

# The scores of Hamilton depression, anxiety, and panic agoraphobia rating scales in patients with acute coronary syndrome

*Akut koroner sendrom nedeni ile tedavi görmüş olan hastalarda Hamilton depresyon, anksiyete ve panik agorafobi düzeyleri*

Mutlu Vural, Mehmet Acer\*, Berfu Akbaş\*\*

From Clinics of Cardiology and \*Psychology, Kırşehir State Hospital, Kırşehir

\*\*Clinic of Psychiatry, School of Medicine, Yeditepe University, İstanbul, Turkey

## ABSTRACT

**Objective:** Psychological factors may influence the development and prognosis of coronary heart disease. The purpose of this study was to measure levels of depression, anxiety, and panic agoraphobia in patients who had been treated for acute coronary syndrome (ACS). We attempted to evaluate the relationship of the scores of depression, anxiety and panic agoraphobia, coronary risk factors, some clinical variables and coronary heart disease.

**Methods:** We evaluated the levels of depression, anxiety, and panic agoraphobia of patients who had been treated for ACS, using the Hamilton depression (HAM-D), the Hamilton anxiety (HAM-A), and the Hamilton panic agoraphobia (HAM-PA) rating scales in 82 patients underwent treatment for acute coronary syndrome in this cross-sectional observational study. The relationship of these psychological variables with gender, presence of diabetes mellitus, hypercholesterolemia and coronary revascularization were assessed. Statistical analysis was performed using unpaired t test for independent samples and Chi-square test

**Results:** The majority of the patients were male (54 males and 28 females); the mean age of the patients was  $61.9 \pm 12.1$  years; 46% were admitted for unstable angina, 37.8% for acute myocardial infarction (MI) with ST elevation, and 16.7% with non-ST-elevation MI. Depressive symptoms (HAM-D score  $>8$ ) were present in 87.8% of the patients. The HAM-D score was closely related to the HAM-A and the HAM-PA scores ( $p < 0.001$ ). The HAM-D, HAM-A, and HAM-PA scores were significantly higher in female patients ( $p < 0.001$ ). After controlling for sex, both the HAM-D score ( $21.05 \pm 7.72$  vs  $15.10 \pm 7.3$ ;  $p = 0.02$ ) and the HAM-A score ( $19.17 \pm 9.50$  vs  $12.96 \pm 7.77$ ;  $p = 0.03$ ) were significantly higher in diabetic patients. The mean HAM-D score was also significantly higher in patients with hypercholesterolemia ( $18.10 \pm 8.23$  vs  $13.97 \pm 6.38$ ;  $p = 0.02$ ), as well as in those with a previous history of cerebrovascular disease (CVD) ( $23.20 \pm 9.62$  vs  $15.89 \pm 7.45$ ;  $p = 0.02$ ). Patients who had undergone coronary artery bypass grafting (CABG) showed significantly lower HAM-D ( $12.5 \pm 7.8$  vs  $16.6 \pm 8.1$ ;  $p = 0.03$ ) and HAM-A ( $9.6 \pm 6.3$  vs  $15.6 \pm 8.5$ ;  $p = 0.01$ ) scores.

**Conclusion:** Higher scores of depression, anxiety, and panic agoraphobia were particularly common findings in female patients and in those patients with diabetes mellitus, hypercholesterolemia, and CVD. Depression and anxiety disorder may be prevalent in patients who had been treated for ACS. We believe that patients should be carefully followed and treated for depression and anxiety disorder after ACS treatment to prevent adverse outcomes. (*Anadolu Kardiyol Derg 2008; 8: 43-7*)

**Key words:** Depression, anxiety, acute coronary syndrome, coronary risk factors, Hamilton depression rating scale, Hamilton anxiety rating scale, Hamilton panic agoraphobia rating scale

## ÖZET

**Amaç:** Psikolojik faktörler koroner arter hastalığı gelişimi ve prognozunu olumsuz etkilemektedir. Bu çalışmada akut koroner sendrom nedeni ile tedavi görmüş olan hastalarda depresyon, anksiyete ve panik agorafobi düzeylerini ölçmeyi amaçladık. Ayrıca; depresyon, anksiyete ve panik agorafobi skorlarının koroner risk faktörleri, bazı klinik değişkenler ve koroner kalp hastalığı ile ilişkisini araştırmayı amaçladık.

