Association between Depression and Anxiety Symptoms and Major Atherosclerosis Risk Factors in Patients with Chest Pain

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VURAL, M., ŞATIROĞLU, O., AKBAS, B., GÖKSEL, I. and KARABAY, O. Association between Depression and Anxiety Symptoms and Major Atherosclerosis Risk Factors in Patients with Chest Pain. Tohoku J. Exp. Med., 2007, 212 (2), 169-175 —— Psychological variables, such as depression and anxiety, are known as independent risk factors for coronary artery disease (CAD), suggesting the interaction of psychological and physiological factors in the development of CAD. In the present study, we analyzed the possible association between depressive and anxiety symptoms and major atherosclerotic risk factors in patients with chest pain warranting coronary angiography. The patients without CAD (n = 159) and those with CAD (n = 155) were evaluated for the severity of depression and anxiety by the symptom scales; high scores indicate severe symptoms. Age, male/female ratio, prevalence of diabetes mellitus (DM), and depression level were significantly higher in the CAD group. Among a total of 314 patients with chest pain, the mean depression score was higher in patients with DM (16.01 ± 8.12 vs 13.01 ± 9.6, p = 0.01) and those with hypercholesterolemia (15.43 ± 9.61 vs 12.53 ± 9.61, p = 0.02). The mean anxiety score was also higher in patients with DM (20.81 ± 12.85 vs 16.51 ± 12.09, p = 0.008), hypercholesterolemia (20.67 ± 13.11 vs 15.29 ± 11.36, p = 0.002), or hypertension (20.74 ± 12.94 vs 14.1 ± 10.8, p = 0.001). Thus, DM and hypercholesterolemia are associated with depression and anxiety, while hypertension is only related to anxiety. In contrast, smoking and family history of atherosclerosis are not related to depression and anxiety scores. These results suggest depression and anxiety symptoms may contribute to the development and progression of CAD, especially in patients with DM or hypercholesterolemia. ——— depression; anxiety; psychological tests; atherosclerosis risk factors; coronary artery disease

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Depression and anxiety scores are elevated in the presence of major atherosclerosis risk factors. For this purpose, we measured depression and anxiety scores using a semistructured psychiatric interview in both male and female patients undergoing coronary angiography for the evaluation of CAD. We showed that depression and anxiety scores were significantly elevated in the presence of some atherosclerosis risk factors in our study sample. The mechanism of psychological variable-atherosclerosis risk factor association is discussed in this paper.

**METHODS**

**Study population**

Between April and May 2006, 1,064 patients were referred to Avrupa Safak Hospital for diagnostic coronary angiography. Inclusion criteria for this cross-sectional study were age older than 18 years, indication of selective coronary angiography to evaluate the etiology of chest pain, and the patient’s informed consent to join the study. Exclusion criteria consisted of current pregnancy, cardiomyopathy, recent myocardial infarction or revascularization procedure (percutaneous transluminal coronary angioplasty or coronary artery bypass grafting), a history of congenital heart disease, insufficient cooperation, and incomplete study forms. From these 1,064 patients, 314 (152 males and 162 females; age, 19-79 years; mean age 56.26 ± 11.68) were enrolled in the study. All patients underwent a physical examination (body mass index [BMI]), coronary angiography, and questionnaire assessments of atherosclerosis risk factors (smoking status, diabetes mellitus [DM], family history, and existing or prior hypertension diagnosis) and educational and income status.

**Atherosclerosis risk factors**

The Turkish Society of Cardiology has defined major atherosclerosis risk factors in the Turkish population as age (> 45 in men, > 55 or premature menopause in women), family history, current smoking, hypertension (> 140/90 mmHg) or use of antihypertensive drugs, hypercholesterolemia (total cholesterol > 200 or low-density lipoprotein > 130 mg/dl), low high-density lipoprotein level (< 35 mg/dl), and DM.

**Evaluation of socioeconomic status**

Two indicators of socioeconomic status were educat-
tion and annual household income. Patients' levels of education were defined as “less than high school,” “high school graduate,” or “beyond high school.” Economic status was classified according to the following annual household income levels: less than US$8,500, between US$8,500 and US$42,500, and more than US$42,500.

**Coronary angiography**

Using the Judkins technique, coronary angiography and left ventriculography were performed in all patients. Each angiogram was interpreted by two cardiologists, who were not aware of the patient’s psychiatric diagnosis during interpretation of coronary angiography. Angiographic findings were evaluated as averages of the reports of the two cardiologists. Findings were classified into two major groups: normal or abnormal coronary angiography. Abnormal coronary angiography was suggested in patients with atherosclerotic disease and/or slow blood flow in coronary arteries. Significant obstructive disease was defined as equal to or greater than 50% stenosis of the luminal diameter in one or more coronary arteries.

