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# Anxiety, a significant risk factor for coronary artery disease: what is the best index

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## Abstract

**Background** Coronary artery disease (CAD) is known as the leading cause of disability and death globally. Anxiety disorders are also recognized as common types of mental disorders that substantially impact global health. Iran ranks among the countries with a high incidence of CAD and anxiety disorders. Therefore, the present study aims to determine the potential association and epidemiological aspects of anxiety and CAD within the population of Mashhad, the second most popoulos city in Iran.

**Methods** The present study is based on extracted data from the Mashhad stroke and heart atherosclerotic disorder (MASHAD) study which is a 10-year prospective cohort study intended to assess the effects of various CAD risk factors among Mashhad city residents. Anxiety scores were assessed at the baseline using Beck Anxiety Inventory and individuals were classified based on the BAI 4-factor structure model which included autonomic, cognitive, panic, and neuromotor components. Accordingly, the association between baseline anxiety scores and the BAI four-factor model with the risk of CAD events was analyzed using SPSS software version 21.

**Results** Based on the results, 60.4% of the sample were female, and 5.6% were classified as having severe forms of anxiety. Moreover, severe anxiety was more prevalent in females. Results showed a 1.7% risk of CAD ($p$-value < 0.001) over 10 years with one unit increase in anxiety score. Based on the 4-factor model structure, we found that only panic disorder could significantly increase the risk of CAD by 1.1% over the 10-year follow-up ($p$-value < 0.001).

**Conclusion** Anxiety symptoms, particularly panic disorder, are independently and significantly associated with an increased overall risk of developing CAD over a 10-year period. Therefore, further studies are warranted to investigate the mechanisms through which anxiety may cause CAD, as well as possible interventions to mitigate these processes.

**Keywords** Coronary artery diseases, Anxiety, Factor structure model, Beck anxiety inventory, Panic disorder

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## Introduction

Cardiovascular diseases (CVDs), with a worldwide prevalence of 573 million, were estimated to account for about 32% of deaths in 2017 [1, 2]. Reported disability-adjusted life years (DALYs) due to CVDs have doubled since 1990; solidifying their status as the leading cause of disability and death globally [1]. Notably, Iran ranks among the countries with the highest age-standardized prevalence of CVDs, with more than 9,000 cases per 100,000 individuals [3]. Additionally, it has been shown that CVDs are responsible for 45.45% of all-cause mortality in Iran [4], signaling a significant transition in the leading causes of death among Iranian people from diarrheal and infectious diseases to CVDs in the last few decades [5]. Coronary heart disease (CHD) may subsequently cause serious complications such as arrhythmias, cardiogenic shock, pericardial effusion, pulmonary embolism, and heart failure [6].

Anxiety is defined as a temporary fear, concern, and ambiguity regarding the future, that varies among individuals on its depth and repetition. In severe forms, it can be considered as a class of anxiety disorders including panic disorder, generalized anxiety disorder, separation anxiety disorder, phobias, etc [7]. Anxiety disorders are among the common types of mental disorders with a substantial impact on global health. According to the Global Burden of Disease Study 2019, the worldwide prevalence of different types of anxiety disorders is up to 300 million; accompanied by an approximate incidence of 45 million [8]. It was reported that the lifetime prevalence of common mental health disorders is up to 29.2% [9]. The prevalence of anxiety disorders in Iran has been estimated as high as 15.6% [10]. Additionally, it has been shown that patients with anxiety are more susceptible to various comorbidities such as gastrointestinal, cardiorespiratory, endocrine, and neurologic illnesses [11].

Anxiety disorders are found to be more prevalent in coronary artery disease (CAD) patients compared to the general population [12]. Although the causal relationship between anxiety disorders and CVDs has not yet been established, a growing number of studies are showing the possible unfavorable effect of anxiety on CVDs, particularly on CAD [13], which is a major and most important subtype of CVDs. Moreover, as already mentioned, both anxiety disorder and CAD exert considerable impact on morbidity, mortality, and quality of life, reinforcing the necessity of additional investigations.

Given that the coexistence of anxiety and CAD may contribute to a higher number of disabilities and mortalities, and considering the limited knowledge of its epidemiological aspects in the Mashhad (the second-most-populous city in Iran) population, the present study aims to determine the association between anxiety and factor models of BAI items with CAD in Mashhad.

## Materials and methods

### Study population

The present study is based on extracted data from the Mashhad stroke and heart atherosclerotic disorder (MASHAD) study which is a 10-year prospective cohort study intended to assess the effects of numerous CAD risk factors such as nutrition, environment, psychological disorders, and genetics on CAD events among Mashhad city residents. Participants were recruited from three regions of Mashhad, the second most populated city of the country located in north-eastern Iran (2016 Census), using a stratified cluster random sampling method. The inclusion criteria were (I) between 35 and 65 years of age; (II) having the physical and mental capability of participating in the clinical examination; (III) having no specific plans to leave the area after the first and second stages of the study. All individuals were well-informed, and their written consent was drawn. During the 10-year follow-up, of the initial 9,704 study participants, 1715 subjects were lost during follow-up due to lack of response, reluctance, lack of access, and migration. Moreover, 429 subjects passed away, leaving 7560 individuals included in the data analysis, and 7389 subjects were recruited in this study (171 missing data in anxiety) [14].