**Yöntemler:** Bu kros-seksiyonel, gözlemsel çalışmada bir zaman diliminde Hamilton depresyon, anksiyete ve panik agorafobi değerlendirme ölçeği (HAM-D, HAM-A ve HAM-PA) kullanılarak hastaların sırasıyla depresyon, anksiyete ve panik agorafobi düzeyleri akut koroner sendrom nedeni ile tedavi görmüş olan 82 hastada değerlendirilmiştir. Bu psikolojik değişkenlerin cinsiyet, diyabet, hiperkolesterolemi ve revaskülarizasyon ile ilişkisi değerlendirilmiştir. İstatistiksel analiz bağımsız olmayan değişkenler için eşsiz t-test ve Ki-kare testi kullanılarak yapılmıştır.

**Bulgular:** Hastaların geneli erkek olup (54 erkek, 28 kadın) yaş ortalaması  $61.9 \pm 12.1$  yıl idi. Toplamda %46 hastada kararsız anjina, %37.8 hastada ST yükselmeli miyokard infarktüsü ve %16.7 hastada ST yükselmez miyokard infarktüsü nedeni ile tedavi uygulanmıştır. Depresif semptomlar (HAM-D skoru  $>8$ ) hastaların %87.8'inde rastlanmıştır. HAM-D HAM-A ve HAM-PA skorları ile yakın ilişki içerisindedir ( $p < 0.001$ ). HAM-D, HAM-A ve HAM-PA skorları kadın hastalarda anlamlı olarak yüksek bulunmuştur ( $p < 0.001$ ).

Cinsiyet kontrol edildikten sonra diyabet bulunan hastalarda hem HAM-D skoru ( $15.10 \pm 7.30$ 'a karşılık  $21.05 \pm 7.72$ ;  $p = 0.02$ ), hem de HAM-A skoru

(12.96±7.77'e karşılık 19.17±9.5; p=0.03) anlamlı olarak yüksek saptanmıştır. Ortalama HAM-D skoru hiperkolesterolemi (13.97±6.38'e karşılık 18.10±8.23; p=0.02) ve serebrovasküler hastalık öyküsü olan hastalarda (15.89±7.45'e karşılık 23,2±9,62; p=0,02) anlamlı olarak yüksek saptanmıştır. Baypas ameliyatı olan hastalarda HAM-D skoru (16.6±8.1'e karşılık 12.5±7.8; p=0.03) ve HAM-A skoru (15.56±8.50'ye karşılık 9.6±6.3; p=0.01) daha düşük düzeydedir.

**Sonuç:** Yüksek depresyon, anksiyete ve panik agorafobi düzeyleri özellikle kadınlarda olmak üzere diyabet, hiperkolesterolemi ve serebrovasküler hastalığı olan hastalarda sık rastlanan bir bulgudur. Depresyon ve anksiyete bozukluğu akut koroner sendrom tedavisi gören hastalarda yaygın olmalıdır. Bize göre akut koroner sendrom tedavisi sonrası hastaların psikolojik yönden yakından izlenmesi ve tedavisi önemlidir. Bu yaklaşımla akut koroner sendromun olası olumsuz sonuçları önenebilir. (*Anadolu Kardiyol Derg 2008; 8: 43-7*)

**Anahtar kelimeler:** Depresyon, anksiyete, akut koroner sendrom, koroner risk faktörleri, Hamilton depresyon ölçeği, Hamilton anksiyete ölçeği, Hamilton panik agorafobi ölçeği

## Introduction

Populationbased epidemiologic studies have demonstrated that depressive symptoms, even at low levels, can predict the incidence of coronary heart disease (CHD) in healthy populations (1, 2). Other studies have identified a relationship between the presence of depressive symptoms or psychological stress and an increased risk of morbidity and mortality after acute myocardial infarction (MI) (3, 4). Despite these negative clinical implications, comorbid depression in patients with a history of acute MI or unstable angina is frequently undiagnosed and/or untreated (5, 6).

