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Exploring the association between healthy lifestyle score and atherogenic indices in a general population of Iranian adults

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Abstract

Background Atherogenic indices outperform traditional lipid markers; however, the combined association of lifestyle habits with these indices remains unclear. This study, which is based on population data, explored the link between the Healthy Lifestyle Score (HLS) and various atherogenic indices.

Methods In this cross-sectional analysis of the 2013 Isfahan Cohort Study 2 (participants aged ≥ 35 years), HLS was derived from four factors: smoking status, body mass index (18.5–24.9 kg/m^2), physical activity (≥ 1350 MET minutes/week), and diet quality (top two quintiles of the Alternate Healthy Eating Index-2010). Each factor was scored as 1 for adherence and zero otherwise, yielding a score of 0–4. The atherogenic indices included the Atherogenic Coefficient (AC), Atherogenic Index of Plasma (AIP), Atherogenic Combined Index (ACI), Castelli Risk Indices I and II (CRI-I/II), non-high-density Lipoprotein Cholesterol (NHC), Lipoprotein Combined Index (LCI), Remnant Lipoprotein Cholesterol (RLPC), and triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio. Logistic and linear regression analyses were conducted to examine these associations after adjusting for confounders.

Results Among 2,256 participants (49.7% men), the overall mean age was 58.15 ± 9.89 years. Across the population, a higher HLS was strongly linked to a decreased likelihood of elevated levels of individual atherogenic indices. Compared to individuals with HLS 0–1, those with HLS 3–4 had notably reduced odds of high AIP (odds ratio (OR): 0.42; 95% CI: 0.30–0.59), ACI (OR: 0.60; 95% CI: 0.47–0.77), and other indices (all *P* for trend < 0.05). Sex-stratified analyses revealed distinct patterns: in men, HLS was strongly associated with lower TG/HDL-C, AIP, and ACI, whereas in women, stronger associations were observed with cholesterol-driven markers (AC, NHC, RLPC, CRI-I, and CRI-II). Linear regression analysis confirmed that each unit increase in HLS corresponded to lower continuous values of these indices in the total population. AIP emerged as the most sensitive marker in both sexes.

Conclusions Adherence to a healthier lifestyle, as measured by the HLS, was significantly associated with lower atherogenic indices, highlighting its role in reducing cardiovascular risk. These results support integrating lifestyle interventions with cardiovascular prevention. Future studies should assess the causal impact of lifestyle modifications on atherogenic profiles.

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Keywords Healthy lifestyle, Atherogenic indices, Lipids, Heart disease risk factors

Background

Atherogenic indices are blood markers representing the balance between lipid components and are increasingly used to assess the risk of atherosclerosis and cardiovascular disease (CVD) [1, 2]. These indices, such as the atherogenic index of plasma (AIP), Castelli risk indices (CRI-I/II), and atherogenic coefficient (AC) offer better predictive values for cardiovascular risk than individual lipid measures [3]. Compared to traditional lipid measures (e.g., low-density lipoprotein-cholesterol (LDL-C) or high-density lipoprotein-cholesterol [HDL-C] alone), atherogenic indices have shown superior predictive value for subclinical atherogenesis, even when conventional lipid profiles are within normal ranges [3].

Lifestyle choices that can be modified, such as eating habits, exercise, body mass, and tobacco use, significantly influence lipid metabolism and, consequently, atherogenic profiles. Edwards et al. found that higher physical activity in NHANES adults lowered elevated AIP risk, while diet quality (measured by the Healthy Eating Index (HEI)-2005) showed no correlation [4]. Furthermore, engaging in either health-enhancing behaviors reduces the odds of elevated AIP by 32–45% in this population [4]. Other studies have linked higher diet quality and non-smoking status to reduced atherogenic indices (e.g., CRI-I/II and AIP) [5, 6].

Although individual lifestyle factors have been examined concerning atherogenic indices, few studies have evaluated their combined impact using an integrated scoring system. An integrated Healthy Lifestyle Score (HLS), which encompasses diet, smoking habits, physical activity, and body mass index (BMI), serves as an effective measure to assess the overall influence of lifestyle choices on lipid metabolism and cardiovascular well-being [7]. Moreover, many previous studies have focused on the association between traditional lipid parameters (e.g., LDL-C, HDL-C, and triglyceride [TG]) and HLS [8, 9], whereas atherogenic indices may offer more comprehensive insights into cardiovascular risk.

Given the limited research examining the collective impact of lifestyle behaviors on atherogenic indices, this research sought to explore the association between a composite HLS and various atherogenic markers among Iranian adults in the general population. It was hypothesized that higher adherence to healthy lifestyle behaviors would be associated with lower levels of atherogenic indices. This study extends the current knowledge by being among the first to explore this relationship using a comprehensive lifestyle score and a wide panel of atherogenic markers in a population-based setting, offering insights beyond traditional lipid parameters.

Methods

Population and design

The data for this cross-sectional study were sourced from the initial stage of the Isfahan Cohort Study 2 (ICS2), which took place in 2013. The ICS2 is a longitudinal cohort study spanning a decade and involving multiple generations. It includes a sub-sample from the original ICS study as well as a newly recruited group of individuals aged 35 and older living in both urban and rural regions of the Isfahan and Najaf-Abad districts in Central Iran [10]. The ICS2 aims to study lifestyle behaviors across three generations: parents, offspring, and grandchildren. The cohort sample was selected using a multistage random sampling method [10], and no separate sample size calculation was conducted for the present analysis, as it relied on the available dataset from ICS2 participants with complete information on lifestyle factors and lipid profiles.

Participants who were pregnant or had a history of pre-existing CVD (such as myocardial infarction, heart failure, or stroke) or inflammatory conditions (such as cancer, autoimmune diseases, and liver and kidney diseases) were excluded [10]. Participants lacking data on lifestyle factors or lipid profiles were excluded. ICS2 data were collected with informed consent under the principles of the Declaration of Helsinki and were approved by the Isfahan Cardiovascular Research Center Ethics Committee and Isfahan University of Medical Sciences. This study adhered to the same ethical standards as a secondary data analysis. Detailed methodological information is available in previous publications [10].

Data collection

Data on demographic, socioeconomic, clinical, and family history variables were obtained through structured interviews administered by trained personnel using a standardized questionnaire. Demographic information included participants' age, gender, and marital status, categorized as married or unmarried (the latter comprising single, divorced, or widowed individuals). Educational attainment was evaluated by years of formal schooling and classified into three groups: 0–5 years (primary education or below), 6–12 years (secondary or high school), and more than 12 years (post-secondary education, such as university or its equivalent).

Socioeconomic status (SES) was evaluated using a previously validated short-form instrument tailored to the Iranian population. This tool includes items such as the educational and employment status of the household head, housing conditions, car ownership, access to digital devices, and international travel for leisure [11].

