



## Food Intake Pattern and Cardiovascular Risk Factors in Patients with Premature Coronary Artery Disease in Iran

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### ABSTRACT

**Background:** There is limited evidence regarding the risk factors and nutritional patterns in patients with premature coronary artery disease (PCAD). This study aims to investigate the relationship between different dietary patterns and risk factors in patients with PCAD. **Methods:** This cross-sectional study was conducted on PCAD patients, including men younger than 55 years and women younger than 65 years, who underwent coronary angiography in the Angiography Department of the Shahid Mohamadi Hospital, Bandar Abbas, Iran. Anthropometric and clinical examination, demographic questionnaires, and containing dietary intake and physical activity questionnaires were filled for all participants. **Results:** The most prevalent risk factors for obstructive PCAD in the 65 selected patients were family history of coronary artery disease (CAD) (73%), hypertension (52%), and overweight/obesity (50%). Daily consumption of hydrogenated fats ( $P = 0.008$ ) and high-fat milk ( $P < 0.001$ ) were significantly higher in obstructive PCAD patients compared to non-obstructive and non-PCAD patients. Daily consumption of fruits was significantly higher in non-obstructive and non-PCAD patients compared to obstructive PCAD patients ( $P = 0.039$ ). **Conclusion:** Family history of CAD, hypertension, and obesity were found to be the most common risk factors among obstructive PCAD patients. According to the findings, increased consumption of high-fat milk and hydrogenated fats may increase the risk of PCAD, whereas, daily consumption of fruits may reduce the risk of PCAD.

**Keywords:** Coronary artery disease; Premature coronary artery disease; Risk factors; Dietary patterns.

### Introduction

Coronary artery disease (CAD) is one of the critical cardiovascular diseases and is the major cause of morbidity and mortality in recent decades (Malakar *et al.*, 2019). CAD has a great burden on health care in Iran and is responsible for

50% of all annual cardiovascular deaths (Hatmi *et al.*, 2007, Malakar *et al.*, 2019). CAD generally occurs in old age; however, the mean age of CAD has decreased in recent decades. Recent studies have shown that about 4%-10% of CAD patients

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aged less than 45 years (Doughty *et al.*, 2002, Poorzand *et al.*, 2019). According to a recent systematic review and meta-analysis, the mean age of onset of CAD has decreased in recent years in Iran (Poorzand *et al.*, 2019).

Different definitions have been used for premature coronary artery disease (PCAD). PCAD is generally defined as the event of acute myocardial infarction (MI) or myocardial ischemia with an obstructive CAD (any stenosis  $\geq 70\%$  or left main [LM] stenosis  $\geq 50\%$ ) in women and men younger than 65 and 55 years, respectively (Iyengar *et al.*, 2017, Mohammad *et al.*, 2015). However, the reported age of PCAD patients ranged from 40 to 65 years in different studies (Mohammad *et al.*, 2015, Poorzand *et al.*, 2019). PCAD is related to various adverse outcomes, which affect quality of life and lead to premature death (Sharma and Ganguly, 2005). Therefore, early diagnosis of PCAD and preventing its exacerbation is crucial. Various risk factors, including tobacco and cocaine abuse, dyslipidemia, diabetes mellitus, and positive family history of PCAD, are associated with PCAD (Cole and Sperling, 2004). These risk factors are similar to the suggested risk factors for CAD. A study by Zeitouni, *et al.* showed that PCAD patients have various modifiable risk factors, among which the most common risk factor was smoking. In addition, almost half of the population in the mentioned study was obese, suggesting obesity as a risk enhancer for PCAD (Zeitouni *et al.*, 2020). Also, in a cohort study on French population elevated serum low-density lipoprotein cholesterol (LDL-c) levels and active smoking were more frequent in the PCAD population compared to general population (Collet *et al.*, 2019). Unhealthy diet is another important but challenging risk factor for CAD as well as PCAD. Several studies have shown that excessive intake of saturated and hydrogenated fats and reduced intake of plant-based foods along with increased consumption of simple carbohydrates are associated with increased risk of cardiovascular disease (Feigin *et al.*, 2016, Forouzanfar *et al.*, 2016, Mensink and World health organization, 2016). Various studies have

been conducted to identify the nutritional risk factors for PCAD; however, there is limited data regarding the risky dietary behaviors for PCAD. These studies separately indicated the role of healthy diet and Mediterranean diet in preventing PCAD but the findings of these studies were inconclusive. It could be due to the existence of various dietary patterns and differences in study populations and racial and geographical diversity of the populations (Kumbhalkar and Bisne, 2019, Osadnik *et al.*, 2018). Therefore, this study aims to define dietary patterns that might increase the risk of PCAD among Iranian population.

