistical analysis

The statistical analysis for the study was conducted using Stata version 14.2 software (Stata Corp, College Station, TX, USA). Descriptive statistics were presented with quantitative variables reported as mean ± standard deviation (SD) and categorical variables as frequency (percentage). To compare the basic characteristics between diabetic and non-diabetic groups, T-tests and Chi-square tests were utilized. One-way ANOVA and Chi-square tests were employed to analyze participant characteristics across different quartiles of the LAP.

Binary logistic regression models were used to evaluate the relationship between T2DM and quartiles of LAP. The multiple model incorporated adjustments for age, family history of T2DM, Body Mass Index (BMI), physical activity, systolic and diastolic blood pressure (SBP and DBP) and SES variables. Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive ability of LAP, WC, and TG for T2DM, using the area under the curve (AUC) with a 95% confidence interval. The ROC curves illustrate the overall diagnostic ability of a test across its entire range of values. The AUC is a measure of the diagnostic power of a test, and it is a widely used metric to evaluate the diagnostic performance of a test or model. The AUC serves as an indicator of a test's

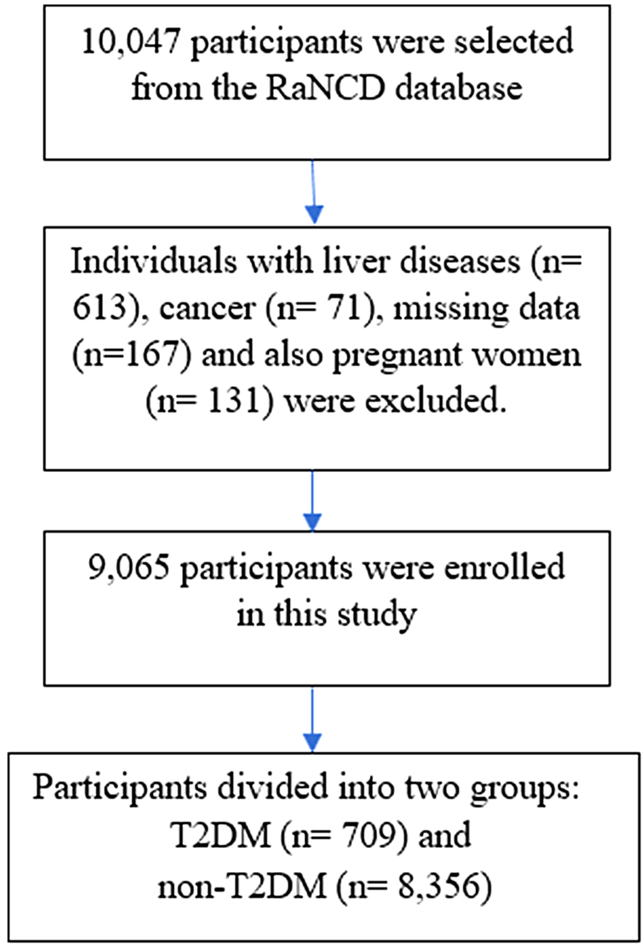

Fig. 1 Flowchart of the study participants

diagnostic effectiveness and is a commonly used measure for evaluating diagnostic performance. It ranges from 0 to 1, with higher values signifying better discriminatory ability. An AUC below 0.60 is deemed to indicate poor diagnostic performance [29, 30]. All p-values reported below 0.05 were considered statistically significant.

Results

A total of 9,065 participants, comprising 49.30% men and 50.70% women, with an average age of 47.24±8.27 years, were included in the study. Among these participants, 7.82% had T2DM, 11.97% were smokers, and 5.02% reported consuming alcohol. Anthropometric indices, such as BMI, WC, and visceral fat area (VFA), were significantly higher in diabetic individuals ($p<0.001$). Additionally, liver enzymes, systolic and diastolic blood pressure were significantly higher in diabetic subjects ($p<0.001$). Except for LDL, all lipid profile indices were significantly different between the two diabetic and non-diabetic groups ($p<0.001$). The average LAP was 53.10±36.60 in the healthy group and 75.51±51.34 in the diabetic group ($p<0.001$) (Table 1).