Individuals were classified into 2 groups based on their cardiovascular health state including healthy and CAD. The 1st group had reported no documented coronary artery disease during the 10-year follow-up and was considered a healthy group ($N$=6623) whilst the 2nd group had documented and confirmed CAD ($N$=766) (Fig. 1). Healthy and CAD groups were further subdivided into 4 categories based on their psychological state and Beck Anxiety Inventory [15] which included, mild, moderate, and severe anxiety as well as healthy group (Fig. 1) (Table 1). All individuals were well informed and their written consent was drawn. Accordingly, the study protocol was validated by the Ethics Committee of the Mashhad University of Medical Sciences (MUMS) and the Institutional Review Board of Mashhad University Medical Center.

### Demographic, anthropometric, and metabolic data

Sociodemographic data were collected from all participants through a questionnaire as described before [14], which included marital status, socioeconomic, job, and smoking status, and education level. Baseline anthropometric data including height, weight, waist and hip circumference, body mass index(BMI), systolic and diastolic blood pressure, and biochemical and hematological measurements were also gathered from all participants as formerly explained [14],

For all subjects, height (in cm), weight (in kg), and body mass index (in kg/m2) were measured. Height and weight were measured in centimeters and the nearest

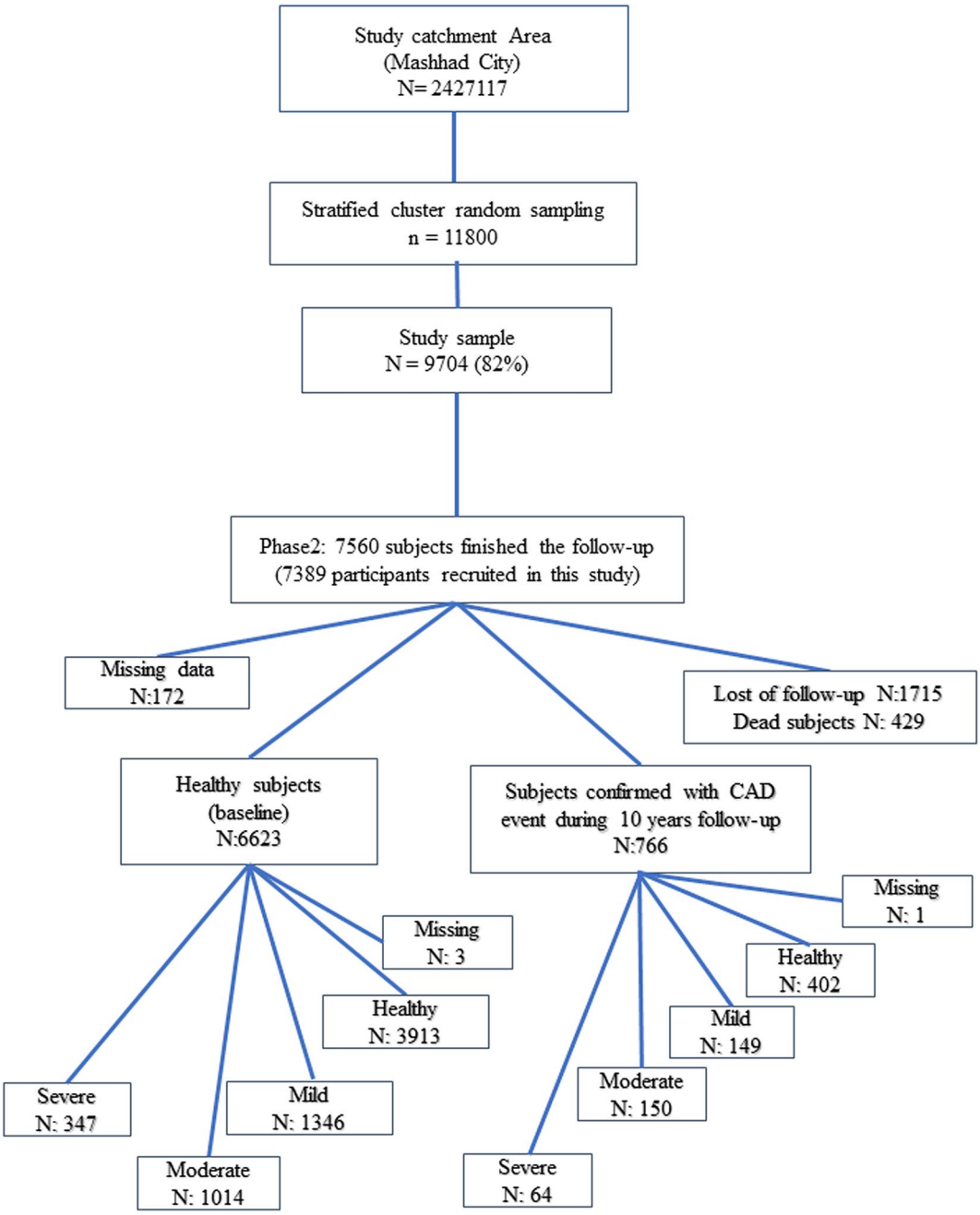


**Fig. 1** Flowchart of study subjects

0.1 cm with a stadiometer (SECA 217, Hamburg, Germany) and calibrated digital balance in kilogram scale (SECA 813, Hamburg, Germany) to the nearest 0.1 kg, respectively. Subsequently, BMI was calculated and categorized into obese (BMI≥30 kg/m2) and non-obese (BMI<30 kg/m2) subjects. Systolic and diastolic blood pressure (SBP and DBP) were measured using a standard sphygmomanometer, twice in the same manner. BP was measured using the left arm with individuals remaining seated after 15 min. We took the third measurement and averaged the two closest readings, if the first two readings differed by >15mmHg for DBP or >25mmHg for SBP. HTN was defined in accordance with the International Diabetic Federation (IDF) criteria for a SBP≥130 mmHg and/or DBP≥85 mmHg and/or if antihypertensive medication was used. Diabetes mellitus was defined as a fasting plasma glucose≥126 mg/dL, or being under treatment with oral hypoglycemic agents or insulin. A total subjects who declared symptoms of CAD were invited to the clinic and visited by an expert cardiologist.

**Table 1** Demographics and clinical features according to anxiety categorized in MASHAD study at baseline

| | | Anxiety | | | | |