### Material and Methods

**Study population:** This cross-sectional study was carried out at Shahid Mohamadi Hospital, Bandar Abbas, Iran. The participants were selected consecutively from the patients who underwent coronary angiography in the angiography department of the Shahid Mohamadi Hospital between May 2017 and February 2018. Due to the low prevalence of PCAD, the global sampling method was used to include all patients with PCAD during the recruitment duration. A total of 65 participants (36 men and 29 women) were enrolled based on global sampling method. After anthropometric and clinical examination, demographic questionnaires, and questionnaires containing dietary intake and physical activity, were filled for all participants. All questionnaires were paper-based, written in Persian language, and administered by a trained interviewer.

The inclusion criteria were as follows: being within the age range of 18 and younger than 55 years in men or 65 years in women, presenting symptoms of acute coronary syndrome (ACS) or acute MI, and undergoing coronary angiography for the first time. Patients with other causes of non-obstructive heart disease, including myocarditis and coronary spasm, were excluded.

**Ethical considerations:** Written informed consent forms were signed by all the participants before the initiation of the study. The study protocol was approved by the Ethics Committee of the Bandar Abbas University of Medical Sciences

(Ethical Code: HUMS.REC.1396.109).

**Measurements:** General demographic data including age, smoking and opioid use, medical history, family history, drug and supplement use, as well as history of chronic diseases were collected by an experienced interviewer who had a degree in nutrition science. Physical activity was investigated by using the validated International Physical Activity Questionnaires (IPAQ). Physical activity level was calculated based on total metabolic equivalent task (MET) minutes per week.

Current smoking was defined as smoking even one cigarette during the last month. Diabetes mellitus was defined as a fasting blood glucose  $\geq$  126 mg/dl, 2 hours postprandial glucose  $\geq$  200 mg/dl, or use of hypoglycemic medications or insulin. Hypertension was defined as a systolic blood pressure  $\geq$  140 mmHg and/or diastolic blood pressure  $\geq$  90 mmHg, and/or use of antihypertensive medication. Dyslipidemia was defined as high-density lipoprotein cholesterol (HDL-c)  $<$  40 mg/dl or triglycerides (TG)  $>$  150 mg/dl and/or LDL-c  $>$  100 mg/dl and/or using lipid-lowering medications.

Height and weight were measured by a trained nurse based on standard protocols. Height was measured to the nearest 0.01 cm by using a standard stadiometer without shoes, in free-standing position with the head in the Frankfurt horizontal plane. Weight was measured by using a clinical Seca scale (Rumily, France), to the nearest 0.1 kilograms. Body mass index (BMI) was calculated by division of weight (kg) by the square of height (m<sup>2</sup>).

A valid and reliable food frequency questionnaire (FFQ) containing 168 food items was administered by trained interviewers to estimate the dietary intake of the study participants. The validity and reproducibility of this FFQ have been reported in previous studies (Djazayery *et al.*, 2008, Mirmiran *et al.*, 2010). For each item in the FFQ, the participants stated their average frequency of consumption over the past year on a daily, weekly, monthly, or yearly basis

over the past year.

Diagnostic coronary angiography was performed by a team of qualified cardiologists. All coronary angiographies were analyzed by at least 2 expert cardiologists. Eyeballing and quantitative coronary angiography (QCA) methods were used to determine the percentage, morphology, and length of the coronary lesions.

The electrocardiographic and echocardiographic data and coronary angiographic findings were recorded. Diameter stenosis  $>$  50% in each left anterior descending (LAD) or right coronary artery (RCA) was defined as obstructive stenosis and stenosis  $<$  50% was considered as non-obstructive stenosis. Therefore, patients were divided into two groups based on the PCAD extent in angiography. Group 1 consisted of patients without any stenosis or with non-obstructive stenosis, while group 2 included patients with obstructive stenosis.