The results indicated that with increasing LAP quartiles, there was a significant increase in the mean BMI, rising from 23.63±3.48 in the first quartile to 30.17±4.31 in the fourth quartile (p-trend<0.001). Similarly, WC, TG, LDL and total cholesterol levels also increased across the LAP quartiles (p-trend<0.001). The average FBS in the fourth quartile of LAP was significantly higher compared to the first quartile (89.80±24.20 vs. 103.85±34.78, p-trend<0.001). Across the quartiles of LAP, vigorous physical activity has decreased and low physical activity has increased. Additionally, the study reported that liver enzymes were significantly higher in the participants belonging to the fourth quartile of the LAP compared to the first quartile ($p<0.001$).

The crude model revealed that the odds of developing T2DM were 1.9 times higher in the second quartile of LAP, 3.20 times higher in the third quartile, and 4.77 times higher in the fourth quartile, compared to the first quartile ($p<0.001$). After adjusting for age, sex and history of diabetes in first-degree relatives, the odds of diabetes were 1.78 (95%CI: 1.32, 2.40) times higher in the second quartile of LAP, 2.90 (95% CI: 2.19, 3.85) times

Table 1 Baseline characteristics of participants this study, (*n* = 9,065)

Parameters	Total (*n* = 9,065)	Non-T2DM (*n* = 8,356)	T2DM (*n* = 709)	*P* value*
Gender, *n* (%)				
Men	4469 (49.30)	4126 (92.32)	343 (7.68)	0.609
Women	4596 (50.70)	4230 (92.04)	366 (7.96)	
Age (year)	47.24 ± 8.27	46.89 ± 8.24	51.44 ± 7.45	< 0.001
Current smoker, *n* (%)	1080 (11.97)	1006 (12.09)	74 (10.45)	< 0.001
Alcohol drinking, *n* (%)	455 (5.02)	425 (5.09)	30 (4.23)	0.317
Physical activity, *n* (%)				
Low	2682 (29.59)	2431 (29.09)	251 (35.40)	< 0.001
Moderate	4287 (47.29)	3952 (47.30)	335 (47.25)	
Vigorous	2096 (23.12)	1973 (23.61)	123 (17.35)	
Socioeconomic status, *n* (%)				
Low	3031 (33.44)	2803 (33.54)	228 (32.16)	0.230
Moderate	3010 (33.20)	2754 (32.96)	256 (36.11)	
Good	3024 (33.36)	2799 (33.50)	225 (31.73)	
Body mass index (kg/m^2)	27.19 ± 4.49	27.10 ± 4.50	28.47 ± 4.14	< 0.001
Waist circumference (cm)	96.63 ± 10.29	96.35 ± 10.30	100.01 ± 9.56	< 0.001
Visceral fat area (cm [2])	118.83 ± 50.28	117.51 ± 50.21	134.51 ± 48.39	< 0.001
Fasting blood sugar (mg/dl)	96.48 ± 29.46	90.23 ± 9.72	170.04 ± 64.14	< 0.001
Triglycerides (mg/dl)	135.01 ± 82.28	131.34 ± 75.22	178.10 ± 133.64	< 0.001
High-density lipoprotein cholesterol (mg/dl)	46.48 ± 11.37	46.7 ± 11.36	44.19 ± 11.20	< 0.001
Low-density lipoprotein cholesterol (mg/dl)	111.37 ± 31.12	111.38 ± 30.85	111.21 ± 34.21	0.443
Total cholesterol (mg/dl)	184.81 ± 37.66	184.30 ± 37.10	190.73 ± 43.48	< 0.001
Systolic blood pressure (mmHg)	108.10 ± 17.04	107.47 ± 16.77	115.23 ± 18.54	< 0.001
Diastolic blood pressure (mmHg)	69.78 ± 9.92	69.52 ± 9.80	72.80 ± 10.83	< 0.001
Alkaline phosphatase (mg/dl)	196.81 ± 62.80	195.01 ± 61.88	218.11 ± 69.25	< 0.001
Aspartate aminotransferase (mg/dl)	21.31 ± 8.95	21.41 ± 8.91	20.24 ± 9.43	< 0.001
Alanine aminotransferase (mg/dl)	24.65 ± 14.65	24.42 ± 14.59	27.37 ± 15.10	< 0.001
Gamma-glutamyl transpeptidase (mg/dl)	24.20 ± 19.35	23.53 ± 18.84	32.10 ± 23.21	< 0.001
Lipid accumulation product	54.82 ± 38.43	53.10 ± 36.60	75.51 ± 51.34	< 0.001
Family history of T2DM, *n* (%)	2213 (24.42)	1900 (22.74)	313 (44.15)	< 0.001

