ASSOCIATION OF ANXIETY DISORDER AND CAROTID ATHEROSCLEROSIS

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Abstract

INTRODUCTION: Anxiety is associated with a higher risk of cardiovascular disease. The present study aims to assess the extent of carotid artery atherosclerosis in patients with and without anxiety disorder.

METHODS: In a cross-sectional study, two groups of participants with and without anxiety disorder (40 and 80 subjects, respectively) according to DSM-IV were selected from the Psychiatry Clinic of Noor Hospital and Mental Health Unit of Isfahan Cardiovascular Research Center by simple sampling method. Evaluation of major risk factors was performed after recording demographic characteristics. Zung questionnaire was used to assess severity of anxiety. Carotid ultrasonography was performed in three portions of carotid arteries, bilaterally, and Intima-Media Thickness (IMT) ≥8 mm was considered as atherosclerosis. Statistical analysis included t-test, χ^2 and logistic regression.

RESULTS: Mean age of participants with and without anxiety disorder was 49.07±12.08 and 48.68±11.02 years, respectively. Major atherosclerosis risk factors did not differ significantly between the two groups. IMT values in all portions were significantly higher in the anxiety group. The presence of anxiety was positively associated with the presence of atherosclerosis in all branches, except for the left common carotid artery.

DISCUSSION: Anxiety increases the risk of cardiovascular disease, hence measures must be adopted to control anxiety with pharmacologic and nonpharmacologic interventions to reduce atherosclerosis.

Keywords ● Anxiety ● Intima-Media thickness ● Atherosclerosis

Introduction

Coronary artery disease is the leading cause of death worldwide.[1] Several risk factors have been identified for this condition, some of which are environmental.[2] Anxiety is associated with a higher risk of cardiovascular disease.[3] Phobic anxiety, generalized anxiety disorder, panic disorder and worry are predictors of myocardial infarction and cardiac death.[4-6] Anxiety affects nearly 25% of the population sometime throughout their life.[7,8]

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Anxiety causes overactivity of the autonomic nervous system, increases catecholamines and cortisol,[9,10] leading to acceleration of heart rate and increase in blood pressure.

On the other hand, anxiety-associated habits of some anxious patients, such as smoking and alcohol use, increase the risk of progression of atherosclerosis.[11,12] However, direct relationship between anxiety and atherosclerosis is to be investigated.

Several studies have reported that atherosclerosis in carotid arteries may be considered a marker of generalized atherosclerosis of the arteries, including the coronaries.[13]

The present study aims to assess the extent of carotid artery atherosclerosis as a marker of coronary atherosclerosis in patients with anxiety disorder and those without anxiety disorder.

Materials and methods

This cross-sectional study was performed in 2004. Samples were selected from medical profiles of patients referring to the Psychiatry Clinic of Noor Hospital and the Mental Health Unit of Isfahan Cardiovascular Research Center during the year preceding the study, using simple non-randomized sampling method. Participants with diagnosis of anxiety disorder (phobic anxiety, generalized anxiety disorder, obsessive-compulsive disorder, panic disorder) according to DSM-IV criteria[14] and no other disorders in axis I (such as schizophrenia, bipolar mood disorder, major depressive disorder and substance abuse) in the preceding year were labeled as the anxious group. Others with no psychiatric disorders or debilitating physical condition based on psychiatric interview and physical examination were recognized as the non-anxious group. The study was approved by the Ethics Committee of Isfahan Cardiovascular Research Center. Written informed consent was obtained from all participants.

Risk factor Assessment

History of major atherosclerosis risk factors, i.e. high blood pressure, overweight, diabetes, hypercholesterolemia and smoking was recorded.

Measurements of blood pressure, body mass index (BMI), fasting blood sugar (FBS), total cholesterol (TC) and smoking status were recorded.

