# Coronary artery disease in Iranian young adults, similarities and differences

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#### **ABSTRACT**

Objective: Due to devastating consequences of coronary artery disease (CAD) in young population, this study was designed to evaluate the prevalence of preventable risk factors and severity of atherosclerosis for Iranian young adults (≤45 years) diagnosed with premature CAD. Method: A cross sectional, descriptive study comprised 1093 consecutive patients (≤45 years), with a diagnosis of CAD, who underwent percutaneous intervention (PCI) or coronary bypass graft (CABG) from 2010 to 2012. Data on demographic features, cardiovascular risk factors, and angiographic findings were studied. Result: There were 1093 young patients (234 females, 859 males) with proven CAD; the mean age of  $39 \pm 3$  years and the mean BMI were  $28 \pm 4.7 \text{ kg/m}^2$ . According to the treatment plan, patients were classified into two groups: PCI and CABG groups (n = 898,195 respectively). Obesity was the most prevalent risk factor (73.6%). In the risk factor assessment, it was noticed: 27% with diabetes mellitus, 37% with hypertension, 38% with family history, 39% with hyperlipidimia, and 54% smokers. Angiographic study revealed that 10 (1%) had left main coronary disease, 747 (68%) patients had single vessel disease, 181 (17%) had twovessel disease and that 155 (14%) had three-vessel disease. The most common anatomical involvement was the anterior wall territory. Conclusion: Young CAD patients from Iran have different risk profile. Although atherosclerosis of the coronary arteries is less prominent in young patients, more often it is accompanied by decreased left ventricular function. There is a need for prevention plan to control obesity by targeting young adults in the population.

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#### **KEYWORDS**

Coronary Heart Disease; Percutaneous Coronary Intervention; Coronary Artery Bypass Graft; Prevention; Body Mass Index; Obesity

#### 1. INTRODUCTION

The coronary artery disease (CAD) as a silent process is regarded as a disease of advanced age, but young population can be affected. The prevalence of young patients (less than 40 to 45 years of age) among CAD patients is from less than 2% to 10% depending on the population studied [1-7]. Acute myocardial infarction (MI) at the young age is associated with high morbidity, the disturbing effects on the more active patients' lifestyle and their families, with higher cardiac mortality. A majority of them develop congestive heart failure (10%), experience re-infarction (15%) and will die within 15 years from their first cardiac events (26%). While its incidence is low, its significance is important in terms of potential life years lost. The importance of screening for identification and clinical management of modifiable risk factors is a paramount part. CAD presenting at the young age shows a different clinical presentation, angiographic findings, pathophysiologic and risk factor profiles compared to older [5-7].

Most of the studies involving young CAD patients are reported from Western countries and might not be directly applicable to the other population.

The proportion of CAD patients under the age of 45 years in Iran is currently increasing because the life style is becoming more westernized, especially among young adults [8,9].

The purpose of this study was to see the frequency of correctable risk factors for CAD in our young, produc-



tive and workforce population with the expectation of using the information as an aid in primary and secondary prevention in the future.

#### 2. METHOD

## 2.1. Study Subjects

The study population consisted of 1093 adult patients ( $\leq$ 45 years) who underwent diagnostic coronary angiography and then referred for percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) in tertiary university hospital, between March 2010 and March 2012 and had at least one coronary artery stenos is  $\geq$ 70%. The cutoff age of 45 years was used to identify young adult patients based on previous epidemiologic studies [2,3,5]. Relevant clinical data (demographic, clinical, angiographic, and type of procedure) were retrieved from the patient's medical records.

The study protocol was approved by the local research Ethics committee of Shahid Beheshti University of Medical Sciences (Ethics Committee reference number 124). Exclusion criteria were CAD patients older than 45 years, spontaneous coronary artery dissection, non-atheromatous CAD such as congenital coronary artery anomalies, drug abuse, hypercoagulable states and insignificant coronary artery stenos is (<70% luminal narrowing).

All patients included in the study underwent angiography. Significant coronary disease was defined as at least a 70% reduction in the internal diameter of coronary artery or more than 50% reduction in internal diameter of left main. The extent of CAD was scored as single, two- and three-vessel disease according to the number of arteries involved.

#### 2.2. Assessment of Risk Factor

We examined the following risk factors: Overweight as body mass index (BMI)  $\geq 25 \text{ kg/m}^2$ . Hypertensive, if the blood pressure was more than 140/90 mmHg or self-reported current use of antihypertensive medication. Family history of premature CAD, angina or MI in the first-degree relatives is younger than 50 years. Diabetics, as fasting plasma glucose, are more than 125 mg/dL or taking hypoglycemic agents. Hyperlipidemic if receiving any lipid-lowering drugs or had serum cholesterol concentration 200 mg/dL. Daily smoking habit was obtained by a self reported questionnaire.