**P* value < 0.005 by t-test or chi^2 test

Table 2 Association of lipid accumulation product and type 2 diabetes mellitus by logistic regression analysis

Lipid accumulation product quartiles	Model 1		Model 2		Model 3	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Q1	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Q2	1.91 (1.42, 2.57)	< 0.001	1.78 (1.32, 2.40)	< 0.001	1.69 (1.25, 2.29)	0.003
Q3	3.20 (2.43, 4.22)	< 0.001	2.90 (2.19, 3.85)	< 0.001	2.67 (2.01, 3.55)	< 0.001
Q4	4.77 (3.65, 6.23)	< 0.001	4.17 (3.18, 5.49)	< 0.001	3.73 (2.83, 4.92)	< 0.001
P value trend	< 0.001		< 0.001		< 0.001	

Model 1: Unadjusted; Model 2: Adjusted for age, sex and family history of T2DM; Model 3: Adjusted for age, sex, family history of T2DM, physical activity, SBP, DBP and smoking

higher in the third quartile, and 4.17 (95% CI: (3.18, 5.49) times higher in the fourth quartile compared to the first quartile. The multiple regression model showed that, the odds of T2DM were 1.69 (95% CI: 1.25, 2.29) times higher in the second quartile of LAP compared to the first quartile. Additionally, the odds of T2DM were 2.67 (95% CI: 2.01, 3.55) times higher in the third quartile, and 3.73 (95% CI: 2.83, 4.92) times higher in the fourth quartile, compared to the first quartile (Table 2).

The ROC curve in Fig. 2 illustrates the predictive performance of the LAP, TG, and WC for the diagnosis of T2DM in the study population. The results of the ROC analysis for predicting T2DM indicated that the LAP has a higher predictive power, with an AUC of 0.66 (95% CI: 0.64, 0.68) compared to TG (AUC: 0.64, 95% CI: 0.62, 0.66) and WC (AUC:0.60, 95% CI: 0.58, 0.62). These findings, summarized in Table 3, indicate that LAP has