We hypothesized that psychological factors are very important and closely associated with clinical parameters in patients with CHD affecting the prognosis of acute coronary syndrome (ACS). Using the Hamilton depression (HAMD), Hamilton anxiety (HAMA), and Hamilton panic agoraphobia (HAMPA) rating scales, we attempted to evaluate some psychological characteristics of patients who had been treated for ACS in this study. We have later compared the results of these symptom scales to coronary risk factors, demographic and some clinical features of the patients.

## Methods

**Study design and patients characteristics:** In this cross-sectional observational study, we first identified 160 patients treated for ACS between 2004 and 2005. Patients who were older than 18 years, treated with ACS in the intensive coronary care unite of Kırşehir State Hospital, discharged at least 6 month ago, and accepted to join the study were eligible for inclusion in the study. Exclusion criteria were the diagnosis other than ACS, death during in-hospital stay or after discharge, inability to contact after discharge, refusing to join to the study. Of 160 patients, two of them died during hospitalization and 19 died 6 to 15 months following hospitalization. We were able to make contact with all of the remaining 139 patients and accepted the first 82 patients (54 males, 28 females) between 40 and 83 years (mean age 61.92±12.16 years) who agreed to participate in this study.

In present study, the diagnosis of ACS consisted of unstable angina, ST elevation, and non-STelevation MI. Overall, the patients included in this study had been admitted for unstable angina (46%), acute MI with ST elevation (37.8%), and nonSTelevation MI (16.7%) (Table 1). Patients with dynamic STT wave changes on their electrocardiograms (ECGs) and creatinine kinase, muscle and brain (CKMB) levels less than 50 U/L were determined to have unstable angina, whereas those with CKMB levels greater than 50 U/L were identified as having an acute MI.

Coronary angiography was performed in 49 patients (37 males, 12 females); percutaneous coronary intervention (PCI) in 14 patients (10 males, 4 females); and coronary artery bypass grafting (CABG) in 18 patients (15 males, 3 females). Of the 82 patients included in this study, 42.8% of the female patients, in comparison to 68.5% of the male patients, underwent coronary angiography. There were sex differences in the application of revascularization procedures: PCI was carried out in 14.2% of female patients and in 18.5% of male patients; CABG was performed in 10.7% of female patients and in 27.7% of male patients.

### Data collection

When performing a chart review of 82 subjects included in the study, we tabulated such factors as previous history of CHD and other cardiovascular diseases, the presence of diabetes mellitus, the type of ACS, the body mass index, medications, treatment interventions, vital signs, physical examination findings, and electrocardiographic findings.

### Psychological assessment

The psychological interview was semistructured, which was carried out by a psychologist (who had received previous training in performing the psychological tests used in this study) and a psychiatrist (one of the authors of this study), involved determining the severity of depression, anxiety and panic agoraphobia by the HAMD, HAMA, and HAMPA as psychological symptoms scales. During the psychological assessment, neither the psychologist nor the psychiatrist was aware of the cardiac status of the patients.

**Hamilton depression rating scale:** This scoring questionnaire was first developed by Hamilton et al. (7). The validity and the reliability of Turkish HAMD scale scores were demonstrated by Akdemir et al. (8). This scale, which consists of 17 questions and has an upper score limit of 53, measures the depression levels of patients. Scores less than 8 are considered normal, scores between 8 and 16 indicate that patients may have mild to moderate depression, and scores equal to and greater than 17 signs that patients may be experiencing major depression.

**Hamilton anxiety rating scale:** This psychological test was also developed by Hamilton et al. (7) The validity and the reliability of Turkish HAMA scale scores were evaluated by Yazıcı et al. (9). This scale is used to determine the anxiety levels and the distribution of symptoms of patients. It consists of 14 questions that evaluate both somatic and mental findings. Using this scale, experienced psychologists can determine the presence and level of each item. Scores equal to and greater than 17 are signs that patients may have anxiety disorder.

