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**Original Article**

# A 10-Year Atherosclerotic Cardiovascular Disease Risk Assessment and 5-Year Follow-Up in the Sabzevar PERSIAN Cohort Center, Northeast Iran

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**Abstract**

**Background:** Atherosclerotic cardiovascular disease (ASCVD) remains a leading cause of global morbidity and mortality. This study assessed the 10-year ASCVD risk and evaluated 5-year follow-up outcomes among adults in the Sabzevar PERSIAN Cohort Center, northeast Iran.

**Methods:** Baseline data were collected in 2018, with follow-up completed in 2023. Risk factors including age, gender, blood pressure, cholesterol levels, smoking status, and diabetes were assessed. The 10-year ASCVD risk was calculated using the American College of Cardiology's risk estimator and categorized as low (<5%), borderline (5–7.4%), intermediate (7.5–19.9%), or high (≥20%). A Cox proportional hazards model evaluated the association between age, gender, diabetes, and ASCVD events.

**Results:** Among 2,871 participants, men had higher blood pressure, while women had higher levels of total cholesterol, HDL, and LDL ($P < 0.05$). Hypertension was more prevalent in men than in women ($P < 0.001$). Diabetes was present in 13.8% (n = 397) of participants, with no significant difference between men and women. The distribution of 10-year ASCVD risk was as follows: low (74.58%), borderline (9.3%), intermediate (13.96%), and high (2.16%). Men had a significantly higher ASCVD risk than women ($P < 0.001$). During the 5-year follow-up, 1.2% (n = 34) of participants experienced ASCVD events. In multivariable analysis, age ($P < 0.001$), male gender ($P < 0.001$), and diabetes ($P = 0.013$) were significant predictors of ASCVD events.

**Conclusion:** ASCVD risk estimation and early intervention, particularly for older adults and individuals with diabetes, are essential. These findings support targeted prevention efforts in northeast Iran and similar populations.

**Keywords:** Atherosclerosis; Cardiovascular diseases; Risk assessment; Longitudinal studies; PERSIAN cohort; Iran


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## Introduction

Atherosclerosis, a chronic inflammatory condition affecting the arteries and serves as the fundamental cause of a wide range of cardiovascular diseases (CVDs), such as coronary artery disease (CAD), peripheral arterial disease (PAD), and cerebrovascular disease (1, 2). The condition is marked by the thickening of arterial walls resulting from the buildup of plaques composed of fatty acids, fibrin, cholesterol, cellular debris, and calcium within the sub-endothelial layer. These plaques can lead to arterial stenosis, restricting blood circulation and can induce hypoxia in essential organs such as the brain, heart, kidneys, and lower limbs (3-5). Furthermore, unstable plaques are prone to rupture, triggering thrombosis—a process that can completely occlude arteries or veins, resulting in acute incidents like myocardial infarction (MI) and stroke (2, 6). These complications of atherosclerosis significantly contribute to global mortality and morbidity, underscoring the need for effective prevention and management strategies (2).

CVDs represent the foremost cause of mortality globally, and Iran is no exception. In Iran, CVD accounts for approximately 46% of all deaths, with coronary artery disease being the predominant contributor (7). Early identification of individuals at risk for CVD is critical for implementing preventive measures and reducing the burden of disease.

Several well-established risk factors play a significant role in the onset of atherosclerosis and subsequent cardiovascular events. These include non-modifiable elements including gender, age, ethnicity, and family history, alongside modifiable elements such as cigarette smoking, diabetes, hypertension, dyslipidemia (e.g., elevated cholesterol and triglyceride levels), and sedentary lifestyle (8-12). While non-modifiable factors cannot be altered, modifiable risk factors offer opportunities for intervention through lifestyle modifications, pharmacological treatments, and public health initiatives (7, 13).