## 2.3. Statistical Analysis

The SPSS software (Chicago, Illinois; Version 16.0) was used for all statistical analyses. Data are presented as percentages for discrete variables and as mean  $\pm$  standard deviation for continuous variables. Differences in baseline characteristics between groups were compared using

unpaired t-test and Fisher's exact. A p value of <0.05 was considered significant.

#### 3. RESULT

There were 1093 young patients (234 females, 859 males) with proven CAD; the mean age of  $39 \pm 3$  years and the mean BMI was  $28 \pm 4.7 \text{ kg/m}^2$ . Of them, 515 (47.1%) suffered a previous myocardial infarction and the mean left ventricular systolic function was 46%. In risk factor assessment it was noticed: 27.5% with diabetes mellitus, 37% with hypertension, 38% with family history, 39% with hyperlipidemia, 54% smokers and; BMI  $\geq$  25 kg/m<sup>2</sup> in 73.6% of patients, in order of frequency. In 2.4% of this population (26 patients), there was none of these conventional risk factors. Angiographic study revealed that 10 (1%) patients had left main coronary disease, 747 (68%) patients had single vessel disease, 181 (17%) patients had two-vessel disease and 155 (14%) patients had three-vessel disease. According to the treatment plan. patients were classified into two groups: PCI and CABG groups (898 and 195 patients, 82.2% and 17.8%, respectively).

In CABG group (n = 195), indication for surgery was left main coronary artery stenos is in five patients, single vessel disease in seven patients, two-vessel disease in 28 patients, and three-vessel disease in 91 patients. Four grafts were done in 59 patients and 5 grafts were done in 5 patients (Table 1). The surgical procedure was carried out by extra corporeal circulation and cardioplegic arrest of the heart in 170 patients and off pump surgery in the remaining 25 cases. A total of 607 grafts were constructed, with a mean of  $3.1 \pm 0.8$  grafts per patient (range 1 - 5 grafts). All patients received the left internal thoracic artery to their left anterior descending coronaryartery (LAD). All saphenous vein grafts were used for diagonal, marginal branches of the circumflex artery (LCX) or to the right coronary artery (RCA) system. No patients had significant heart valve dysfunction.

Distribution of coronary artery stenos is in PCI group

Table 1. Distribution of coronary artery disease in groups.

	PCI group (n = 898)	CABG group (n = 195)
Left main disease	5 (0.6%)	5 (2.5%)
One vessel disease	740 (82.4%)	7 (3.5%)
Two-vessel disease	153 (17%)	28 (14.3%)
Three-vessel disease: Three graft		91 (46.6%)
Four graft		59 (30.2%)
Five graft		5 (2.5%)

PCI, Percutanous Coronary Intervention; CABG, Coronary Artery Bypass Graft.

(n = 898) is displayed in **Table 1**. It is shown that left main lesion represent only 0.6% of total lesion, LAD was the most frequently affected vessel (48.3%) followed by LCX and RCA which represent 21.2% and 13% respectively. Combination of LAD + LCX lesions was more than LAD + RCA or LCX + RCA lesions, 11.9% vs 3.5% and 1.5% respectively.

Clinical variables at baseline of both groups are summarized in **Table 2**. Approximately one-half of the patients in each group had previous MI at the time of initial admission. Obesity and smoking were the most prevalent factors in both groups. In CABG group 4% of patients had a history of previous PCI and in PCI group 12.7% had a history of previous coronary surgery. Decreased EF was seen in both groups, and was less in CABG group (p value: 0.02) but it was not important clinical impression.

Comparison of risk factor profiles was made between women and men patients (**Table 3**). Twenty one percent of the patients were women. The mean age at presentation was 39 for both of them. The average EF in the study was more in women (p value: 0.001), without significant clinical impression. Men had more prior MI

**Table 2.** Demographic data and cardiovascular risk factors of patients according to treatment plan.

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	PCI group (n = 898)	CABG group (n = 195)	P value
Age (years)	$39 \pm 3$	$40\pm2$	0.001
Sex (male)	718 (80%)	141 (72.3%)	0.02
BMI $(kg/m^2)$	$28.2 \pm 4.7$	$26.9{\pm}~4.3$	0.001
Current Smoking (%)	492 (54.8%)	106 (54.4%)	0.9
Family history of CAD (%)	319 (35.5%)	100 (51.3%)	0.001
Diabetes mellitus (%)	221 (24.6.1%)	80 (41%)	0.001
Dyslipidemia (%)	335 (37.3%)	92 (47.2%)	0.005
Hypertension (%)	311 (34.6%)	96 (49.2%)	0.001
CVA history (%)	19 (2.1%)	8 (4.4%)	0.11
COPD (%)	11 (1.2%)	3 (1.7%)	0.7
PVD (%)	9 (1%)	1 (0.6%)	1
Renal failure (%)	28 (3.1%)	11 (7.9%)	0.013
$BMI \ge 25 \ (kg/m^2)$	673 (74.9%)	131 (67.2%)	0.03
Previous MI (%)	423 (47.1%)	92 (52.3%)	0.2
Previous surgery (%)	113 (12.7%)	3 (1.9%)	0.001
Thrombolytic therapy (%)	134 (14.9%)	8 (1.9%)	0.001
LVEF (%)	47 ± 11	44 ± 11	0.02