|---|---|---|---|---|---|---|
| | | **No (0–9)** | **Mild (10–16)** | **Moderate (17–29)** | **Severe (30–63)** | ***p*-value** |
| N, %7389 | | 4315 (58.4%) | 1495 (20.2%) | 1169 (15.8%) | 411 (5.6%) | |
| Age | | 48.2±8.23 | 48.01±8.25 | 48.14±8.33 | 47.55±8.22 | 0.15 |
| Sex | Male 2928 (39.6) | 2023 (69.1%) | 501 (17.1%) | 311 (10.6%) | 93 (3.2%) | < 0.001 |
| | Female 4457 (60.4%) | 2292(51.4%) | 994 (22.3%) | 853 (19.1%) | 318 (7.1%) | |
| Marriage | Single, 40(0.5%) | 19 (47.5%) | 9 (22.5%) | 10 (25%) | 2 (5%) | 0.001 |
| | Married, 6949(94.1%) | 4109 (59.1%) | 1387 (20%) | 1070 (15.4%) | 383 (5.5%) | |
| | Divorced, 86 (1.2%) | 37 (43%) | 22 (25.6%) | 20 (23.3%) | 7 (8.1%) | |
| | Widow, 310(4.2%) | 150 (48.4%) | 77 (24.8%) | 64 (20.6%)* | 19 (6.1%) | |
| Smoking | No, 5217(70.6%) | 3150 (60.4%) | 1038 (19.9%) | 762 (14.6%) | 267 (5.1%) | < 0.001 |
| | Former, 663(9%) | 389 (58.7%) | 128 (19.3%) | 112 (17%) | 33 (5%) | |
| | Current, 1505 (20.4%) | 776 (51.6%) | 329 (21.9%) | 289 (19.2%) | 271 (7.4%)* | |
| Job status | Employed, 2836 (38.4%) | 1873(66%) | 517 (18.2%) | 337 (11.9%) | 109 (3.8%) | < 0.001 |
| | Unemployed, 3862 (52.3%) | 2000 (51.8%) | 839 (21.7%) | 743 (19.2%)* | 280 (7.3%) | |
| | Retired, 684 (9.3%) | 440 (64.3%) | 138 (20.2%) | 84 (12.3%) | 22 (3.2%) | |
| Education level | Low, 3887 (52.7%) | 2195 (56.5%) | 796 (20.5%) | 659 (17%) | 237 (6.1%) | < 0.001 |
| | Moderate, 2640 (35.8%) | 1549 (58.7%) | 531 (20.1%) | 414 (15.7%) | 146 (5.5%) | |
| | High, 852 (11.5%) | 569 (66.8%)* | 166 (19.5%) | 90 (10.6%) | 27 (3.2%) | |
| Clinical feature | | | | | | |
| Obesity | No, 5154 (69.9%) | 3145 (61%) | 1026 (19.9%) | 718 (13.9%) | 265 (5.1%) | < 0.001 |
| | Yes, 2220 (30.1%) | 1161 (52.3%) | 467 (21%) | 446 (20.1%)* | 146 (6.6%) | |
| Diabetes | No, 6380 (87.6%) | 3780 (59.2%) | 1273 (20.0%) | 992 (15.5%) | 335 (5.3%) | 0.015 |
| | Yes, 907 (12.4%) | 495 (54.6%) | 195 (21.5%) | 151 (16.6%) | 66 (7.3%)* | |
| Hypertension | No, 5207 (70.7%) | 3089 (59.3%) | 1061 (20.4%) | 790 (15.2%) | 267 (5.1%) | < 0.001 |
| | Yes, 2159 (29.3%) | 1215 (56.3%) | 430 (19.9%) | 372 (17.2%) | 142 (6.6%)* | |
| CAD | No, 6620 (89.6%) | 3913 (59.1%) | 1346 (20.3%) | 1014 (15.3%) | 347 (5.2%) | < 0.001 |
| | Yes, 766 (10.4%) | 402 (52.5%) | 149 (19.5%) | 151 (19.6%) | 64 (8.4%)* | |

Chi-square test or one-way ANOVA has been done; data presented as Mean ± SD or number and percentage

*CAD* coronary artery disease

Patients were checked and the diagnosis was confirmed by utilizing stress echocardiography, radioisotope scan, coronary angiography, computed tomography (CT), or exercise tolerance test (ETT). In ten years follow-up, 17.5% CABG, 6.7% MI, 44.4% PCI, 23.3% stable angina and 8.1% unstable angina were confirmed.

