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A cross- sectional study on the association between lifestyle factors and coronary artery stenosis severity among adults living in central Iran: A protocol for the Iranian- CARDIO study

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Original Article

Abstract

BACKGROUND: Although several studies have attempted to identify coronary artery disease (CAD) risk factors, few have explored the association between lifestyle-related factors and the severity of coronary artery stenosis. The present study was designed to assess the association between a combination of lifestyle, dietary, cardiometabolic, psychological, and mental factors, and CAD severity in adults undergoing angiography.

METHODS: This cross-sectional study aimed to recruit a total of 700 patients (aged 35 to 75 years) who met the inclusion criteria and were referred for angiography between July 2020 and November 2021 to Afshar Hospital, a central heart disease hospital in Yazd city, Iran. To assess the presence and intensity of CAD, we used the Gensini and SYNTAX scores. Biochemical factors were measured using standard kits from serum samples, and extra serum and whole blood samples were retained for further analyses. Data on general information, dietary food and supplement intake, eating habits, medicinal herbs consumption, psychological and mental state, sleep quality, and other variables were gathered by trained interviewers using specific questionnaires.

RESULTS: In total, 720 participants (444 males and 276 females) aged 56.57±9.78 years were included in the current study. Moderate to severe coronary artery stenosis was prevalent in 47.0% and 17.9% of participants based on Gensini and SYNTAX scores, respectively.

CONCLUSION: The results of this study will enhance our understanding of the association between different risk factors and the severity of coronary artery stenosis.

Keywords: Life style; Risk factors; Coronary artery stenosis; Cardiovascular Diseases; Cross-Sectional studies

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Introduction

Despite advances in diagnostic and therapeutic methods, cardiovascular disease remains the leading cause of mortality and disability worldwide[1, 2]. Ischemic heart disease (IHD), also known as coronary artery disease (CAD) and atherosclerotic cardiovascular disease (ACD), accounts for approximately 9 million deaths. The current incidence rate of 1,655 in a population of 100,000 is projected to exceed 1,845 by 2030[3]. The economic impact of CAD is significant [4]; for instance, in 2004, CAD resulted in more than 44 billion US dollars in inpatient hospital charges in the United States[5]. Although gender, age, and modifiable risk factors such as unhealthy diet, obesity, smoking, dyslipidemia, diabetes, and hypertension are known to contribute to CAD occurrence[6-11], data on CAD severity risk factors are still lacking. Research indicates that the Gensini and SYNTAX scores are the preferred scoring systems to measure the intensity of coronary artery occlusion, as both primarily assess anatomic and angiographic findings. Moreover, these scores have prognostic value for cardiovascular events, including myocardial infarction (MI) and cardiac death among CAD patients[12, 13].

Recently, studies have been conducted on the association between various cardiovascular risk factors and the severity of coronary artery occlusion predicted by these scores. For instance, several investigations have reported that serum low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels are potent predictors of CAD severity[14-16]. There was also a positive correlation between fasting blood glucose (FBS) and Gensini score among MI patients[17]. Furthermore, a higher Gensini score has been observed in pre-diabetic and diabetic patients than in normoglycemic patients[18]. Obesity is also proposed to be associated with the disease. Although obesity has been known as an independent risk factor for CAD for many years, a better prognosis for CAD has been observed in individuals with a higher body mass index (BMI)[19-21].

Previous investigations have also examined the association between psychological disorders and CAD severity; however, they have led to inconsistent results. Some studies, but not all, have indicated a notable positive association between CAD severity and depression, anxiety, and perceived stress[22, 23]. On the other hand, Assari et al.[24] discovered a negative association between anxiety symptoms and CAD severity; however, results from Salari et al.'s study showed no significant association between depression symptoms and the number of impaired vessels[25].

Although the role of diet as a modifiable risk factor for the prevention of CAD has been extensively investigated[26, 27], there are limited studies examining the association between whole diet expressed as dietary patterns and the severity of coronary artery stenosis[28, 29]. Dietary patterns were introduced as a new approach to examining the association between diet and chronic disease because the effects of combining foods or their components in the context of dietary patterns might be greater than the effects of individual foods or nutrients, as dietary patterns express the interactions of nutrients comprehensively[30-34]. Also, as far as we know, none of the previous studies have evaluated the association between dietary habits and consumption of herbal medicines with CAD severity in an observational study.

On the other hand, each of the CAD risk factors alone might have limited ability to predict CAD development[35], whereas the coexistence of several CAD risk factors such as diabetes, dyslipidemia, hypertension, and current smoking increases their effect on the risk of developing CAD [36]. A few studies have been conducted regarding the association between the coexisting CAD risk factors and CAD severity. For example, it was shown that concurrent diabetes and hypertension increase the risk of CAD more than these factors alone [37]. This suggests that studying the combination of risk factors might provide more information than examining the univariate association with the severity of CAD[38]. Therefore, the need for a comprehensive study that can simultaneously investigate the association between different modifiable and non-modifiable risk factors and CAD severity was felt. This protocol describes the details of a cross-sectional study which aimed to gather data on age, sex, education, occupation, economic status, physical activity, tobacco and alcohol use, cardiometabolic markers, anthropometric indices, patients' disease history, depression, anxiety, mental state, sleep quality, dietary food, nutrients, and supplements intake, dietary food habits, herbs consumption, and CAD severity (assessed by using Gensini and SYNTAX scores) among adults undergoing coronary angiography.