**Data analysis:** All statistical analyses were carried out by using the Statistical Package for Social Sciences (SPSS) version 16 software. The Nutritionist IV software was used to calculate daily nutrient intakes for each participant. The normality of quantitative data was determined by using the Kolmogorov-Smirnov test. Normally distributed quantitative data were described using mean and standard deviation, and non-normally distributed data were described using median and interquartile range (IQR). Qualitative data were described by frequency and percentages. To compare quantitative parametric and non-parametric variables between groups, independent t-test and Mann-Whitney U test were used, respectively. The chi-square or Fisher exact tests were used to compare the distribution of quantitative variables between groups. Further statistical tests could not be performed due to the heterogeneity of the patients in the study groups. A P-value  $<$  0.05 was defined as statistically significant.

## Results

The general characteristics of the study population are summarized in **Table 1**. The mean  $\pm$  SD for the age of the study participants was  $51.05 \pm 7.6$  years. The mean  $\pm$  SD value of BMI

was  $25.4 \pm 4.2 \text{ kg/m}^2$ . Half of the patients had a  $\text{BMI} \geq 25 \text{ kg/m}^2$ . No significant difference was observed between groups in terms of age, sex, anthropometric parameters, level of education, and physical activity.

Among the participants, 10 (15.4%) had no coronary artery stenosis (no apparent PCAD), 3 (4%) had arterial stenosis between 20-50% (non-obstructive PCAD), and 52 (80%) had arterial stenosis above 50% (obstructive PCAD). According to angiographic information (Table 2), single vessel disease (1VD), two-vessel disease (2VD), and three-vessel disease (3VD) were observed in 33.8%, 38.5%, and 12.3% of the participants, respectively. Single vessel disease was the most common in (LAD) (69.2%), followed by RCA (44.6%), and left circumflex artery (LCX) (15.4%). The frequency of 1VD, 2VD, 3VD, and the involvement of LAD and RCA were significantly higher in group 2 (Includes obstructive PCAD patients) compared to group 1 (Includes non-PCAD and non-obstructive PCAD

patients,  $P > 0.05$ ).

Frequency of cardiovascular risk factors in the study groups are shown in Figure 1. The most prevalent risk factors in group 2 were family history of CAD (73%), hypertension (52%), and overweight/obesity (50%). Prevalence of all risk factors except dyslipidemia were higher in obstructive PCAD patients compared to non-obstructive and non-PCAD patients; however, this difference was not statistically significant ( $P > 0.05$ ).

There was no significant difference between the daily consumption of grains, eggs, fish, red meat, chicken, snacks, sweets, sugars, vegetables, soft drinks, animal fats, and vegetable oils between study groups ( $P > 0.05$ ) (Table 3). Daily consumption of hydrogenated fats ( $P = 0.008$ ) and milk ( $P < 0.001$ ) were significantly higher in the group 2 compared to group 1, while daily consumption of fruits ( $P = 0.039$ ) was significantly higher in group 1 compared to group 2 (Table 3).

Table 1. Baseline characteristics of the study population.

Variables	Total (N=65)	Group 1 (N=13)	Group 2 (N=52)	P-value <sup>a</sup>
Age (years)	$51.05 \pm 7.60^b$	$49.77 \pm 7.30$	$51.37 \pm 7.70$	0.50
Weight (kg)	$70.67 \pm 11.90$	$66.09 \pm 13.20$	$71.80 \pm 11.40$	0.15
Height (cm)	$167.01 \pm 9.50$	$162.00 \pm 13.70$	$168.20 \pm 7.90$	0.17
Body mass index ( $\text{kg/m}^2$ )	$25.40 \pm 4.20$	$25.29 \pm 4.90$	$25.42 \pm 4.10$	0.92
Physical activity (Baecke score)	$6.34 \pm 1.10$	$6.51 \pm 1.40$	$6.30 \pm 1.00$	0.55
Education level				
<High school	45 (69.2) <sup>c</sup>	6 (13.3)	39 (86.7)	0.09
High school or vocational	16 (24.6)	5 (31.3)	11 (68.8)	
College <	4 (6.2)	2 (50.0)	2 (50.0)	
Sex				
Men	36 (55.4)	5 (13.9)	31 (86.1)	0.17
Women	29 (44.6)	8 (27.6)	21 (72.4)	

<sup>a</sup>: Chi-square test; <sup>b</sup>: Mean  $\pm$  SD; <sup>c</sup>: n (%); PCAD: premature coronary artery disease; Group 1: includes non-PCAD and non-obstructive PCAD patients; Group 2: includes obstructive PCAD patients.

Table 2. Angiographic characteristics of the study population.