### Measurement of anxiety

The Beck Anxiety Inventory [15] was exerted for evaluating anxiety symptoms in this study [16]. It is a 21-question inquiry that investigates the frequency of the patient's anxiety symptoms [17]. Questions are based on a 4-point Likert scale and each one may attain a score from 0 to 3. The cumulative score can range from 0 to 63 and is divided into 4 levels to determine the severity of anxiety [16]. Kaviani et al. demonstrated that the Persian-translated edition of BAI retains assuring validity ($r$=0.72, $P$<0.001), reliability ($r$=0.83, $P$<0.001), and internal consistency (Alpha=0.92) [18]. Additionally, Clark et al. investigated various factor structure models for the BAI among CVD patients and suggested the four-factor model as a more compatible method in this population [19]. It was based on autonomic, cognitive, panic, and neuromotor components which we also applied to our classification method [19, 20].

### Statistical analyses

SPSS software version 21 was used to analyze the data (IBM SPSS, Inc., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to determine the normality of the data. Descriptive analysis, qualitative and quantitative variables were reported as the frequency (%) and mean ± standard deviation (SD), respectively. The Chi-Square test was used for statistical analysis to assess the relationship between qualitative variables and One-Way analysis of variance (ANOVA) or sample t-test was used to examine the means of quantitative variables among separate groups. Anxiety ratings were classified based on severity, with individuals in the first group (no or minimum anxiety) serving as a control group. Also, a Cox regression model was developed for evaluation of the CAD and anxiety as an independent variable. Moreover, data was adjusted by age, sex, marital status, smoking status, job, and education levels. Every analysis was two-sided, and a p-value of 0.05 or lower was regarded as significant. Graph pad prism was used for drawing figures

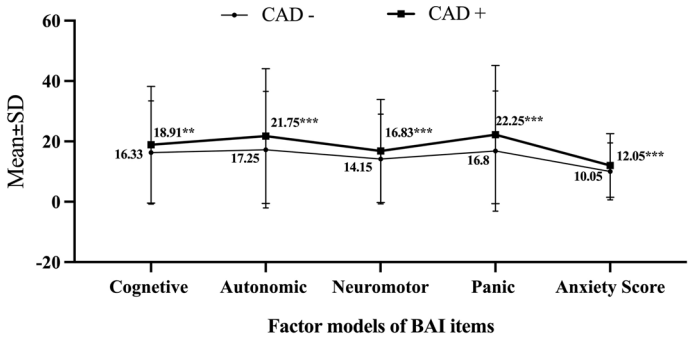


**Fig. 2** Mean of anxiety total score and factor models of BAI items in MASHAD cohort study according to the CAD event after 10 years follow-up; ***$p < 0.001$

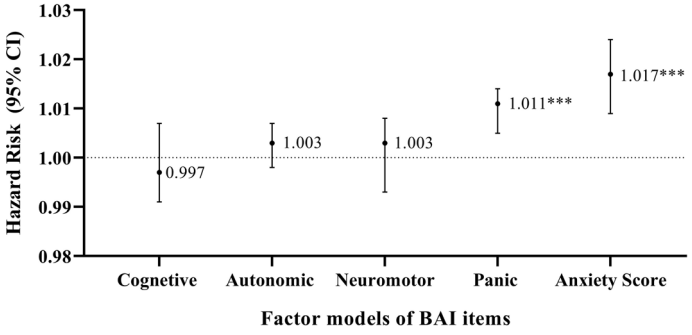


**Fig. 3** Relative risk of CAD event according to anxiety total score and factor models of BAI items in MASHAD study at baseline; sex, age, marriage status, job status, education level, smoking status, obesity, diabetes. ***$p < 0.001$

## Results

Population characteristics are comprehensively demonstrated in Table 1. 60.4% of the sample were female, approximately 35.8% were considered moderate to highly educated, and 52.7% had low education levels. Most participants were non-smokers (70.6%) and married (94.1%). Regarding the results of the BAI, individuals were divided into 4 different groups at the time of admission into our study (Table 1) [16]. 58.4% of subjects were healthy for anxiety, whereas 5.6% were classified as having severe forms of anxiety (Table 1). Most healthy participants were employees (66%). However, the prevalence of moderate anxiety in unemployed subjects was significantly higher than other groups, and it was 19.2% (Table 1).

The overall anxiety scores were evaluated at the baseline of the study among all participants including healthy individuals (10.05± 9.45) as well as participants who experienced coronary artery events during our 10-year follow-up (12.05±10.53) (Fig. 2). All individuals were classified as one property of the four anxiety structure model which includes cognitive, autonomic, neuromotor, and panic, by considering their answers to the 21 questions of BAI (Fig. 2) [20]. For simplicity and clearness, the results of each category were calculated as percentages and expressed as mean ± standard deviation (Fig. 2).

