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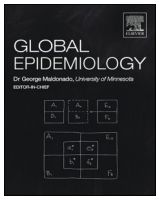

Is the prevalence of risk factors, clinical presentations and severity of coronary artery diseases (CAD) in patients with very early and premature CAD are different from mature CAD patients?: A registry- based cross-sectional study

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ABSTRACT

Introduction: The present study aims to compare the risk factors, clinical presentation, and severity of coronary artery involvement in young compared to elderly CAD patients to assess the cardiovascular health status for better disease management and control of these specific patients.
Methods: This registry-based cross-sectional study was conducted using Coronary Angiography and Angioplasty Registry (CAAR) patients in east of Tehran, Iran. The data were extracted from 330 patients with confirmed CAD recorded by the CAAR during July 2021 to August 2023.
Results: The majority of patients in MCAD (68.2%) and VECAD (80%) were male, while the majority of PCAD patients were female (51.8%). Among PCAD patients, the prevalence of diabetes (38.1%) was higher than in other groups. The presence of IHD history in the father (38.1%) and mother (26.3%) was higher in the VECAD group. The mean total cholesterol, LDL, and LDL/HDL ratio were higher in the VECAD group. Among MCAD group (75.4%) compared to PCAD (58.1%) and VECAD (47.2%) groups, the multi-vessel disease was more common.MCAD patients had the highest median Gensini score compared to PCAD and VECAD patients. Also, in male compared to female the mean Gensini score was higher by 8 units (ß = 8.26, 95%CI = 0.24, 16.28).
Conclusion: Modifiable risk factors in young CAD patients are common. High LDL-C levels and smoking were the common modifiable CVD risk factors in young patients, indicating the significant role of these traditional risk factors in early atherosclerosis development alongside inheritable risk-factors such as positive family history that were more common in young CAD patients. While, the severity of coronary artery involvement in individuals with MCAD was higher, but the priority of involvement based on the type of vessel was almost the same in all CAD groups.

Introduction

Among the various types of cardiovascular diseases, coronary artery disease is one of the most common disorders, also known as Ischemic Heart Disease (IHD) [1]. This type of disease is caused by the accumulation of plaque due to the deposition of cholesterol and other substances in the arteries' walls. Over time, these plaques narrow the blood vessels, leading to partial disruption in blood supply and, in severe cases, complete blockage of blood flow to the heart and other organs, known as atherosclerosis [1]. Atherosclerosis can lead to various symptoms such as angina or chest pain and heart attacks. Coronary artery disease is a chronic process that begins in early adulthood and gradually progresses

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[2]. Epidemiological studies have shown that although most cases of coronary artery disease and heart attacks occur in individuals over 55 years of age, >5 to 10% of cases occur in younger individuals. Additionally, the occurrence of atherosclerosis and its complications at a younger age tends to be more severe and progressive than in older individuals [3].

Risk factors for coronary artery disease include obesity, hyperlipidemia, hypertension, diabetes, stress and anxiety, lack of physical activity, unhealthy diet, and the use of tobacco and alcohol. Non-modifiable risk factors include age, gender, family history, and genetics. Individuals with a family history of coronary artery disease, especially at a young age, are particularly at risk of developing this type of disease [1,4,5]. In recent decades, the high prevalence of these risk factors has led to an increased incidence of obstructive vascular diseases worldwide, especially in Iran [6].

Based on available reports in Iran, ischemic heart diseases, including coronary artery diseases, are the most common cardiovascular diseases and have become the leading cause of mortality and disease burden [7]. Given the differences in the natural course of CAD in young and older individuals, the present study aims to compare the risk factors, clinical presentation, and severity of coronary artery involvement in individuals under 45 years, under 65 years, and over 65 years of age, based on their gender, to assess the cardiovascular health status for better disease management and control of these specific patients.

Material and methods

Study design and participants

This single-center registry-based cross-sectional-comparative study was conducted using Coronary Angiography and Angioplasty Registry (CAAR) patients. CAAR contains a prospective follow-up of patients under coronary angiography, presenting to Imam Hossein Hospital, one of the main educational hospitals in east of Tehran, Iran. In this registry system the inclusion criteria was adult patients (aged 18 years and older) who underwent coronary angiography or angioplasty. In this study, the data were extracted from 330 patients with confirmed coronary artery diseases recorded by the CAAR during July 2021 to August 2023. The protocol of CAAR system was approved by review board of Vice-Chancellor for Research and Technology, Shahid Beheshti University of Medical Sciences (SBMU) and has been approved by review board of the Ethics Committee (IR.SBMU.RETECH.REC.1400.256).In addition, this study was approved by the research ethics committee of the vice-chancellor for Research, SBMU (IR.SBMU.RETECH.REC.1400.732). In this registry system, the written informed consent was obtained from all the participants.

Inclusion criteria

In this study, adult's patients with confirmed CAD using coronary angiography with specific conditions were included as follows:

Mature coronary artery diseases (MCAD): CAD occurring (at least one vessel involvement with stenosis ≥50%) in men and women older than 55 and 65 years, respectively [8].

Premature coronary artery diseases (PCAD): CAD occurring (at least one vessel involvement with stenosis ≥50%) in men and women younger than 55 and 65 years, respectively [8].

Very early coronary artery diseases (VECAD): CAD occurring (at least one vessel involvement with stenosis ≥50%) in men and women younger 45 years [9].

In addition about patients with multiple coronary angiography results during study time, we considered only first result of their coronary angiography.