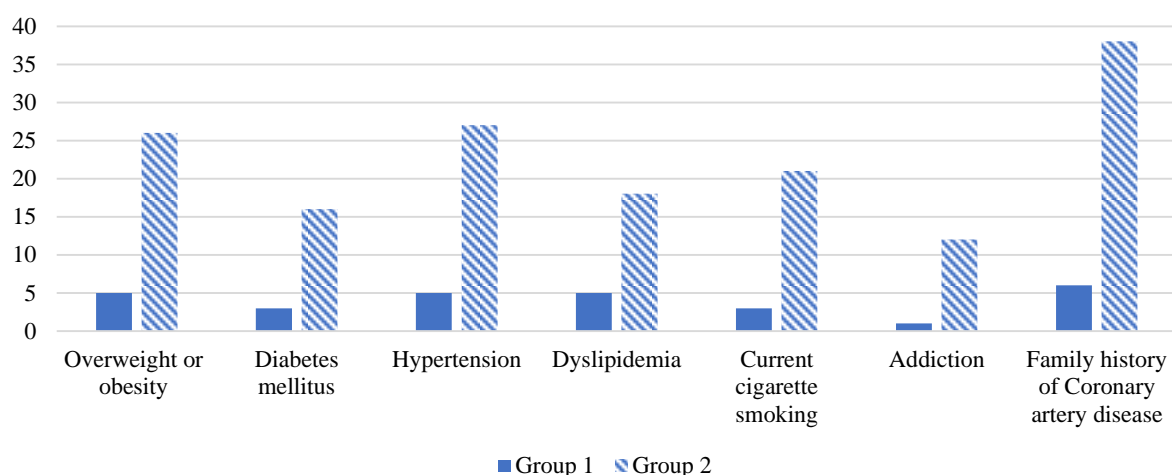
Variables	Total (N=65)	Group 1 (N=13)	Group 2(N=52)	P-value <sup>a</sup>
Involved coronary arteries				
Left anterior descending artery	45 (69.2) <sup>b</sup>	1 (7.7)	44 (84.6)	<0.001
Left circumflex artery	10 (15.4)	1 (7.7)	9 (17.3)	0.390
Right coronary artery	29 (44.6)	1 (7.7)	28 (53.8)	0.003
Major coronary arteries involved				
Single vessel disease	22 (33.8)	2 (15.4)	20 (38.5)	<0.001
Two-vessel disease	25 (38.5)	1 (7.7)	24 (46.2)	<0.001
Three-vessel disease	8 (12.3)	0 (0.0)	8 (15.4)	<0.001*

<sup>a</sup>: Chi-square test; <sup>b</sup>; <sup>c</sup>: n (%); PCAD: premature coronary artery disease; Group 1: includes non-PCAD and non-obstructive PCAD patients; Group 2: includes obstructive PCAD patients.

Table 3. Comparison of daily consumption of food groups between study groups.

Food groups (g/day)	Food items	Group 1 (N=13)	Group 2 (N=52)	P-value <sup>a</sup>
Whole grains	Dark breads (Iranian), barley bread, popcorn, cornflakes, wheat germ, bulgur	31.75 ± 41.90 <sup>b</sup>	23.30 ± 40.70	0.77
Refined grains	White breads, noodles, pasta, rice, toasted bread, milled barley, sweet bread, white flour, starch, biscuits	300.60 ± 141.40	307.42 ± 148	0.91
Milk	High-fat, low-fat and flavored milk	33.78 ± 74.10	119.01 ± 131.91	<0.001
Legumes	Beans, peas, lima beans, broad beans, lentils, soy	15.95 ± 20.90	13.97 ± 28.44	0.53
Fruit	Fruit	666.93 ± 104.10	205.55 ± 566.25	0.03
Vegetable	Vegetable	256.87 ± 264.80	203.94 ± 237.50	0.67
Red meats and organ meats	Beef, Lamb meat, Camel meat, organ meat	15.31 ± 14.20	6.81 ± 5.50	0.09
Poultry	Chicken and Ostrich meat	12.44 ± 12.50	7.40 ± 4.60	0.27
Fish	Canned tuna fish, other fish	13.11 ± 8.90	11.26 ± 7.50	0.47
Processed meats	Sausages	1.12 ± 1.70	2.90 ± 4.70	0.22
Egg	Egg	14.76 ± 11.90	23.63 ± 53.66	0.81
Animal fats	Animal fats And Butter	0.67 ± 1.90	4.50 ± 11.80	0.25
Hydrogenated fats	Hydrogenated fats, and Margarine	1.65 ± 5.00	13.50 ± 27.00	0.008
Vegetable oils	Sesame oil, olive oil, canola oil and corn oil	16.51 ± 14.90	11.76 ± 11.80	0.13
Nuts	Peanuts, almonds, pistachios, hazelnuts, roasted seeds, walnuts	18.87 ± 19.70	10.20 ± 19.50	0.13
Sweets	Sugars, desserts candies, Jam, jelly, honey, biscuits, Candy, Cake, Iranian sweets	44.96 ± 43.30	62.57 ± 129.90	0.70
Soft drinks	Soft drinks	10.04 ± 10.20	57.90 ± 90.10	0.22
Salt	Salt	16.31 ± 9.30	16.20 ± 6.40	0.67
Tea	Black and green tea	647.61 ± 489.50	436.68 ± 397.30	0.88
Coffee	Coffee	45.27 ± 126.10	26.55 ± 57.08	0.67