A composite SES score, ranging from 0 to 17, was calculated, with higher values reflecting greater socioeconomic advantage [11].

Each participant provided a fasting blood sample, which was processed to separate the serum and subsequently stored at −70 °C. Biochemical assessments were performed on the stored serum samples, including the evaluation of fasting blood glucose (FBS), total cholesterol (TC), LDL-C, HDL-C, and TG levels using standardized methods. Participants were classified as hypertensive if they had a systolic blood pressure (SBP) of 140 mmHg or higher, a diastolic pressure (DBP) of at least 90 mmHg, or were receiving antihypertensive treatment. DM was identified by either a FBS level of 126 mg/dL or greater or the reported use of glucose-lowering medications, including insulin or oral antidiabetic drugs. Moreover, TC level ≥ 240 mg/dL indicated hypercholesterolemia. Information on family history of hypertension (HTN), dyslipidemia, CVD, and DM was collected using a binary format, denoting whether or not these conditions were present in the participant's family members.

Healthy lifestyle score

Lifestyle factors contributing to HLS were assessed using validated methods integrating smoking status, physical activity, BMI, and dietary intake. Smoking status was assessed through interviews and classified as non-smoker, former smoker, or current smoker.

Physical activity levels were assessed using the validated International Physical Activity Questionnaire (IPAQ) [12], with participants engaging in ≥ 1350 MET minutes per week classified as active [8, 13]. BMI was computed as weight (kg) divided by height (m^2) and categorized as normal (18.5–24.9 kg/m^2) or abnormal (< 18.5 or ≥ 25 kg/m^2).

Dietary intake was assessed through in-person interviews carried out by trained dietitians using a culturally adapted, validated semi-quantitative food frequency questionnaire (FFQ) comprising 110 items [14]. Detailed information on food consumption frequency over the previous year was collected in an open-ended format, with participants reporting their daily, weekly, or monthly food intakes. These responses were subsequently converted into an average daily intake to standardize the dietary assessment [14]. These data were used to compute the Alternate HEI 2010 (AHEI-2010), an enhanced version of the HEI, and a validated diet quality measure [15].

Because of cultural and methodological limitations, alcohol intake was not assessed due to religious restrictions in Iran. Sodium intake was not included in the analysis, as the 110-item FFQ employed in this study does not provide an accurate estimate of sodium consumption. Accordingly, the AHEI-2010 was calculated based on nine components [16]. Each component of the index was scored on a scale of 0 to 10, resulting in a total possible score of 0 to 90. Individuals whose scores fell within the top 40% were classified as having a healthier dietary pattern [13].

being a non-smoker, engaging in sufficient physical activity (≥ 1350 MET minutes/week), maintaining a healthy diet (top two quintiles of AHEI-2010), and having a normal BMI. A final score between 0 and 4 was assigned, with higher values corresponding to better adherence to a healthy lifestyle.

Atherogenic indices

Multiple atherogenic indices were computed to assess lipid-associated cardiovascular risk among participants in this study. All lipid measurements were obtained in mg/dL, and the indices were computed accordingly. Table S1 presents the formulas and definitions of each index. For high-level cut-offs, values above the following thresholds were defined as indicative of increased atherogenic risk: For the AC, values exceeding 3 were considered high [3]. For AIP, a threshold of 0.24 was used [17], and for the Atherogenic Combined Index (ACI), high levels were determined relative to the sample median [18].

Thresholds for elevated CRI-I were set at > 3 for women and > 3.5 for men, while CRI-II values exceeding 2.5 in females and 3 in males were considered high [3, 19]. Non-High-Density Lipoprotein Cholesterol (NHC) was considered high if it exceeded 130 mg/dL [20]. For both the Lipoprotein Combined Index (LCI) and Remnant Lipoprotein Cholesterol (RLPC), values above the median of the study sample were considered indicative of high risk, and a TG/HDL-C ratio greater than 3 was used as the cut-off for increased atherogenic risk [21–23].

Statistical analysis

For continuous variables, data are expressed as mean ± standard deviation (SD) or median (interquartile range [IQR]) based on distribution. Categorical variables are presented as frequencies and percentages. HLS was categorized into three groups: low adherence (scores 0–1), moderate adherence (score 2), and high adherence (scores 3–4). Comparisons across HLS categories were performed using analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables.

The association between HLS and the risk of high atherogenic indices was assessed using multivariable logistic regression models, and results were presented as odds ratios (OR) and 95% confidence intervals (CI). For atherogenic indices considered continuous variables, multivariable linear regression models were applied, and the results were reported as beta coefficients (β) with 95% CI. Two hierarchical models were used to adjust for potential

confounding variables: Model 1 was adjusted for age and sex; Model 2 was additionally adjusted for educational level, marital status, SES, DM, total energy intake, and family histories of DM, HTN, CVD, and dyslipidemia. Potential confounding variables were selected based on their demonstrated associations with HLS categories, their established relevance in previous studies, and their contribution to improving model performance and overall goodness of fit. In the logistic regression analyses, *P* for linear trends was analyzed by HLS and treated as a continuous variable in the models.

The potential interactions between HLS components (BMI, smoking, physical activity, diet quality, and smoking status) and other variables in a two-by-two manner were systematically evaluated. For statistically significant interactions, the results were analyzed and reported in detail. Additionally, due to the significant interaction effects observed between sex and HLS on several atherogenic indices, subgroup analyses stratified by sex were conducted. All statistical analyses were performed using SPSS for Windows version 23 (IBM Corp. IBM SPSS Statistics for Windows [Internet]. Armonk, NY: IBM Corp; 2015). A two-sided *P*-value of less than 0.05 was considered statistically significant.

Results

Among 2,256 participants (49.7% men, mean age 58.15 ± 9.89 years) in the ICS2, 42.4% exhibited low adherence to a healthy lifestyle (HLS 0–1), 39.0% moderate adherence (HLS 2), and 18.7% high adherence (HLS 3–4). Baseline characteristics (Table 1) revealed that participants with higher HLS were more likely to be men ($P = 0.015$), have higher educational attainment ($P = 0.018$) and SES ($P < 0.001$), and demonstrate healthier behaviors, including lower smoking rates, higher physical activity, normal BMI, and better diet quality (all *P*-values < 0.001). Clinically, higher HLS was associated with lower SBP, FBS, TG, and the prevalence of HTN and DM (all *P*-values < 0.05), as well as higher HDL-C and total energy intake (both *P*-values < 0.05). No significant differences were observed in age, marital status, DBP, TC, LDL-C, or hypercholesterolemia (all *P*-values > 0.05). Family histories of HTN, DM, and dyslipidemia were less frequent with higher HLS (all *P*-values < 0.05), but family history of CVD did not differ ($P = 0.295$).