Definition of the risk factors

In this registry system, hypertension defined as ≥140/90 mmHg or a history of antihypertensive therapy [10]. Diabetes was defined as a fasting blood glucose level of ≥126 mg/dl or HbA1C of ≥6.5% or the use of either oral anti-diabetes agents or insulin [11]. Based on American Heart Association's classification dyslipidaemia defined as total cholesterol >200 mg/dl, LDL >100 mg/dl, HDL <35 mg/dl, triglycerides >150 mg/dl (or a combination thereof) or a history of antilipemic agents [12]. Who smoked cigarettes at the time of examination defined as current smoker and who was smoke free (at least one month) at the time of the examination was classified as ex-smoker [13]. All of the information about patients' habits, medical history and family history are based on patients' self-reporting, their medical and laboratory records and clinical visits.

Coronary angiography and Gensini score

The Gensini score is considered a measure of the severity of coronary stenosis and was estimated by a cardiologist who was blinded to the patients' group of study and all angiograms were interpreted by the same cardiologist. Gensini score was estimated as follows: First, degree of stenosis for each coronary artery was defined and rated to 1, 2, 4,8,16 and 32. Then importance of the lesion was rated as maximum 5 point to minimum 0.5 point based on type of involved coronary vessel and location of that lesion (proximal, midpart or distal part). Finally, the Gensini score was estimated using summation of each coronary segment score [14].

Sampling method and sample size calculation

Patients included in this study were randomly selected from the database of CAAR based on age and gender classification. Simple randomization was performed in six steps: [1] the CAD population based on age and gender was defined; [2] the sample size was estimated; [3] MCAD, PCAD and VECAD as CAD groups were listed in CAAR database; [4] numbers were assigned to the units based on each CAD group; [5] random numbers were assigned using "rand" function in excel; and [6] our sample was selected.

Considering a prevalence of diabetes of at least 14% in PCAD patients and 30% in MCAD patients [15,16], an error type one of 5% ($\alpha = 0.05$), and a power of 80% ($ß = 0.2$), the minimum sample size estimated in each group is 110 CAD patients (total $n = 330$).

Statistical analysis

First, the normality of continuous variables was assessed using histogram. Continuous variables described as mean and standard deviation (SD) or median and interquartile range (Q1-Q3) and categorical variables reported as frequency and percentage. To compare the means in more than two groups was used from one-way Anova or Kruskal–Wallis tests based on normality distribution of variables. The homogeneity of variance was assessed using Bartlett's test for normally distributed data following one-way Anova test. In addition, for comparing the frequency of categorized variables, was used from chi-square or Fisher's exact test. So that, if ≤20% of the expected number of cells was <5, we used the chi-square test. If >20% of the expected number of cells was <5, Fisher's exact test was used.

Univariate and multivariable linear regression models were used to detect the association between related factors and Gensini score as a CAD severity index. For selecting the best variables to enter the last multivariable model, a backward stepwise approach with *P*-value <0.2 was used. Also, about some variables such as total cholesterol and HbA1c values that did not have statistical criteria for entering in multivariable model (P-value >0.2), due to probable role of residual confounding of these variables, were adjusted in last multivariable

model. Before running the final multivariable linear regression model, the linearity of quantitative predictors such as age, HbA1c, and total cholesterol with Gensini score was assessed using a two-way scatter plot. The fitting of the final model was assessed using the adjusted R-square statistic with a value closer to 1 that indicating a better fit. Also, homogeneity of the variance test and normality of residuals were assessed. All of the statistical analysis was set as *P*-value <0.05 (two-tailed) and was performed using STATA version 14.

Results

General characteristics and prevalence of risk factors

The mean age of the 330 CAD patients was 55.1 ± 13.2 years, and 216 (65.5%) were male. The majority of patients in MCAD (68.1%) and VECAD (80%) were male, while the majority of PCAD patients were female (51.8%).

Totally, the mean of Body Mass Index (BMI) among CAD patients was 27.8 ± 4.9 kg/m^2. No difference was observed in mean of BMI and median of hip circumference among the three study groups. However, median of waist circumference was higher in the PCAD (median = 99, IQR =92–108) and VECAD (median = 98, IQR = 89–105.5) groups compared to the MCAD (median = 94, IQR = 87–102) group.

The median years of being a smoker (median = 40, IQR = 20–40) in MCAD patients have been higher compared to other groups, but the prevalence of current smoker was higher in VECAD patients compared to the other two groups. Specifically, 49% of VECAD patients were current smokers, while this percentage was 30% and 30.9% in PCAD and MCAD patients, respectively.

In CAD patients, hypertension (50.4%), dyslipidaemia (33%) and diabetes (32.8%) were the most prevalent underlying diseases, respectively. Among PCAD patients, the prevalence of diabetes (38.1%) was higher than in other groups, while the prevalence and median of disease onset age of other diseases was higher among MCAD patients compared to the PCAD and VECAD groups (Fig. 1).

In addition, 16.3%, 14.9% and 4.5% in MCAD, VECAD and PCAD had history of PCI, respectively.

In terms of the family history of CVA/TIA, the presence of a history of CVA/TIA in the father was higher in the VECAD group (10%). Additionally, in the VECAD group, the positive history of IHD in the father (38.1%) and mother (26.3%) especially at their young age was higher (Fig. 1).

The laboratory findings were also compared among the three groups. After excluding the patients who were under treatment with antilipemic agents, it was observed that the median of total cholesterol, LDL, and LDL/HDL ratio were higher in the VECAD group compared to the other groups. However, no differences were observed in the levels of FBS, HbA1c, Triglyceride and HDL among the groups. Table 1 provides more detailed information about the variables studied and the results obtained in the comparison of the three groups (Table 1).