<sup>a</sup>: Mann-Whitney test; <sup>b</sup>: Mean ± SD; PCAD: premature coronary artery disease; Group 1: includes non-PCAD and non-obstructive PCAD patients; Group 2: includes obstructive PCAD patients.



**Figure 1.** Cardiovascular risk factors of the study population

Values are presented as the number; Group 1 includes non-PCAD and non-obstructive PCAD patients; Group 2 includes obstructive PCAD patients.

## Discussion

This study aims to evaluate the cardiovascular-related risk factors and dietary patterns in PCAD patients. To the best of the authors' knowledge, this is the first study to investigate dietary patterns as well as cardiovascular risk factors in PCAD patients in Iran.

Although previous epidemiologic studies have identified the important risk factors for PCAD, most of these risk factors were not specific to young adults and it was difficult to differentiate between PCAD and CAD risk factors. Nonetheless, some risk factors, including cigarette smoking, cocaine abuse, and diabetes appear to be more specific for PCAD (Cole and Sperling, 2004).

According to the findings of this cross-sectional study, the most common risk factor among PCAD patients was positive family history for CAD, followed by hypertension, overweight/obesity, current cigarette smoking, dyslipidemia, diabetes mellitus, and addiction. This finding was similar to the findings of Framingham studies, that reported family history of CAD as an independent risk factor for PCAD (Myers *et al.*, 1990). Similarly, in a study by Poorzand *et al.*, which compared the risk factors for PCAD and late-onset CAD in an Iranian population, it was reported that family

history of CAD and smoking were the most prevalent risk factors in PCAD patients. However, hypertension and diabetes mellitus were not prevalent (Poorzand *et al.*, 2019). Also, in another study by Che *et al.* in China, family history of PCAD was the most common risk factor in PCAD among other conventional risk factors (Che *et al.*, 2013).

In addition to a family history of CAD, hypertension and obesity were other common risk factors of PCAD in the current study. Aggarwal *et al.* revealed that the prevalence of hypertension was higher in young patients with CAD compared to healthy individuals (Aggarwal *et al.*, 2016). Several previous studies have shown obesity as an independent risk factor for coronary atherosclerosis and PCAD (Marcial and Altieri, 2015, Shah *et al.*, 2016, Wilson *et al.*, 2002).

Moreover, the findings of the current study revealed that daily consumption of hydrogenated fats and milk, as the sources of saturated fatty acids (SFAs) and trans-fatty acids (TFAs), were significantly higher in obstructive PCAD patients compared to non-obstructive or non-PCAD patients.

Several studies evaluating the association between fat intake and cardiovascular diseases (CVD), reported controversial findings (Berger *et*

al., 2015, Mcgee et al., 1984, Nettleton et al., 2017, Posner et al., 1991). For decades, a high intake of SFAs was thought to undermine heart health. It has been demonstrated that dietary cholesterol and saturated fats increase serum total and LDL-c (Steinberg, 2005). The oxidized LDL particles are scavenged by macrophages around the heart which leads to atherosclerosis and CAD (Libby, 2000). However, some recent studies (De Souza et al., 2015, Siri-Tarino et al., 2010) demonstrated that consumption of SFAs was not associated with coronary heart disease (CHD), stroke mortality, and MI. Interestingly, some randomized clinical trials suggest that high consumption of SFAs is associated with decreased small-dense LDL and increased large buoyant LDL, which are protective against CHD (Campos et al., 2001, Dreon et al., 1998, Mora et al., 2007). Nonetheless, it is proven that replacing SFAs with polyunsaturated fatty acids (PUFA) may be associated with a lower risk of CAD compared to high consumption of SFAs (Hooper et al., 2020, Jakobsen et al., 2009).

