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Hypertension and 10-year risk of coronary artery diseases in adult population: Yazd healthy heart project

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Abstract

BACKGROUND: The incidence of coronary artery disease (CAD) is influenced by several risk factors, including hypertension. Although the association between hypertension and CAD has been investigated in Western countries, limited research has been conducted in Asia and the Middle East. We investigated the association between hypertension and the 10-year risk of CAD in the adult population.

METHODS: In this cohort study, 2,000 participants aged 20 to 74 years in the Yazd Healthy Heart Project were enrolled in 2005–2006 and followed up to 2015–2016. Participants with a history of CAD were excluded. At baseline, data on demographic characteristics, anthropometric measurements, biochemical blood tests, and lifestyle factors were collected. The association between hypertension and approximately 10-year CAD risk was assessed using the Cox regression model.

RESULTS: The baseline prevalence of hypertension among adults was 36.1%. During the ten-year follow-up, CAD incidence was 16.8% in men, 12.0% in women, and 14.5% in the total population. After adjusting for potential confounders, hypertension increased the risk of CAD in men (HR = 1.64; 95% CI: 1.09–2.46), women (HR = 2.16; 95% CI: 1.15–4.05), and the whole sample (HR = 1.73; 95% CI: 1.23–2.43). This association was similar in men and women (p for interaction ≥0.05).

CONCLUSION: This study demonstrated a significant association between hypertension and CAD risk, highlighting the need for targeted interventions in populations with hypertension to reduce CAD risk.

Keywords: Coronary Artery Disease; Hypertension; Incidence; Risk Factors; Cohort Studies

Introduction

Coronary artery disease (CAD) is a cardiovascular disease (CVD) and one of the most common causes of death worldwide, responsible for approximately 8.9 million deaths annually[1]. Despite the decline in CAD mortality in Western nations over the past decade, it still accounts for approximately one-third of deaths among individuals aged 35 and older[2]. In 2022, an estimated 315 million people worldwide were affected by CAD, with an age-standardized prevalence of approximately 3,605 cases per 100,000 people[3]. The development of CAD is influenced by multiple risk factors, among which hypertension plays a particularly prominent role[4,5].

Hypertension is associated with 40% of deaths worldwide[6]. The American Heart Association estimates that by 2030, the direct and indirect costs related to hypertension will reach $200 billion and $40 billion, respectively[7]. The global prevalence of hypertension is 31.1%, and it is particularly high in low-income and middle-income countries[7]. A meta-analysis projected a 20% prevalence in Iran in 2018[8], whereas recent analyses report an overall prevalence of 26.26% among adults, with 25.11% in women and 26.22% in men[9]. It has been shown that hypertension is present in 63% of patients with CVD, suggesting a significant association between the two conditions[10]. Extensive evidence has demonstrated a strong association between elevated blood pressure and CAD incidence[11]. However, most research to date has centered on Western and East Asian populations, leaving a notable gap in studies involving Middle Eastern groups[12–14]. To address this gap, the present study used data from the Yazd Healthy Heart Project (YHHP) to assess the association between hypertension and the ten-year risk of CAD among urban adults in Yazd, Iran.

Methods

Study design and participants

The YHHP is a prospective study conducted in the urban population of Yazd, Iran. This study registered 2,000 participants (1,000 men and 1,000 women) aged 20–74 years between 2005 and 2006 using a cluster random sampling method and was followed up until 2015–2016 (median = approximately 10 years and interquartile range = 0.88). Individuals with CAD at baseline were excluded from the study. The data collected at baseline and during Phase II included demographic information, blood pressure measurements, CAD evaluation, biochemical blood tests, anthropometric measurements, and lifestyle.

Data collection

The methodology has been thoroughly detailed in a previous study; thus, only a concise overview is provided here[15].

Blood pressure assessment

At baseline, blood pressure measurements were obtained twice from the right arm using an automatic digital monitor (M6 Comfort from Omron Co., Osaka, Japan) with a five-minute interval between measurements. Hypertension was classified as systolic blood pressure (SBP) ≥ 140 mmHg, or diastolic blood pressure (DBP) ≥ 90 mmHg, or medication consumption for hypertension according to prevalent guidelines[5].