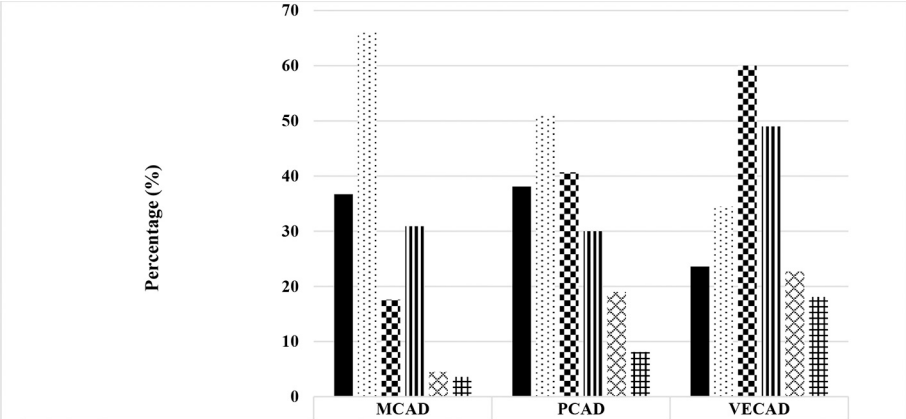
Clinical presentations in admission time

Based on results of Table 2, in CAD patients, chest pain (71.8%) and dyspnea (46.6%) were the most prevalent chief complaints at the time of admission, respectively. In the VECAD group, 75 patients, (68.1%), presented with typical chest pain, while this percentage was 61.8% in the PCAD group and 43.6% in the MCAD group. This indicates that more patients in the VECAD and PCAD groups presented with typical chest pain. In the MCAD group, prevalence of patients without any symptoms (15.4%) was higher than others.

In CAD patients, unstable angina (45.1%), stable angina (20.1%) and ST-Segment Elevation Myocardial Infarction (STEMI) (12.4%) were the most prevalent cardiac presentations at the time of admission, respectively. The most common cardiac presentations compared to other groups were 55.4% unstable angina, 29% stable angina and 19% STEMI in MCAD, PCAD and VECAD, respectively. On the other hand, in the MCAD group, a greater number of patients presented with non-ischemic symptoms compared to the other two groups (Table 2, Fig. 2).

Angiography's results and Gensini score

Most of the CAD patients (60.3%) had multi-vessel disease. The prevalence of single-vessel disease (SVD) among VECAD (52.7%) and PCAD (41.8%) was higher than MCAD group (24.5%). The median score of Gensini was different among the three groups, so that MCAD patients (median = 34, IQR = 16–54) had the highest median score (more severe) compared to PCAD (median = 22, IQR = 10–36) and VECAD patients (median = 18, IQR = 10–30) (Fig. 3). In addition, in CAD patients, LAD (73.9%), RCA (51.21%) and diagonal (37.8%) were the most type of vessels' involvement, respectively. This priority of involvement based on the type of vessel was almost the same in all CAD groups. With the minor difference that in the PCAD group, involvement in the LCX was in the third order (LAD =79%, RCA = 50.9% and LCX = 33.6%). It should



	MCAD	PCAD	VECAD
Diabetes	36.7	38.1	23.6
Hypertension	66	50.9	34.5
LDL > 100 mg/dl	17.6	40.7	60
Smoking	30.9	30	49
History of IHD in mother ≤ 65 years	4.5	19	22.7
History of IHD in father ≤ 55 years	3.6	8.1	18.1

Fig. 1. Prevalence of modifiable and non-modifiable risk factors in MCAD, PCAD and VECAD patients.

Table 1
General and clinical characteristics of patients based on CAD groups.

Variables	MCAD (n = 110)	PCAD (n = 110)	Very early CAD (n = 110)	Total (n = 330)	P_value
General information:					
Age (years)	69.9 ± 8.6	53.9 ± 4.9	41.5 ± 4.6	55.1 ± 13.2	<0.001
Gender					
Female	35 (31.8)	57 (51.8)	22 (20.0)	114 (34.5)	<0.001
Male	75 (68.2)	53 (48.2)	88 (80.0)	216 (65.5)	
Anthropometric assessment:					
Waist circumference (cm)	94 (87–102)	99 (92–108)	98 (89–105.5)	97 (89–105)	0.010
Hip circumference (cm)	96 (88.5–103.5)	100 (91–107)	100 (92–108)	99 (90–107)	0.216
Body Mass Index (BMI, kg/m^2)	27.46 ± 4.8	28.24 ± 5.4	27.90 ± 4.5	27.87 ± 4.9	0.453
Habits and underlying diseases (Yes):					
Current smoker	34 (30.9)	33 (30.0)	54 (49.0)	121 (36.6)	0.004
Duration of smoking (years)	40 (20–40)	25 (20–30)	20 (10–20)	20 (15–30)	<0.001
Ex-smoker	7 (6.4)	3 (2.7)	4 (3.9)	14 (4.3)	0.403
Opium addiction	21 (19.0)	19 (17.2)	22 (20.0)	62 (18.7)	0.870
History of diabetes	40 (36.7)	42 (38.1)	26 (23.6)	108 (32.8)	0.041
Diabetes onset time (years)	9 (2–15)	13 (3–19)	5.5 (2.5–8.5)	8 (3–15)	0.097
History of hypertension	72 (66.0)	56 (50.9)	38 (34.5)	166 (50.4)	<0.001
Hypertension onset age (years)	6.5 (2–15)	2 (1–7)	3 (1–8)	4 (1–10)	0.008
History of dyslipidemia	42 (38.1)	37 (33.6)	30 (27.2)	109 (33.0)	0.225
History of Ischemic Heart Disease (IHD)	42 (38.1)	24 (21.8)	20 (18.1)	86 (26.0)	0.002
History of Myocardial Infarction (MI)	11 (10.1)	5 (4.5)	10 (9.0)	26 (7.6)	0.262
History of heart failure	35 (32.1)	17 (15.4)	16 (14.8)	68 (20.8)	0.002
History of PCI	17 (16.3)	5 (4.5)	16 (14.9)	38 (11.8)	0.014
History of CABG	2 (1.9)	0 (0.0)	2 (2.1)	4 (1.3)	0.395
History of Cerebral Vascular Accident / Transient Ischemic Attack(CVA/TIA)	9 (8.2)	6 (5.4)	3 (2.7)	18 (5.4)	0.203
History of Chronic Kidney Disease (CKD)	12 (10.9)	1 (0.9)	3 (2.7)	16 (4.8)	0.001
Family history of CVA/TIA					
Mother	8 (7.2)	1 (0.9)	4 (3.6)	13 (3.9)	0.056
Disease onset in age of ≤55 years (mother)	3 (2.7)	1 (0.9)	2 (1.8)	6 (1.8)	0.874
Father	4 (3.6)	1 (0.9)	11 (10.0)	16 (4.8)	0.006
Disease onset in age of ≤55 years (father)	1 (0.9)	0 (0.0)	3 (2.7)	4 (1.2)	0.329
Family history of IHD /MI					
Mother	13 (11.8)	26 (23.6)	29 (26.3)	68 (20.6)	0.018
Disease onset in age of ≤65 years (mother)	5 (4.5)	21 (19.0)	25 (22.7)	51 (15.4)	<0.001
Father	13 (11.8)	23 (20.9)	42 (38.1)	78 (23.6)	<0.001
Disease onset in age of ≤55 years (father)	4 (3.6)	9 (8.1)	20 (18.1)	33 (10.0)	0.001
Laboratory results[1]**:**					
HbA1c (%)	6.3 (5.9–6.4)	6 (5.8–6.2)	5.9 (5.7–6.4)	6 (5.8–6.3)	0.211
Fasting blood sugar (mg/dl)	106 (98–137)	99 (86–120)	102 (91–116)	103 (91–119)	0.256
Triglyceride (mg/dl)	110 (94–128)	117 (92–139)	133 (92–189)	123.5 (92–154)	0.137
Total Cholesterol (mg/dl)	138 (115–187)	148 (128–168)	163.5 (146–195)	157.5 (131–182)	0.019
LDL (mg/dl)	74.5 (59–85)	88.5 (76–105)	107 (95–127)	96 (81–114)	<0.001
HDL (mg/dl)	35 (32–44)	35 (30–40)	37 (33–46)	36 (32–42)	0.144
LDL/HDL ratio	1.9 (1.6–2.4)	2.5 (2.0–2.8)	2.7 (2.3–3.4)	2.5 (2.0–3.1)	0.007