Associations with atherogenic indices in the total population

A higher HLS was strongly associated with reduced odds of elevated atherogenic indices in the total population (Table 2). Compared to participants with low HLS (0–1), those with high HLS (3–4) had significantly lower odds of elevated levels across all indices: AC (OR: 0.61, 95% CI: 0.47–0.79), AIP (OR: 0.42, 95% CI: 0.30–0.59), ACI (OR: 0.60, 95% CI: 0.47–0.77), CRI-I (OR: 0.62, 95% CI: 0.41–0.92), CRI-II (OR: 0.66, 95% CI: 0.51–0.85), NHC (OR: 0.69, 95% CI: 0.53–0.91), LCI (OR: 0.67, 95% CI: 0.52–0.86), RLPC (OR: 0.68, 95% CI: 0.52–0.88), and TG/HDL-C (OR: 0.62, 95% CI: 0.48–0.79; all *P*-values for trend < 0.05). The strongest associations were observed for AIP and ACI, reflecting their sensitivity to lifestyle factors.

Linear regression analyses (Table 3) corroborated these findings, showing that each unit increase in HLS was associated with significantly lower levels of all atherogenic indices in the crude and adjusted models (all *P*-values < 0.05).

Sex-stratified associations

Sex-stratified analyses revealed distinct patterns in the associations between HLS and atherogenic indices in male and female populations (Tables 2 and 3).

In Males, higher HLS was significantly associated with lower odds of elevated AIP (OR: 0.37, 95% CI: 0.22–0.63), ACI (OR: 0.58, 95% CI: 0.41–0.82), CRI-II (OR: 0.71, 95% CI: 0.50–1.00), and TG/HDL-C (OR: 0.55, 95% CI: 0.39–0.78; all *P for trend* < 0.05). Linear regression analysis confirmed these findings, with significant reductions per HLS unit increase in AIP, ACI, CRI-II, and TG/HDL-C (all *P*-values < 0.05). Additionally, AC, CRI-I, and LCI showed significant inverse associations in the linear models (all *P*-values < 0.05) despite non-significant ORs in the logistic regression. Associations with NHC and RLPC were not significant in either the logistic regression or linear models.

In Females: Higher HLS was significantly associated with lower odds of elevated AC (OR: 0.48, 95% CI: 0.33–0.70), AIP (OR: 0.45, 95% CI: 0.28–0.72), ACI (OR: 0.61, 95% CI: 0.42–0.89), CRI-I (OR: 0.51, 95% CI: 0.27–0.95), CRI-II (OR: 0.59, 95% CI: 0.41–0.87), NHC (OR: 0.47, 95% CI: 0.31–0.71), and RLPC (OR: 0.40, 95% CI: 0.27–0.59). All *P* values for trends were significant, except for the CRI-I trend. Linear regression analysis confirmed these findings, with significant reductions per HLS unit increase in AC, AIP, ACI, CRI-I, NHC, and RLPC (all *P*-values < 0.05). However, CRI-II did not show a significant association in the linear model. Associations regarding LCI and TG/HDL-C were insignificant in either logistic regression or linear models.

Interactions among HLS components

Pairwise interaction analyses (Table S2) identified significant interactions between BMI and smoking status on CRI-I ($P = 0.006$) and LCI ($P = 0.026$), and between physical activity and smoking status on CRI-II ($P = 0.036$).

Table 1 Baseline characteristics of study participants based on the healthy lifestyle score groups

Variable	Healthy Lifestyle Score (HLS)			*P*
	0–1 (*n* = 956)	2 (*n* = 879)	3–4 (*n* = 421)	
Age, years (mean ± SD)	57.87 ± 8.87	58.54 ± 10.53	57.97 ± 10.70	0.312
Sex (Men), n (%)	462 (48.3)	423 (48.1)	236 (56.1)	**0.015**
Married, n (%)	839 (89.1)	759 (87.2)	366 (88.4)	0.169
Education, n (%)				**0.018**
0–5 years	519 (54.7)	442 (50.8)	199 (47.4)	
6–12 years	321 (33.9)	300 (34.5)	148 (35.2)	
>12 years	108 (11.4)	128 (14.7)	73 (17.4)	
SES score	4.20 ± 2.82	4.29 ± 2.96	4.87 ± 2.97	**< 0.001**
HLS Smoking status, n (%)				**< 0.001**
Never	752 (78.7)	828 (94.2)	411 (97.8)	
Ever smoking	204 (21.3)	51 (5.8)	10 (2.4)	
Physical activity (METs-min/wk)[a]	595.71 (349.46-862.29)	730.71 (403.57-1279.50)	1566.00 (797.50–2673.00)	**< 0.001**
HLS Physical activity (METs-min/wk)[b]				**< 0.001**
High physical activity	23 (2.4)	201 (22.9)	272 (64.6)	
Low physical activity	933 (97.6)	678 (77.1)	149 (35.4)	
BMI (kg/m^2)	29.23 ± 4.22	27.65 ± 4.81	24.77 ± 3.73	**< 0.001**
Weight status, n (%)[c]				**< 0.001**
Underweight	13 (1.4)	16 (1.8)	0 (0)	
Normal	66 (6.9)	266 (30.3)	292 (69.4)	
Overweight	528 (55.2)	346 (39.4)	86 (20.4)	
Obesity	349 (36.5)	251 (28.6)	43 (10.2)	
HLS BMI[d](kg/m^2)				**< 0.001**
Normal BMI	66 (6.9)	266 (30.3)	292 (69.4)	
Abnormal BMI	890 (93.1)	613 (69.7)	129 (30.6)	
AHEI-2010 (score)	41.39 ± 8.33	50.05 ± 10.81	55.86 ± 8.92	**< 0.001**
HLS AHEI-2010 (score)				**< 0.001**
Upper 40%	48 (5.0)	463 (52.7)	337 (80.0)	
Lower 60%	908 (95.0)	416 (47.3)	84 (20.0)	
SBP (mmHg)	129.28 ± 17.60	127.10 ± 18.75	124.55 ± 18.02	**< 0.001**
DBP (mmHg)	84.51 ± 9.02	83.54 ± 9.81	83.95 ± 9.11	0.082
Total Energy Intake (kcal/day)	1297.39 ± 610.84	1436.58 ± 584.54	1566.45 ± 578.72	**< 0.001**
FBS (mg/dl)	107.13 ± 37.41	105.53 ± 34.00	100.63 ± 28.42	**0.006**
TC (mg/dl)	197.07 ± 40.38	195.34 ± 41.02	192.64 ± 37.85	0.165
LDL-C (mg/dl)	112.94 ± 28.92	112.38 ± 30.44	111.18 ± 26.78	0.588
HDL-C (mg/dl)	43.33 ± 12.37	44.41 ± 11.19	44.85 ± 10.99	**0.041**
TG (mg/dl)	163.91 ± 105.24	152.21 ± 77.70	145.92 ± 90.03	**0.001**
Hypertension, n (%)	493 (51.6)	380 (43.2)	1553 (36.4)	**< 0.001**
Diabetes Mellitus, n (%)	295 (30.9)	255 (29.0)	88 (20.9)	**0.001**
Hypercholesterolemia, n (%)	129 (13.5)	115 (13.2)	40 (9.5)	0.103
Family history of hypertension, n (%)	468 (49.1)	392 (44.6)	178 (42.4)	**0.005**
Family history of diabetes mellitus, n (%)	360 (37.7)	319 (36.4)	109 (25.9)	**< 0.001**
Family history of dyslipidemia, n (%)	398 (41.6)	330 (37.7)	133 (31.6)	**0.006**
Family history of CVD, n (%)	316 (33.1)	260 (29.9)	137 (32.8)	0.295