The variations in the mortality and incidence of atherosclerotic cardiovascular disease (ASCVD) at both regional and national levels, further complicate the global burden of CVD. These differences are attributed to disparities in genetic predisposition, the prevalence of risk factors, and access to healthcare services (13). This underscores the importance of conducting population-specific studies to better understand local risk factors and develop tailored prevention strategies.

In this context, the objective of the current research was to calculate the 10-year risk of ASCVD among participants enrolled in the Sabzevar PERSIAN Cohort Center, northeast Iran, utilizing the ASCVD Risk Estimator developed by the American College of Cardiology (ACC). Additionally, the study aimed to assess the 5-year incidence of ASCVD events, such as coronary heart disease and stroke, in this specific population. By identifying high-risk individuals and evaluating the distribution of ASCVD risk factors, this study seeks to inform targeted prevention strategies and enhance cardiovascular health outcomes in northeast Iran.

## Materials and Methods

### *Data Source*

This study utilized data from the Sabzevar PERSIAN Cohort Center, a branch of the Prospective Epidemiological Research Studies in Iran (PERSIAN) Cohort. The PERSIAN Cohort is a large-scale, population-based investigation designed to investigate the prevalence and risk factors associated with non-communicable diseases (NCDs) in Iran. The methodology of the PERSIAN Cohort has been described in detail elsewhere (14). In summary, a total of 4,241 residents from Sabzevar were enrolled in 2018 using a census-based purposive sampling strategy. Trained personnel conducted door-to-door visits based on a preliminary population census of the defined geographic area to identify and invite all eligible individuals to participate. Inclusion criteria required participants to be Iranian nationals, aged 35 to 70 years, and re-

siding within the study area. All participants provided written informed consent before enrollment (14).

### Study population

From the Sabzevar PERSIAN Cohort Center, participants aged 40 to 70 years were selected for this study. Individuals with pre-existing cardiovascular diseases (CVDs), including coronary artery disease, typical angina, congestive heart failure, carotid artery disease, peripheral vascular disease, or electrocardiographic evidence of myocardial infarction (MI) or ischemic heart disease, were excluded. These exclusions were essential to establish a primary prevention cohort, allowing us to focus on the incidence of new ASCVD events in a population initially free of established disease. Additionally, participants with the following laboratory and clinical parameters were included:

- Systolic blood pressure (SBP): 90–200 mmHg
- Diastolic blood pressure (DBP): 60–130 mmHg
- Total cholesterol levels: 130–320 mg/dL
- High-density lipoprotein (HDL) levels: 20–100 mg/dL
- Low-density lipoprotein (LDL) levels: 30–300 mg/dL

Excluding individuals outside these defined ranges was necessary to ensure that the study population fell within parameters typically used for ASCVD risk assessment and to avoid confounding effects from extreme metabolic conditions.

### Ethics

The study protocol was approved by the Research Ethics Committee of Sabzevar University of Medical Sciences, Sabzevar, Iran (Approval IDs: IR.MEDSAB.REC.1398.098 and IR.MEDSAB.REC.1401.018).

### Ten-year ASCVD risk calculation

The 10-year risk of atherosclerotic cardiovascular disease (ASCVD) was calculated for each participant using the ACC's ASCVD Risk Estimator (15). This tool estimates the 10-year risk of ASCVD based on these variables: age, gender, ethnicity, systolic and diastolic blood pressure, total cholesterol, low-density lipoprotein (LDL), HDL levels, history of diabetes, and smoking status. It is important to note that the ACC ASCVD Risk Estimator was developed and validated primarily in U.S. populations. While widely used, its direct applicability and predictive accuracy in the Iranian population require further local validation. Based on the ASCVD Risk Estimator scores, participants were categorized as low (<5%), borderline (5–7.4%), intermediate (7.5–19.9%), or high (≥20%) risk groups (15).