The hazard risk of developing CAD over a 10-year follow-up was calculated after adjustment for potential confounding variables including age, sex, marriage status, job, smoking status, education level, and having existing comorbidities such as diabetes, and obesity (Fig. 3). Our results showed a 1.7% risk of CAD (HR = 1.017, p-value < 0.001, 95% CI: 1.009–1.024) over 10 years with one unit increase in anxiety score (Fig. 3). Accordingly, based on the 4-factor model structure, we found that only panic disorder could significantly increase the risk (HR = 1.011, p-value < 0.001, 95%, CI: 1.005–1.014) of CAD by 1.1% over the 10-year follow-up (Fig. 3).

## Discussion

Regarding the possible deteriorating effects of anxiety in various cardiovascular diseases (CVDs) such as heart failure [21], CHD [22, 23], acute coronary syndrome (ACS) [24], and hypertension [25], investigating their interrelation is an important field of study. Various studies have indicated a prospective link between anxiety and CVD [26, 27], and one study has established a dose-response correlation between these two entities [28]. Accordingly, some studies have attributed the higher CAD incidence among patients with high anxiety levels to the accelerated hypothalamic-pituitary-adrenal axis, and the possible existence of a pro-atherosclerotic state in these patients [29, 30].

To the best of our knowledge, there is limited data about the association between the severity of anxiety

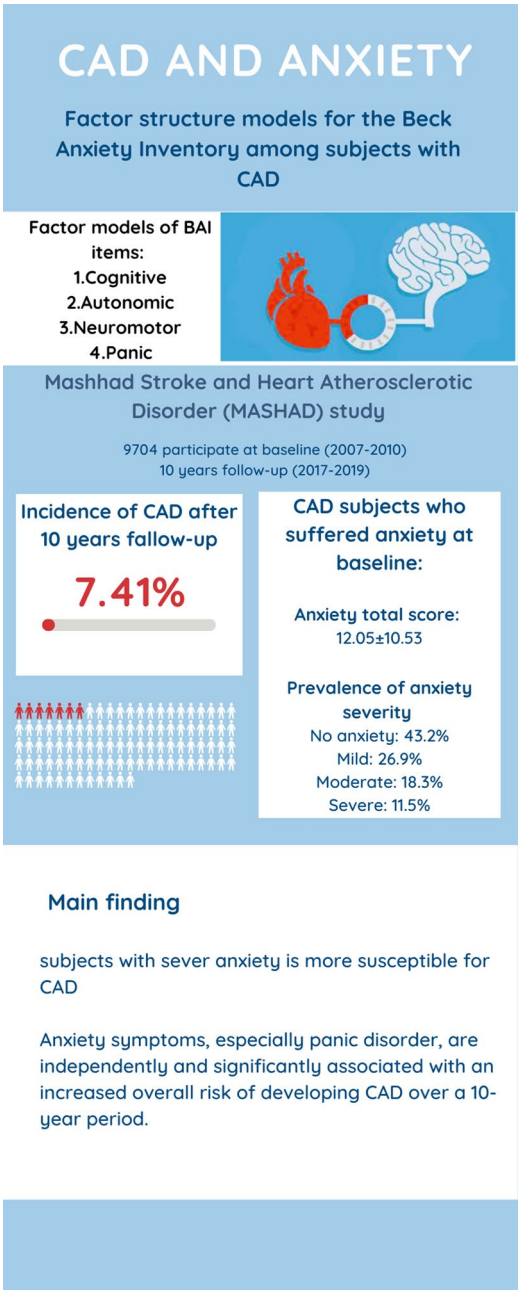


**Fig. 4** Summary of result

symptoms and the risk of CAD incidence in initially healthy subjects among Iranians. Hosseini et al. utilized the BAI to evaluate anxiety scores in patients following new-onset myocardial infarction (MI) and found no relationship between anxiety and cardiac mortality during a 5-year follow-up [31]. In addition, Najafipour and colleagues established a meaningful correlation between anxiety and cardiac risk factors including opium usage and low physical activity [32]. Another investigation conducted by Abbasi et al. also determined an association between anxiety and various cardiac risk factors such as opium usage, positive family history of CAD, duration of CAD, hypertension, serum creatinine levels, and major adverse cardiac events (MACE) [33]. However, it is noteworthy that none of these studies have prospectively evaluated the effects of anxiety score severity on the incidennce rate of CAD, which directed us to investigate the possible correlation.

This study evaluated the correlation between anxiety and documented CAD of a well-characterized 10-year prospective cohort study among MASHAD cohort study. We found an increased based-line mean anxiety score among participants who experienced CAD during 10-year follow-up compared to the healthy group. This increase was seen in all properties of the four-factor model BAI which includes cognitive, autonomic, neuromotor, and panic. We observed a dose-response relationship between increased anxiety levels and CAD risk. Also, we showed that patients with higher anxiety levels were at a greater risk of CAD, in which every unit increase in the baseline BAI score was associated with a 1.7% higher risk of developing CAD over the next 10 years. In fact, in this study, we illustrated that anxiety was significantly associated with an increased risk of CAD, and we also found that anxiety total score and related disorders were meaningfully more severe among patients with established CAD.