[a] Reported as median (interquartile range)

[b] High physical activity was defined as ≥ 1350 METs-min/week, and low physical activity was defined as < 1350 (METs-min/week)

[c] Underweight was defined as BMI < 18.5 kg/m^2, normal weight as BMI 18.5–24.99 kg/m^2, overweight as BMI 25–29.99 kg/m^2, and obesity as BMI ≥ 30 kg/m^2

[d] Normal BMI was defined as BMI = 18.5–24.99 kg/m^2, and abnormal BMI was defined as BMI < 18.5 kg/m^2 or BMI ≥ 25 kg/m^2

Abbreviations. *P* = *P*-value (resulted from ANOVA or Chi-square for continuous and categorical variables, respectively); SES = socioeconomic status, BMI = body mass index; AHEI = alternate healthy eating index; kcal = kilocalories; SBP = systolic blood pressure; DBP = diastolic blood pressure; FBS = fasting blood sugar; TC = total cholesterol; LDL-C = low-density lipoprotein cholesterol; HDL-C = low-density lipoprotein cholesterol; CVD = cardiovascular disease

Table 2 Multiple adjusted logistic regression presented with odds ratios and 95% confidence interval for the association of atherogenic indices and healthy lifestyle score

Atherogenic indices	Healthy Lifestyle Score (Total Population)			*P* for linear trend	Healthy Lifestyle Score (Male)			*P* for linear trend	Healthy Lifestyle Score (Female)			*P* for linear trend
	0–1 (*n* = 956)	2 (*n* = 879)	3–4 (*n* = 421)		0–1 (*n* = 462)	2 (*n* = 423)	3–4 (*n* = 236)		0–1 (*n* = 494)	2 (*n* = 456)	3–4 (*n* = 185)	
High AC												
Crude Model	1 (Ref)	0.77 (0.63, 0.95)	0.62 (0.49, 0.80)	**< 0.001**	1 (Ref)	0.73 (0.53, 0.99)	0.73 (0.51, 1.06)	0.056	1 (Ref)	0.80 (0.61, 1.05)	0.45 (0.32, 0.65)	**< 0.001**
Model 1	1 (Ref)	0.77 (0.62, 0.95)	0.58 (0.45, 0.75)	**< 0.001**	1 (Ref)	0.73 (0.53, 1.00) [a]	0.73 (0.51, 1.06)	0.061	1 (Ref)	0.80 (0.61, 1.05)	0.45 (0.31, 0.65)	**< 0.001**
Model 2	1 (Ref)	0.80 (0.64, 0.98)	0.61 (0.47, 0.79)	**< 0.001**	1 (Ref)	0.73 (0.53, 1.01)	0.76 (0.52, 1.11)	0.098	1 (Ref)	0.86 (0.65, 1.15)	0.48 (0.33, 0.70)	**< 0.001**
High AIP												
Crude Model	1 (Ref)	0.60 (0.45, 0.81)	0.40 (0.29, 0.56)	**< 0.001**	1 (Ref)	0.48 (0.29, 0.77)	0.34 (0.20, 0.57)	**< 0.001**	1 (Ref)	0.70 (0.48, 1.02)	0.41 (0.26, 0.64)	**< 0.001**
Model 1	1 (Ref)	0.60 (0.45, 0.81)	0.38 (0.27, 0.54)	**< 0.001**	1 (Ref)	0.49 (0.30, 0.80)	0.35 (0.21, 0.58)	**< 0.001**	1 (Ref)	0.70 (0.48, 1.02)	0.41 (0.26, 0.64)	**< 0.001**
Model 2	1 (Ref)	0.62 (0.46, 0.84)	0.42 (0.30, 0.59)	**< 0.001**	1 (Ref)	0.49 (0.30, 0.79)	0.37 (0.22, 0.63)	**< 0.001**	1 (Ref)	0.74 (0.50, 1.10)	0.45 (0.28, 0.72)	**0.001**
High ACI												
Crude Model	1 (Ref)	0.74 (0.61, 0.90)	0.60 (0.48, 0.77)	**< 0.001**	1 (Ref)	0.67 (0.51, 0.89)	0.59 (0.42, 0.82)	**0.001**	1 (Ref)	0.81 (0.62, 1.05)	0.57 (0.40, 0.82)	**0.002**
Model 1	1 (Ref)	0.74 (0.61, 0.90)	0.59 (0.46, 0.75)	**< 0.001**	1 (Ref)	0.68 (0.51, 0.90)	0.59 (0.42, 0.82)	**0.001**	1 (Ref)	0.81 (0.62, 1.05)	0.57 (0.40, 0.82)	**0.002**
Model 2	1 (Ref)	0.74 (0.61, 0.91)	0.60 (0.47, 0.77)	**< 0.001**	1 (Ref)	0.65 (0.49, 0.87)	0.58 (0.41, 0.82)	**0.001**	1 (Ref)	0.86 (0.65, 1.13)	0.61 (0.42, 0.89)	**0.013**
High CRI-I												
Crude Model	1 (Ref)	0.69 (0.49, 0.96)	0.58 (0.39, 0.85)	**0.003**	1 (Ref)	0.61 (0.40, 0.94)	0.73 (0.43, 1.22)	0.130	1 (Ref)	0.82 (0.48, 1.40)	0.44 (0.24, 0.80)	**0.011**
Model 1	1 (Ref)	0.69 (0.49, 0.96)	0.60 (0.40, 0.89)	**0.004**	1 (Ref)	0.62 (0.40, 0.95)	0.73 (0.44, 1.23)	0.137	1 (Ref)	0.82 (0.48, 1.40)	0.44 (0.24, 0.80)	**0.011**
Model 2	1 (Ref)	0.70 (0.50, 0.98)	0.62 (0.41, 0.92)	**0.011**	1 (Ref)	0.61 (0.39, 0.94)	0.68 (0.40, 1.15)	0.082	1 (Ref)	0.90 (0.52, 1.56)	0.51 (0.27, 0.95)	0.052
High CRI-II												
Crude Model	1 (Ref)	0.77 (0.64, 0.93)	0.63 (0.49, 0.80)	**< 0.001**	1 (Ref)	0.64 (0.48, 0.84)	0.72 (0.52, 1.00) [b]	**0.012**	1 (Ref)	0.92 (0.71, 1.20)	0.55 (0.38, 0.80)	**0.005**
Model 1	1 (Ref)	0.78 (0.64, 0.94)	0.65 (0.51, 0.83)	**< 0.001**	1 (Ref)	0.65 (0.49, 0.85)	0.72 (0.52, 1.00) [a]	**0.015**	1 (Ref)	0.92 (0.71, 1.20)	0.55 (0.38, 0.80)	**0.005**
Model 2	1 (Ref)	0.78 (0.64, 0.95)	0.66 (0.51, 0.85)	**< 0.001**	1 (Ref)	0.62 (0.46, 0.82)	0.71 (0.50, 1.00) [b]	**0.011**	1 (Ref)	1.01 (0.77, 1.33)	0.59 (0.41, 0.87)	**0.027**
High NHC												
Crude Model	1 (Ref)	0.71 (0.58, 0.88)	0.67 (0.52, 0.87)	**0.001**	1 (Ref)	0.74 (0.55, 0.99)	0.88 (0.62, 1.25)	0.278	1 (Ref)	0.68 (0.50, 0.92)	0.49 (0.33, 0.73)	**< 0.001**
Model 1	1 (Ref)	0.71 (0.57, 0.88)	0.68 (0.52, 0.88)	**0.001**	1 (Ref)	0.74 (0.55, 0.99)	0.88 (0.62, 1.25)	0.279	1 (Ref)	0.68 (0.50, 0.92)	0.49 (0.33, 0.73)	**< 0.001**
Model 2	1 (Ref)	0.73 (0.59, 0.90)	0.69 (0.53, 0.91)	**0.002**	1 (Ref)	0.74 (0.55, 1.00) [b]	0.91 (0.63, 1.31)	0.371	1 (Ref)	0.70 (0.51, 0.96)	0.47 (0.31, 0.71)	**< 0.001**
High LCI												
Crude Model	1 (Ref)	0.73 (0.60, 0.88)	0.65 (0.51, 0.82)	**< 0.001**	1 (Ref)	0.70 (0.53, 0.92)	0.72 (0.52, 1.00) [b]	**0.017**	1 (Ref)	0.78 (0.60, 1.02)	0.54 (0.38, 0.77)	**0.001**
Model 1	1 (Ref)	0.73 (0.61, 0.89)	0.64 (0.50, 0.81)	**< 0.001**	1 (Ref)	0.70 (0.53, 0.92)	0.73 (0.52, 1.00) [a]	**0.22**	1 (Ref)	0.78 (0.60, 1.02)	0.54 (0.38, 0.77)	**0.001**
Model 2	1 (Ref)	0.75 (0.62, 0.91)	0.67 (0.52, 0.86)	**< 0.001**	1 (Ref)	0.68 (0.51, 0.90)	0.75 (0.53, 1.05)	**0.037**	1 (Ref)	0.58 (0.40, 0.84)	0.85 (0.64, 1.11)	**0.006**
High RLPC												
Crude Model	1 (Ref)	0.72 (0.59, 0.89)	0.61 (0.48, 0.79)	**< 0.001**	1 (Ref)	0.79 (0.59, 1.05)	0.91 (0.65, 1.29)	0.415	1 (Ref)	0.65 (0.48, 0.88)	0.39 (0.27, 0.56)	**< 0.001**
Model 1	1 (Ref)	0.72 (0.58, 0.88)	0.62 (0.48, 0.80)	**< 0.001**	1 (Ref)	0.78 (0.58, 1.04)	0.91 (0.64, 1.28)	0.379	1 (Ref)	0.65 (0.48, 0.88)	0.39 (0.27, 0.56)	**< 0.001**
Model 2	1 (Ref)	0.76 (0.62, 0.94)	0.68 (0.52, 0.88)	**0.001**	1 (Ref)	0.82 (0.61, 1.10)	1.02 (0.71, 1.45)	0.828	1 (Ref)	0.69 (0.51, 0.94)	0.40 (0.27, 0.59)	**< 0.001**
High TG/HDL-C												
Crude Model	1 (Ref)	0.75 (0.62, 0.91)	0.62 (0.49, 0.79)	**< 0.001**	1 (Ref)	0.72 (0.54, 0.95)	0.54 (0.39, 0.76)	**< 0.001**	1 (Ref)	0.77 (0.59, 1.00) [b]	0.64 (0.45, 0.92)	**0.007**