Diagnosis and evaluation of CAD

The primary outcome of CAD was defined as a composite of fatal and nonfatal CAD, myocardial infarction (MI), percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), and new angina pectoris. A previous study provided a comprehensive overview of the diagnosis of new angina, time of CAD outcome, and other related tests[15].

Assessment of other variables

Demographic variables such as sex, age, economic status, and education level were collected at baseline using validated questionnaires and interviews. Additionally, anthropometric measurements, including height (in meters), weight (in kilograms), and waist circumference (in centimeters), were taken using standardized equipment. The body mass index (BMI) was calculated by dividing weight (kg) by height squared (m^2). We also recorded the physical activity levels and smoking status

of each participant. Following an overnight fast, blood samples (5 cc) were collected in the morning after 9 to 12 hours. Fasting blood sugar (FBS) and lipid profiles, including triglycerides (TG), total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL), were assessed in a single laboratory.

Statistical analyses

Categorical data were presented as the number of participants and percentage, and between-group (hypertensive and non-hypertensive) comparisons were performed using the chi-square test. Continuous data were presented as average ± standard deviation (SD), and between-group comparisons were performed using the t-test. The Cox regression model was used to assess the association between hypertension and incidence of CAD over a mean follow-up of 10 years. Crude and multivariable-adjusted models were used in this study. Model I was adjusted for age and sex. Model II included the previous variables plus smoking (smoker and non-smoker), physical activity (low, moderate, and vigorous), and educational (low, moderate, and high) levels. The results were expressed as hazard ratios (HR) and 95% confidence intervals (CIs). Statistical analyses were conducted with SPSS version 19 (IBM Corp., Armonk, NY, USA), using a two-sided test to determine significance at $p<0.05$.

Ethics approval

Ethics approval and consent to participate**:** Approval for the study was granted by the Ethics Committee of Shahid Sadoughi University of Medical Sciences under ethical code IR.SSU. REC.1400.071. Informed consent was obtained from all participants in both phases of the study.

Results

The prevalence of CAD was 4.1% among men, 2.1% among women, and 3.1% in the overall population. Following the exclusion of sixty-two participants (3.1%), a total of 1,938 individuals with a mean age of 48.3±15.20 years were enrolled for a ten-year follow-up. During the 2015–2016 reassessment, 385 participants (19.9%) were lost to follow-up, resulting in 1,553 individuals included in the final analysis (Fig. 1).

