

# Anxiety and Depression in Patients with Coronary Artery Disease

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## ÖZET:

Koroner arter hastalığı olan hastalarda anksiyete ve depresyon

**Amaç:** Önceki prospektif çalışmalarda depresyonun miyokardiyal enfarktüs ve kardiyovasküler mortalite için bağımsız bir risk faktörü olduğu bildirilmiştir. Anksiyete bozukluklarının da koroner arter hastalığı (KAH) ile ilişkili olduğu bilinmektedir. Psikolojik faktörler de sigara içme, azalmış fiziksel aktivite, kötü diyet ve tedaviye uyumun azalması gibi davranışsal mekanizmalar ile KAH seyrini etkileyebilmektedir. Bu çalışmanın amacı KAH şüphesiyle elektif olarak koroner anjiyografi yapılmak üzere kabul edilmiş hastalarda anksiyete ve depresyon düzeylerini araştırmak ve aterosklerotik risk faktörlerini saptamaktır.

**Yöntem:** Çalışma örneklemini ardışık olarak elektif koroner anjiyografi yapılan 116 hastadan oluşmuştur. Bulgular iki majör grup olarak sınıflandırıldı: normal ve anormal koroner anjiyografi. Koroner arterlerinde aterosklerotik hastalık saptanan (%50 ya da daha fazla darlık) ve/veya koroner arterlerinde yavaş kan akımı olan hastaların anjiyografileri anormal olarak değerlendirilmiştir. Hastaların anksiyete ve depresyon düzeyleri öz bildirimde dayalı Beck Depresyon Envanteri, Beck Anksiyete Envanteri ve Spielberger'in Durumluluk-Süreklilik Anksiyete Envanteri kullanılarak ölçülmüştür.

**Bulgular:** Altmışüç hastada (44 erkek, ortalama yaş: 52.2±11.1 yıl) anormal koroner anjiyografi bulgusu saptanmışken elli üç hastanın (40 erkek, ortalama yaş: 54.5±10.5 yıl) anjiyografisi normal olarak değerlendirilmiştir. Sosyodemografik özellikler ve aterosklerotik risk faktörleri her iki grupta benzerdi. Anormal koroner anjiyografi bulguları saptanan hastalar, normal bulgular saptanan hastalarla karşılaştırıldığında, anlamlı olarak daha yüksek depresyon ve anksiyete düzeylerine sahipti. Logistik regresyon analizinde sadece Beck Anksiyete Envanteri skorunun 15'den daha yüksek (odds ratio: 13.2, CI: 3.8-46.4) ve Durumluluk Anksiyete Envanteri skorunun 42'den yüksek olması (odds ratio: 4.9, CI: 1.7-14.2) koroner arter hastalığı için bağımsız belirleyicisidir.

**Sonuç:** Her iki grup için kardiyovasküler risk faktörleri benzer iken koroner arter hastalığı ile depresyon ve anksiyete düzeyleri arasında anlamlı bir ilişkinin olabileceği gösterilmiştir.

**Anahtar sözcükler:** koroner arter hastalığı, anksiyete, depresyon

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## ABSTRACT:

Anxiety and depression in patients with coronary artery disease

**Objective:** Previous prospective studies have reported depression as an independent risk factor for myocardial infarction and cardiovascular mortality. Anxiety disorders are also known to be associated with coronary artery disease (CAD). Psychological factors may also affect the course and outcome of CAD through behavioral mechanisms such as smoking, decreased physical activity, poor diet, and reduced compliance to treatment. The aim of this study was to explore the anxiety and depression levels and to determine the atherosclerotic risk factors in patients admitted for elective coronary angiography due to suspected CAD.

**Methods:** The study population consisted of 116 patients, who were consecutively admitted for elective coronary angiography. Findings were classified into two major groups: normal or abnormal coronary angiography. Abnormal coronary angiography was suggested in patients with atherosclerotic disease (equal to or greater than 50% stenosis) and/or slow blood flow in coronary arteries. Anxiety and depression symptom severities were assessed by self-reported scales, including the Beck Depression Inventory, Beck Anxiety Inventory and Spielberger's State-Trait Anxiety Inventory.