Data describes as n (%) or mean ± standard deviation or median and interquartile range (Q1-Q3).
[1] The values are based on the exclusion of patients with a history of antilipemic or anti-diabetic agents /insulin use.

be noted that left main involvement was reported in 11 patients out of all patients(3.3% of all CAD patients). Details are described in Table 2.

Associated factors to severity of vessel involvement

The univarte linear regression showed that only age and CAD groups had an association with the Gensini score as severity index. The results of adjusted linear regression model revealed that after adjusting confounding variables, in male compared to female the mean Gensini score was higher by 8 units (ß = 8.26, 95%CI = 0.24, 16.28). In addition, in PCAD (ß = −18.33, 95%CI = −34.30, −2.35) and VECAD (ß = −25.93, 95%CI = −49.07, −2.79) compared to MCAD patients the mean Gensini score was lower (Table 3).

Discussion

This study was conducted to investigate and compare the prevalence of risk factors and the severity of CAD in three groups of patients: MCAD, PCAD, and Very early CAD, undergoing diagnostic coronary angiography. In general, according to the study results, it can be said that the prevalence of modifiable and non-modifiable risk factors in patients with PCAD, VECAD, and MCAD are different.

The Gensini score comprehensively considers the number, location, and severity of coronary artery lesions, providing a more scientifically rigorous standard for evaluating coronary artery disease. Additionally, this scoring system has been widely used in relevant studies to assess clinical outcomes in CAD [14]. In our study, we also utilized this scoring system to evaluate the severity of coronary artery disease in the mentioned groups. Patients with MCAD had the highest Gensini score compared to patients with PCAD and Very early CAD, demonstrating the strong influence of increasing age on the severity of coronary artery disease. According to the results of the current study, coronary artery disease was not only more prevalent in men compared to women, but it was also associated with greater severity. Additionally, individuals with PCAD and VECAD had lower severity of coronary artery disease compared to patients with MCAD. Our study revealed that 51.8% of patients with PCAD were female, while 80% of the VECAD group comprised males. The difference in the prevalence of risk factors in men and women may also have an impact on the prevalence of coronary artery disease.

As reported in the Sharma SK, et al. study [17], the prevalence of diabetes, hypertension, and dyslipidemia in women with PCAD was higher than in men with PCAD. Furthermore, according to the definition of PCAD in our study, the occurrence of cardiovascular disease among

Table 2
Clinical presentation, angiography's finding and prognosis of CAD patients.