Methods

Study objectives and design

Our study, the Iranian Coronary Artery Disease Observation (Iranian CARDIO), aims to examine the prevalence of specific risk factors and their association with the severity of CAD using a cross-sectional approach

Study setting

The study was conducted at Afshar Referral Heart Hospital in Yazd, Iran, which is a referral hospital for cardiovascular diseases in Yazd city, Yazd province, central Iran. Data gathering was initiated in July 2020 and continued until November 2021. The Ethics Committee of the National Institute for Medical Research and Development granted primary approval on December 7, 2019, with the code IR.NIMAD. REC.1398.393, and the Shahid Sadoughi University of Medical Sciences Review Board granted approval with the code IR.SSU. SPH. REC.1399.092 on July 13, 2020. Written informed consent will also be obtained from all participants

Study population

In this study, adults aged 35 to 75 years, whose physicians suspected coronary artery occlusion based on symptoms such as angina pectoris and abnormalities in one or more signs such as electrocardiogram (EKG) records, exercise test, blood test, CT angiography, or nuclear heart scan, were selected using convenience sampling. These individuals were recommended to Afshar Heart Hospital for coronary angiography for the first time.

Persons with a history of cancer, chronic heart failure, heart attack, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), stage 3 or above of chronic kidney disease, decompensated liver disease, neurocognitive or psychiatric conditions, immunodeficiency or autoimmune deficiency syndrome (AIDS) were excluded. Persons with excessive obesity (BMI > 40 kg/m^2), any restrictions in receiving an oral diet or being on a special diet, as well as pregnant or lactating women, were also excluded.

After confirming the conditions for entering the study, written informed consent was obtained from the eligible individuals. A convenience sampling method was used: the selection of participants depended on the availability of people at the hospital at the time when the interviews were being conducted.

Determination the CAD severity

The angiography was performed using a Siemens Axiom Artis angiogram from Germany. The severity of CAD was assessed by two scoring systems: the Gensini and SYNTAX scores. For this purpose, the coronary angiography was evaluated by an experienced cardiologist who was blinded to all collected data except for age and sex. To ensure accuracy, a second cardiologist randomly evaluated the Gensini and SYNTAX scores for several participants as a confirmation of the initial interpretation.

Gensini score: In order to calculate the gender score for 1 to 25% occlusion, score 1 for 26 to 50% occlusion, score 2 for 51 to 75% occlusion, score 4 for 76 to 90 % occlusion, score 8 for 91 to 99% occlusion, score 16 and for complete occlusion score 32 were considered. Also, a coefficient was assigned to each segment depending on the functional significance of the area supplied by that segment: 5 for the left main coronary artery, 2.5 for the proximal segment of the left anterior descending (LAD) coronary artery and the proximal segment of the circumflex artery, 1.5 for the mid-segment of the LAD, 0.5 for second diagonal branch and posterolateral branch, and 1 for the other branches. The final Gensini score was obtained from the total score of all segments. A Gensini score of 20 or more was categorized as moderate to severe occlusion[39-41].

SYNTAX Score

Version 2 of the internet-based SYNTAX calculator was used to calculate the SYNTAX score. The SYNTAX score raises questions about the functional and anatomical domains of lesions with more than 50% stenosis and 1.5 mm in diameter. To determine the final SYNTAX score, we added up the scores of all lesions. Scores 0-22 reflect no/mild occlusion, 23-32 reflect moderate occlusion, and scores greater than 32 reflect severe occlusion, respectively[13, 42].

Blood sampling

Five ml of venous blood was collected from all participants after overnight fasting and equally transferred to two separate EDTA blood tubes. Then,

the samples were transported to the biochemistry laboratory of the School of Public Health, Shahid Sadoughi University of Medical Sciences, using an insulated shipping container containing dry ice. One of the two blood samples taken from participants was centrifuged at 2500 rpm for 3 minutes to separate the serum from blood cells. The measurements of serum triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and fasting blood sugar (FBS) were carried out using standard detection kits (Pars Azmoon, Iran). Additionally, alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea, and creatinine were measured in the serum using a BiorexFars kit (BiorexFars, Fars, Iran). The other blood sample was homogenized and then stored in two DNase/RNase-free microtubes at -70 ºC for future purposes.

Anthropometric and blood pressure measurement

Height measurements (in meters) were accurately taken using a wall height gauge with a precision of 0.1 cm. Weight (kg) and body composition (% fat mass, % skeletal muscle, and visceral fat %) were assessed with a bioelectrical impedance analyzer, without shoes, and with minimal clothing (mode BF51, Omron, Japan). The body mass index (BMI) of patients was calculated by dividing weight in kilograms by the square of height in meters. Waist circumference was measured at the midpoint between the lower rib edge and the iliac crest using a tape measure. All anthropometric measurements were performed by trained nutritionists.

Before participants underwent coronary angiography, their blood pressure was recorded by a nurse working in the cardiovascular care unit (CCU). Measurements were taken using the right hand of subjects who were completely at rest and lying on their backs using a pressure gauge (NIBP version 3, Sazgan Gostar, Iran) connected to the bedside monitor (Vectra, Sazgan Gostar, Iran). The systolic and diastolic blood pressure displayed on the monitor was registered.