**Results:** Sixty-three patients (44 male, mean age: 52.2±11.1 years) had abnormal coronary angiography while fifty-three patients (40 male, mean age: 54.5±10.5 years) had normal findings. Sociodemographic characteristics and atherosclerotic risk factors were similar for both groups. Patients with abnormal coronary angiography had significantly higher depression and anxiety scores compared to patients with normal coronary angiography. In logistic regression analyses, only a Beck Anxiety Inventory score over 15 (odds ratio: 13.2, CI: 3.8-46.4) and State-Trait Anxiety Inventory score over 42 (odds ratio: 4.9, CI: 1.7-14.2) were independent predictors of coronary artery disease.

**Conclusions:** We have demonstrated a significant relationship between depression and anxiety scores and coronary artery disease while cardiovascular risk factors were similar for both groups.

**Keywords:** coronary artery disease, anxiety, depression

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## INTRODUCTION

Coronary artery disease (CAD) is one of the most common chronic diseases in our country (1). The rate of psychiatric disorders is very high and depressive symptoms are seen in 20% of the Turkish population. The prevalence of clinical depression is nearly 10% (2). General psychological stress, especially depression, is thought to increase the risk of cardiovascular disorders. Previous studies have showed that the presence of psychosocial risk factors such as depression, anxiety, anger, stress and lack of adequate social support increased the risk of acute coronary syndrome (ACS) (3). Depending on changes in health status, increases in levels of anxiety and depression can be seen in patients with CAD (4-6). Depressive symptoms generally seen in patients with CAD can also be frequently observed in patients with heart failure (7,8). As a result, depression affects significantly and negatively the course of cardiovascular diseases and may be considered as an important risk factor for cardiovascular diseases (9,10).

Anxiety, which is another psychological factor, also plays a role in the development of cardiovascular disorders (11). Anxiety is often seen in patients with CAD and, because of the risk of a heart attack at any moment, it reduces the quality of life and causes unnecessary use of health care services (12,13). As a result of psychological factors, smoking, reduced physical activity, poor diet and reduction of adherence to treatment affect the development of the CAD. Related to these psychosocial factors, the risk of atherosclerosis, myocardial infarction, arrhythmias associated with electrical instability, sudden death and hypertensive attacks increases (14,15). The aim of this study was to evaluate the levels of anxiety and depression in patients undergoing elective coronary angiography due to suspected CAD and to determine their relationship with other coronary artery disease risk factors.

## METHODS

### Study Population

Between June 2012 and August 2012, 116 consecutive patients scheduled for elective coronary angiography were included in the study in the Cardiology Clinic of Marmara University Training and Research Hospital. The study was approved by the hospital ethics committee and written informed consent was obtained from all patients participating in the study. According to the results of the coronary angiography, patients were divided into two groups, abnormal or normal coronary angiography (CAG). The abnormal CAG group was defined as patients with coronary artery stenosis equal to or greater than 50% and / or slow flow detected in coronary arteries. The group with normal CAG was defined as patients with normal coronary arteries or stenosis less than 50% (16). CAD risk factors and socio-demographic data of all patients were recorded. In order to determine the levels of anxiety and depression, the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and the Spielberger's State-Trait Anxiety Inventory (STAI) tests were applied to all study patients before coronary angiography. Sixty-three patients in the abnormal CAG group (44 male; mean age:  $52.2 \pm 11.1$  years) and 53 patients in the normal CAG group (40 male; mean age:  $54.5 \pm 10.5$  years) were enrolled in the study.