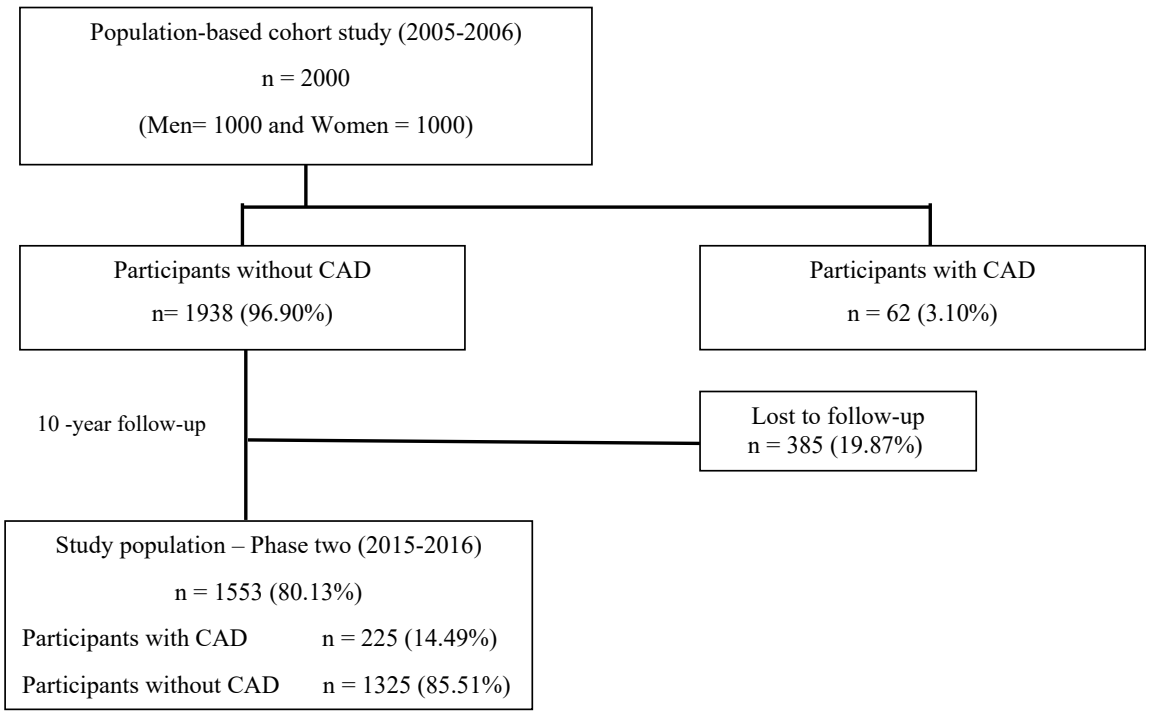

Fig. 1. Flowchart of Participant Enrollment and Follow-up in the YHHP Cohort Study

The prevalence of hypertension was 35.8% in men, 36.5% in women, and 36.1% in the overall sample. Table 1 presents a comparison between hypertensive and non-hypertensive participants. Those with hypertension were generally older and had higher body weight, body mass index, and waist circumference. They also exhibited elevated glucose and lipid levels (except for HDL cholesterol) and were more likely to have a lower socioeconomic status and lower levels of physical activity.

Table 2 compares participants who completed follow-up with those who did not. There were no significant differences between the two groups for most characteristics, except for waist circumference.

After ten years of follow-up, the incidence of CAD was 16.8% in men, 12.0% in women, and 14.5% in the overall sample. The association between hypertension and the ten-year risk of CAD in men, women, and the total cohort was (HR=1.64; 95% CI: 1.09–2.46), (HR=2.16;

Table 1. Comparison of characteristics between participants with and without hypertension at the baseline

	Hypertension	No hypertension	P value
Number of participants	684	1254	-
Women (%)	353 (51.6)	628 (50.1)	0.537
Age (years)	58.0 ± 11.6	43.0 ± 14.3	<0.001
Anthropometric parameters			
BMI (Kg/m^2)	27.3 ± 4.3	25.5 ± 4.5	<0.001
Waist circumference (cm)	98.5 ± 11.0	90.7 ± 12.1	<0.001
Blood Pressure			
SBP (mm Hg)	143 ± 14	120 ± 9	-
DBP (mm Hg)	90 ± 8	78 ± 5	-
Fasting Blood sugar (mg/dL)	113 ± 51	96 ± 40	<0.001
Lipid levels (mg/dL)			
Triglyceride	202 ± 113	160 ± 102	<0.001
Cholesterol	209 ± 44	194 ± 67	<0.001
LDL	115 ± 36	105 ± 37	<0.001
HDL	53 ± 14	54 ± 14	0.076
Smoking Status (%)			
Current smokers	114 (16.8)	219 (17.5)	0.705
Non-smoker	564 (83.2)	1030 (82.5)	
Physical activity (%)			
Low	371 (73.8)	537 (65.4)	0.006
Moderate	112 (22.2)	242 (29.5)	
Vigorous	20 (4.0)	42 (5.1)	
Socioeconomic Status (%)			
Low	117 (41.5)	151 (26.0)	<0.001
Moderate	105 (37.2)	240 (41.4)	
High	60 (21.3)	189 (32.6)	
Education (%)			
Primary	529 (77.6)	612 (50.7)	<0.001
High school	110 (16.1)	466 (38.6)	
Academic	43 (6.3)	130 (10.8)	

Results are expressed as percentage for categorical variables and as mean ± standard deviation for continuous variables. BMI, Body Mass Index; SBP: Systolic Blood Pressure; DBP, Diastolic Blood Pressure

Table 2. Baseline comparison of characteristics between participants who completed follow-up and those who did not