Table 2 (continued)

Atherogenic indices	Healthy Lifestyle Score (Total Population)			*P* for linear trend	Healthy Lifestyle Score (Male)			*P* for linear trend	Healthy Lifestyle Score (Female)			*P* for linear trend
	0–1 (*n* = 956)	2 (*n* = 879)	3–4 (*n* = 421)		0–1 (*n* = 462)	2 (*n* = 423)	3–4 (*n* = 236)		0–1 (*n* = 494)	2 (*n* = 456)	3–4 (*n* = 185)	
Model 1	1 (Ref)	0.75 (0.62, 0.91)	0.59 (0.46, 0.75)	**< 0.001**	1 (Ref)	0.73 (0.55, 0.96)	0.55 (0.39, 0.76)	**< 0.001**	1 (Ref)	0.77 (0.59, 1.00) [b]	0.64 (0.45, 0.92)	**0.007**
Model 2	1 (Ref)	0.75 (0.61, 0.94)	0.62 (0.48, 0.79)	**< 0.001**	1 (Ref)	0.70 (0.52, 0.93)	0.55 (0.39, 0.78)	**< 0.001**	1 (Ref)	0.81 (0.61, 1.07)	0.70 (0.48, 1.02)	**0.040**

Abbreviations CI = confidence interval; *P* = *P*-value; AC = atherogenic coefficient; AIP = atherogenic index of plasma; ACI = atherogenic combined index; CRI-I = Castelli risk index I; CRI-II = Castelli risk index II; NHC = non-HDL-cholesterol; LCI = lipoprotein combined index; RLPC = remnant lipoprotein cholesterol; TG/HDL-C = triglyceride to high-density lipoprotein ratio

[a]: *P*-value ≥ 0.05

[b]: *P*-value < 0.05

Model 1. Adjusted for age and sex.