### Five-year follow-up

In addition to the baseline risk assessment, a five-year follow-up was conducted from 2019 to 2023 to evaluate the incidence of ASCVD events, including coronary heart disease and stroke, among cohort participants. The ascertainment of ASCVD events during the 5-year follow-up involved active communication with participants via phone calls to inquire about new diagnoses of coronary heart disease or stroke. For any reported events, medical records from local healthcare facilities were reviewed to confirm diagnoses and dates, ensuring accuracy and completeness of event data (14).

### Statistical analysis

All analyses were performed using SPSS version 19 (IBM Corp., Armonk, NY, USA). Descriptive statistics summarized demographic and clinical characteristics. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Group differences in ASCVD risk categories by age and gender were assessed using chi-square or Fisher's exact tests. Participants were grouped into three age categories (40–49, 50–59, and 60–70 years) to examine age-specific trends. To evaluate predictors of ASCVD events over the 5-year follow-up, a multivariable Cox proportional hazards model was applied, including age, gender, and diabetes as covariates. Hazard ratios (HRs), 95% confidence intervals (CIs), and P-values were reported. Statistical significance was set at $P < 0.05$.

## Results

### *Study Population*

A total of 4,241 individuals were initially referred to the Sabzevar PERSIAN Cohort Center. After applying exclusion criteria, 2,871 participants were included in the final analysis. Exclusions were made for these reasons: pre-existing cardiovascular disease (428 individuals), age below 40 years (652 individuals), incomplete file information (75 individuals), HDL levels outside the range of 20–100 mg/dL (3 individuals), cholesterol levels outside the range of 130–320 mg/dL (115 individuals), diastolic blood pressure outside the range of 60–130 mmHg (36 individuals), systolic blood pressure outside the range of 90–200 mmHg (61 individuals).

### *Demographic Characteristics*

The study population comprised 45.4% men (n = 1,303) and 54.6% women (n = 1,568). The average age of the study cohort was 50.86 ± 7.46 years (range: 40–70 years). The age distribution was as follows: 40–49 years, 47.3% (n = 1,358); 50–59 years, 38.3% (n = 1,101); 60–70 years, 14.4% (n = 412). Men had a slightly higher mean age than women (52 vs. 50 years). The gender distribution across age groups is presented in Table 1.

**Table 1:** Gender distribution across age groups in the Sabzevar PERSIAN Cohort Center (n=2871)

| Age group(yr) | Total (n=2,871) N(%) | Men (n=1,303) N(%) | Women (n=1,568) N(%) |
|---|---|---|---|
| 40-49 | 1358 (47.30) | 554 (42.51) | 804 (51.27) |
| 50-59 | 1101 (38.35) | 516 (39.60) | 585 (37.30) |
| 60-70 | 412 (14.35) | 232 (17.80) | 180 (11.48) |
| *Data are presented as numbers and percentages* | | | |

### *Cardiovascular disease risk factors*

The mean diastolic blood pressure was 73.06 ± 10 mmHg (range: 60–116 mmHg), and the average systolic blood pressure was 116.42 ± 15.73 mmHg (range: 90–200 mmHg). Women exhibited lower average values for both systolic and diastolic blood pressure compared to men. ($P < 0.05$). The mean lipid profile values were as follows: total cholesterol, 196.60 ± 35.79 mg/dL (range: 130–320 mg/dL); HDL, 52.87 ± 10.42 mg/dL (range: 21.80–98 mg/dL); and LDL, 113.95 ± 31.17 mg/dL (range: 15.76–223.40 mg/dL). Women had higher mean total cholesterol, HDL, and LDL levels compared to men ($P < 0.05$). Of the participants, 15% (n = 431) were smokers, with the majority being men (96.7%). Diabetes was present in 13.8% (n = 397) of participants, with no significant difference between men and women. Hypertension (defined as SBP ≥140 mmHg or DBP ≥90 mmHg on two separate occasions) was observed in 11% (n = 315) of participants, with a significantly higher prevalence in men than in women (62% vs. 38%; $P < 0.001$).