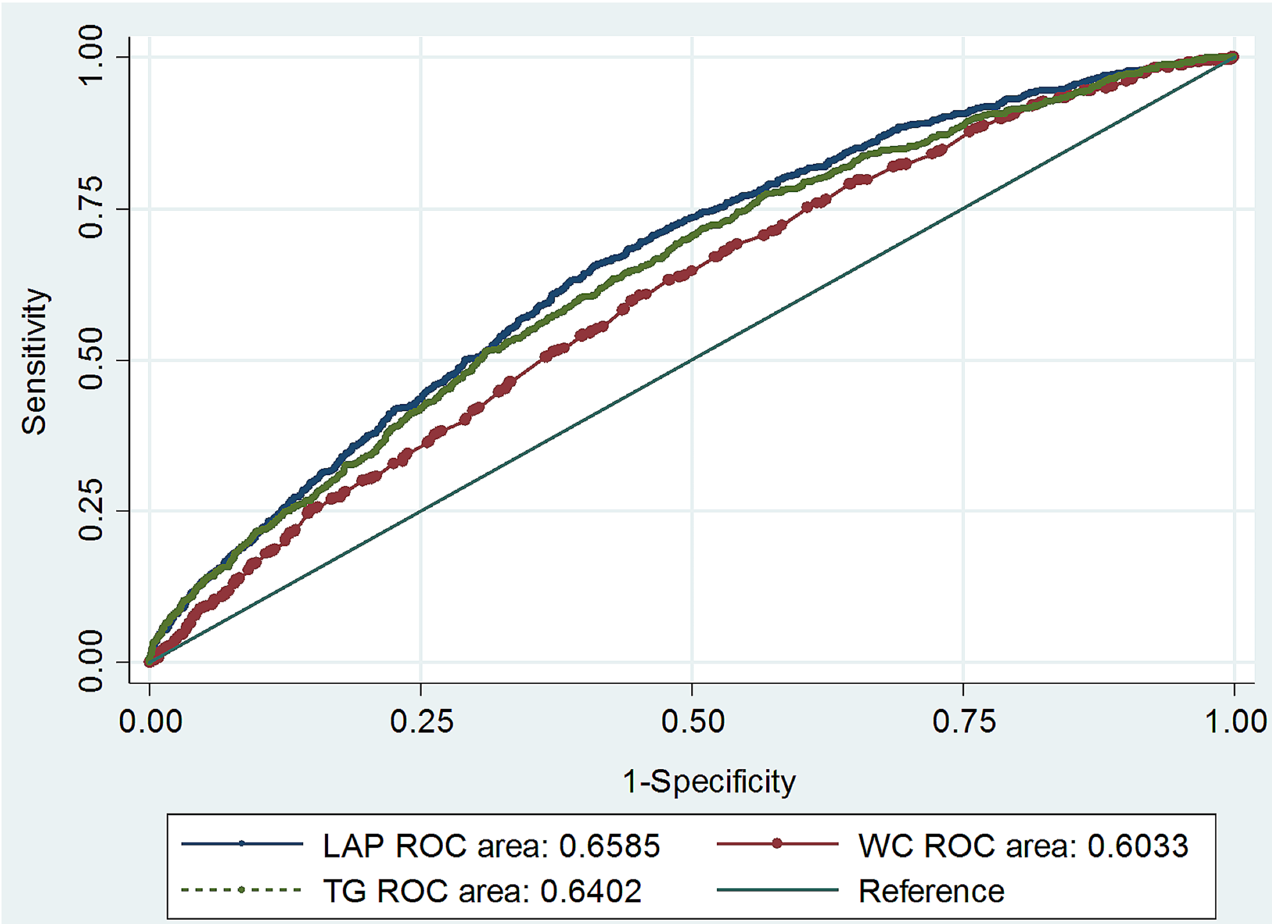

Fig. 2 ROC curve analysis of lipid accumulation product and its components for predicting of type 2 diabetes mellitus risk

Table 3 ROC curve analysis of lipid accumulation product and its components for predicting of type 2 diabetes mellitus risk

Variables	Cut-points	AUC ROC (95% CI)	Sensitivity (%)	Specificity (%)	Youden J-index
Lipid accumulation product	46.24	0.66 (0.64, 0.68)	0.70	0.57	27%
Triglycerides	120.40	0.64 (0.62, 0.66)	0.65	0.54	19%
Waist circumference	100.2	0.60 (0.58, 0.62)	0.78	0.41	19%

superior diagnostic value for predicting T2DM compared to TG and WC in the studied population.

Discussion

This population-based study found that higher levels of the LAP were significantly associated with increased odds of T2DM among adults in western Iran. Specifically, individuals in the second, third, and fourth LAP quartiles had 1.60, 2.43-, and 3.36-times higher odds of T2DM, respectively, compared to those in the first quartile.

The positive association between LAP and T2DM has been observed in various demographic and ethnic subgroups. For instance, in the Japanese population, high LAP levels were found to increase the risk of T2DM by 76% over time [23]. Similar results have been reported in studies involving Chinese adults and middle-aged Koreans [31, 32]. This is consistent with the well-established finding that obesity is a significant risk factor for the development of T2DM [33].

The excessive accumulation of lipids, or liver fat, leads to non-alcoholic fatty liver disease (NAFLD) and insulin resistance (IR), which are significant contributors to the development and progression of T2DM [11, 12, 34]. Additionally, WC is a more accurate measure than BMI for assessing excess visceral fat, although it does not clearly differentiate between subcutaneous and visceral fat in the abdominal area [34]. Moreover, dyslipidemia, hypertriglyceridemia, and low HDL cholesterol levels are associated with T2DM [35]. The LAP, as a composite index of WC and TG, reflects the state of visceral fat and blood lipids. Research has shown a strong correlation between higher LAP levels and an increased risk of metabolic diseases such as CVD and hypertension [22, 36].

