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Anxiety is Related to Increased Carotid Intima-Media Thickness in Patients with First Acute Myocardial Infarction

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Abstract

Purpose: We examined the association of anxiety and depression with carotid intima media thickness in CAD patients during their hospitalization for acute myocardial infarction (MI).

Methods: A cohort of 74 consecutive patients (age: 59±10, range: 30 to 75 years) with a first episode of myocardial infarction (MI) (64% STEMI and 36% Non STEMI) were included. Mean intima-media thickness (IMT) in common carotids and carotid bulbs using ultrasound imaging was measured at study entry. All patients completed the Hospital Anxiety and Depression Scale (HADS) in the first 3 days of admission and the corresponding anxiety and depression scores were calculated. Patients were interviewed according to the structured clinical interview of the *DSM-IV* masked to the self-reports of symptoms.

Results: Patients with MI and pre-infarction angina had a higher incidence of anxiety (75% *vs.* 25% P<0.01) compared to those without. There were no difference in atherosclerotic risk factors medication and socioeconomic status, location of MI and STEMI between patients with (n=49 (67%)) and without anxiety. However patients with anxiety had increased IMT compared to those without (0.1 ±0.01 *vs*. 0.08 ±0.01 cm p<0.05). The anxiety score as assessed by HADS was related with IMT (r=0.40 p<0.01). After adjustment for atherosclerotic risk factors, (hyperlipidemia, diabetes, smoking, hypertension, socioeconomic status and medication), anxiety was independently associated with increased IMT values (b regression coefficient =0.37 p<0.05).

Conclusion: The present study suggests that increased anxiety is an independent determinant of IMT, an established surrogate marker of atherosclerosis, in patients with acute myocardial infarction.

Keywords: IMT and anxiety; Depression; First MI; Carotid atherosclerosis

Introduction

Phobic anxiety, generalized anxiety disorder, panic disorder and worry are predictors of myocardial infarction and cardiac death [1-12]. Anxiety affects nearly 25% of the population sometime throughout their life [13,14]. Anxiety causes over activity of the autonomic nervous system, increases catecholamines and cortisol, [15,16] 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 [17,18]. 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 [19]. As such, the association between sustained anxiety and carotid atherosclerosis is consistent with the reported association between chronic anxiety disorders and cardiovascular events. Sustained anxiety has also been shown [20] as a risk factor for the progression of carotid atherosclerosis, especially in men. Matthews et al. [21] found that baseline trait anxiety measured with the Spielberger Inventory scale did not predict average carotid intima-media-thickness (IMT) scores 10 years later in a group of 200 healthy postmenopausal women. In the same study, measures of trait anger and anger-in (a tendency to suppress anger) were associated with higher carotid IMT. Concerning depression, in cross-sectional studies, both concurrent depressive symptoms and clinically diagnosed depression have been associated with greater carotid IMT in selected healthy samples [22,23]. However, other cross-sectional work has noted a lack of

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association between current depressive symptoms and both carotid IMT and plaque [24]. Furthermore, lifetime history of clinical depression has been linked with presence of carotid plaque, but not carotid IMT, among middle-aged women [24]. Longitudinal research has identified baseline depressive symptoms [25] and hopelessness [26] as predictors of accelerated progression of carotid IMT over a 3- or 4- year follow-up. In addition, elevated depressive symptoms at baseline have been found to predict presence of carotid plaque at a 10-year follow-up27. A particular weakness of the current literature involves a nearly exclusive reliance on measurement of depression or depressive symptoms at a single time point (with the exception of Everson et al. [26], who studied hopelessness only). Because the relation between depressive symptoms and carotid IMT is unlikely to be a static one, additional research examining the relation between change in depressive symptoms and carotid IMT may help elucidate existing inconsistencies in the literature. In this study the association of anxiety and depression with carotid intima media thickness in CAD patients during their hospitalisation for acute myocardial infarction (MI) was examined.