### Risk Factors for Coronary Artery Disease

All participants were evaluated for the presence of cardiovascular risk factors such as hypertension, hyperlipidemia, diabetes mellitus, smoking, and family history of CAD. Hypertension was defined as systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg, previously diagnosed hypertension, or use of any antihypertensive medications. Diabetes mellitus was defined as fasting plasma glucose levels more than 126 mg/dL in multiple measurements, previously diagnosed diabetes mellitus or use of

antidiabetic medications such as oral anti-diabetic agents and/or insulin. Hyperlipidemia was defined as serum total cholesterol  $\geq 240$  mg/dl, serum triglycerides  $\geq 200$  mg/dl, low-density lipoprotein cholesterol  $\geq 130$  mg/dl, previously diagnosed hyperlipidemia, or use of lipid-lowering medication. Smoking status was defined as the history of tobacco use at admission or in the 6 months prior to the visit. A family history of CAD was considered to be a history of documented CAD or sudden cardiac death in a first degree relative before the age of 55 years for men and 65 years for women.

### Self-Report Questionnaires

The BDI was developed by Beck et al. (17) in 1961 in order to measure behavioral signs of depression in adolescents and adults. Revision of the original version was developed by Beck during the 1970s and copyrighted in 1978. Reliability and validity of the BDI in Turkish was demonstrated by Hisli (18) in 1989. The BDI was designed to identify disease, measure the severity of depression and monitor the changes with treatment. The BAI was developed by Beck and colleagues in 1988 according to the cognitive approach. Turkish reliability and validity of the BAI was evaluated by Ulusoy et al. (19) in 1993. The BAI is a scale for rating anxiety in people (20). The STAI which was developed in order to determine the levels of state and trait anxiety separately by Spielberg and his colleague in 1970,

stemmed from Spielberger's two-factor theory of anxiety (21). Reliability and validity of the STAI in Turkish was shown by Le Compte and Oner in 1985. The STAI consists of two scales designed to differentiate between the temporary condition of the state of anxiety (STAI-1) and the more general and long-standing quality of trait anxiety (STAI-2). The STAI requires an individual describe how he/she feels at a specific time and in a specific circumstance and take into account his/her feelings relevant to the situation under consideration. The Trait Anxiety Scale requires the individual to describe generally how he/she feels. Scores range from 20 to 80, with higher scores correlating with greater anxiety.

### Statistical Analysis

Statistical analysis was performed using SPSS 15.0 software for Windows. The Kolmogorov-Smirnov test was used to evaluate the data distribution. Continuous variables are presented as mean  $\pm$  standard deviation and categorical variables are expressed as proportions. To compare parametric and nonparametric variables between the two groups, the Student t-test or the Mann-Whitney U test were used, respectively. Logistic regression analysis was performed to determine the independent predictors of coronary artery disease. The level of significance was determined to be  $P < 0.05$ . A 95% confidence interval for the percentage of prevalence was calculated using Wilson's method.

**Table 1: Sociodemographic characteristics and clinical data of the study population**

	Abnormal CAG Group (n= 63)	Normal CAG Group (n= 53)	P
Age (years)	52.2 $\pm$ 11.1	54.5 $\pm$ 10.5	0.260
Male (n-%)	44 (69.9%)	40 (75.5%)	0.499
Married (n-%)	55 (87.3%)	46 (86.8%)	0.935
Literate (n-%)	58 (92.1%)	51 (96.2%)	0.348
Working (n-%)	41 (65.1%)	41 (77.4%)	0.148
Smoke (n-%)	25 (39.7%)	29 (54.7%)	0.106
Hypertension (n-%)	41 (65.1%)	25 (47.2%)	0.052
Diabetes Mellitus (n-%)	30 (47.6%)	17 (32.1%)	0.089
Hyperlipidemia (n-%)	29 (46.0%)	17 (32.1%)	0.126
Family History of CAD (n-%)	29 (46.0%)	22 (41.5%)	0.625

CAG: Coronary Angiography, CAD= Coronary Artery Disease

**Table 2: Depression and anxiety score of the study population**

	<b>Abnormal CAG Group (n= 63)</b>	<b>Normal CAG Group (n= 53)</b>	<b>P</b>
BDI Scores	15.0±9.8	9.2±7.6	0.001
BAI Scores	20.7±10.9	8.2±4.1	<0.001
STAI-1 Scores	43.0±5.3	40.4±4.3	0,010
STAI-2 Scores	49.5±7.6	45.3±5.5	0.003

Data are presented as mean±standard deviation.