### *Ten-year ASCVD risk assessment*

The 10-year ASCVD risk was calculated using the ACC's ASCVD Risk Estimator. The distribution of risk groups was as follows: low risk (74.58%, n = 2,141), borderline risk (9.3%, n = 267), intermediate risk (13.96%, n = 401), and high-risk (2.16%, n = 62).

### *Gender-specific ASCVD risk*

The 10-year ASCVD risk distribution by gender revealed that 54% of men and 90.4% of women were in the low-risk category. For borderline risk, 15.6% of men and 5.2% of women were classified. In the intermediate-risk category, 25.9% of men and 4.1% of women were included, while 4.5% of men and 0.2% of women were classified as high-risk (Table 2). A statistically significant association was observed between ASCVD risk and gender ($P < 0.001$), with men having a significantly higher 10-year ASCVD risk compared to women.

### *Age-specific ASCVD risk*

The 10-year ASCVD risk varied notably across different age categories. Among participants aged 40–49 years, 96.17% were classified as low risk, 2.72% as borderline risk, 1.03% as intermediate risk, and 0.07% as high risk. In the 50–59 years age group, 68.39% were low risk, 15.07% borderline risk, 15.53% intermediate risk, and 1% high risk. For participants aged 60–70 years, 19.90% were low risk, 15.53% borderline risk, 52.42% intermediate risk, and 12.13% high risk .These findings reveal a distinct pattern of increasing ASCVD risk associated with advancing age ($P < 0.001$). Table 2 presents the distribution of estimated 10-year ASCVD risk categories by age group and gender in the study population.

**Table 2:** Distribution of estimated 10-year ASCVD risk categories by age group and gender in the Sabzevar PERSIAN Cohort (n = 2,871)

| Age group | Gender | Total in group (n) | Low Risk n (%) | Borderline Risk n (%) | Intermediate Risk n (%) | High Risk n (%) |
|---|---|---|---|---|---|---|
| 40-49 | Overall | 1358 | 1306 (96.17) | 37 (2.72) | 14 (1.03) | 1 (0.07) |
| | Men | 554 | 505 (91.15) | 34 (6.14) | 14 (2.53) | 1 (0.18) |
| | Women | 804 | 801 (99.63) | 3 (0.37) | 0 (0.00) | 0 (0.00) |
| 50-59 | Overall | 1101 | 753 (68.39) | 166 (15.07) | 171 (15.53) | 11 (1.00) |
| | Men | 516 | 202 (39.15) | 140 (27.13) | 163 (31.59) | 11 (2.13) |
| | Women | 585 | 551 (94.19) | 26 (4.44) | 8 (1.37) | 0 (0.00) |
| 60-70 | Overall | 412 | 82 (19.90) | 64 (15.53) | 216 (52.42) | 50 (12.13) |
| | Men | 232 | 6 (2.59) | 20 (8.62) | 159 (68.53) | 47 (20.26) |
| | Women | 180 | 76 (42.22) | 44 (24.44) | 57 (31.67) | 3 (1.67) |

*Data are presented as numbers (percentages) for each category.*

### *Five-year follow-up outcomes*

In the course of the five-year follow-up, 1.2% (n = 34) of participants developed ASCVD events. Among these 34 individuals, the majority were men, comprising 82.4% (n=28) of the cohort, while 17.6% (n=6) were women. The mean age of participants who experienced an ASCVD event was 56 ± 7 years, ranging from 41 to 69 years. The average 10-year ASCVD risk for these individuals was 14.16% ± 8.41. The mean time to an ASCVD event during the five-year follow-up was 19.41 months, with events occurring as early as 3 months and as late as 39 months after baseline assessment. The descriptive statistics for key continuous variables among the participants with ASCVD events are presented in Table 3.