Physical activity assessment

The level of physical activity in patients was measured using the short version of the International Physical Activity Questionnaire (IPAQ), which has been validated in the Iranian population[43]. The data collected for activity were then converted to metabolic equivalents per minute per day (Met-min/week)[44].

Dietary intake assessment

To evaluate the dietary intakes of participants, a valid and reliable 182-item semi-quantitative multiple-choice food frequency questionnaire (FFQ) was used, which covered the past year[45]. This study modified the 178-item FFQ, which was previously validated to assess the dietary intake of adults living in Yazd, Iran[45]. Participants were required to indicate how frequently they consumed each item over the past year on a 10-point scale ranging from never to ten or more times per day. The recorded frequencies of each item were then converted to the number of times it was consumed per day. The recorded intake was then converted to grams per day by multiplying the recorded intake by the predefined standard portion size.

Moreover, data regarding supplement intake (including calcium, vitamin D, folic acid, iron, fish oil (or omega-3), vitamin C, vitamin E, and multivitamin-mineral) was obtained using a separate multiple-choice questionnaire. All data on dietary and supplement intake were collected by expert nutritionists.

Dietary habits

Based on earlier studies, dietary habits were assessed using 42 multiple-choice questions regarding meal patterns (9 questions), eating rate (3 questions), intra-meal fluid intake (3 questions), meal-to-sleep interval (3 questions), fatty food intake (6 questions), difficulty in chewing and digestive problems (2 questions), oral and dental problems (7 questions), amount and type of water consumed (2 questions), type of juice consumed (1 question), amount of sweets consumed with a cup of tea (1 question), usual soy intake (1 question), the spices consumed (2 questions), the type of dairy consumed (1 question), and adding salt to food when eating (1 question).

Regarding meal patterns, participants were asked about their typical meal frequency (including major meals and snacks) per day, how often they consume meals, how many times they have main meals (breakfast, lunch, and dinner) daily, and the difference in the amount of food received on holidays compared to weekdays.

We asked participants about their chewing and eating times, their fluid intake, and the time between the end of a meal and bedtime. Participants reported their weekly consumption of fried foods and fatty meats and the type of oil used for frying. They also reported the level of fat in their primary meals as low-fat, moderate-fat, or high-fat, as well as the rate of trimming visible fat from meat and removing skin from chicken.

Assessment of medicinal herbs consumption

Dietary herb intake was evaluated using a researcher-made questionnaire that asked about the frequency of use for 39 widely used herbs in Iran. Participants were asked about their herb consumption frequency over the last year using an 8-point scale, ranging from never to five or more times per day on average. Data on the consumption of the following herbs were gathered: *Cinnamon, Cuminum Cyminum, Carum Carvi L, Zataria multiflora, Mentha, Mentha pulegium L, Ginger (Zingiber officinale), Foeniculum vulgare, Saffron (Crocus sativus L), Rosa damascene, Echium amoenum, Descurainia Sophia, Basil seeds (Ocimum basilicum L seeds), Licorice (Glycyrrhiza glabra), Green Tea, Stachys lavandulifolia, Ziziphus jujuba, Matricaria chamomilla, Achillea millefolium, Alhagi maurorum, Citrus aurantium, Chicory (Cichorium intybus L.), Salix aegyptiaca, Salix, Fumaria officinalis, Lavandula angustifolia, Balangu (Lallemantia royleana), Plantago major, Fumaria officinalis, Alcea rosea, Dill (Anethum graveolens L), Berberis vulgaris, Sumac (Rhus Coriaria), Nigella Sativa, Cardamom, Heracleum persicum, pepper, Clove (Syzygium aromaticum), Garlic (Allium Sativum), and Turmeric (Curcuma longa L.).*

Psychological assessment

Depression

Two questionnaires, the Persian version of the Beck Depression Inventory II (BDI-II) and the Patient Health Questionnaire-9 (PHQ-9), whose validity and reliability have been confirmed in coronary heart disease patients, were employed to evaluate the severity of depression and its symptoms [46, 47]. The BDI-II questionnaire comprises 21 items that are graded on a 4-point Likert scale from 0 to 3. Based on their total scores, the participants were divided into four groups: minimal depression (0-13), mild depression (14-19), moderate depression (20-28), and severe depression (29-63). The PHQ-9 questionnaire was also used to assess depression symptoms on a 4-point Likert scale from 0 to 3. Higher scores indicate a higher level of depression symptoms. Scores of 0-4 reflect no depression, while scores of 5-9, 10-14, 15-19, and 20-27 reflect mild, moderate, moderately severe, and severe depression, respectively.

Anxiety

Anxiety symptoms were assessed using the Beck Anxiety Inventory (BAI) over the two weeks prior to the patient's admission. The BAI contains 21 items, with each item scoring between 0 and 3. A higher score indicates greater anxiety intensity. BAI scores were categorized as minimal anxiety (0-7), mild anxiety (8-15), moderate anxiety (16-25), and severe anxiety (26-63). Furthermore, the Generalized Anxiety Disorder (GAD-7), a 7-item questionnaire, was used to assess how often individuals have been affected by anxiety symptoms in the last two weeks. Each item's score ranged from 0 (not at all) to 3 (nearly every day). Participants were categorized into four groups based on the following criteria: none/mild anxiety (0-9) and moderate/severe anxiety (≥ 10). It has been confirmed that both questionnaires are valid and reliable for use in the Iranian population[48].