The results of several meta-analyses confirmed that anxiety disorders increase the chance of subsequently developing CAD among healthy individuals [13, 27, 34]. Accordingly, our findings also showed a 1.7% increment in CAD incidence with every unit increase of anxiety score after adjustments for confounding variables such as age, sex, marriage status, job, smoking status, education level, and having existing comorbidities such as diabetes, and obesity. Additionally, a recent meta-analysis of 17 studies has evaluated the effects of anxiety on clinical outcomes among ACS patients. They reported that patients with concurrent ACS and anxiety are at a 47% greater risk of MACEs and a 21% higher risk of mortality. However, several studies did not find any association between anxiety disorders and clinical prognosis in CAD patients [35–38].

Various potential processes have been suggested to provide a reliable prediction for the correlation between anxiety disorders and CAD including cardiac arrhythmias [39], attenuated heart rate variability [40], and atherosclerosis development [30]. Although the exact mechanism by which anxiety may cause CAD is yet to be determined, several cardiac risk factors were found to be linked with augmented anxiety levels such as opium usage, positive family history of coronary artery diseases (CAD), duration of CAD, hypertension, low physical activity, serum creatinine levels, and major adverse cardiac events (MACE) [32, 33].

Multiple studies have shown a significant correlation between a variety of anxiety disorder categories and CAD [34, 41, 42], whereas some others have only reported meaningful correlations with panic disorder [13, 43, 44]. Similarly, we have found a significantly increased risk of developing CAD only within individuals experiencing panic disorder. In addition, as there is an overlap between symptoms of CAD and anxiety, and as CADs are thought to be more prevalent among patients diagnosed with anxiety [45], we also propose that underdiagnosis of cardiac diseases ought to be an area of concern in anxiety patients which might primarily occur due to falsely attributing cardiac symptoms to their underlying anxiety disorder.

The strengths of this study were, Firstly, we utilized an immense sample of individuals as our baseline population which truly represented the general population of our target city. Secondly, we followed all participants for a long period of 10 years, and all of the cardiac events were documented and confirmed by expert academic cardiologists. Thirdly, our results are collected prospectively which makes it more competent to draw a conclusion.

The present study also comprises some limitations which we will discuss to guide future research. Firstly, even though we have excluded individuals with preexisting CAD at the baseline of our study, we are not able to exclude the odds of reverse causality due to a possible existing early-stage or asymptomatic CAD in our baseline sample. Secondly, our data showed that anxiety was correlated with several CAD risk factors such as obesity and diabetes. Although we have adjusted for these covariates in our analyses, there might be some other mediators missed in our considerations, such as having an unhealthy lifestyle, having simultaneous depression, or being a second-hand smoker.

## Conclusion

In conclusion, our 10-year prospective cohort study within the MASHAD cohort sheds light on the relationship between anxiety and the incidence of CAD (Fig. 4). We discovered that anxiety symptoms, especially panic disorder, are independently and significantly associated with an increased overall risk of developing CAD over a 10-year period. Based on our knowledge, recognition of subjects with panic disorder for a long time and treatment of them may decrease the risk of CAD. However, as there is a lack of evidence regarding the potential mechanisms, further studies are warranted to investigate the possible biological processes by which anxiety may cause CAD as well as proper interventions to slow down these mechanisms.

### Abbreviations

| | |
|---|---|
| ACS | Acute coronary syndrome |
| BAI | Beck Anxiety Inventory |
| BMI | Body mass index |
| CAD | Coronary artery disease |
| CHD | Coronary heart disease |
| CVD | Cardiovascular disease |
| DALY | Disability-adjusted life year |
| MACE | Major adverse cardiac event |
| MASHAD | Mashhad Stroke and Heart Atherosclerotic Disorder |
| MI | Myocardial infarction |
| SD | Standard deviation |

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### Author contributions

Mojtaba Rezaee (pcycologic scientific consultant) Susan Darroudi, Leila Etemad, Arya Nasimi Shad (wrote manuscript) Haniyeh Darroudi, Zahra Zardast, Houra Kohansal, Fatemeh Sadeghian (data gathering) Susan Darroudi, Habibollah Esmaeili (Data analysis and study design)Gordon A. Ferns (scientific and grammatical editing) Habibollah Esmaily, Majid Ghayour-Mobarhan (study design) Mohsen Moohebati (corresponding author, designed the study).

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### Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## Declaration

### Ethical approval and consent to participate

All individuals were well informed and their written consent was drawn. Accordingly, the study protocol was validated by the Ethics Committee of the Mashhad University of Medical Sciences (MUMS) and the Institutional Review Board of Mashhad University Medical Center. This project is supported by Mashhad University of Medical Sciences. Funding number: 85134.

### Consent for publication

This section as not applicable. It is not applicable to the Consent of Image Publication for this manuscript. The figures were designed only in this manuscript to present the results of the current paper.

### Competing interests

The Authors declare that there is no conflict of interest.