Blood pressure was measured by a general practitioner using a standard mercury sphygmomanometer in sitting position, after a 10-minute rest, on the right arm. Mean of two blood-pressure readings was recorded. High blood pressure was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥95 mmHg.[15]

BMI was calculated as weight divided by height squared. The subjects were weighed barefoot with light-weight clothing using a Seca Scale. Height was measured with standard method. BMI ≥25 was considered as overweight.[16]

Smoking status was determined based on patient reports. Daily consumption of any number of cigarettes during the preceding year was recorded as active smoking.[17] Blood specimens for measuring TC and FBS were taken after 12 hours of fasting. TC measurement was performed via spectrophotometry using an autoanalyzer.[18] FBS ≥126 mg/dl or consumption of anti-diabetics was considered as diabetes.[19] TC level ≥240 mg/dl or using lipid-lowering agents during the preceding year was considered as hypercholesterolemia.[18]

Anxiety Measures

All participants were assessed with Zung questionnaire for severity of anxiety. This is a 20-item questionnaire with a four-point scale, which has been validated in the Iranian population. Scores ≥45 are considered as indicating anxiety disorder.[20]

Carotid Ultrasonography

Participants underwent carotid ultrasonography with a transducer frequency of 7 MHz. Ultrasonographic assessment was performed in three portions: 1) terminal part (2-cm segment) of common carotid artery, 2) carotid bulb, and 3) origin (1-cm segment) of internal carotid artery, bilaterally. These segments were examined for plaques, in longitudinal and transverse planes. Those with plaques were excluded from the study. Intima-Media thickness (IMT) was measured twice in every portion, and the mean value was recorded. IMT ≥8 mm was considered as atherosclerosis.[21]

Statistical Analysis

Statistical analysis included t-test and χ2 to compare the two groups. A binary logistic Regression model was also used. Unconditional logistic regression (method: Enter) was used for assessing the relationship of carotid atherosclerosis (IMT≥8 mm) in three portions of carotid artery bilaterally with the presence of anxiety disorder adjusted for major cardiovascular risk factors. Presence of anxiety required DSM-IV criteria. This binary variable was used as an independent variable and its relationship with atherosclerosis was adjusted for other risk factors including categorical variables: blood pressure (normotensive/hypertensive), BMI, (normal/overweight), Smoking (smoker/nonsmoker), FBS (diabetic/non-diabetic), and TC (normal/hypercholesterolemia). Atherosclerosis in the right common carotid (RCC), left common carotid (LCC), right carotid bulb (RCB), left carotid bulb (LCB), right internal carotid (RIC) or left internal carotid (LIC) was considered as a dependent variable.

SPSS11 (statistical package for social sciences, SPSS Inc, Illinois, USA) was used for all statistical

calculations. All reported P values were based on two-sided tests and were compared to a significance level of 5%.

Results

The study was performed on 120 subjects, 40 participants with anxiety, with a mean age of 49.07± 12.08 years, and 80 participants without anxiety, with a mean age of 48.68±11.02 years. Demographic characteristics of the participants are presented in Table 1. Major cardiovascular risk factors did not differ significantly between the two groups. In the anxious and non-anxious groups, antihypertensive drugs were used by 4 and 7 participants, respectively.

Antidiabetic agents were used by 2 and 4 participants in anxious and non-anxious groups, respectively.
Table 2 presents mean and standard deviation of IMT in three portions of left and right carotid arteries.
All values are significantly different between the two groups.
Multivariate logistic regression analysis adjusted for sex and major risk factors of coronary arthrosclerosis (high blood pressure, overweight, diabetes, hypercholesterolemia and smoking) showed that atherosclerosis in the carotid arteries was associated with increased risk of anxiety.
Thus, given the adjustment for major risk factors, the presence of anxiety was positively associated with atherosclerosis (Table 3).