BMI, Body Mass Index; CAD, Coronary Artery Disease; MI, Myocardial Infarction; LVEF, Left Ventricular Ejection Fraction, PCI, Percutanous Coronary Intervention; CABG, Coronary Artery Bypass Graft.

Table 3. Risk factor characteristics according to gender.

	Male (n = 859)	Female $(n = 234)$	p value
Age (years)	$39.7 \pm 3.1$	$39.8 \pm 3.4$	0.5
BMI (kg/m²)	$28.2 \pm 4.6$	$27.3 \pm 5.1$	0.02
$BMI \geq 25 \ kg/m^2$	646 (59.1%)	158 (67.5%)	0.01
Current smoking (%)	563 (65.5%)	35 (15%)	0.001
Family history of CAD (%)	330 (38.4%)	89 (38%)	0.9
Diabetes mellitus (%)	192 (22.4%)	109 (46.6%)	0.001
Dyslipidemia (%)	314 (36.6%)	112 (47.9%)	0.006
Hypertension (%)	274 (31.9%)	133 (56.8%)	0.001
Previous MI (%)	448 (53.1%)	67 (29.1%)	0.001
LVEF (%)	$45.9 \pm 12$	$49.5\pm10$	0.001
Thrombolytic therapy (%)	134 (16%)	8 (3.5%)	0.001
PCI	718	180	0.02
CABG	141	54	
Number of treated vessels	$1.9\pm0.9$	$2 \pm 0.9$	0.02

BMI, Body Mass Index; CAD, Coronary Artery Disease; CVA, Cerebrovascular Accident; PVD, Peripheral Vascular Disease; MI, Myocardial Infarction; LVEF, Left Ventricular Ejection Fraction.

events at the time of initial admission (41% vs 6%, p value < 0.001). Smoking was more common risk factor in men (51% vs 3%, p value < 0.001). Although obesity was higher frequency in women (p value 0.01), it was the most common risk factor in both.

Because of high prevalent obesity in this population, clinical data were compared according to BMI classification, with results detailed in Table 4. Briefly patients with BMI  $\geq$  25 were more likely to have positive family history, hyperlipidemia, previous MI event and PCI treatment, with significant statistical differences.

#### 4. DISCUSSION

Ischemic heart disease is an age related progressive condition, this is probably the reason that most available data refer to the elderly population. The CAD management in the young patients is of particularly important subject because of a longer life expectancy and greater functional requirements for the normal life. To define the risk factors and angiographic data of the Iranian patients under age 45 who present to the cardiac ward of a tertiary hospital, a retrospective cross-sectional study was conducted over a 2-year period. The major finding of the present study in 1093 patients with symptomatic premature CAD requiring PCI or CABG is that prevalence of obesity and smoking is greater than other cardiac risk factors. Due to the social reasons, smoking is very infer-

Table 4. Demographic data of patients according to BMI.

	$BMI \ge 25 \text{ kg/m}^2$ $(n = 804)$	BMI < 25 kg/m (n = 289)	$n^2 P$ value
Age (years)	39 ± 3	39 ± 2	0.09
Sex(male)	646	213	0.01
Current smoking (%)	436	162	0.6
Family history of CAD (%)	326	93	0.01
Diabetes mellitus (%)	216	85	0.4
Dyslipidemia (%)	329	97	0.02
Hypertension (%)	309	98	0.1
Previous MI (%)	400	115	0.01
LVEF (%)	$47 \pm 11$	$45 \pm 12$	0.09
PCI	673	225	0.03
CABG	131	64	

BMI, Body Mass Index; CAD, Coronary Artery Disease; MI, Myocardial Infarction; LVEF, Left Ventricular Ejection Fraction, PCI, Percutanous Coronary Intervention; CABG, Coronary Artery Bypass Graft.

quent among Iranian women. The results of previous studies have similarly suggested smoking is strongly associated with CAD in young men patients. But increased BMI was the most risk factor in young Iranian women. The clinical implications of these novel data appear relevant for the therapeutic view.

The primary finding of this study is that obesity is a correctable and important risk factor for premature CAD in this population. Truncal obesity and increased BMI have been suggested as potential factor for CAD. About 30% - 50% of young CAD patients are obese in other studies [1,10-12].