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**References**

1. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, Barengo NC, Beaton AZ, Benjamin EJ, Benziger CP, et al. Global Burden of Cardiovascular diseases and Risk factors, 1990–2019: Update from the GBD 2019 study. J Am Coll Cardiol. 2020;76(25):2982–3021.
2. Global regional. National age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the global burden of Disease Study 2017. Lancet. 2018;392(10159):1736–88.
3. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, Ahmed M, Aksut B, Alam T, Alam K, et al. Global, Regional, and National Burden of Cardiovascular diseases for 10 causes, 1990 to 2015. J Am Coll Cardiol. 2017;70(1):1–25.
4. Global regional. National disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the global burden of Disease Study 2017. Lancet. 2018;392(10159):1859–922.
5. Sarrafzadegan N, Mohammmadifard N. Cardiovascular Disease in Iran in the last 40 years: Prevalence, Mortality, Morbidity, challenges and Strategies for Cardiovascular Prevention. Arch Iran Med. 2019;22(4):204–10.
6. Shao C, Wang J, Tian J, Tang YD. Coronary artery disease: from mechanism to clinical practice. Adv Exp Med Biol. 2020;1177:1–36.
7. Cohen BE, Edmondson D, Kronish IM. State of the art review: depression, stress, anxiety, and Cardiovascular Disease. Am J Hypertens. 2015;28(11):1295–302.
8. Yang X, Fang Y, Chen H, Zhang T, Yin X, Man J, Yang L, Lu M. Global, regional and national burden of anxiety disorders from 1990 to 2019: results from the global burden of Disease Study 2019. Epidemiol Psychiatr Sci. 2021;30:e36.
9. Steel Z, Marnane C, Iranpour C, Chey T, Jackson JW, Patel V, Silove D. The global prevalence of common mental disorders: a systematic review and meta-analysis 1980–2013. Int J Epidemiol. 2014;43(2):476–93.
10. Hajebi A, Motevalian SA, Rahimi-Movaghar A, Sharifi V, Amin-Esmaeili M, Radgoodarzi R, Hefazi M. Major anxiety disorders in Iran: prevalence, sociodemographic correlates and service utilization. BMC Psychiatry. 2018;18(1):261.
11. Culpepper L. Generalized anxiety disorder and medical illness. J Clin Psychiatry. 2009;70(Suppl 2):20–4.
12. Jia Z, Du X, Du J, Xia S, Guo L, Su X, Dong Z, Yuan Y, Zheng Y, Wu S, et al. Prevalence and factors associated with depressive and anxiety symptoms in a Chinese population with and without cardiovascular diseases. J Affect Disord. 2021;286:241–7.
13. Tully PJ, Turnbull DA, Beltrame J, Horowitz J, Cosh S, Baumeister H, Wittert GA. Panic disorder and incident coronary heart disease: a systematic review and meta-regression in 1131612 persons and 58111 cardiac events. Psychol Med. 2015;45(14):2909–20.
14. Ghayour-Mobarhan M, Moohebati M, Esmaily H, Ebrahimi M, Parizadeh SM, Heidari-Bakavoli AR, Safarian M, Mokhber N, Nematy M, Saber H, et al. Mashhad stroke and heart atherosclerotic disorder (MASHAD) study: design, baseline characteristics and 10-year cardiovascular risk estimation. Int J Public Health. 2015;60(5):561–72.
15. Gong P, Chang X, Chen X, Bai X, Wen H, Pi S, Yang W, Wang L, Chen F. Metabolomics study of cadmium-induced diabetic nephropathy and protective effect of caffeic acid phenethyl ester using UPLC-Q-TOF-MS combined with pattern recognition. Environ Toxicol Pharmacol. 2017;54:80–92.
16. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 1988;56(6):893–7.
17. Muntingh AD, van der Feltz-Cornelis CM, van Marwijk HW, Spinhoven P, Penninx BW, van Balkom AJ. Is the Beck anxiety inventory a good tool to assess the severity of anxiety? A primary care study in the Netherlands Study of Depression and anxiety (NESDA). BMC Fam Pract. 2011;12:66.
18. Hossein Kaviani H, Mousavi AS. Psychometric properties of the Persian version of Beck anxiety inventory (BAI). Tehran Univ Med J. 2008;66(2):136–40.
19. Clark JM, Marszalek JM, Bennett KK, Harry KM, Howarter AD, Eways KR, Reed KS. Comparison of factor structure models for the Beck anxiety inventory among cardiac rehabilitation patients. J Psychosom Res. 2016;89:91–7.
20. Wetherell JL, Areán PA. Psychometric evaluation of the Beck anxiety inventory with older medical patients. Psychol Assess. 1997;9(2):136.
21. Tsuchihashi-Makaya M, Kato N, Chishaki A, Takeshita A, Tsutsui H. Anxiety and poor social support are independently associated with adverse outcomes in patients with mild heart failure. Circ J. 2009;73(2):280–7.
22. Watkins LL, Koch GG, Sherwood A, Blumenthal JA, Davidson JR, O'Connor C, Sketch MH. Association of anxiety and depression with all-cause mortality in individuals with coronary heart disease. J Am Heart Assoc. 2013;2(2):e000068.