BDI= Beck Depression Inventory, BAE= Beck Anxiety Inventory, STAI-1= State Anxiety Inventory, STAI-2= Trait Anxiety Inventory, CAG: Coronary Angiography

## RESULTS

Sixty-three patients (44 male, mean age: 52.2±11.1 years) had abnormal coronary angiography while fifty-three patients (40 male, mean age: 54.5±10.5 years) had normal findings. Socio-demographic and clinical data of the two groups are displayed in the Table 1. There were no statistical differences between the groups regarding age, gender, marital status, educational level or working status. In terms of risk factors for coronary artery disease such as smoking, hypertension, diabetes, hyperlipidemia, and family history of CAD, the groups were similar ( $p=0.106$ , 0.052, 0.089, 0.126 and 0.625 respectively).

The abnormal and normal CAG groups were compared in terms of depression and anxiety levels in Table 2. The BDI level was 15.0±9.8 in the abnormal CAG group and was 9.2±7.6 in the normal CAG group ( $p=0.001$ ). The BAI level was 20.7±10.9 in the abnormal CAG group and 8.2±4.1 in the normal CAG group ( $p<0.001$ ). The STAI-1 level was 43.0±5.3 in the abnormal CAG group and was 40.4±4.3 in the normal CAG group ( $p=0.01$ ). The STAI-2 level was 45.3±5.5 in the abnormal CAG group and 49.5 7.6 in the normal CAG group ( $p=0.003$ ).

In a univariate analysis, hypertension, diabetes mellitus, BDI more than 12, BAI more than 15, STAI-1 more than 42, and STAI-2 more than 48 were among predictors of coronary artery disease. In logistic regression analyses, only BAI more than 15 (odds ratio: 13.2, CI: 3.8-46.4) and STAI-1 more than 42 (odds ratio: 4.9, CI: 1.7-14.2) were independent predictors of coronary artery disease.

## DISCUSSION

In patients with a chronic disease, perceived or experienced anxiety and depression are the most commonly seen psychological problems. Anxiety and depression are also common in patients with CAD. In patients with CAD, symptoms related to depression were observed in 65% of patients after ACS and 16-22% of them were at the level of major depression. In the first year after ACS, major depression developed in nearly 35% of patients (22). Epidemiological studies assessing the relationship between CAD and depression have showed that there was a strong correlation between the presence of episodes of major depression and CAD (23,24). A previous study has reported that there was a tendency towards anxiety and depression in patients with CAD and that this tendency was associated with the number of diseased vessels (25).

Psychological factors play an important role in the pathogenesis, evaluation and treatment of diseases. Some pathophysiological mechanisms have been suggested to explain the effects of psychiatric disorders on the cardiovascular system. One of the proposed pathophysiological mechanisms that triggered or accelerated the development of cardiovascular disease was cardiovascular reactivity, which was defined as the increase in blood pressure and pulse rate leading to more sympathetic stimulation of the heart muscle, parasympathetic slowdown and, as a result, increased cardiac output and vascular resistance (26,27). In addition, some factors that often occur in these patients, such as neuroendocrine system degradation, increase in

blood cortisol levels, increase in plasma and urinary catecholamine levels, platelet dysfunction, increased leukocyte adhesion and aggregation, increased inflammatory cytokines, increased heart rate and decreased heart rate variability are important in the development of CAD (28,29). Activation of the immune system leads to deterioration of endothelial function, thereby accelerating development of atherosclerosis in coronary arteries, resulting in ACS by cracking of the atherosclerotic plaques in these patients (30). Stress-induced increases in plasma catecholamines may lead to myocardial “stunning” mimicking acute myocardial infarction or Takotsubo syndrome, which is characterized by severe left ventricular systolic dysfunction (31).