Sleep quality assessment

The sleep quality of participants in the last month was assessed by the Persian version of the Pittsburgh Sleep Quality Index (PSQI) questionnaire. It contains 19 questions across seven domains: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disorders, use of sleep medication, and diurnal dysfunction. Each domain is scored between 0 and 3 points. A total PSQI score of ≥ 5 indicates poor sleep quality. The validity and reliability of the Persian version of the PSQI questionnaire have been previously confirmed in the Iranian population[49].

Cognitive function

The Mini-Mental State Examination (MMSE) questionnaire, which has acceptable validity and reliability, was employed to measure cognitive function[50]. The MMSE questionnaire examines various cognitive functions, including concentration, memory, language and comprehension, orientation, and the ability to copy a figure. The total score of this questionnaire ranges from 1 to 3, with a higher score indicating better cognitive performance.

Data collection on other variables

Data on age, gender, marital status (single/married/widowed), family size, and smoking status were collected. The smoking status included details such as whether the participant had ever smoked a cigarette, when they first smoked, how often they smoked cigarettes, the number of cigarettes smoked per day, if the participant had stopped smoking and for how long, the participant's exposure to cigarette smoke and its duration, and history of smoking naswar, hookah, and pipe. Information on alcohol use, including whether or not a participant had drunk alcohol and how often, was also collected.

In addition, data on drug addiction, including the history of drug use, how often they used the drug, and the type of drug, were gathered. The history of the participant's and their family's chronic diseases (diabetes, hypertension, dyslipidemia, fatty liver, hepatitis, gallstone, cancer, kidney failure, kidney stone, heart failure, blood clotting disease, hypo/hyperthyroidism, multiple sclerosis, lupus, psychiatric disorders, Alzheimer's, osteoporosis and arthritis, chronic pulmonary disease), and history of surgery were also collected using a questionnaire.

Furthermore, participants' education level, occupational status, ethnicity, home-ownership, the house type, its location, the number of rooms in the house, the number of cars, the type of car, the number of computers and laptops in the house, and whether they had a dishwasher at home were recorded. Information about menstrual status and pregnancy were also collected for female participants. All questionnaire-based data were gathered in an interview with trained researchers.

Sample size calculation and statistical analysis

Regarding a 5% significance level and at least 80% power, and according to the mean difference for adherence to dietary patterns between individuals with a SYNTAX score higher than the median [standard deviation (SD) = 2.6] and participants with a SYNTAX score lower than the median (SD = 2.84) [28], at least 288 participants were needed [51]. The formula below was utilized to determine the sample size:

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2 / \kappa)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

To calculate the value of Δ, as difference in group means, the following variables need to be known: n1 (the sample size of Group 1), n2 (the sample size of Group 2), σ1 (the standard deviation of Group 1), σ2 (the standard deviation of Group 2), and K (the ratio of n1 to n2). $Z_{1-\alpha/2}$ is two-sided Z value (for instance1.96 for 95% confidence interval) and $Z_{1-\beta}$ is power.

Given that we had access to a sufficient number of participants, and that several factors other than diet were going to be assessed, we aimed to recruit 700 participants to allow for a high dropout rate.

To assess the normal distribution of continuous variables, we used a histogram and a Kolmogorov-Smirnov test. We compared continuous and categorical variables between males and females using the independent-samples t-test and the chi-square test, respectively. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, version 15.0 for Windows, 2006, SPSS, Inc, Chicago, IL). Results were considered statistically significant if the p-value was less than 0.05.

Results

In total, 720 participants (444 males and 276 females) aged 56.57±9.78 years were included in the current study. Detailed information about the participants' characteristics is presented in Table 1. The analyses revealed that male participants were significantly younger than females. Furthermore, they had higher weight, BMI, skeletal mass, and visceral fat percentages, as well as more physical activity and a lower total body fat percentage compared to females (P<0.05). Hypertension, dyslipidemia, and type 2 diabetes were reported more by females compared with males (P<0.05); however, moderate to severe coronary artery occlusion was higher in male participants (P<0.01), as shown in Table 1.

Discussion

Coronary artery disease (CAD) is a significant contributor to mortality and incurs substantial costs during hospitalization. The most costly hospital expenses are associated with patients undergoing percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) for CAD[2, 4, 52]. Decreasing the severity of CAD could reduce cardiac adverse events and CAD hospitalization.

Table 1. shows characteristics of the Iranian Cardio Study participants[1]