Model 2. Further adjusted for education level, marital status, socioeconomic status (SES), diabetes mellitus, total energy intake, and family history of diabetes, hypertension, cardiovascular disease, and dyslipidemia

Discussion

This study is one of the earliest to thoroughly examine the association between composite HLS and multiple atherogenic indices in a large Iranian adult population. Higher HLS (scores 3–4) was linked to 31–58% lower odds of elevated indices than low HLS (0–1), with significant inverse trends. AIP and ACI showed the strongest association. Linear regression analysis confirmed that the levels of all indices per HLS unit increased. Sex-stratified analyses revealed stronger associations in women. Among female participants, those with elevated HLS had decreased odds of AC, AIP, ACI, CRI-I/II, NHC, and RLPC (all *P* for trend < 0.05, except CRI-I), with linear models supporting reductions in AC, AIP, ACI, CRI-I, NHC, and RLPC. The LCI and TG/HDL-C were not significant. For men, the indices significantly related to HLS included AIP, ACI, CRI-II, and TG/HDL-C (*P* for trend < 0.05), with linear models supporting AC, CRI-I, and LCI but not NHC or RLPC. These patterns suggest that sex-specific differences in lifestyle influence lipid metabolism.

In the present study, women exhibited stronger associations between higher HLS and reduced cholesterol-driven indices, such as AC, NHC, RLPC, and Castelli Risk Indices. Men showed more pronounced associations with TG-driven markers, notably the TG/HDL-C ratio and ACI. These patterns likely stem from physiological differences: women's higher baseline HDL-C, influenced by estrogen [24], may enhance responsiveness to lifestyle modifications, like physical activity and smoking cessation, reducing cholesterol-related indices [25, 26]. Men with higher baseline TG [27] may benefit more from weight loss and lower TG-driven indices [28]. Behavioral factors also contribute; a higher smoking prevalence in men may limit HDL-C improvements [29], while women's lower smoking rates support greater cholesterol-driven benefits. Clinically, AIP and ACI were robust markers of lifestyle adherence across sexes, with AIP showing the strongest association. For risk stratification, AC, NHC, and RLPC are particularly relevant for women, whereas the TG/HDL-C ratio is key for men. These findings underscore the need for sex-specific lipid markers to assess cardiovascular risk and tailor lifestyle interventions.

The atherogenic markers assessed in this study reflect distinct aspects of lipid-related cardiovascular risk. AC reflects the ratio between harmful lipoproteins and protective HDL-C, indicating an overall atherogenic risk [30]. AIP is related to LDL particle size, with higher values suggesting smaller, denser, and atherogenic LDL that are more likely to promote plaque formation than larger LDL particles [31]. ACI quantifies the cumulative atherogenic risk by incorporating TG, non-HDL-C, and HDL-C into a single composite measure, including

Table 3 Multivariable adjusted linear regression coefficient presented with β and 95% confidence interval for the association of atherogenic indices with the healthy lifestyle score

Atherogenic indices	Healthy Lifestyle Score (Total Population *n* = 2256)						Healthy Lifestyle Score (Male *n* = 1121)						Healthy Lifestyle Score (Female *n* = 1135)					
	Crude Model		Model 1		Model 2		Crude Model		Model 1		Model 2		Crude Model		Model 1		Model 2	
	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*
AC	-0.15 (-0.21, -0.09)	**< 0.001**	-0.16 (-0.22, -0.10)	**< 0.001**	-0.13 (-0.19, -0.07)	**< 0.001**	-0.17 (-0.25, -0.08)	**< 0.001**	-0.17 (-0.25, -0.08)	**< 0.001**	-0.15 (-0.23, -0.06)	**0.001**	-0.14 (-0.23, -0.06)	**< 0.001**	-0.14 (-0.23, -0.06)	**< 0.001**	-0.11 (-0.20, -0.02)	**0.019**
AIP	-0.04 (-0.05, -0.03)	**< 0.001**	-0.04 (-0.05, -0.03)	**< 0.001**	-0.04 (-0.05, -0.02)	**< 0.001**	-0.05 (-0.06, -0.03)	**< 0.001**	-0.05 (-0.06, -0.03)	**< 0.001**	-0.04 (-0.06, -0.03)	**< 0.001**	-0.03 (-0.05, -0.01)	**0.002**	-0.03 (-0.05, -0.01)	**0.002**	-0.02 (-0.04, -0.00)	**0.020**
ACI	-0.05 (-0.06, −0.03)	**< 0.001**	-0.05 (-0.06, −0.03)	**< 0.001**	-0.04 (-0.06, −0.03)	**< 0.001**	-0.05 (-0.07, −0.03)	**< 0.001**	-0.05 (-0.07, −0.03)	**< 0.001**	-0.05 (-0.07, −0.02)	**< 0.001**	-0.05 (-0.07, −0.02)	**< 0.001**	-0.05 (-0.07, −0.02)	**< 0.001**	-0.04 (-0.06, −0.01)	**0.002**
CRI-I	-0.15 (-0.21, -0.09)	**< 0.001**	-0.16 (-0.21, -0.10)	**< 0.001**	-0.13 (-0.19, -0.07)	**< 0.001**	-0.17 (-0.25, -0.08)	**< 0.001**	-0.17 (-0.25, -0.08)	**< 0.001**	-0.15 (-0.23, -0.06)	**0.001**	-0.14 (-0.23, -0.06)	**0.001**	-0.14 (-0.23, -0.06)	**0.001**	-0.11 (-0.20, -0.02)	**0.019**
CRI-II	-0.07 (-0.0.11, -0.03)	**< 0.001**	-0.08 (-0.0.12, -0.04)	**< 0.001**	-0.07 (-0.0.11, -0.03)	**0.001**	-0.08 (-0.0.13, -0.03)	**0.003**	-0.08 (-0.0.13, -0.02)	**0.005**	-0.08 (-0.0.14, -0.03)	**0.003**	-0.08 (-0.0.14, -0.02)	**0.011**	-0.08 (-0.0.14, -0.02)	**0.011**	-0.05 (-0.0.11, 0.01)	0.087
NHC	-2.64 (-4.62, -0.67)	**0.009**	-2.55 (-4.52, -0.58)	**0.011**	-2.09 (-4.09, -0.08)	**0.042**	-0.42 (-3.00, 2.15)	0.747	-0.43 (-3.01, 2.16)	0.746	-0.10 (-2.74, 2.54)	0.941	-5.46 (-8.51, -2.41)	**< 0.001**	-5.41 (-8.49, -2.36)	**0.001**	-4.97 (-8.10, -1.84)	**0.002**
LCI	-7610.48 (-12139.27, -3081.68)	**< 0.001**	-7670.39 (-12196.31, -3144.48)	**0.001**	-6250.22 (-10869.59, -1630.85)	**0.008**	-9323.68 (-15638.47, -3008.90)	**0.004**	-8850.27 (-15145.92, -2554.63)	**0.006**	-7780.07 (-14217.08, -1343.06)	**0.018**	-5524.89 (-12045.06, 995.282)	0.097	-5430.34 (-11950.06, 1089.39)	0.102	-3583.21 (-10305.51, 313.9.09)	0.296
RLPC	-1.96 (-3.12, -0.81)	**0.001**	-1.96 (-3.11, -0.80)	**0.001**	-1.46 (-2.64, -0.28)	**0.016**	-1.36 (-2.99, 0.27)	0.101	-1.41 (-3.04, 0.22)	0.091	-0.73 (-2.40, 0.93)	0.389	-2.75 (-4.40, -1.10)	**0.001**	-2.73 (-4.38, -1.08)	**0.001**	-2.53 (-4.23, -0.84)	**0.003**
TG/HDL-C	-0.38 (-0.55, -0.21)	**< 0.001**	-0.39 (-0.56, -0.22)	**< 0.001**	-0.34 (-0.51, -0.16)	**< 0.001**	-0.57 (-0.83, -0.31)	**< 0.001**	-0.55 (-0.81, -0.29)	**< 0.001**	-0.49 (-0.75, -0.22)	**< 0.001**	-0.15 (-0.35, 0.05)	0.136	-0.15 (-0.35, 0.05)	0.138	-0.10 (-0.30, 0.11)	0.372