Variables	MCAD (n = 110)	PCAD (n = 110)	Very early CAD (n = 110)	Total (n = 330)	P_value
LVEF (eyeball,%)	50 (35–55)	50 (45–55)	50 (40–55)	50 (40–55)	0.095
Chief complaints:					
Chest pain	61 (55.4)	79 (71.8)	97 (88.1)	237 (71.8)	<0.001
Chest pain types:					
Non-anginal / Atypical chest pain	14 (12.7)	11 (10.0)	23 (20.9)	48 (14.5)	0.058
Typical chest pain	48 (43.6)	68 (61.8)	75 (68.1)	191 (57.8)	0.001
Abdominal pain	0 (0.0)	5 (4.5)	1 (0.9)	6 (1.8)	0.051
Dyspnea	56 (50.9)	51 (46.3)	47 (42.7)	154 (46.6)	0.476
Weakness	13 (11.8)	7 (6.3)	5 (4.5)	25 (7.5)	0.105
Palpitation	14 (12.7)	6 (5.4)	8 (7.2)	28 (8.4)	0.131
Without symptoms	17 (15.4)	9 (8.1)	6 (5.4)	32 (9.7)	0.035
CAD presentation:					
Stable angina	14 (12.7)	32 (29.0)	23 (20.9)	69 (20.9)	0.012
Unstable angina	61 (55.4)	42 (38.1)	46 (41.8)	149 (45.1)	0.025
Non-STEMI	8 (7.2)	10 (9.0)	15 (13.6)	33 (10.0)	0.269
STEMI	10 (9.0)	10 (9.0)	21 (19.0)	41 (12.4)	0.034
Heart failure	6 (5.4)	9 (8.1)	3 (2.7)	18 (5.4)	0.205
Without CAD presentation	18 (16.3)	7 (6.3)	5 (4.5)	30 (9.0)	0.005
Coronary artery involvement:					
Ectasia	11 (10.0)	16 (14.5)	10 (9.0)	37 (11.2)	0.389
Muscle bridge	1 (0.9)	2 (1.8)	0 (0.0)	3 (0.9)	0.776
Slow flow	3 (2.7)	2 (1.8)	2 (1.8)	7 (2.1)	1.000
Single vessel disease (SVD)	27 (24.5)	46 (41.8)	58 (52.7)	131 (39.7)	0.001
Two-vessel disease (2VD)	40 (36.3)	32 (29.0)	30 (27.2)	102 (30.9)	
Three-vessel disease (3VD)	43 (39.0)	32 (29.0)	22 (20.0)	97 (29.3)	
Gensini score	34 (16–54)	22 (10–36)	18 (10−30)	23 (12–40)	<0.001
Type of vessel involvement:					
Left main	5 (4.5)	3 (2.7)	3 (2.7)	11 (3.3)	0.798
Proximal LAD	16 (14.5)	2 (1.8)	11 (10.0)	29 (8.7)	0.003
LAD	81 (73.6)	87 (79.0)	76 (69.0)	244 (73.9)	0.239
Diagonal	56 (50.9)	33 (30.0)	36 (32.7)	125 (37.8)	0.002
LCX	44 (40.0)	37 (33.6)	21 (19.0)	102 (30.9)	0.003
OM	50 (45.4)	35 (31.8)	29 (26.3)	114 (34.5)	0.009
Ramus	7 (6.3)	6 (5.4)	6 (5.4)	19 (5.7)	0.946
RCA	67 (60.9)	56 (50.9)	46 (41.8)	169 (51.2)	0.018
PDA	23 (20.9)	8 (7.2)	8 (7.2)	39 (11.8)	0.001
PLV	9 (8.1)	2 (1.8)	5 (4.5)	16 (4.8)	0.088
SVG	2 (1.8)	0 (0.0)	0 (0.0)	2 (0.6)	0.331
LIMA	2 (1.8)	0 (0.0)	1 (0.9)	3 (0.9)	0.776
Recommendation					
Only medical treatment and life style modification	27 (24.5)	22 (20.0)	32 (29.0)	81 (24.5)	0.293
PCI	43 (39.0)	56 (51.3)	49 (44.9)	148 (45.1)	0.188
CABG	11 (10.0)	7 (6.4)	10 (9.0)	28 (8.5)	0.615
Outcome					
Alive discharge	108 (98.1)	109 (100.0)	108 (100.0)	325 (99.3)	0.331
Died	2 (1.8)	0 (0.0)	0 (0.0)	2 (0.6)	

Data describes as n (%) or median and interquartile range (Q1-Q3).

women was in the 45 to 65 age range, which is typically associated with the menopausal period, a decrease in estrogen levels, and consequently, susceptibility to CAD. Therefore, it is possible that the prevalence of CAD in Iranian women aged 45 to 65 may be higher compared to other age groups [18]. In the present study, diabetes was more common in individuals with PCAD compared to the other two groups, and the median time of onset of diabetes in this group was observed to be higher than in the other groups. The prevalence of diabetes at a young age, especially from the age of 40, due to an unhealthy lifestyle [19] and its impact on the occurrence of coronary artery disease, can be a reason for its higher prevalence in patients with PCAD compared to other groups under study. Although, these results were contrary to the findings of Sharma SK, et al. [17].

In the present study, the prevalence of hypertension was higher in MCAD compared to PCAD, which may be due to the association of this risk factor with increasing age. In fact, since MCAD occurs at older ages, high blood pressure is more commonly observed in these patients [20].

In our study, the prevalence of dyslipidemia (based on self-reporting of patients) was not statistically difference in the three CAD groups. However, based on laboratory results, it was observed that markers related to dyslipidemia (including total cholesterol, LDL, and LDL/HDL ratio) were higher in the VECAD and PCAD groups compared to the MCAD group after excluding individuals with a history of lipid-lowering drug use, which is consistent with the findings of the Vikulova DN, et al. study [21]. This indicates three important points: firstly, it highlights the strong association of dyslipidemia with early onset coronary artery disease as a highly modifiable risk factor in this group of patients. Secondly, it is unclear whether the high prevalence of dyslipidemia in younger patients is due to genetic factors or changes in lifestyle and the prevalence of unhealthy diets in society. Therefore, further studies are needed for a better understanding. Lastly, it can be said that the lack of awareness among patients about their health status due to a reluctance to undergo screening and assessment for cardiovascular risk factors, especially in young individuals, can lead to concealment and consequently an increase in prevalence of cardiovascular risk factors.