Variable	Follow-up	Loss to Follow-up	P value
Number of participants	1553	385	-
Age (years)	48.64 ± 14.73	47.07 ±16.94	0.07
Anthropometric parameters			
BMI (Kg/m^2)	26.17 ± 4.35	26.07 ± 5.02	0.72
Waist circumference (cm)	93.79 ± 12.11	92.05 ± 12.90	0.013
Blood Pressure			
SBP (mm Hg)	128.26 ± 15.46	127.08± 16.39	0.187
DBP (mm Hg)	82.67 ± 8.76	81.81± 9.29	0.088
Fasting Blood Sugar (mg/dL)	103.07 ±45.96	98.34 ± 40.63	0.067
Lipid levels (mg/dL)			
Triglyceride	176.75 ± 109.22	166.23 ± 103.96	0.09
Cholesterol	199.30± 45.12	197.68 ± 100.12	0.638
LDL	109.20 ± 36.79	105.58 ± 35.36	0.088
HDL	54.13 ± 13.8	53.62 ± 13.16	0.517
Smoking Status (%)			
Current smokers	280 (18.1)	53 (14)	0.058
Non-smoker	1268 (81.9)	326 (86)	
Physical activity (%)			
Low	720 (67.9)	188 (71.2)	0.573
Moderate	290 (27.4)	64 (24.2)	
Vigorous	50 (4.7)	12 (4.5)	
Socioeconomic Status (%)			
Low	212 (30.2)	56 (35.0)	0.06
Moderate	275 (39.2)	70 (43.8)	
High	215 (30.6)	34 (21.3)	
Education (%)			
Primary	904 (59.8)	237 (62.7)	0.153
High school	460 (30.4)	116 (30.7)	
Academic	148 (9.8)	25 (6.6)	

Results are expressed as percentage for categorical variables and as mean ± standard deviation for continuous variables. BMI, Body Mass Index; SBP: Systolic Blood Pressure; DBP, Diastolic Blood Pressure

95% CI: 1.15–4.05), and (HR=1.73; 95% CI: 1.23–2.43), respectively (Table 3). Although the hazard ratio was numerically higher in women, the interaction test did not reach statistical significance.

Discussion

This study provides valuable insights into the prevalence and effects of hypertension on CAD risk in Iranian adults. The prevalence of hypertension (36.1%) is higher than previously reported national estimates and is consistent with trends observed in other Asian populations[9,16–18]. The prevalence of hypertension in Iran's western neighbors varies from 32% in Jordan to 34% in Turkey[16–18]. The findings highlight the necessity for implementing specific public health strategies in Iran and in similar regions. It is reported that hypertension is the primary preventable risk factor for CVD, especially in developing countries[19].

After a decade of follow-up, the incidence of CAD in the total population was 14.5%. Those with hypertension had a 1.73 times higher risk

Table 3. Association between hypertension and 10-year risk of coronary artery disease in men, women and the overall sample, Yazd prospective study, Iran

	Case/Participants	Crude	Model I	Model II
Men				
No	53\521	1	1	1
Yes	82\284	2.68 (1.90-3.79)	1.56 (1.08-2.25)	1.64 (1.09-2.46)
P value		<0.001	0.018	0.017
Women				
No	31\474	1	1	1
Yes	59\274	3.10 (2.00-4.79)	1.41 (0.87-2.28)	2.16 (1.15-4.05)
P value		<0.001	0.168	0.017
P for interaction		0.632	0.874	0.740
Total				
No	84\995	1	1	1
Yes	141\558	2.81 (2.14-3.68)	1.50 (1.12-2.01)	1.73 (1.23-2.43)
P value		<0.001	0.007	0.002

Results are reported as hazard ratio with 95% confidence interval. Model I: adjusted for age; Model II: adjusted for age, smoking, economic status, physical activity and education. For the overall analysis (Total), a further adjustment for gender was performed in both models.