Anxiety leads to deterioration of the autonomic nervous system and causes death due to arrhythmia. Autonomic dysfunction could involve either increased sympathetic stimulation, which has been related to the occurrence of arrhythmias and sudden death (32), or decreased vagal control, which has also been related to increase cardiac mortality (33). Kawachi et al. have showed that CAD is associated with anxiety and also that there was a link between high levels of anxiety and decreased heart rate variability (34). Patients who had increased anxiety symptoms had a concomitant reduction in heart rate variability. This association supports the hypothesis that the relation of anxiety with sudden cardiac death due to arrhythmias (35) may be related to ventricular arrhythmias. In a recent study, Habibović et al. demonstrated that anxiety was associated with an increased risk of ventricular arrhythmias and mortality 1 year after intracardiac defibrillator implantation, independent of demographic and clinical covariates (36). In patients with anxiety, acute coronary syndrome may develop due to coronary vasospasm. Vasospasm induced endothelial dysfunction facilitates the development of atherosclerotic plaques (37). In addition to the effects of psychological factors in these patients, behavioral factors, such as an increase in the frequency of smoking, deterioration in eating habits, an increase in the

consumption of alcohol and substance abuse and treatment non-compliance, affect the development of CAD (22). Anxiety has an impact on heart rhythm such as sinus tachycardia, atrial and ventricular premature beats or sinus bradycardia with vasovagal syncope. In a recent study, it was shown that anxiety increased susceptibility to ventricular arrhythmias and risk of sudden death by reducing the heart rate variability and increasing the QT dispersion (38).

In this study, levels of anxiety and depression in patients undergoing coronary angiography and socio-demographic variables that affect depression and anxiety were analyzed. According to the results of coronary angiography, groups with and without CAD were compared with each other. Soon after the diagnosis of patients with CAD, screening for anxiety and depression is important, and there are several reasons for it. Depression, rather than having an effect on cardiac function, has a significant impact on the quality of life and physical limitation in patients with CAD (39). For example, the presence of depression in patients with CAD decreases patient adherence to treatment and increases the risk of disease progression. After coronary angiography in patients diagnosed with CAD, health care workers have an important role in noting the occurrence of anxiety and depression. Patients should be evaluated using appropriate scales and clinical interviews. These assessments would be further improved by re-evaluating the patient a few weeks after discharge (40). Thus, the negative effects of depression on CAD could be reduced by early diagnosis and treatment of cases. Health care professionals that follow-up the patients should be aware of patients' doubts and concerns and should assist their adaptation to the treatment. At the same time, education of the family members and friends about depression can help them to understand and to assist the patient in developing coping strategies for their disease. It has been shown that family support causes better results in patients with major depression (40).

Treatment of depression is important in patients with CAD for several reasons. Successful

treatment of depression has been shown to improve patients' quality of life and decrease cardiovascular events (41). A previous study has showed that decreased emotional distress in the short-term may improve long-term mortality in patients with CAD (42). Although treatment of depression is possible in patients with cardiovascular disease, there is still a fear of cardiac toxicity of antidepressant drugs. Treatment with selective serotonin reuptake inhibitors (SSRIs) is safe and effective in patients with CAD (43). Behavioral treatments such as a lifestyle change program, vegetarian diet and moderate exercise reduce cardiovascular risks by decreasing atherosclerotic lesions (44).

The results of our study have important clinical implications. Our study is the second in the literature that reports associations between depression, anxiety and angiographic CAD in a population without previously documented CAD. In a previous study, Vural et al. (45) showed that there was no association between anxiety score and CAD while depression was associated with increased abnormal coronary angiographic findings. Our study confirmed not only the results of that study in terms of the association between depression and CAD but also extended further the

understanding of this association to anxiety. Therefore, screening and early detection of anxiety and/or depression in patients undergoing CAG might be helpful.

### Study Limitations

Our study had some limitations. One of them was the small sample size. Our study had a cross-sectional design; it would be better to follow up the patients with depression or anxiety and look for risk factors in those who develop coronary artery disease after a certain period of time. In addition, we could not examine the effect of medical treatments of the patients on their cardiovascular system.

## CONCLUSIONS

We conclude that anxiety and depression are important factors in patients with CAD. We have demonstrated a significant relationship between depression and anxiety scores and CAD while cardiovascular risk factors were similar for both groups. The results of the present study warrant large scale prospective studies to further elucidate this relationship.

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