**Psychological tests**

Psychological evaluation was carried out using the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI) in a semistructured psychiatric interview. The BDI is a 21-item scale developed by Beck et al. (1961) and is widely used to measure the severity of depression. Each item was scored from 0 to 3. The scores marked for each of these 21 items were added up at the end of the psychological evaluation. Accuracy and reliability studies of the BDI were conducted by Hisli (1989), and a score of 17 was accepted as a pathologic cut-off value for major depression in the Turkish population. To distinguish patients with depression, Carney et al. (1987) used a BDI score greater than or equal to 10, which revealed a moderate sensitivity (78%) and specificity (90%). The BAI was applied in a manner similar to the BDI. The validity and accuracy of the BAI has been studied in the Turkish population. Anxiety disorders can be diagnosed when a BAI score is equal to or greater than 17 in the Turkish population. Scores lower than 8 are considered normal in both inventories. Scores between 8 and 16 in the BDI and BAI show mild to moderate depression and anxiety, respectively. The suitability of the BDI and BAI scores in our patients was controlled by an experienced psychologist and a psychiatrist. Neither the psychologist nor the psychiatrist was aware of the clinical status or angiographic results of the patients.

**Statistics**

We investigated possible relationships between the atherosclerosis risk factors and the scores of depression and anxiety in a moderately large population. Patient characteristics are summarized as mean ± s.d. and percentages and compared with paired t-tests and $\chi^2$ tests, respectively. A multivariate regression analysis was performed to disclose possible confounding effects of age, BMI, gender, socioeconomic variables, and angiographic findings. A $p$ value < 0.05 was considered statistically significant.

**RESULTS**

Demographic and clinical parameters of the patients with and without CAD are summarized in Table 1. Coronary angiography was normal in 159 patients; 52% of all patients who were regarded as the patients without CAD. We suppose that chest pain may be related to cardiac and non-cardiac etiologies in these patients, such as syndrome X and gastroesophageal reflux disease. On the other hand, coronary angiography was abnormal in 155 patients, who were regarded as the patients with CAD. Smoking, family history, hypertension and hypercholesterolemia were similarly seen in the patients with or without CAD ($p > 0.05$). However, DM was prevalent in the patients with CAD ($p = 0.02$). We have also noted that the patients with CAD had significantly older age and increased male/female ratio.

The mean depression score was significantly different between patients with and without CAD (Table 1). In this analysis, the mean BDI score was higher in patients with CAD ($14.69 \pm 9.92$ vs $12.87 \pm 8.65; p = 0.03$). However, the mean BAI score was similar between the patients with and without CAD ($17.73 \pm 11.09$ vs $17.45 \pm 11.09; p = 0.75$) (Table 1).

The mean depression and anxiety scores were higher in females than in males, despite female patients had CAD less frequently (Table 2). Both the BDI score ($15.45 \pm 9.54$ vs $15.92 \pm 9.29; p = 0.81$) and the BAI score ($21.71 \pm 13.11$ vs $22.14 \pm 11.8; p = 0.89$) were slightly lower for
### Table 1. Patient characteristics and clinical data.

<table>
<thead>
<tr>
<th>Characteristics and clinical parameters</th>
<th>Patients without CAD ((n = 159))</th>
<th>Patients with CAD ((n = 155))</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53.8</td>
<td>58.7</td>
<td>0.03</td>
</tr>
<tr>
<td>Female/male</td>
<td>95/64</td>
<td>67/88</td>
<td>0.01</td>
</tr>
<tr>
<td>Family history</td>
<td>56 (35%)</td>
<td>78 (50%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Smoking</td>
<td>39 (24%)</td>
<td>27 (17%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>57 (35%)</td>
<td>77 (49%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Hypertension</td>
<td>83 (52%)</td>
<td>82 (52%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>32 (20%)</td>
<td>47 (30%)</td>
<td>0.02</td>
</tr>
<tr>
<td>BDI score</td>
<td>12.87 ± 8.65</td>
<td>14.69 ± 9.92</td>
<td>0.03</td>
</tr>
<tr>
<td>BAI score</td>
<td>17.45 ± 11.09</td>
<td>17.73 ± 11.09</td>
<td>0.75</td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; \(n\), number of patients; %, percentage of atherosclerosis risk factors; NS, not significant; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory.