The prevalence of CAD in young adult has progressively increased during the latter half of the current century in Iran, although there was a few studies about that [8,9]. It was a previous study on young Iranian CAD population with different design. The effect of smoking and hypertension on the number and severity of vessel involvement and EF was evaluated. But they included only these 2 factors and the other risk factors including obesity were kept out [8]. In similar study the angiographic and demographic finding of 108 Iranian patients less than 35 years of age with acute ST elevation myocardial infarction was compared with the control group of CAD patients aged >35, the mean BMI was more than 27 kg/m² in both groups [9].

Changing the pattern of diseases towards chronic and non-communicable diseases and prevalence of obesity in the world was reported by the World Health Organization [12]. There is a progressive growth of obesity in Iranian young population. The importance of obesity is that as opposed to non modifiable risk factors, such as genetic

predisposition, aggressive control of it may pay large dividends in decreasing the incidence of CAD in young adult patients. There were comparable studies for young CAD population in neighborhood countries [6,7,9,13-16]. It was displayed that smoking and hypertension were the leading risk factors in young CAD patients in Pakistan, Turkey, Kuwait and Iraq. The frequency of BMI  $\geq 25 \text{kg/m}^2$  in these populations is being reported between 16% - 35%. But the result in Oman study was somewhat different. Obesity was the prominent risk factor (in 72% of young CAD population) followed by smoking and family history (47% and 16%, respectively), different profile that was in agreement with the Iranian patients [13]. Although this discrepancy cannot be explained precisely, it is possible that gender and cultural factors may be involved.

Recent data on three other Asian countries was gathered. A comparable study in Dhaka, Bangladesh was consistent with Middle East finding [17]. Smoking and family history were the most risk factor, obesity was seen in 30% of young CAD population. In similar study of young CAD patients in China, BMI ≥ 25 kg/m² was observed in 44% of patients [18]. The Chinese have a low rate of CAD despite high prevalent rate of hypertension and smoking; it may be due to anti-atherogenic lipid profile of them. It is believed that CAD occurs at least ten years earlier in Indian population, with dominancy of smoking as the main risk factor [8,19-21].

There was matching study in three European countries. Increased BMI in young Poland population was reported 5% - 19% and smoking was the strongest risk factor regardless of gender [2]. In Switzerland young CAD patients, smoking was the first (77%); family history and obesity both were the second risk factor (55%) [22]. In Spain population, CAD represented the main cause of sudden death in young adult and the mean BMI in this group was 31 kg/m². Hyperlipidemia and obesity were the modifiable risk factors in association with higher risk of sudden death from CAD [23]. In assessment of 12 European cohort studies, it was emphasized that increased BMI is related strongly to CAD mortality, especially in young adult [11].

The current study shows that young adult have a high frequency of single vessel disease, the most common anatomical location for the significant was the anterior wall particularly in LAD territory. Similar result has been reported by other authors [8,14-17,24].

Most evidence from previous studies had shown that CAD in young patients has less extensive disease, higher EF, fewer comorbidities and a more favorable prognosis than older patients [2,10,24,25]. Data from our study showed that about one half of this young population had MI event prior to admission. This may interpret that why the mean EF was less than 50%. Both of them are important prognostic determinant of adverse cardiac events

[3,26]. This result may be due to differences in genetic predisposition, as the EF was less than 50% in half of the young CAD patients in the two other Iranian studies [8,9]. It was contrast to the finding of Cole *et al.* that in spite of the previous MI event in young population with the same rate, EF had been preserved [25]. In Kuwait study, MI was seen in half of young patients and EF < 50% in one third of them [14]. In Turkish population, there was about 20% prevalence of MI with significant dominancy in men [16]. The rate of MI was the less (13%) in Oman population [13].

#### 5. LIMITATIONS

It is the observational and retrospective analysis. The possible confounding variables are not controlled in the study. We evaluated the standard coronary risk factors. Other newer risk factors such as lipoprotein abnormalities and elevated homocysteine levels were not studied. Furthermore, non-atherosclerotic coronary disease, which should be considered in young patients with CAD, was not evaluated. This study included patients from a single centre, resulting in a small sample size of patients, its reliance on a sample of the general population.

To our knowledge, this is the first epidemiological study to identify risk factors for CAD in this subset of population. However, this is the largest series to date reporting specifically on young adult patients who underwent coronary revascularization (PCI or CABG) in Iran. Our observations will need confirmation from a larger prospective study.

#### 6. CONCLUSION

CAD is increasing in our young population due to imperfect life style. It leads to the loss of work days, transition from an active to sedentary working life and decreased efficiency. Preventing the disease is probably the best way to improve results by modifying life style, dietary habits, public awareness programs and regular exercise. Prevention and treatment of obesity must become a major public health priority in the prevention of premature CAD.

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# DECLARATION OF CONFLICTING INTERESTS

None declared.

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