**Table 3:** Descriptive statistics of key variables for participants with ASCVD events (n=34)

| Variable | Mean | Minimum | Maximum | SD |
|---|---|---|---|---|
| Age (year) | 56 | 41 | 69 | 7 |
| SBP (mmHg) | 123 | 102 | 156 | 14 |
| DBP (mmHg) | 76 | 60 | 98 | 9 |
| Cholesterol (mg/dL) | 201.36 | 131.20 | 274 | 37.51 |
| HDL (mg/dL) | 50.24 | 34.30 | 73.90 | 10.10 |
| LDL (mg/dL) | 120.29 | 55.54 | 201.48 | 30.43 |
| Ten-year risk (%) | 14.16 | 2.10 | 35.70 | 8.41 |
| Time to ASCVD event (months) | 19.41 | 3 | 39 | 10.10 |

*SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure*

In the multivariable Cox proportional hazards model including age, gender, and diabetes status, all variables were significantly associated with the risk of ASCVD events during the 5-year follow-up

period. Each one-year increase in age was associated with an 8.1% higher hazard of ASCVD (Hazard Ratio [HR] = 1.081; 95% Confidence Interval [CI]: 1.04–1.13; $P < 0.001$). Gender was also a significant predictor, with women having a substantially lower risk of ASCVD events (HR = 0.21; 95% CI: 0.09–0.50; $P < 0.001$). Participants with diabetes had a nearly threefold increase in hazard (HR = 2.95; 95% CI: 1.25–6.90; $P = 0.013$).

## Discussion

The 10-year risk of atherosclerotic cardiovascular disease (ASCVD) varies significantly across regions and populations due to differences in genetic predisposition, lifestyle factors, and access to healthcare. In this study, we assessed the 10-year ASCVD risk among participants of the Sabzevar PERSIAN Cohort Center in northeast Iran, providing significant insights into the distribution of cardiovascular risk factors in this population. Our findings underscore the necessity of calculating 10-year ASCVD risk scores as a critical step in implementing targeted prevention strategies, including smoking cessation, management of lipid profiles, control of blood pressure, and regulation of glucose, to reduce the burden of cardiovascular diseases (16-21).

Our results revealed that men exhibited a notably elevated 10-year ASCVD risk compared to women, with a greater proportion of men in the borderline, intermediate, and high-risk categories. This finding aligns with earlier research that has consistently reported a higher prevalence of cardiovascular disease in men than in women (22, 23). The gender disparity in ASCVD risk may be attributed to a complex interplay of biological and sociocultural factors. Biologically, hormonal differences, particularly the protective effects of estrogen in premenopausal women, are thought to play a role (24). Socioculturally, men often exhibit higher rates of traditional risk factors such as smoking (as observed in our study where 96.7% of smokers were men) and may engage in less healthy lifestyle behaviors. Differences in health-seeking behaviors and access to early preventive care might also contribute to these disparities (23, 25). For instance, in our study, 15% of participants were smokers, with the majority being men (96.7%). Smoking is a well-established risk factor for endothelial dysfunction and arterial stiffness, which contribute to the development of ASCVD (16, 26). A meta-analysis by Alicia Saz-Lara et al. demonstrated that smoking cessation improves arterial stiffness, highlighting the importance of targeted interventions for high-risk groups (16). Similarly, Duncan et al. reported that smoking cessation significantly diminishes the risk of cardiovascular events within five years compared to continued smoking (17).

Our research also emphasized that dyslipidemia and hypertension are key modifiable risk factors for ASCVD, alongside smoking. Lipid-lowering therapies, particularly those targeting low-density lipoprotein (LDL) cholesterol, have demonstrated a substantial decrease in the risk of cardiovascular events (21). Furthermore, Pierdomenico et al. emphasized that effective blood pressure control—particularly in patients with responder hypertension (defined as normal blood pressure in both clinical and non-clinical settings)—is associated with a lower cardiovascular risk compared to those with masked hypertension (normal blood pressure in the clinic but elevated levels outside the clinic) (18). These findings highlight the importance of early identification and management of hypertension and dyslipidemia in high-risk individuals.