### Table 2. Depression and anxiety scores in male and female patients.

<table>
<thead>
<tr>
<th>Psychological tests</th>
<th>Gender</th>
<th>(n)</th>
<th>Mean score ± S.D.</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck Depression Inventory</td>
<td>Female</td>
<td>162</td>
<td>15.54 ± 9.47</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>152</td>
<td>11.88 ± 8.82</td>
<td></td>
</tr>
<tr>
<td>Beck Anxiety Inventory</td>
<td>Female</td>
<td>162</td>
<td>21.79 ± 12.86</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>152</td>
<td>13.11 ± 10.18</td>
<td></td>
</tr>
</tbody>
</table>

\(n\), number of patients; S.D., standard deviation; \(p\), \(p\) value on comparison of Beck Depression Inventory and Beck Anxiety Inventory scores between the female and male groups.

### Table 3. Depression and anxiety scores in the presence of diabetes mellitus, hypercholesterolemia, hypertension and menopause.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Presence of disease</th>
<th>(n)</th>
<th>Mean BDI score ± S.D.</th>
<th>(p)</th>
<th>Mean BAI score ± S.D.</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>Yes</td>
<td>79</td>
<td>16.01 ± 8.12</td>
<td>0.01</td>
<td>20.81 ± 12.85</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>235</td>
<td>13.01 ± 9.60</td>
<td></td>
<td>16.51 ± 12.09</td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>Yes</td>
<td>134</td>
<td>15.43 ± 9.61</td>
<td>0.02</td>
<td>20.67 ± 13.11</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>180</td>
<td>12.53 ± 9.61</td>
<td></td>
<td>15.29 ± 11.36</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>Yes</td>
<td>165</td>
<td>14.25 ± 8.83</td>
<td>0.33</td>
<td>20.74 ± 12.94</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>149</td>
<td>13.23 ± 9.85</td>
<td></td>
<td>14.1 ± 10.80</td>
<td></td>
</tr>
<tr>
<td>Menopause</td>
<td>Yes</td>
<td>134</td>
<td>15.45 ± 9.54</td>
<td>0.81</td>
<td>21.71 ± 13.11</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>28</td>
<td>15.92 ± 9.29</td>
<td></td>
<td>22.14 ± 11.8</td>
<td></td>
</tr>
</tbody>
</table>

\(n\), number of patients; BDI, Beck Depression Inventory; S.D., standard deviation; BAI, Beck Anxiety Inventory; \(p\), \(p\) value between the BDI scores and the atherosclerosis risk factors; \(P\), \(p\) value between the BAI scores and the atherosclerosis risk factors.
women in menopause although the difference was not statistically significant (Table 3). Socioeconomic variables were not significantly related to the BDI and BAI scores ($p > 0.05$).

After controlling for socioeconomic variables, age, gender, BMI, and angiographic results, significant associations were found between the BDI and BAI scores and some of the major coronary risk factors. The mean BDI and BAI scores in the presence of DM, hypercholesterolemia, and hypertension are summarized in Table 3. The mean BDI and BAI scores were significantly higher among patients with DM or hypercholesterolemia. All diabetic patients had type II DM in our study. No significant relationship was shown between the presence of hypertension and the mean BDI score, whereas the mean BAI score was significantly higher in patients with hypertension.

We could not find any association between the BDI and BAI scores and smoking or family history. The BDI score was $17.1 \pm 8.54$ in smokers and $15.32 \pm 9.6$ in nonsmokers ($p = 0.44$). The BAI score was $22.52 \pm 12.26$ in smokers and $21.69 \pm 12.98$ in nonsmokers ($p = 0.79$). Patients with a family history of CAD showed slightly elevated anxiety scores. However, neither the BDI score ($15.48 \pm 8.63$ vs $15.58 \pm 10.32$; $p = 0.94$) nor the BAI ($23.08 \pm 11.97$ vs $20.46 \pm 13.66$; $p = 0.19$) score was statistically different in patients with or without a family history of CAD.

**DISCUSSION**

Although rapid advances in cardiovascular therapeutics have reduced mortality in patients admitted to hospital with acute myocardial infarction, about one third of cardiac deaths occur within the first hour of a patient’s first attack and, thus, before any opportunity for medical intervention exists. This fact underlines the importance of primary prevention to reduce the risk of CAD before its clinical presentation. Behavioral risk factors for CAD (such as smoking, overeating, physical inactivity, and poor compliance with the management of DM, hypercholesterolemia, and hypertension) are the main targets of primary preventive medicine (Shapiro 2000).