Methods

A cohort of 74 consecutive patients (age: 59±10, range: 30 to 75 years) with a first episode of myocardial infarction (MI) (64% STEMI and 36% Non STEMI) were included. The study was approved by the Ethics committee of ATTIKON University Hospital [27]. All patients gave written informed consent before participating in the research protocol. Inclusion criteria to the study were patients < 75 years of age with MI with diagnosed and stable CAD or undiagnosed CAD. Exlusion criteria were: patients with known psychiatric illness, more than one MI, and patients with known but un stabilized CAD with frequent chest pain (Canadian class 3-4). Four patients were excluded for previous psychiatric illness and 6 patients for second episode of MI. Anxiety and depression was assessed with the HADS (Hospital Anxiety and Depression Scale) a scale found to perform well in assessing the symptom severity and caseness of anxiety disorders and depression in both somatic, psychiatric and primary care patients and in the general population [28] validated in Greece [29]. Patients were also interviewed according to the structured clinical interview of the *DSM-IV* masked to the self-reports of symptoms. Both measurements were attained in the first 3 days of hospitalization by a psychologist. In the HADS scale we used a cutoff point of 10, an indication of either high level anxiety symptoms or high level depression symptoms. Data describing how the patient was treated (medically, percutaneous transluminal coronary angioplasty, or coronary bypass grafting surgery), type of medications, comorbid conditions, and cardiovascular risk factors (lipid profile, smoking history, family history, body weight) were obtained by the medical records [30]. Mean intima-media thickness (IMT) in common carotids and carotid bulbs using ultrasound imaging was measured at a period of 30 days after MI. Endothelium dependent FMD of the right brachial artery was determined in all patients. All subjects were studied in the morning, having abstained from alcohol, caffeine and food for 8 hprior to the study; all vasoactive medications were withheld for 48 h before the study. Optimal imaging of the brachial artery was obtained and a resting scan was recorded using an Echo-Doppler ultrasound system (Vivid 7; GE Medical systems) and a 10 MHz transducer. Reactive hyperaemia was then induced by inflation of a blood pressure cuff on the forearm at a pressure of 200 mmHg for 5 min and subsequent deflation; the brachial artery was scanned continuously 30 s before and 90 s after cuff deflation. All images were recorded on super VHS videotape for off-line analysis. Artery diameter measurements were made using electronic calipers from the anterior to the posterior m line. FMD was calculated as the percentage increase in arterial diameter during hyperaemia as compared with the resting scan. B-modeul trasonographic examination was performed in all patients using the same Echo-Doppler ultrasound. Scanning included left and right carotid arteries for the measurement of the IMT; all scans were performed by the same operator. The carotid artery image was focused in the far wall and two segments were identified on each side: the distal 1.0 cm of the common carotid proximal to the bifurcation and the carotid bulb. The mean value of all four sites was used for analysis. All scans were digitally stored (Echopac; GE Medical Systems), and recorded on super VHS videotape for off-line analysis. The associations between vascular indices and the clinical characteristics of the patient are presented by means of standardized regression coefficient $P<0.05$ was considered to be the level of statistical significance. All statistical tests were two tailed. SPSS 11.5 software was used for statistical analysis. All variables are expressed as means ±S.D. Categorical data were compared by means of the 2-test. Variables with a P value of <0.1 in univariate analysis or of major clinical significance (e.g. sex, blood pressure, glucose, cholesterol, smoking, age, education level) were entered in multiple regression models. All co-variables included in the final models were tested for interactions.

Table 1: Descriptive measurements, A: patients with anxiety, NA: non-anxiety patients.

	Mean ± sd	
	A (*n*=34)	**NA (n=40)**
Age	59±10	56±10
Men (*n*)	32	39
Glucose (mg/dl)	94±44	112±35
Diameter of brachial artery baseline	0.45±.07	0.42±0.07
Diameter of brachial artery after nitrate	0.51±0.06	0.47.±0.06
FMD	0.044±0.02	0.043±0.01
IMTmean	0.13±0.03	0.11±0.02
chol	197.95±50.51	198.92±50.53
Trg	159.63±88.81	157.67±82.62
Hdl	39.18±12.82	37.32±14.72
Ldl	141.07±37.56	139.02±35.32
Glu	116.80±43.14	118.43±39.14
Anxiety	8.17±3.85	8.3±4.44
Depression	7. 05±4.07	6.9±3.6

Results

Patients with MI and pre-infarction angina had a higher incidence of anxiety (75% *vs.* 25% P<0.01) (Table 1) compared to those without. Overall, the correlation of anxiety (A) and depression (D) scores of self report (HADS) and interview (DSM) was statistically significant (A: p=0, 86 at 0, 01, D: p=0, 64 at 0,01) . There is atendency of self reported depression to be lower than diagnosed especially in the patients group. Anxiety was more easily detected by both the patient and the clinician. There was no difference in atherosclerotic risk factors, medication and socioeconomic status, location of MI and STEMI between patients with and without anxiety. Patients with anxiety had increased IMT compared to those without (0.1

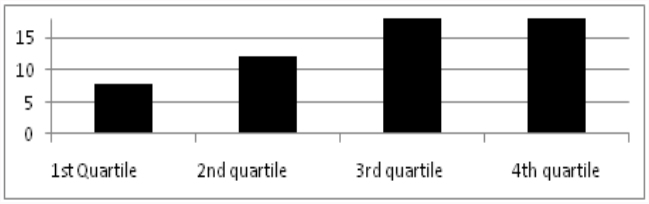

Figure 1: Drawing 1: Anxiety score and IMT.