TABLE 1. Demographics, major risk factors and Zung score in anxious and non-anxious groups

	Anxious group	Non-anxious group	P value
Age*	49.07 ± 12.08	48.68 ± 11.02	0.728[‡]
Sex (male)(%)	20 (50)	40 (50)	1.000[†]
Over weight (%)	18 (45)	33 (41.2)	0.812[†]
Diabetes (%)	2 (5)	5 (6.3)	0.783[†]
Hypertension (%)	9 (22.5)	14 (17.5)	0.512[†]
Current smoking (%)	7 (17.5)	13 (16.3)	0.862[†]
Hypercholesterolemia (%)	13 (32.5)	25 (31.2)	0.854[†]
Zung score*	46.56 ± 22.41	12.83 ± 10.21	0.000[‡]

* Mean ±SD
‡ t-test
† Chi-square test

TABLE 2. Intima-Media Thickness of several carotid artery portions in anxious and non-anxious group

	Anxious group Mean ± SD	Non-anxious group Mean ± SD	P value ‡
Right common carotid	74.27 ± 12.60	57.88 ± 11.89	0.000
Left common carotid	72.85 ± 13.22	57.01 ± 11.58	0.000
Right carotid bulb	71.51 ± 12.84	54.12 ± 10.79	0.000
Left carotid bulb	69.12 ± 13.92	53.80 ± 10.19	0.000
Right internal carotid	64.02 ± 12.14	49.05 ± 9.67	0.000
Right internal carotid	63.55 ± 12.18	49.71 ± 8.82	0.000

‡ t-test

TABLE 3. Association of anxiety (independent) with atherosclerosis in different portions of carotid artery (dependent)

Dependent variable	Odds ratio	CI 95%	P value
Right common carotid	3.2	1.2 - 6.2	0.001
Left common carotid	2.8	0.94 - 6.3	0.232
Right carotid bulb	3.2	1.8 - 5.4	0.008
Left carotid bulb	4.1	1.9 - 8.1	0.01
Right internal carotid	2.4	1.1 - 8.2	0.01
Right internal carotid	2.1	1.2 – 7.3	0.05

Discussion

The results of the present study show a positive association between the presence of anxiety and carotid artery atherosclerosis, which is observed after adjustment for several major atherosclerosis risk factors.

A previous study performed by Stevens et al on the relationship between psychological/personality factors and carotid artery atherosclerosis yielded similar results. In this study 237 men with a mean age of 56 years and mild to moderate hypertension were studied. Intima-Media Thickness measured by B-mode ultrasonography showed that those with psychiatric disorder had higher IMT scores.[22]

In another study performed by Matthews et al on 200 premenopausal women on the relationship between IMT and psychiatric disorder, women with higher scores of psychiatric disorder had higher IMT scores ten years later. Our study included those with at least 1 year of anxiety disorder; still the same results were obtained, even after adjustment for major cardiovascular risk factors.[23] A study on 336 middle-aged women on the relationship between chronic anxiety and carotid artery atherosclerosis showed such a relationship; individuals with chronic anxiety and frequent anxiety symptoms had a twice greater risk of atherosclerosis carotid artery plaques (OR: 2.30, CI 95%: 1.10-4.82). This study suggests anxiety as a risk factor for carotid artery atherosclerosis.[24] Our study yielded similar results.

Several factors might play a role in the association between anxiety and atherosclerosis. One is that anxiety ensues from cardiovascular problems.

However, one study excluded symptomatic cardiovascular patients in the presence of such an association.[25] Another explanation might be the confounding effect of cardiovascular risk factors. In our study, the relation existed even after adjustment for known risk factors. The third explanation is anxiety-related biological events that promote atherosclerosis either through unhealthy lifestyle habits or directly.[26] Anxiety is associated with sympathetic activation, which has been suggested to alter endothelial integrity. These effects could contribute to the progression of arteriosclerosis. Anxious patients may have sympathetic nervous system hyperreactivity, i.e. exaggerated heart rate and blood pressure responses to behavioral stimuli, which is associated with more rapid progression of atherosclerosis.[27]

Based on results of our study and similar studies, it can be concluded that anxiety is a factor that increases the risk of cardiovascular disease.

Hence, controlling and reducing anxiety via pharmacologic and non-pharmacologic measures such as education and consultation might reduce the risk of CVD through controlling anxiety. Also evaluating patients with anxiety disorder for concomitant CAD seems reasonable.

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