23. Stewart RAH, Colquhoun DM, Marschner SL, Kirby AC, Simes J, Nestel PJ, Glozier N, O'Neil A, Oldenburg B, White HD, et al. Persistent psychological distress and mortality in patients with stable coronary artery disease. Heart. 2017;103(23):1860–6.
24. Li J, Ji F, Song J, Gao X, Jiang D, Chen G, Chen S, Lin X, Zhuo C. Anxiety and clinical outcomes of patients with acute coronary syndrome: a meta-analysis. BMJ Open. 2020;10(7):e034135.
25. Lim LF, Solmi M, Cortese S. Association between anxiety and hypertension in adults: a systematic review and meta-analysis. Neurosci Biobehav Rev. 2021;131:96–119.
26. Janszky I, Ahnve S, Lundberg I, Hemmingsson T. Early-onset depression, anxiety, and risk of subsequent coronary heart disease: 37-year follow-up of 49,321 young Swedish men. J Am Coll Cardiol. 2010;56(1):31–7.
27. Roest AM, Martens EJ, de Jonge P, Denollet J. Anxiety and risk of incident coronary heart disease: a meta-analysis. J Am Coll Cardiol. 2010;56(1):38–46.
28. Gustad LT, Laugsand LE, Janszky I, Dalen H, Bjerkeset O. Symptoms of anxiety and depression and risk of acute myocardial infarction: the HUNT 2 study. Eur Heart J. 2014;35(21):1394–403.
29. Berge LI, Skogen JC, Sulo G, Igland J, Wilhelmsen I, Vollset SE, Tell GS, Knudsen AK. Health anxiety and risk of ischaemic heart disease: a prospective cohort study linking the Hordaland Health Study (HUSK) with the Cardiovascular diseases in Norway (CVDNOR) project. BMJ Open. 2016;6(11):e012914.
30. Paterniti S, Zureik M, Ducimetière P, Touboul PJ, Fève JM, Alpérovitch A. Sustained anxiety and 4-year progression of carotid atherosclerosis. Arterioscler Thromb Vasc Biol. 2001;21(1):136–41.
31. Hosseini SH, Ghaemian A, Mehdizadeh E, Ashraf H. Levels of anxiety and depression as predictors of mortality following myocardial infarction: a 5-year follow-up. Cardiol J. 2014;21(4):370–7.
32. Najafipour H, Banivaheb G, Sabahi A, Naderi N, Nasirian M, Mirzazadeh A. Prevalence of anxiety and depression symptoms and their relationship with other coronary artery disease risk factors: a population-based study on 5900 residents in Southeast Iran. Asian J Psychiatr. 2016;20:55–60.
33. Abbasi SH, Kassaian SE, Sadeghian S, Karimi A, Saadat S, Peyvandi F, Jalali A, Davarpasand T, Akhondzadeh S, Shahmansouri N, et al. Factors Associated with anxiety in premature coronary artery Disease patients: THC-PAC study. Acta Med Iran. 2016;54(4):261–9.
34. Emdin CA, Odutayo A, Wong CX, Tran J, Hsiao AJ, Hunn BH. Meta-analysis of anxiety as a risk factor for Cardiovascular Disease. Am J Cardiol. 2016;118(4):511–9.
35. Ahern DK, Gorkin L, Anderson JL, Tierney C, Hallstrom A, Ewart C, Capone RJ, Schron E, Kornfeld D, Herd JA, et al. Biobehavioral variables and mortality or cardiac arrest in the Cardiac Arrhythmia Pilot Study (CAPS). Am J Cardiol. 1990;66(1):59–62.
36. Frasure-Smith N, Lespérance F. Depression and other psychological risks following myocardial infarction. Arch Gen Psychiatry. 2003;60(6):627–36.
37. Kornerup H, Zwisler AD, Prescott E. No association between anxiety and depression and adverse clinical outcome among patients with cardiovascular disease: findings from the DANREHAB trial. J Psychosom Res. 2011;71(4):207–14.
38. Lane D, Carroll D, Ring C, Beevers DG, Lip GY. Mortality and quality of life 12 months after myocardial infarction: effects of depression and anxiety. Psychosom Med. 2001;63(2):221–30.
39. van den Broek KC, Nyklícek I, van der Voort PH, Alings M, Meijer A, Denollet J. Risk of ventricular arrhythmia after implantable defibrillator treatment in anxious type D patients. J Am Coll Cardiol. 2009;54(6):531–7.
40. Martens EJ, Nyklícek I, Szabó BM, Kupper N. Depression and anxiety as predictors of heart rate variability after myocardial infarction. Psychol Med. 2008;38(3):375–83.
41. Tully PJ, Cosh SM, Baune BT. A review of the affects of worry and generalized anxiety disorder upon cardiovascular health and coronary heart disease. Psychol Health Med. 2013;18(6):627–44.

42. Vogelzangs N, Seldenrijk A, Beekman AT, van Hout HP, de Jonge P, Penninx BW. Cardiovascular disease in persons with depressive and anxiety disorders. J Affect Disord. 2010;125(1–3):241–8.
43. Celano CM, Daunis DJ, Lokko HN, Campbell KA, Huffman JC. Anxiety disorders and Cardiovascular Disease. Curr Psychiatry Rep. 2016;18(11):101.
44. Caldirola D, Schruers KR, Nardi AE, De Berardis D, Fornaro M, Perna G. Is there cardiac risk in panic disorder? An updated systematic review. J Affect Disord. 2016;194:38–49.
45. Todaro JF, Shen BJ, Raffa SD, Tilkemeier PL, Niaura R. Prevalence of anxiety disorders in men and women with established coronary heart disease. J Cardiopulm Rehabil Prev. 2007;27(2):86–91.

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