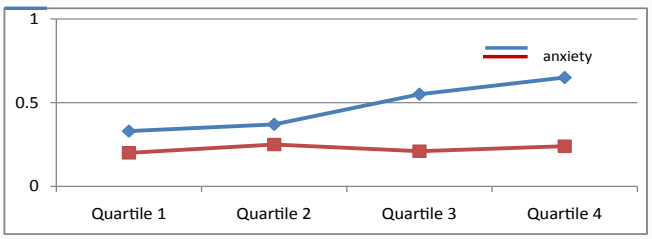

Figure 2: Regression analysis of depression and anxiety in HADS (Hospital Anxiety and Depression Scale) and IMT.

±0.01*vs.* 0.08 ±0.01 cm p<0.05). The anxiety score as assessed by HADS was related with IMT (r=0.40 p<0.01). After adjustment for atherosclerotic risk factors, (hyperlipidemia, diabetes, smoking, hypertension socioeconomic status and medication) anxiety was independently associated with increased IMT values (b regression coefficient =0.37p<0.05). In multivariate regression analysis the most important determinant of increased IMT was anxiety (Beta=-.04, p<0.05) and age (Beta=.028, p<0.05).

Patients were divided in four groups according to their IMT measurement (1st quartile: 0.06-0.09, 2nd quartile: 0.1-0.12, 3rd quartile: 0.13-0.15, 4th quartile: 0.18-0.21). The results of the one way analysis of variance with tests of linear trend showed that the growth of the quartile distribution is related to the increase of the anxiety score in HADS (p<0.05) and age (p<0.05) (Figure 1,2).

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

Discussion

The present study suggests that increased anxiety is related to IMT in patients with acutemyocardial infarction. In interpreting the present results, it is important to note the following limitations. We did not measure carotid IMT at the baseline – before the MI. Thus, it is possible that there are common pathophysiological processes behind the association between depressive or anxiety symptoms and increased IMT or that depressive or anxiety symptoms are affected by changes in IMT. According to our results, there was no relationship between continuous depressive symptoms and IMT. It could be that only high levels of depressive symptoms contribute to the progression of early atherosclerosis. A dichotomization of the depression measure so to select a group with a substantial level of depressive symptoms might be more appropriate only if we could define a clinically significant cutoff point for the level of depression.

It seems that ultrasound measures of carotid IMT and plaque can provide an indirect test of the coronary risk associated with psychological factors. It is possible that anxiety triggers clinical events as opposed to contributing to the development of atherosclerosis. One possible explanation for the association between anxiety and the progression of atherosclerosis is that cardiovascular problems may produce anxiety.

Anxiety is associated with sympathetic activation. The effect of this activation could be the influence and possibly alteration of endothelial integrity [31-36], a strong indicator of progression of atherosclerosis. The relationship with anxiety reflects in the condition of anxious patients: they have sympathetic nervous system hyper reactivity [34].As such, diminished autonomic control of the heart and may induce higher blood pressure variability, with effects on the coronary endothelium and plaque formation [35]. Several population-based studies show that high levels of IMT in asymptomatic men and women predict new clinical CHD and stroke even when controlling statistically for major cardiovascular risk factors21. Thus, ultrasound measures of carotid IMT and plaque can provide an indirect test of the coronary risk associated with psychosocial attributes. It is possible that anxiety triggers clinical events as opposed to contributing to the development of atherosclerosis. For example, high anxiety scores are associated with reduced heart rate variability30 and reduced heart rate variability predicts mortality after myocardial infarction, which suggests that anxiety contributes to clinical events.

Concerning depression, despite the well-known association between depression and CHD, little is known about the mechanisms responsible for the link. The diagnosis of CHD may increase depressive symptoms, and depressive patients with CHD may have a worse outcome. Previous studies on the relationship between depression or negative feelings and progression of IMT have been conducted among middle-aged or hypertensive men, whereas women have been almost totally ignored in these studies.

The lack of association between depressive symptoms and atherosclerotic process in women should be verified in other studies. Lack of correlation between depression and IMT in this study might give an indication that depressive symptoms may act as a marker rather than a predictor of IMT. Compared with other large arteries, atherosclerosis of the common carotid artery tends to develop relatively late in life, and lower degrees of common carotid IMT may indicate the presence of atherosclerosis elsewhere in the arterial system. This finding might imply links of the pathophysiology of emotional disorders to CAD and vascular structure. Treating anxiety disorder might also have cardiac prognostic implications.

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