Variable	Men (n=444)	Women (n=276)	Total (n=720)	P-value
Age (mean ± SD)	55. 95 ± 9. 88	57. 56 ± 9. 56	56.57±9.78	0. 04[a]
Weight (mean ± SD)	76. 97 ± 12.90	69. 49 ± 11. 27	74.04±12.81	< 0. 001[a]
BMI (mean ± SD))	26. 60 ± 3. 92	28.98 ± 4.56	27.53±4.33	< 0. 001[a]
Waist circumference (mean ± SD)	99. 49 ± 12.01	100.69 ± 12. 83	99.96±12.34	0. 23[a]
Fat mass percentage (mean ± SD)	25.78 ± 7. 19	42. 54 ± 7. 79	32.25±11.04	< 0. 001[a]
Skeletal muscle mass percentage (mean ± SD)	33.90 ± 10.61	24. 55 ± 5.87	30.29±10.16	< 0. 001[a]
Visceral fat percentage (mean ± SD)	11. 73 ± 6.12	9.97 ± 2.93	11.05±5.19	< 0. 001[a]
Physical activity (Met-min/week)	5312.31±8373.92	2360.52±4486.07	4187.35±7284.96	< 0. 001[a]
Current cigarette smoking	48.9	5.1	32.1	< 0. 001[b]
History of Hypertension (%)	40. 5	60. 8	48.3	< 0. 001[b]
History of Dyslipidemia (%)	36.7	56. 3	44.2	< 0. 001[b]
History of Diabetes type 1 (%)	3. 2	3. 4	3.3	0. 54 [b]
History of Diabetes type 2 (%)	26.5	40.3	31.8	<0. 001[b]
Moderate to sever CAD assessed based on gensini score (%)	58.8	28. 2	47.0	< 0. 001[b]
Moderate to sever CAD assessed based on SYNTAX score (%)	24. 3	7.8	17.9	,0. 001[b]

[1] Data was presented in the format of mean ± (SD).otherwise explained.
[a]T-test; [b]Chi-square test

Although several studies have investigated the association between CAD severity and lipid profile[53], serum glucose level[54], and anthropometric indices[55], research on the association between other risk factors, including blood pressure[56] and psychological disorders[57]), and CAD severity has not been conclusive. The association between dietary patterns and CAD severity, assessed using a standard scoring system, is also understudied[28]. On the other hand, despite the widespread use of herbs and the existence of unique dietary habits in Asian countries such as Iran, no research has been conducted to date on the association between the use of medicinal herbs and dietary habits with CAD severity in the context of an observational study.

In addition, the data gathered in this study can be used to evaluate the interaction between lifestyle factors such as smoking, diet, physical activity, and mental status, and elements of metabolic syndrome and severity of CAD. CAD risk factors tend to cluster in individuals[35]. For instance, it has been shown that approximately two-thirds of diabetic patients have simultaneous hypertension[58, 59]. Also, the loss of skeletal muscle mass and obesity exacerbate cardiometabolic risk factors such as hyperglycemia, hypertension, insulin resistance, and dyslipidemia compared with sarcopenia or obesity alone[60].

Although the simultaneous presence of two or more coronary heart disease risk factors compared to each alone could increase their effects on developing CAD, there have been few studies exploring the association between various CAD risk factors and the extent of occlusion in the coronary arteries [37]. Also, the extra blood samples collected from all the participants will enable further investigation of gene-gene, gene-diet, and gene-other environmental and lifestyle factors interaction in the future.

By following participants, investigators can also evaluate the association between different CAD risk factors and major adverse cardiac events such as myocardial infarction (MI) and deaths from CAD, as well as any recurrent PCI or CABG due to restenosis. Furthermore, the present study can serve as a basis for designing clinical trial studies to investigate the cause-and-effect association between the risk factors and the severity of coronary artery disease.

Strengths and limitations

The present study is one of the few studies regarding the association between several CAD risk factors and the severity of coronary artery stenosis in the Middle East. Also, to our knowledge, this is the first study attempting to investigate the association between dietary habits and herbal medicine consumption and CAD severity. Afshar Hospital is a central hospital for heart diseases, to which patients from the Yazd

province are referred for angiography. Hence, the findings of this research can be applied to the general Iranian population living in central Iran. In addition, two standard scoring systems were used to measure the severity of coronary artery occlusion.

It's important to take into account several limitations when interpreting the results of the study. Due to the cross-sectional design of the present study, it is not possible to conclude the causality relationships between the severity of coronary artery stenosis and the risk factors. Although we have tried to gather data to control for several potential confounders, the effect of unknown or unmeasured confounders cannot be excluded. It should be noted that the questionnaires used for the assessment of dietary habits and medicinal herb consumption are not validated yet. We will try to assess their face validity and their reliability in future investigations. Furthermore, despite using validated questionnaires, it is inevitable to incur some level of measurement error and misclassification.

Conclusion

In summary, the present cross-sectional research may provide a valuable opportunity to evaluate the association between a combination of CAD risk factors and CAD severity. The findings will be beneficial for researchers and decision-makers to identify and develop preventive and treatment strategies for individuals at risk or with CAD.

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Conflict of Interest

The authors declare that they have no personal or financial conflicts of interest. The corresponding author asserts that he has full access to the data generated from this project.

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Author's Contributions

ASA conceived the study. ASA, SB, and MM designed the study protocol. ASA and MT wrote the first draft of the manuscript. All authors critically reviewed the manuscript and approved the final version. All authors agreed to be accountable for all aspects of the work.