AbbreviationsCI = confidence interval; *P* = *P*-value; AC = atherogenic coefficient; AIP = atherogenic index of plasma; ACI = atherogenic combined index; CRI-I = Castelli risk index I; CRI-II = Castelli risk index II; NHC = non-HDL-cholesterol; LCI = lipoprotein combined index; RLPC = remnant lipoprotein cholesterol; TG/HDL-C = triglyceride to high-density lipoprotein ratio

Model 1. Adjusted for age and sex

Model 2. Further adjusted for education level, marital status, socioeconomic status (SES), diabetes mellitus, total energy intake, and family history of diabetes, hypertension, cardiovascular disease, and dyslipidemia

often-overlooked VLDL and IDL [18]. Higher values of CRI-I and CRI-II have been linked to an increased likelihood of developing atherosclerosis, coronary events, and insulin resistance [32]. In individuals with hypertriglyceridemia, NHC is considered the secondary treatment target following LDL-C and is regarded as a reliable surrogate for ApoB in reflecting the total atherogenic lipoprotein burden [33, 34]. LCI enhances risk stratification, particularly for metabolic disorders and atherosclerosis risk [21]. RLPC serves as an indicator of residual cardiovascular risk that persists even when LDL-C levels are within the target range [22]. The TG/HDL-C ratio is commonly associated with insulin resistance, small HDL particles, LDL phenotype B, and increased arterial stiffness [35]. Together, these markers offer a more complete picture of lifestyle-related atherogenic risk, supporting their inclusion in reflecting the different aspects of atherogenesis.

Each component of HLS contributes to improving lipid metabolism through distinct yet connected mechanisms. Smoking cessation has been associated with favorable changes in lipid profiles and vascular health, including increased HDL, reduced LDL, and small dense LDL levels, and improvements in markers of inflammation (e.g., interleukin-6 [IL-6]), oxidative stress (e.g., uric acid, vitamin C), and endothelial function [36–38]. Regular physical activity enhances lipoprotein lipase activity, improves insulin sensitivity, and increases the expression of ABCA1 and LXR, key mediators of reverse cholesterol transport [39, 40]. These changes contribute to elevated HDL-C, reduced TG, and improved LDL particle size and density [40].

Maintaining a healthy BMI, especially by preventing central obesity, helps lower insulin resistance and inflammation [41], key contributors to dyslipidemia and atherogenic risk. Higher AHEI scores have been associated with increased HDL-C levels, partly due to components such as nuts and soy, which are rich in isoflavones and lecithin that support reverse cholesterol transport and activate lipoprotein lipase, thereby improving dyslipidemia [42]. Greater adherence to the AHEI has been associated with decreased circulating concentrations of C-reactive protein (CRP) and IL-6 [43]. Sotos-Prieto et al. showed that greater HLS was linked to lower IL-6 and tumor necrosis factor-alpha (TNF-α) but not CRP after adjustment [44]. The combined association of these factors in the composite HLS is likely to influence lipid-related cardiovascular risk more than each factor alone.

Previous research has explored single lifestyle factors. For example, Zeinalabedini et al. reported a 44% reduction in high AIP risk with higher HEI-2015 adherence, though no link was observed with CRI-I or CRI-II [45]. Studies have also shown that smokers often exhibit elevated atherogenic indices, such as CRI-I, CRI-II, AIP, AC, and TG/HDL-C [46, 47]. For BMI, previous studies mentioned that obese individuals had notably higher TG/HDL-C, CRI-I/II, and non-HDL-C than non-obese individuals; however, another study found no significant correlation between BMI and TG/HDL-C, CRI-I/II, AC, and AIP [48, 49]. Edwards et al. reported that physical activity is the most influential factor in lowering AIP [50]. Earlier studies have consistently shown that higher physical activity is linked to lower atherogenic index levels [51, 52]. Discrepancies with earlier studies may stem from differences in design, sample characteristics, or how lifestyle and lipid metrics were defined and assessed. For example, using a composite HLS in the present study may capture synergistic associations that individual factor analyses in prior studies could not detect.

Nevertheless, diet, physical activity, smoking, and BMI can affect atherogenic indices, so their combination may provide a more accurate cardiovascular risk assessment [53]. This study reinforces the existing evidence by linking cumulative HLS scores to multiple atherogenic indices, highlighting the value of integrated lifestyle assessment in cardiovascular risk. Dyslipidemia exacerbates vascular inflammation and vice versa [54]. Reactive oxygen species (ROS) and immune cell infiltration amplify oxidative stress and LDL oxidation, thereby worsening lipid imbalance [54]. These adverse effects may be effectively mitigated when multiple lifestyle factors are optimized together rather than individually. This aligns with previous research, where interventions targeting multiple lifestyle domains (diet, exercise, and weight control) yielded a significantly improved lipid profile [55, 56]. Analysis of 80 studies revealed that integrating dietary changes with physical activity led to greater lipid profile improvements than using either strategy independently in individuals with excess weight [57].

Prior studies have explored composite lifestyle scores, such as Life Essential 8 (LE8) and Ideal Cardiovascular Health (CVH), integrating multiple risk factors to assess overall heart health [58]. Among 8,215 adults, elevated LE8 scores were linked to a 49% lower AIP, suggesting strong cardiometabolic benefits [58]. Similar to the HLS score, this score uses the HEI-2015 as a dietary status indicator, demonstrating that the HEI is a valuable index for researching cardiometabolic disorders [59]. Similarly, a study on CVH metrics in a Chinese cohort found that individuals with no ideal metrics experienced 6.5 times greater odds of high AIP than those with 5–7 ideal metrics [60]. Both studies highlighted the importance of integrating multiple lifestyle factors into a composite score rather than assessing them individually. However, unlike LE8 and CVH, which include clinical factors such as blood glucose and blood pressure, HLS focuses purely on behavioral risk factors.