The literature indicates that psychosocial factors influence the development and prognosis of CAD (Ruberman et al. 1984; Frasure-Smith et al. 1995; Musselman et al. 1998; Rozanski et al. 1999). However, the pathophysiological mechanisms through which psychosocial factors affect CAD outcomes remain undefined. In this study, we detected some associations between the severity of depression and anxiety symptoms and major atherosclerosis risk factors in a moderately large population. We also showed a significant relationship between the severity of depression and CAD. The mean depression and anxiety scores gradually increased as the severity of CAD increased. These analyses will be continued and discussed in a future paper. Coronary angiographic findings were controlled during statistical analysis in the present study.

Female gender predisposed our patients to have increased depression and/or anxiety scores. The BDI and BAI scores were significantly higher among female patients. In previous studies, the prevalence of depression was also higher in women with or without CAD (Blazer 2000; Naqvi et al. 2005; Perez et al. 2005). It seems that psychosocial distress is prospectively associated with increased risk of the development of CAD and premature mortality from cardiovascular events in women (Penninx et al. 1999; Wamala et al. 1999).

Although men had CAD more frequently based on coronary angiography, they had lower depression and anxiety scores in present study. As a result, gender difference was controlled during statistical analysis of this study.

A significant association was found between depression and anxiety scores and DM. In previous studies, diabetic patients were commonly known to have more frequent psychiatric disorders. Murrel et al. (1983) reported that the prevalence of depression in a diabetic population was 13.4% and 25.4% in male and female patients, respectively. In a study from Turkey, Gulseren et al. (2001) determined that the prevalence of major depression was 15% in a diabetic population. Jacobson et al. (2002) proposed that DM, especially type 1 DM, may place patients at risk for a
depressive disorder through a biological mechanism related to the metabolic changes of DM on the structure and function of the brain. McIntyre et al. (2006) showed that the treatment of depression with the use of serotonergic antidepressants (e.g., fluoxetine) may reduce hyperglycemia, normalize blood glucose level, and increase insulin sensitivity in diabetic patients. Elevated depression scores increase the risk of having carotid plaques at the 10-year follow-up in a prospective study (Haas et al. 2005). Diabetic patients have already shown elevated depression scores and a tendency for cerebrovascular diseases. The latter event may aggravate depression in diabetics. Elevated BAI score in diabetics may predispose them to hypertension, which may also contribute to this complicated phenomenon. We believe that the association between depression and anxiety symptoms and DM is likely a bidirectional phenomenon. In other words, depression and anxiety disorders may worsen the course of DM, which then predisposes patients to have psychiatric diseases more frequently.

The mean depression score was also significantly higher among patients with hypercholesterolemia in present study. Statin treatment was shown to increase the tendency for depression; for example, simvastatin was shown to increase depression level significantly but did not affect anxiety level (Hyypa et al. 2003). In another study, depressive patients refractory to antidepressant treatment had significantly increased blood cholesterol level (Papakostas et al. 2003). Patients with hypercholesterolemia had also the higher anxiety scores in the present study.

Because hypertensive patients in the present study had significantly elevated BAI scores, anxiety might have a role in the pathogenesis of hypertension (Kaplan and Nunes 2003). Our data are also compatible with the study in which oral diazepam (5 mg) and captopril (25 mg) were compared in two similar groups with excessive hypertension (Grossman et al. 2005). The anti-anxiety treatment was found to be effective in lowering blood pressure in hypertensive patients. Increased sympathetic stimulation or disregulation of the autonomic nervous system, hypothalamic-pituitary-adrenal axis stimulation, increased heart rate and stroke volume, and disregulation of vasomotor tone have been proposed as mechanisms of hypertension in patients with excessive anxiety.

In conclusion, this study demonstrated a significant relationship between depression and anxiety symptoms and some of the major atherosclerosis risk factors in patients with chest pain. Hypertension, hypercholesterolemia, and DM were among the atherosclerotic risk factors, which were associated with the higher depression or anxiety scores. These findings suggest that depression and anxiety disorders may contribute to the development and progression of CAD through their associations with major atherosclerosis risk factors. Moreover, severe depression symptoms were directly associated with the presence of CAD. Therefore, depression and anxiety disorders can be considered within the primary preventive intervention and secondary therapeutic options of CAD, especially in patients with DM, hypercholesterolemia, and hypertension.

**Study limitations**

We cannot rule out the effects of unmeasured third variables, such as viral infections and other psychological parameters, or interactions among several variables, which may have influenced the psychological variable-coronary risk factor associations observed here. This study is also a cross-sectional study. It would be better to follow the changes in depression and anxiety scores in our patients and the effects of these changes on blood pressure, blood glucose, and lipid levels, and the course of CAD in a prospective study.

**References**


Depression and Anxiety Symptoms and Coronary Risk Factors