References

1. Yalcin G, Ozsoy E, Karabag T. The relationship of body composition indices with the significance, extension and severity of coronary artery disease. Nutr Metab Cardiovasc Dis. 2020;30(12):2279-85. https://doi.org/10.1016/j.numecd.2020.07.014
2. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med. 2016;4(13):256. https://doi.org/10.21037/atm.2016.06.33
3. Khan MA, Hashim MJ, Mustafa H, Baniyas MY, Al Suwaidi S, AlKatheeri R, et al. Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study. Cureus. 2020;12(7):e9349. https://doi.org/10.7759/cureus.9349
4. Gholami SS, Azar FEF, Rezapour A, Tajdini M. Cost-effectiveness of coronary artery bypass graft and percutaneous coronary intervention compared to medical therapy in patients with coronary artery disease: a systematic review. Heart Fail Rev. 2019;24(6):967-75. https://doi.org/10.1007/s10741-019-09811-3
5. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. Heart disease and stroke statistics-2014 update: a report from the American Heart Association. Circulation. 2014;129(3):e28-e29.
6. Bechthold A, Boeing H, Schwedhelm C, Hoffmann G, Knüppel S, Iqbal K, et al. Food groups and risk of coronary heart disease, stroke and heart failure: A systematic review and dose-response meta-analysis of prospective studies. Crit Rev Food Sci Nutr. 2019;59(7):1071-90. https://doi.org/10.1080/10408398.2017.1392288
7. Malakar AK, Choudhury D, Halder B, Paul P, Uddin A, Chakraborty S. A review on coronary artery disease, its risk factors, and therapeutics. J Cell Physiol. 2019;234(10):16812-23. https://doi.org/10.1002/jcp.28350

8. Phrommintikul A, Krittayaphong R, Wongcharoen W, Boonyaratavej S, Wongvipaporn C, Tiyanon W, et al. Management and risk factor control of coronary artery disease in elderly versus nonelderly: a multicenter registry. J Geriatr Cardiol. 2016;13(12):954-9.
9. Weber T, Lang I, Zweiker R, Horn S, Wenzel RR, Watschinger B, et al. Hypertension and coronary artery disease: epidemiology, physiology, effects of treatment, and recommendations: A joint scientific statement from the Austrian Society of Cardiology and the Austrian Society of Hypertension. Wien Klin Wochenschr. 2016;128(13-14):467-79. https://doi.org/10.1007/s00508-016-0998-5
10. Park SJ, Yang HM, Seo KW, Choi SY, Choi BJ, Yoon MH, et al. The relationship between coronary atherosclerosis and body fat distribution measured using dual energy X-ray absorptiometry. Atherosclerosis. 2016;248:190-5. https://doi.org/10.1016/j.atherosclerosis.2016.03.014
11. Akhabue E, Thiboutot J, Cheng JW, Vittorio TJ, Christodoulidis G, Grady KM, et al. New and emerging risk factors for coronary heart disease. Am J Med Sci. 2014;347(2):151-8. https://doi.org/10.1097/MAJ.0b013e31828aab45
12. Sinning C, Lillpopp L, Appelbaum S, Ojeda F, Zeller T, Schnabel R, et al. Angiographic score assessment improves cardiovascular risk prediction: the clinical value of SYNTAX and Gensini application. Clin Res Cardiol. 2013;102(7):495-503. https://doi.org/10.1007/s00392-013-0555-4
13. Yadav M, Palmerini T, Caixeta A, Madhavan MV, Sanidas E, Kirtane AJ, et al. Prediction of coronary risk by SYNTAX and derived scores: synergy between percutaneous coronary intervention with taxus and cardiac surgery. J Am Coll Cardiol. 2013;62(14):1219-30. https://doi.org/10.1016/j.jacc.2013.06.047
14. Alber HF, Wanitschek MM, de Waha S, Ladurner A, Suessenbacher A, Dörler J, et al. High-density lipoprotein cholesterol, C-reactive protein, and prevalence and severity of coronary artery disease in 5641 consecutive patients undergoing coronary angiography. Eur J Clin Invest. 2008;38(6):372-80. https://doi.org/10.1111/j.1365-2362.2008.01954.x
15. Zhang Y, Wu NQ, Li S, Zhu CG, Guo YL, Qing P, et al. Non-HDL-C is a Better Predictor for the Severity of Coronary Atherosclerosis Compared with LDL-C. Heart Lung Circ. 2016;25(10):975-81. https://doi.org/10.1016/j.hlc.2016.04.025
16. Zhao X, Sun D, Xu RX, Guo YL, Zhu CG, Wu NQ, et al. Low-density lipoprotein-associated variables and the severity of coronary artery disease: an untreated Chinese cohort study. Biomarkers. 2018;23(7):647-53. https://doi.org/10.1080/1354750X.2018.1474256
17. Qin Y, Yan G, Qiao Y, Ma C, Liu J, Tang C. Relationship between Random Blood Glucose, Fasting Blood Glucose, and Gensini Score in Patients with Acute Myocardial Infarction. Biomed Res Int. 2019 Oct 15;2019:9707513. https://doi.org/10.1155/2019/9707513
18. Muhammed A, Zaki MT, Elserafy AS, Amin SA. Correlation between prediabetes and coronary artery disease severity in patients undergoing elective coronary angiography. Egypt Heart J. 2019;71(1):1-7. https://doi.org/10.1186/s43044-019-0034-y
19. Parsa AFZ, Jahanshahi B. Is the relationship of body mass index to severity of coronary artery disease different from that of waist-to-hip ratio and severity of coronary artery disease? Paradoxical findings: cardiovascular topic. Cardiovasc J Afr. 2015;26(1):13-6. https://doi.org/10.5830/CVJA-2014-054
20. Rubinshtein R, Halon DA, Jaffe R, Shahla J, Lewis BS. Relation between obesity and severity of coronary artery disease in patients undergoing coronary angiography. Am J Cardiol. 2006;97(9):1277-80. https://doi.org/10.1016/j.amjcard.2005.11.061
21. Nabati M, Moosazadeh M, Soroosh E, Shiraj H, Gholami M, Ghaemian A. Correlation between overweightness and the extent of coronary atherosclerosis among the South Caspian population. BMC Cardiovasc Disord. 2020;20(1):1-11. https://doi.org/10.1186/s12872-020-01534-w
22. Ekici B, Ercan EA, Cehreli S, Töre HF. The effect of emotional status and health-related quality of life on the severity of coronary artery disease. Kardiol Pol. 2014;72(7):617-23. https://doi.org/10.5603/KP.a2014.0023
23. Kahraman S, Cam Kahraman F, Zencirkiran Agus H, Kalkan AK, Uzun F, Karakayalı M, et al. Perceived stress level is associated with coronary artery disease severity in patients with ST-segment elevation myocardial infarction. Turk Kardiyol Dern Ars. 2020;48(5):494-503. https://doi.org/10.5543/tkda.2020.30020
24. Assari S, Zandi H, Ahmadi K, Kazemi Saleh D. Extent of Coronary Stenosis and Anxiety Symptoms among Patients Undergoing Coronary Angiography. J Tehran Heart Cent. 2017 Oct;12(4):155-159.
25. Salari A, Ashouri A, Moghtader AJ, Ahmadnia Z, Alizadeh I. The relationship between depression symptoms and severity of coronary artery disease in patients undergoing angiography. Iran J Psychiatry. 2020;15(4):370. https://doi.org/10.18502/ijps.v15i4.4305
26. Hou L, Li F, Wang Y, Ou Z, Xu D, Tan W, et al. Association between dietary patterns and coronary heart disease: a meta-analysis of prospective cohort