Contrary to expectations, the prevalence of smoking in VECAD patients was higher than in the other two groups, with 49% of VECAD patients being smokers. Smoking is one of the most important modifiable risk factors for premature atherosclerosis [22]. In addition to considering genetic factors, it can be noted that one of the important causes of atherosclerosis in young people in recent years [23,24] is the increase in tobacco use, which requires further studies. However, according to the results of Morris P·B, et al. study [25], in agreement with our study, the median duration of smoking in the MCAD group was higher than in the other groups. It can be said that prolonged exposure to smoking can still be related to coronary artery disease in middle and old age, and its consequences, which need to be considered in the context of preventive measures and encouragement to quit unhealthy habits in the community.

According to our study results, the high prevalence of positive family history of IHD in the parents of VECAD patients compared to the other

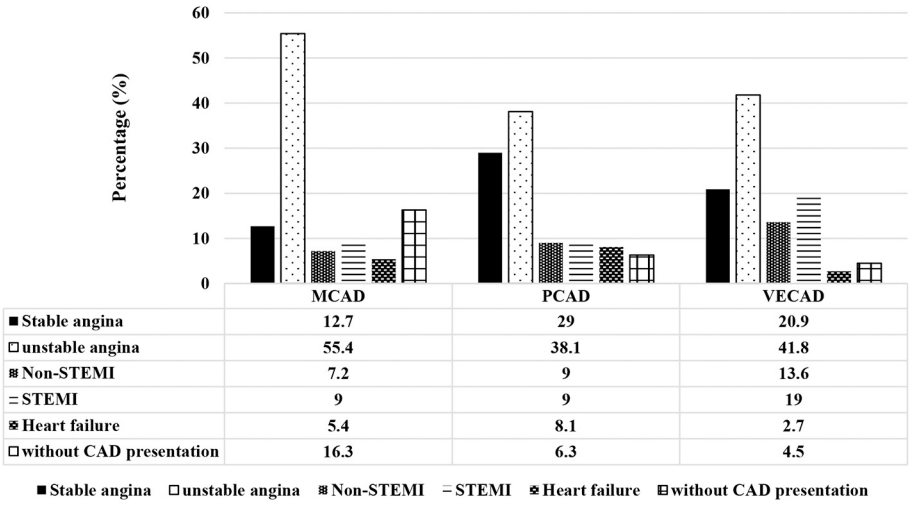


Fig. 2. Cardiac presentation in admission time in MCAD, PCAD and VECAD patients.

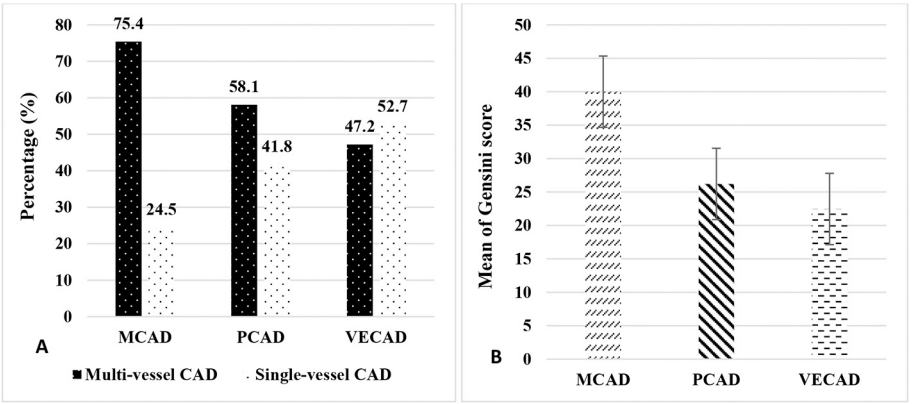


Fig. 3. Prevalence of multi-vessel CAD (A) and the mean of Gensini score (B) (as severity of coronary artery involvement) in MCAD, PCAD and VECAD patients.

Table 3
Factors associated to severity of coronary artery disease (Gensini score) based on univariate and multivariable linear regression model.

Variables	Crude β [1](95%CI)	Adjusted β[1] (95%CI)
Gender		
Female	Reference	Reference
Male	3.58 (−2.11, 9.27)	8.26 (0.24, 16.28)
Age (years)	0.52 (0.32, 0.72)	−0.06 (−0.82, 0.68)
History of ischemic heart diseases		
No	Reference	Reference
Yes	4.14 (−2.01, 10.31)	1.59 (−7.10, 10.28)
CAD category based on age		
MCAD	Reference	References
PCAD	−13.79 (−20.13, −7.44)	−18.33 (−34.30, −2.35)
VECAD	−17.54 (−23.88, −11.19)	−25.93 (−49.07, −2.79)
Total cholesterol (mg/dl)	0.005 (−0.06, 0.07)	0.01 (−0.06, 0.09)
HbA1c (%)	0.42 (−1.39, 2.23)	1.43 (−0.37, 3.25)

[1] Coefficient (ß), 95% Confidence Interval.

groups under investigation may indicate differences in the pathophysiology of coronary artery disease at different ages. In agreement with previous studies [26], it can be said that common (traditional) risk factors over time lead to vascular involvement and cardiovascular events with increasing age, but genetic factors may affect the vascular system at younger ages due to the potential expression of genes from early life [27]. The common occurrence of a positive family history in patients with coronary artery disease at a young age may be due to the potential genetic role and susceptibility of individuals in terms of having risk factors, especially lipid disorders and diabetes, in the development of PCAD [28].