The positive relationship between LAP and diabetes is well-established. In overweight individuals, excessive fat tissue, overeating, and chronic inflammation can lead to IR and disrupt glucose metabolism [37]. IR is a critical stage in the progression of T2DM [38], and chronic inflammation, along with impaired mitochondrial function due to obesity, can exacerbate IR [39–41]. Prolonged exposure to fatty acids can diminish insulin secretion, disrupt insulin gene expression, and increase β-cell death [42, 43]. Given the gradual onset of T2DM, early diagnosis and prevention are crucial. With the rising prevalence of T2DM and its serious complications, there is a need for a low-cost, easy-to-calculate index for early identification. Previous studies have indicated that LAP has a higher diagnostic value for predicting T2DM compared to BMI, WC, A Body Shape Index (ABSI), Visceral Adiposity Index (VAI), and waist/height ratio (WHtR) [23, 44]. The current study also demonstrates that LAP (AUC=0.66) outperforms WC (AUC=0.60) and TG (AUC=0.64) in predicting T2DM. Additionally, a cross-sectional study of 744 Chinese adults found that LAP had the highest predictive power for early T2DM, with an AUC of 0.742 [45].

Furthermore, LAP has been identified as a useful indicator for predicting metabolic diseases like hypertension and CVD [21, 22]. These findings suggest that LAP is a more accurate and comprehensive index for predicting T2DM compared to other commonly used indicators, such as WC and TG, in the studied populations.

The study had several limitations. Firstly, it was a cross-sectional analysis, meaning that the observed relationships cannot be assumed to be causal. However, causal relationships have been noted in longitudinal studies conducted in other population groups. Secondly, the study focused on adults in western Iran, so caution is advised when generalizing the results to other populations. It is recommended that similar studies be conducted in diverse population subgroups. Additionally, the study did not measure HbA1c levels or oral glucose tolerance test variables, which could provide further insights. However, a significant advantage of this study is its large sample size. Furthermore, the comprehensive collection of lifestyles, anthropometric, and biochemical variables, along with the adjustment for numerous confounding factors, strengthens the findings.

Conclusion

The study found a significant increase in the risk of T2DM with rising LAP levels in the adult population of western Iran. According to the ROC curve analysis, LAP was identified as an accessible and cost-effective tool for screening diabetes in adults, with a higher predictive value compared to triglyceride levels and obesity.

The key takeaway is that the LAP index shows promise as a useful screening and monitoring tool for T2DM, potentially outperforming traditional markers like TG levels and obesity. Further research in diverse populations is recommended to validate these findings.

Abbreviations

LAP	Lipid Accumulation Product
T2DM	Type 2 diabetes mellitus
RaNCD	Ravansar non-communicable diseases study
ROC	Receiver operating characteristic
WHO	World Health Organization
NCDs	Non-communicable diseases
CVD	Cardiovascular disease
WC	Waist circumference
PERSIAN	Prospective Epidemiological Research Studies in Iran
SES	Socioeconomic status
BMI	Body mass index
VFA	Visceral fat area
FBS	Fasting blood sugar
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
GGT	Gamma-glutamyl transferase
ALP	Alkaline phosphatase
TG	Triglyceride
TC	Total cholesterol
HDL	High-density lipoprotein cholesterol
LDL	Low-density lipoprotein
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
ABSI	A Body Shape Index
VAI	Visceral adiposity index
WHtR	Waist/height ratio

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-024-01682-6.

Supplementary Material 1

Acknowledgements

The authors thank the PERSIAN cohort Study collaborators and of Kermanshah University of Medical Sciences.

Author contributions

Authors' contributionsSS and AA conceived the idea of the study. FN developed the statistical analysis plan and conducted statistical analyses. YP, SS and AA contributed to the interpretation of the results. SS and AA drafted the original manuscript. AA, YP and FN supervised the conduct of this study. All authors reviewed the manuscript draft and revised it critically on intellectual content. All authors approved the final version of the manuscript to be published.

Funding

This research was supported by Kermanshah University of Medical Sciences (grant number: 92472). The Iranian Ministry of Health and Medical Education has also contributed to the funding used in the PERSIAN Cohort through Grant no 700/534.

Data availability

The data analyzed in the study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the ethics committee of Kermanshah University of Medical Sciences (KUMS.REC.1394.318). All methods were carried out in accordance with relevant guidelines and regulations. All the participants were provided oral and written informed consent. This study was conducted by the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 25 May 2024 / Accepted: 7 August 2024
Published online: 12 August 2024

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