studies. Int J Clin Exp Med. 2015 Jan 15;8(1):781-90.
27. Kahleova H, Levin S, Barnard ND. Vegetarian Dietary Patterns and Cardiovascular Disease. Prog Cardiovasc Dis. 2018 May-Jun;61(1):54-61. https://doi.org/10.1016/j.pcad.2018.05.002
28. Waldeyer C, Brunner FJ, Braetz J, Ruebsamen N, Zyriax BC, Blaum C, et al. Adherence to Mediterranean diet, high-sensitive C-reactive protein, and severity of coronary artery disease: Contemporary data from the INTERCATH cohort. Atherosclerosis. 2018 Aug;275:256-61. https://doi.org/10.1016/j.atherosclerosis.2018.06.877
29. Oikonomou E, Psaltopoulou T, Georgiopoulos G, Siasos G, Kokkou E, Antonopoulos A, et al. Western Dietary Pattern Is Associated With Severe Coronary Artery Disease. Angiology. 2018 Apr;69(4):339-46. https://doi.org/10.1177/0003319717721603
30. van Dam RM. New approaches to the study of dietary patterns. Br J Nutr. 2005 May;93(5):573-4. https://doi.org/10.1079/BJN20051453
31. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol. 2002 Feb;13(1):3-9. https://doi.org/10.1097/00041433-200202000-00002
32. Kahleova H, Salas-Salvadó J, Rahelić D, Kendall CW, Rembert E, Sievenpiper JL. Dietary Patterns and Cardiometabolic Outcomes in Diabetes: A Summary of Systematic Reviews and Meta-Analyses. Nutrients. 2019 Sep 13;11(9):2209. https://doi.org/10.3390/nu11092209
33. Chiavaroli L, Viguiliouk E, Nishi SK, Blanco Mejia S, Rahelic D, Kahleova H, et al. DASH Dietary Pattern and Cardiometabolic Outcomes: An Umbrella Review of Systematic Reviews and Meta-Analyses. Nutrients. 2019 Feb 5;11(2):338. https://doi.org/10.3390/nu11020338
34. Fabiani R, Naldini G, Chiavarini M. Dietary Patterns in Relation to Low Bone Mineral Density and Fracture Risk: A Systematic Review and Meta-Analysis. Adv Nutr. 2019 Mar 1;10(2):219-36. https://doi.org/10.1093/advances/nmy073
35. Poulter N. Coronary heart disease is a multifactorial disease. Am J Hypertens. 1999 Oct;12(10 Pt 2):92S-95S. https://doi.org/10.1016/S0895-7061(99)00163-6
36. Kannel W. Importance of hypertension as a major risk factor in cardiovascular disease. Hypertension: McGraw-Hill, New York; 1977;888-910.
37. Jiang Y, Li Y, Shi K, Wang J, Qian WL, Yan WF, et al. The additive effect of essential hypertension on coronary artery plaques in type 2 diabetes mellitus patients: a coronary computed tomography angiography study. Cardiovasc Diabetol. 2022 Jan 4;21(1):1. https://doi.org/10.1186/s12933-021-01438-9
38. Kim CH, Noh IK, Ryu JM, Bae EJ, Cho HJ, Kim MS. Canonical Correlation between Behavioral-Psychological Variables and Predictors of Coronary Artery Disease Prognosis. Int J Environ Res Public Health. 2020 Mar 2;17(5):1608. https://doi.org/10.3390/ijerph17051608
39. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol. 1983 Feb;51(3):606. https://doi.org/10.1016/S0002-9149(83)80105-2
40. Mazzotta C, Basu S, Gower AC, Karki S, Farb MG, Sroczynski E, et al. Perivascular Adipose Tissue Inflammation in Ischemic Heart Disease. Arterioscler Thromb Vasc Biol. 2021 Mar;41(3):1239-50. https://doi.org/10.1161/ATVBAHA.120.315865
41. Rampidis GP, Benetos G, Benz DC, Giannopoulos AA, Buechel RR. A guide for Gensini Score calculation. Atherosclerosis. 2019 Aug;287:181-3. https://doi.org/10.1016/j.atherosclerosis.2019.05.012
42. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention. 2005 Aug;1(2):219-27.
43. Vasheghani-Farahani A, Tahmasbi M, Asheri H, Ashraf H, Nedjat S, Kordi R. The Persian, last 7-day, long form of the International Physical Activity Questionnaire: translation and validation study. Asian J Sports Med. 2011 Jun;2(2):106-16. https://doi.org/10.5812/asjsm.34781
44. Hagströmer M, Oja P, Sjöström M. The International Physical Activity Questionnaire (IPAQ): a study of concurrent and construct validity. Public Health Nutr. 2006 Sep;9(6):755-62. https://doi.org/10.1079/PHN2005898
45. Zimorovat A, Moghtaderi F, Amiri M, Raeisi-Dehkordi H, Mohyadini M, Mohammadi M, et al. Validity and Reproducibility of a Semiquantitative Multiple-Choice Food Frequency Questionnaire in Iranian Adults. Food Nutr Bull. 2022 Jun;43(2):171-188. https://doi.org/10.1177/03795721221078353
46. Ahmadi SM, Masjediarani A, Bakhtiari M, Davazdahemamy MH, Mohamadian R. Psychometric properties of Persian version of Beck depression inventory in coronary patients. Universa Med. 2019;38(1):33-40. https://doi.org/10.18051/UnivMed.2019.v38.33-40
47. Ahmadi SM, Arani AM, Bakhtiari M, Emamy M. Psychometric properties of the persian versions of patient health questionnaire-9 and patient health questionnaire-2 in patients with coronary heart