According to our study results, it was observed that unlike MCAD patients, VECAD and PCAD patients had more cardiac symptoms upon admission to the hospital, while in MCAD patients, silent ischemia was more common. Interestingly, in patients under 45 years of age, STEMI as a clinical manifestation led to hospitalization, was more common. In terms of vascular involvement, although the prevalence of multi-vessel disease was higher in all CAD patients, the VECAD group mostly had single-vessel disease. Additionally, the severity of coronary artery disease based on the Gensini score was lower in PCAD and VECAD compared to MCAD patients. The most commonly involved arteries in all groups were LAD and RCA, indicating that the pattern of coronary involvement was not age-dependent. The results of the current study are consistent with previous research, particularly studies conducted in South Asia, such as India [29–32]. Although the results of the current study are in contrast to studies conducted in the UK and the US [33,34] and Sharma SK, et al. study in India [17], one possible reason for the differences in these results could be the variation in patient ethnicity, risk factors, and lifestyle, as well as differences in research methodology. Further investigation and studies are needed to understand the various reasons for these discrepancies.

Limitation

Due to the fact that the information in this study is based on the single-center CAAR system in east of Tehran, the study results can be generalized only to patients in Tehran. On the other hand, it is possible that due to the probable presence of response or recall bias from patients during data gathering the results related to the prevalence of habits and underlying diseases may be underestimated. Also, unmeasured confounding factors in this study such as patients' lifestyle and genetic factors may be effective in these results. So, we propose to assess these factors in future studies.

Conclusion

The study findings indicate that, overall, the prevalence of modifiable and non-modifiable risk factors, clinical presentations and the severity of CAD in patients with PCAD, VECAD, and MCAD are different. This difference is evident in terms of gender, smoking, family history of heart disease, lipid profile, clinical signs and symptoms, cardiac presentations, coronary involvement severity based on the Gensini Score, and the number of involved vessels. According to the present study findings, patients with MCAD had the highest mean Gensini Score compared to patients with PCAD and VECAD, and coronary involvement severity was higher in men than in women. In addition, the priority of involvement based on the type of vessel was almost the same in all CAD groups. In fact, based on our findings, modifiable risk factors in young CAD patients are common. High LDL-C levels and smoking were the common and important modifiable CVD risk factors in young patients, indicating the significant role of these traditional risk factors in early atherosclerosis development alongside inheritable risk-factors such as positive family history that were more common in young CAD patients. Therefore, public health interventions such as screening and identification of susceptible and at-risk populations, patient self-care education for those at risk, and control of cardiovascular risk factors contribute to reducing the epidemic and premature cardiovascular disease outcomes.

Ethical approval

Ethical approval has been granted by Deputy for Research Affairs, Shahid-Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1400.732). Recruitment of all patients was voluntarily and based on written informed consent from participants or their legal guardians.

Consent for publication

Not applicable.

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Availability of data and materials

The data that support the findings of this study are available from the scientific committee of the Coronary Angiography and Angioplasty Registry (CAAR) system but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the scientific committee of the CAAR system.

CRediT authorship contribution statement

Mohammad Haji Aghajani: Writing – review & editing, Project administration, Conceptualization. **Niloufar Taherpour:** Writing – original draft, Methodology, Formal analysis. **Mohammad Parsa Mahjoob:** Writing – review & editing, Conceptualization. **Naser Kachoueian:** Writing – review & editing. **Milad Alipour:** Writing – original draft. **Saman Ghorbani:** Writing – original draft, Supervision, Data curation.

Declaration of competing interest

The authors declare that they have no competing interests.

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References

[1] Coronary Artery Disease. Available at: https://www.cdc.gov/heartdisease/coronary_ad.htm; 2019. Access Oct, 2023.
[2] Mousavinasab N, Yazdani Cherat J, Bagheri B, Bakhti FS, Bakhti Z. Identifying the risk factors for cardiovascular disease in individuals aged above 35 years using logistic regression model. J Mazandaran Univ Med Sci 2017 Jan 10;26(144):50–6.
[3] Soleymani A, Dastgiri S, Yaghoubi A, Golestan B, Imani S, Hemmati N, et al. Comparison of coronary artery disease risk factors between patients below and above 45 years old. J School Publ Health Inst Publ Health Res 2012 Jan 1;9(3).
[4] Cardiovascular Diseases. Available at: https://www.who.int/health-topics/cardiovascular-diseases/#tab=tab_1; 2020. Access Oct, 2023.
[5] Non communicable diseases. Available at: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases; 2018. Access Oct 2023.
[6] Emamian MH, Hashemi H, Fotouhi A. Predicted 10-year risk of cardiovascular disease in Shahroud, Islamic Republic of Iran and the body mass index paradox. East Mediterr Health J 2020;26.
[7] Iran (Islamic Republic of Iran). IHME. Institute for Health Metrics and Evaluation; 2019. Available at: http://www.healthdata.org/iran. Access Oct, 2023.
[8] Lilly LS, Braunwald E. Braunwald's heart disease: a textbook of cardiovascular medicine. Elsevier Health Sciences; 2012.
[9] Iribarren C, Go AS, Husson G, Sidney S, Fair JM, Quertermous T, et al. Metabolic syndrome and early-onset coronary artery disease: is the whole greater than its parts? J Am Coll Cardiol 2006 Nov 7;48(9). 1800–7.
[10] Weber MA, Schiffrin EL, White WB, Mann S, Lindholm LH, Kenerson JG, et al. Clinical practice guidelines for the management of hypertension in the community: a statement by the American Society of Hypertension and the International Society of Hypertension. J Clin Hypertens (Greenwich) 2014;16:14–26.
[11] American Diabetes Association criteria for the diagnosis of diabetes. Available at: https://www.uptodate.com/contents/image?imageKey=ENDO%2F61853; 2021. Access Oct, 2023.
[12] Stone Neil J, Bailey Alison L, Beam Craig, Birtcher Kim K, Roger S. Blumenthal et al.American Heart Association Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2018;139(25): e1082–143. https://doi.org/10.1161/CIR.0000000000000625. 18 June 2019.
[13] Balter LJ, Good KP, Barrett SP. Smoking cue reactivity in current smokers, former smokers and never smokers. Addict Behav 2015;45:26–9.
[14] Nurkalem Z, Hasdemir H, Ergelen M, Aksu H, Sahin I, Erer B, et al. The relationship between glucose tolerance and severity of coronary artery disease using the Gensini score. Angiology 2010;61(8):751–5. https://doi.org/10.1177/0003319710373747.
[15] Nadeem M, Ahmed SS, Mansoor S, Farooq S. Risk factors for coronary heart disease in patients below 45 years of age. Pak J Med Sci 2013 Jan;29(1):91–6. https://doi.org/10.12669/pjms.291.2828. PMID: 24353515; PMCID: PMC3809218.
[16] Esteghamati A, Abbasi M, Nakhjavani M, Yousefizadeh A, Basa AP, Afshar H. Prevalence of diabetes and other cardiovascular risk factors in an Iranian population with acute coronary syndrome. Cardiovasc Diabetol 2006;5:15. Published 2006 Jul 17, https://doi.org/10.1186/1475-2840-5-15.
[17] Sharma SK, Makkar JS, Bana A, Sharma K, Kasliwal A, Sidana SK, et al. Premature coronary artery disease, risk factors, clinical presentation, angiography and interventions: hospital based registry. Indian Heart J 2022 Sep 1;74(5):391–7.
[18] El Khoudary SR, Aggarwal B, Beckie TM, Hodis HN, Johnson AE, Langer RD, et al. American Heart Association Prevention Science Committee of the Council on Epidemiology and Prevention; and Council on Cardiovascular and Stroke Nursing. Menopause transition and cardiovascular disease risk: implications for timing of early prevention: a scientific statement from the American Heart Association. Circulation 2020 Dec 22;142(25):e506–32.
[19] Lascar N, Brown J, Pattison H, Barnett AH, Bailey CJ, Bellary S. Type 2 diabetes in adolescents and young adults. Lancet Diabetes Endocrinol 2018;6(1):69–80. https://doi.org/10.1016/S2213-8587(17)30186-9.