Although the relationship between combined lifestyle factors has been studied, research on HLS and its impact on lipid metabolism remains limited. According to Vajdi et al., a higher HLS corresponds to an 18% decrease in TG, with no significant association observed for HDL-C [8]. Another investigation found that greater adherence to HLS corresponded to reduced TG and LDL-C, alongside increased HDL-C, suggesting that a healthier lifestyle improves lipid metabolism [9]. These discrepancies may stem from differences in the definition of HLS, population characteristics, statistical adjustments, and the fact that in this study, atherogenic indices were assessed, which provide a more comprehensive view of lipid-related risk rather than simple parameters.

Given the scarcity of studies investigating the relationship between HLS and lipid ratios, the current study provides valuable insights into this association, as these non-traditional lipid profiles have shown better predictability in assessing cardiovascular risk [3]. The observed results indicate that maintaining a healthier lifestyle may offer protective benefits against dyslipidemia and cardiovascular risk. A combined HLS has also been linked to a lower risk of non-communicable diseases like type 2 DM [13], uncontrolled HTN [61], coronary artery disease [62], metabolic syndrome [8, 63], and nonalcoholic fatty liver disease [59, 64], along with reduced overall mortality [65–67]. Zhao et al. likewise found that greater HLS reduced CVD risk and lessened the negative effects of systemic inflammation [68].

A critical limitation of conventional lipid markers is their inability to capture lipid interactions and balance, which are crucial for determining atherogenic potential. Atherogenic indices provide a more detailed risk assessment using the ratios of lipid components to HDL-C, offering a nuanced evaluation of cardiovascular risk [69]. Evidence suggests that patients who maintain LDL-C levels within the target range continue to experience residual coronary artery disease (CAD) risk [70, 71]. Olamoyegun et al. reported that lipid ratios like AIP, CRI-I/II, and TG/HDL-C were linked to a higher CVD risk [3].

A recent meta-analysis found that elevated AIP was linked to greater CAD risk, severity, and worse outcomes [31]. In those with existing CAD, higher AIP also predicted more cardiovascular events, reinforcing its predictive power beyond traditional lipid markers [72]. Given this, the study's finding that higher HLS scores are most strongly linked to reduced AIP levels reinforces the clinical relevance of AIP as a superior risk predictor.

This study focused on smoking, BMI, diet quality, and physical activity as key components of HLS, aligning with widely accepted cardiovascular research frameworks and similar studies [8, 59]. While some studies included alcohol consumption, it was excluded here as it is prohibited in the country, and no valid data were collected on this factor. Given the well-established impact of each selected factor on lipid metabolism, this study evaluated their combined association with atherogenic lipid ratios to provide a more targeted approach for assessing cardiovascular risk.

Although this study focused on the direct association between HLS and atherogenic indices, future studies could examine whether metabolic conditions, such as DM, mediate this relationship. Mediation analyses using longitudinal data help clarify the indirect pathways linking healthy lifestyle behaviors to atherogenic risk. In addition, future studies should consider using more diverse settings, objective physical activity assessment measures, and dietary intake.

Study strengths and limitations

This study has several strengths. It used a large population-based sample from both urban and rural settings, increasing generalizability. The HLS was based on validated behavioral factors assessed through standardized tools. A wide range of atherogenic indices was analyzed, providing a more comprehensive view of lipid-related cardiovascular risk. Additionally, sex-stratified analyses and the use of both logistic and linear regression models strengthened the validity of the findings.

However, there are some limitations to consider. For instance, the cross-sectional nature prevents drawing definitive causal links between lifestyle behaviors and atherogenic indices. Although strong associations were observed, future longitudinal studies are necessary to determine whether changes in lifestyle behaviors directly result in improvements in lipid profiles over time.

Moreover, dependence on self-reported information for diet and physical activity poses a risk of recall bias. In addition, due to cultural and methodological constraints, alcohol and sodium intakes were not assessed. Alcohol consumption is prohibited in Iran, and the dietary assessment tool used (a 110-item semi-quantitative FFQ) has not yet been validated for estimating sodium intake. However, alcohol intake affects lipid levels, especially HDL-C and TG [73], and its exclusion may limit the interpretation of lifestyle–lipid associations. Finally, although the study benefited from a large sample, it was conducted in a specific geographic region (Isfahan), which can potentially reduce the generalizability.

Conclusions

This study underscores the protective effect of higher HLS, reflecting healthy diet, nonsmoking, physical activity, and normal BMI, in lowering atherogenic indices. By combining multiple lifestyle factors into a single score, HLS may be a stronger predictor of atherogenic risk. These results highlight the clinical value of HLS as both a risk stratification tool and a guide for preventive action.

Implementing structured lifestyle programs that promote smoking cessation, healthy weight, physical activity, and dietary quality could substantially reduce lipid-related cardiovascular risk. Future longitudinal studies are warranted to explore whether improvements in HLS over time lead to sustained reductions in atherogenic markers and cardiovascular events, thereby advancing personalized preventive cardiology.

Abbreviations

AHEI	2010–Alternate Healthy Eating Index–2010
AC	Atherogenic Coefficient
ACI	Atherogenic Combined Index
AIP	Atherogenic Index of Plasma
BMI	Body Mass Index
CVD	Cardiovascular Disease
CRI	I–Castelli Risk Index
FFQ	Food Frequency Questionnaire
FBS	Fasting Blood Glucose
HDL	C–High–Density Lipoprotein Cholesterol
HLS	Healthy Lifestyle Score
ICS2	Isfahan Cohort Study 2
IPAQ	International Physical Activity Questionnaire
LDL	C–Low–Density Lipoprotein Cholesterol
LCI	Lipoprotein Combined Index
MET	Metabolic Equivalent
NHC	Non–High–Density Lipoprotein Cholesterol
RLPC	Remnant Lipoprotein Cholesterol
SES	Socioeconomic Status
TC	Total cholesterol
TG	Triglycerides

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions
R. (A) B.: Conceptualization, Project administration, Software, Formal analysis, Supervision, Writing– original draft, and Writing– review and editing, Visualization. (B) D.: Data curation, Resources, Methodology, and Writing– original draft. N. M.: Conceptualization, Project administration, Data curation, Methodology, and Writing– review and editing. A. F.: Software, Formal analysis, Writing– review and editing. M. B.: Data curation, Investigation, and Writing– review and editing. F. H.: Data curation, Investigation, and Writing– review and editing. M. B.: Data curation, Investigation, and Writing– review and editing. N. G.: Validation and Writing– review and editing. N. S.: Data curation, Validation, and Writing– review and editing. All authors have reviewed the manuscript.

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Data availability
The datasets created and analyzed during this research are not released publicly, yet they can be accessed from the corresponding author if a reasonable request is made.

Declarations

Ethics approval and consent to participate
This study protocol received ethical clearance from the Research Ethics Committee of Isfahan University of Medical Sciences (IR.ARI.MUI.REC.1403.037). Written informed consent was obtained from all participants prior to their enrollment.

Competing interests
The authors declare no competing interests.

Consent for publication
Not applicable.

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