disease. Int Cardiovasc Res J. 2019;13(2):45-9.
48. Kaviani H, Mousavi A. Psychometric properties of the Persian version of Beck Anxiety Inventory (BAI). Tehran Univ Med J. 2008;66(2):136-40.
49. Nazifi M, Mokarami H, Akbaritabar A, Kalte HO, Rahi A. Psychometric properties of the Persian translation of Pittsburgh sleep quality index. Health Scope. 2014;3(2):e15547. https://doi.org/10.17795/jhealthscope-15547
50. Ansari NN, Naghdi S, Hasson S, Valizadeh L, Jalaie S. Validation of a Mini-Mental State Examination (MMSE) for the Persian population: a pilot study. Appl Neuropsychol. 2010 Jul;17(3):190-5.
51. Rosner B. Fundamentals of biostatistics: Cengage learning; 2015.
52. Tarver T. Heart Disease and Stroke Statistics-2014 Update: A Report From The American Heart Association. J Consum Health Internet. 2014;18(2):209. https://doi.org/10.1080/15398285.2014.902284
53. A Razik N, Deep A, Abokrisha M, Mosad E, Hasan-Ali H. The relationship between lipid parameters after fat loading and coronary artery disease severity. ARYA Atheroscler. 2022;18(5):1-9. https://doi.org/10.48305/arya.2022.16286.2416
54. Kilic A, Baydar O. Relationship Between Fasting Glucose, HbA1c Levels, and the SYNTAX Score 2 in Patients With Non-ST-Elevation Myocardial Infarction. Angiology. 2022 Feb;73(2):177-81. https://doi.org/10.1177/00033197211014678
55. Yassir S, Adhikari P, Rao NL, RM P. Association of anthropometric measurements with angiographic findings among diabetic patients with coronary artery disease. J Cardiovasc Dis Res. 2021;12(1):39-43. https://doi.org/10.31838/jcdr.2021.12.01.10
56. Tsukihashi Y, Shiga Y, Suematsu Y, Idemoto Y, Tashiro K, Yano Y, et al. Presence and severity of coronary artery disease in patients who achieved intensive blood pressure reduction at the time of coronary computed tomography angiography. Hypertens Res. 2021 Feb;44(2):206-14. https://doi.org/10.1038/s41440-020-00545-6
57. Ramesh S, Besharat MA, Nough H. Spiritual well-being and coronary artery diseases severity: Mediating effects of anger rumination and worry. Health Educ J. 2021;80(5):501-12. https://doi.org/10.1177/0017896920976697
58. Ferrannini E, Cushman WC. Ferrannini E, Cushman WC. Diabetes and hypertension: the bad companions. Lancet. 2012 Aug 11;380(9841):601-10. https://doi.org/10.1016/S0140-6736(12)60987-8
59. Muntner P, Whelton PK, Woodward M, Carey RM. A Comparison of the 2017 American College of Cardiology/American Heart Association Blood Pressure Guideline and the 2017 American Diabetes Association Diabetes and Hypertension Position Statement for U.S. Adults With Diabetes. Diabetes care. 2018;41(11):2322-9. https://doi.org/10.2337/dc18-1307
60. Jun JE, Kang M, Jin SM, Kim K, Hwang YC, Jeong IK, et al. Additive effect of low skeletal muscle mass and abdominal obesity on coronary artery calcification. Eur J Endocrinol. 2021 May 6;184(6):867-77. https://doi.org/10.1530/EJE-20-0885

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