[20] Pinto E. Blood pressure and ageing. Postgrad Med J 2007 Feb;83(976):109–14. https://doi.org/10.1136/pgmj.2006.048371. PMID: 17308214; PMCID: PMC2805932.
[21] Vikulova DN, Grubisic M, Zhao Y, Lynch K, Humphries KH, Pimstone SN, et al. Premature atherosclerotic cardiovascular disease: trends in incidence, risk factors, and sex-related differences, 2000 to 2016. J Am Heart Assoc 2019 Jul 16;8(14): e012178.
[22] Siasos G, Tsigkou V, Kokkou E, Oikonomou E, Vavuranakis M, Vlachopoulos C, et al. Smoking and atherosclerosis: mechanisms of disease and new therapeutic approaches. Curr Med Chem 2014 Nov 1;21(34):3936–48.
[23] Meysamie A, Ghalehtaki R, Ghodsi S, Esteghamati A, Mohammad K, Etemad K, et al. Trend of cigarette smoking in Iranian adult population from 2000 to 2011 based on four national surveys. Soc Determin Health 2017 Jan 1;3(3):148–59.
[24] Ghelichkhani P, Baikpour M, Mohammad K, Fattah FH, Rezaei N, Ahmadi N, et al. Age, period and cohort analysis of smoking prevalence in Iranian population over a 25-year period. Arch Iran Med 2021 Jan 1;24(1):7–14.
[25] Morris PB, Ference BA, Jahangir E, Feldman DN, Ryan JJ, Bahrami He, Sanchez Shields M, et al. Cardiovascular effects of exposure to cigarette smoke and electronic cigarettes: clinical perspectives from the prevention of cardiovascular disease section leadership council and early career councils of the American College of Cardiology. J Am Coll Cardiol 2015;66(12):1378–91.
[26] Mohammad AM, Jehangeer HI, Shaikhow SK. Prevalence and risk factors of premature coronary artery disease in patients undergoing coronary angiography in Kurdistan. Iraq BMC Cardiovasc Disord 2015 Dec;15(1):1–6.
[27] Poorzand H, Tsarouhas K, Hozhabrossadati SA, Khorrampazhouh N, Bondarsahebi Y, Bacopoulou F, et al. Risk factors of premature coronary artery disease in Iran: a systematic review and meta-analysis. Eur J Clin Investig 2019 Jul; 49(7):e13124.
[28] Wang H, Liu Z, Shao J, Jiang M, Lu X, Lin L, et al. Pathogenesis of premature coronary artery disease: focus on risk factors and genetic variants. Genes Dis 2022 Mar 1;9(2):370–80.
[29] Tewari S, Kumar S, Kapoor A, et al. Premature coronary artery disease in North India: an angiography study of 1971 patients. Indian Heart J 2005;57:311–8.
[30] Prajapati J, Jain S, Virpariya K, et al. Novel atherosclerotic risk factors and angiographic profile of young Gujarati patients with acute coronary syndrome. J Assoc Phys India 2014;62:584–8.
[31] Sinha SK, Krishna V, Thakur R, et al. Acute myocardial infarction in very young adults: a clinical presentation, risk factors, hospital outcome index and their angiographic characteristics in North India- AMIYA study. ARYA Atheroscler 2017; 13:79e87.
[32] Michos ED, Choi AD. Coronary artery disease in young adults: a hard lesson but a good teacher. J Am Coll Cardiol 2019 Oct 15;74(15):1879–82.
[33] Volgman AS, Palaniappan LS, Aggarwal NT, et al. Atherosclerotic cardiovascular disease in south Asians in the United States: epidemiology, risk factors and treatment. Circulation 2018;138:e1ee34.
[34] Bhopal RS. Epidemic of cardiovascular disease and diabetes: explaining the phenomenon in south Asians worldwide. Oxford: Oxford University Press; 2019.