of developing CAD, which aligns with extensive global research that underscores the association of hypertension with the incidence of CAD and other cardiovascular events[20,21]. The study demonstrated that among participants with hypertension (n = 558), 25.27% developed CAD, compared to 8.50% of those without hypertension. These results showed a significant difference in CAD incidence between individuals with and without hypertension, which aligns with previous research[22]. According to a large-scale meta-analysis, for each 20 mm Hg increase in SBP and 10 mm Hg increase in DBP, the risk of death from CAD doubled[20]. These findings highlight the considerable association between hypertension and the development of CAD. After adjusting for confounding variables, such as age, sex, socioeconomic status, education, smoking, and physical activity, the increased risk of hypertension on CAD decreased from 2.81-fold to 1.73-fold. The results revealed that hypertension remains a significant contributor to CAD; therefore, it can be concluded that hypertension is an independent risk factor for CAD[5]. In addition, demographic and lifestyle factors affect the association between hypertension and CAD, which aligns with previous studies indicating that additional risk factors, including age, smoking, physical activity, socioeconomic status, family history, and other variables, are also critical determinants in the development of CAD[4]. The association between CAD and its related risk factors depends in part on the geographical area and racial differences[23].

Notably, a network analysis also showed a linear relationship between mean BP and CVD risk, with the lowest CVD risk among the groups with an SBP of 120–124[21]. A meta-analysis of 123 studies with 613,815 participants found that a 10 mm Hg reduction in SBP led to a reduction in the risk of CAD[24]. These findings are consistent with our results showing a lower incidence of CAD in the non-hypertensive group and highlight the essential role of early detection and management of hypertension in preventing CAD[14,21].

After adjusting for potential confounding factors, hypertension was associated with a 64% higher risk of CAD in men (HR = 1.64) and a 116% higher risk, or more than double the risk, in women (HR = 2.16). The Framingham study reported that the relative risks of CAD associated with the first and second stages of hypertension were 1.03 and 1.67 for men, and

1.73 and 2.20 for women, respectively[25]; these findings are consistent with those of the present study. In the current study, while the HR was numerically higher in women, the interaction test was not statistically significant. An Iranian cohort study found that hypertension increased the CAD risk by 59% in men and 78% in women[26]. In contrast, increased systolic blood pressure was significantly associated with higher CAD incidence in men (P trend = .0002), but not in women, while diastolic blood pressure showed no significant association with CAD in either sex[27]. While another study in Asia reported no significant sex difference in the CAD risk associated with hypertension[28], our study found a higher, though statistically non-significant, risk estimate in women (HR = 2.16) than in men (HR = 1.64). This suggests that hypertension may contribute differently to CAD by sex. For women, the decline in estrogen during menopause could amplify the risk related to hypertension[29,30], while in men, higher baseline risk from androgen activity[30]. Differences between men and women in healthcare utilization, symptom presentation, or lifestyle may further influence these risk estimates. It seems that, even if there is no statistically significant interaction in our study, the way hypertension contributes to CAD could differ by sex. This shows the importance of considering sex as a key biological and social determinant in both epidemiological studies and clinical work, no matter the results of conventional interaction tests.

This study represents the first cohort investigation of adults in Yazd examining the association between blood pressure and the CAD risk over a mean follow-up of 10 years. This study had several limitations. The study did not account for potential confounding factors such as genetic predisposition, dietary habits, sleep patterns, and mental health status. Blood pressure was measured at baseline and the 10-year follow-up, which may have led to an overestimation of the prevalence of hypertension and consequently a reduction in relative risks. Furthermore, this study did not distinguish between individuals with controlled and uncontrolled hypertension. Additionally, there was a 19.87% loss to follow-up during the study period, which could have been considered an attrition bias.

Conclusion

This study provides the first population-based prospective evidence from central Iran demonstrating that hypertension is associated with an increased risk of CAD over a decade. Although the hypertension–CAD link is well established globally, our findings quantify this risk in an understudied region with a high hypertension burden (36.1%). The notably elevated hazard ratio in women, despite a non-significant interaction, suggests that sex-specific risk assessment remains important. These results emphasize the necessity for targeted public health interventions and enhanced clinical management of hypertension in central Iran and similar regions, where long-term, region-specific studies have been limited.

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Conflict of interests

The authors declare no conflict of interest.

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Author's Contributions

Study Conception or Design: MS; MM; SM; HM; LH
Data Acquisition: MS; PV; AK; SN
Data Analysis or Interpretation: MS; PV; AK; SN
Manuscript Drafting: MS; MM; SM; HM
Critical Manuscript Revision: MM; LH; PV; AK; SN
All authors have approved the final manuscript and are responsible for all aspects of the work.

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