Diabetes, another major risk factor for ASCVD, was present in 13.8% of our study population. Intensive glucose management has been shown to decrease the risk of myocardial infarction and microvascular complications in patients with type 2 diabetes (20). The long-term benefits of glucose control were further supported by Holman et al., who reported sustained improvements in microvascular risk and reduced myocardial infarction risk after 10 years of follow-up (19). These results underscore the essential importance of glycemic control in preventing ASCVD progression.

Our study also demonstrated that ASCVD risk increases significantly with age, with the highest risk observed in participants aged 60–70 years. This finding is compatible with numerous studies that

have established a strong association between advancing age and elevated cardiovascular risk (27-29). Age-related changes in vascular function and structure, coupled with the cumulative impact of risk factors over time, contribute to this increased risk. These findings emphasize the need for age-specific prevention strategies and regular monitoring of cardiovascular risk factors in older adults.

One of the key strengths of this study is its use of data from the Sabzevar PERSIAN Cohort, a large, population-based investigation that provides a representative sample of the Iranian population. The inclusion of a 5-year follow-up further enhances the validity of our findings by enabling the assessment of cardiovascular event incidence within this cohort. Despite a relatively low number of ASCVD events (n = 34) during the five-year follow-up, we conducted a multivariable Cox regression analysis to identify independent predictors of ASCVD risk. The analysis revealed several significant predictors, including age, gender, and diabetes status. Increasing age was associated with a significantly elevated hazard of ASCVD, with each additional year increasing risk by approximately 8%. This finding is aligned with existing literature that identifies age as one of the most powerful and consistent predictors of cardiovascular events (30, 31). Similarly, gender was a strong determinant, with women demonstrating a significantly lower risk compared to men. This sex-based disparity in ASCVD risk has been widely reported and may be attributed to a combination of biological (e.g., hormonal protection in premenopausal women) and behavioral factors (25, 32). The presence of diabetes mellitus was associated with a nearly threefold increase in ASCVD risk, reinforcing its role as a major cardiovascular risk enhancer. This is consistent with multiple studies that show diabetes contributes to endothelial dysfunction, accelerated atherosclerosis, and heightened inflammatory responses, all of which predispose individuals to cardiovascular events (33-35).

This study has several limitations that warrant consideration. Firstly, the ACC ASCVD Risk Estimator, while widely used, was developed and validated in U.S. populations. Its direct applicability and predictive accuracy in the Iranian population remain uncertain and require further local validation. However, such validation was beyond the scope of this study; therefore, the results should be interpreted with this limitation in mind. Secondly, the 5-year follow-up period is relatively short, especially for evaluating a model designed to predict 10-year risk. Thirdly, the number of ASCVD events was relatively low (n = 34), which may be attributed to the short follow-up duration, the inclusion of a lower-risk primary prevention population, or potential underreporting of events despite active follow-up efforts. Fourthly, this low number of events constrained the number of predictors that could be included in the multivariable model and may limit the generalizability of the findings. Although predictors were carefully selected to minimize the risk of overfitting, the low event rate may have introduced instability in the estimates or masked smaller effect sizes. Finally, potential residual confounding cannot be ruled out, particularly from unmeasured variables such as physical activity, dietary habits, socioeconomic status, or medication adherence.

## Conclusion

This study highlights the value of 10-year ASCVD risk estimation to identify high-risk individuals and guide targeted prevention strategies, particularly for men and older adults. Addressing modifiable risk factors such as smoking, diabetes, and hypertension is essential to reduce ASCVD burden. While the findings offer important public health insights for northeast Iran, they should be interpreted with caution due to limitations including the limited applicability of the risk estimator to the Iranian population, a short 5-year follow-up period, a small number of ASCVD events, and potential residual confounding from unmeasured variables. Future research with longer follow-up periods and larger event counts is needed to fully validate risk prediction models in the Iranian context.

## Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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## Conflict of Interest

The authors declare no competing interests.

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