Moreover, according to the epidemiological studies, there is a positive association between TFAs intake and LDL-c levels (Benesch et al., 2014, Vineis and Wild, 2014). Therefore, dietary sources of TFA, such as hydrogenated fats have potential effects on CAD (Ahmed et al., 2018).

The results of the study by Amani et al. showed that high intake of hydrogenated fats was related to increased risk of CAD in Iranian population, which is in line with the findings of the present study (Amani et al., 2010).

In regard to milk, although in the present study consumption of milk was higher in obstructive PCAD patients compared to non-obstructive or non-PCAD patients, many recent studies have reported that whole milk intake was not associated with higher risk of CVD (Avalos et al., 2013, Dehghan et al., 2018, Soedamah-Muthu et al., 2011). In a recent study by Ghosh et al. higher intake of whole milk was related to decreased coronary artery calcification progression (Ghosh et al., 2020). It seems that the effects of milk on CVD might not originate from the traditional risk factors

like cholesterol; therefore, various components of lipid in milk should be considered.

Another important finding of the current study was the higher intake of fruits in non-obstructive and non-PCAD patients compared to obstructive PCAD patients. The initial observational studies have shown that vegetable and fruit consumption have a protective effect against CVD. However, results from randomized controlled trials do not conclusively approve this theory (Abbasalizad Farhangi et al., 2016, Alissa and Ferns, 2017). Fruits and vegetables contain large amounts of fiber, fat- and water-soluble vitamins, sterols, and phytochemicals, so they play a role in preventing CVD and reducing the risk of chronic diseases and premature mortality through various mechanisms (Tuso et al., 2015). The protective mechanisms of fruit and vegetables may include improving lipid profile, and insulin sensitivity, reducing blood pressure, and oxidative stress (Grosso et al., 2017, Tuso et al., 2015). A meta-analysis of prospective studies reported an inverse association between the intake of fruits and vegetables, and the risk of CAD and CVD (Aune, 2019). However, the epidemiological evidence for causality is inconclusive and controversial (Alissa and Ferns, 2017, Wang et al., 2014). Therefore, further research on this issue seems necessary.

Although no significant difference was found in case of vegetables, vegetable consumption was higher in non-obstructive PCAD and non-PCAD patients compared to PCAD patients, which confirmed the findings of previous studies.

This study was one of the few studies that assessed nutritional intake in PCAD patients and was the first study in Iran. However, the current study had some limitations. First, it was a cross-sectional study, which made it difficult to assign a causal relationship between PCAD and dietary patterns and cardiovascular risk factors. Second, this study was a single-center experience with a small sample size that could result in a referral bias. Third, due to the small sample size, it was not possible to determine the dietary pattern of the study population; therefore, the daily consumption of food groups was compared between groups.

Nevertheless, in this study, which is the first study on the dietary pattern of PCAD patients in Iran, possible cardiovascular and dietary risk factors of PCAD were identified.

### Conclusion

According to the results of this study, family history of CAD, hypertension, and obesity are the most common risk factors for obstructive PCAD patients. Moreover, the findings suggest that high consumption of milk and hydrogenated fats as sources of saturated and Trans-fatty acids may be associated with increased risk of PCAD. However, daily consumption of fruits, as a rich source of fiber and antioxidants, maybe related to a lower risk of PCAD. Further studies with a larger sample size are needed to determine the dietary pattern of PCAD patients.

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### Conflict of interest

The authors declare that they have no competing interests to report.

### Authors 'contributions

Norouzian Ostad A, Razmpour F, Dehnavi Z, and Farshidi H equally contributed to the conception and design of the research; Norouzian Ostad A contributed to the acquisition, analysis, and interpretation of the data; Ezati Rad R, Behrooj S and Razmpour F was responsible for patient recruitment and follow-up, Dehnavi Z and Norouzian Ostad A contributed to the analysis of the data; Aghamolaei T, and Madani A responsible for data acquisition and critical revision of the manuscript; Norouzian Ostad A, Dehnavi Z, and Jafarzadeh Esfahani A drafted the manuscript and critically revised the manuscript. All authors agree to be fully accountable for ensuring the integrity and accuracy of the work and read and approved the final manuscript.

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