**Hamilton panic agoraphobia rating scale:** This questionnaire, which is complementary to HAMA, consists of 14 questions that evaluate both panic attacks and agoraphobia. Using this scale,

experienced psychologists can evaluate the level of these findings during the clinical examination of their patients.

**Statistical analysis**

Study sample size (n) was estimated according to the formula defined by Karasar (10). As a result, minimum sample size was calculated as 42 patients. In our study, the sample size was 82 to avoid possible turnaround missing.

All statistical analyses were performed using the Statistical Program for the Social Sciences (SPSS for Windows, Chicago, IL, USA). The primary analyses used continuous measures of depression, anxiety, and panic agoraphobia scores to assess correlations among these attributes. Patient characteristics were summarized using mean ±SD values and percentages and then compared with t tests and Chisquare tests, respectively. The distribution of psychological variables was similar between the patient groups checked by using a KolmogorovSmirnov Z test. The unpaired t test for independent samples was used to examine relationship of HAMD, HAMA, and HAMP A scores with clinical variables as gender, diabetes mellitus, history of cerebrovascular disease, hypercholesterolemia and coronary revascularization. Adjustment for gender and some other covariates were also controlled during statistical analyses. A p value <0.05 was considered statistically significant.

**Results**

Of the patients included in the study sample, 87.8% had HAMD scores greater than 8. Moderate and major depression (HAMD ≥14) was found in 92.8% of female patients and in 40.7%

**Table 1. Characteristics and atherosclerosis risk factors of patients**

Characteristics	Findings
Age, years	61.92 ± 12.16
Gender	28 females, 54 males
Smoking, %	42.7
Hypertension, %	55
Hypercholesterolemia, %	55 (18 females and 31 males)
Diabetes mellitus, %	22
Family history of atherosclerosis, %	27
Previous history of CHD, %	33
Previous history of CVD, %	6.7 (2 females and 4 males)
Previous history of PAD, %	3.3 (3 males )
CHD - coronary heart disease, CVD - cerebrovascular disease, PAD - peripheral arterial disease	

**Table 2. Depression, anxiety, and panic agoraphobia scores among male and female patients**

Psychological symptom scales	Gender	n	Mean± SD	p*
Hamilton Depression Rating Scale	female	28	21.50±7.05	<0.001
	male	54	13.66±6.69	
Hamilton Anxiety Rating Scale	female	28	20.21±8.33	<0.001
	male	54	11.16± 6.79	
Hamilton Panic Agoraphobia Rating Scale	female	27	18.29±8.63	<0.001
	male	52	10.75±5.69	
*- unpaired t test				

of male patients. As shown in Table 2, the HAMD, HAMA, and HAMP A scores were higher in female patients as compared with male patients (p<0.001 for all). Hamilton scales have considerable overlap. Depressed patients tend to be anxious, and anxious patients tend to be depressed.

The HAMD score was significantly higher in patients with a history of stroke or carotid atherosclerosis; the HAMD score was 23.2±9.62 among patients with cerebrovascular disease (CVD) and 15.89±7.45 among the other patients. After controlling for sex, a significant relationship between patients with CVD and the HAMD score (p=0.02) was found. No significant relationship was determined between patients with a previous history of CVD and HAMA/HAMP A scores. In addition, no significant relationship was found between patients with a previous history of CHD/peripheral arterial disease and HAMD/HAMA/HAMP A scores.

The HAMD and HAMA scores were found to be significantly higher in diabetic patients than in nondiabetic patients (p=0.02 and p=0.03, respectively) (Table 3). The HAMD score was also significantly higher in patients with hypercholesterolemia than in those without hypercholesterolemia (p=0.02) (Table 4). After controlling for sex, the HAMD and HAMA scores were determined to be significantly lower among patients who underwent CABG than in patients without history of CABG. The HAMD score was 12.5±7.8 among those patients who underwent CABG in comparison to 17.4±7.4 among the other patients (p=0.03). Among those patients who underwent CABG, the HAMA score was 9.6±6.3, whereas the HAMA score was 15.56±8.5 among the other patients (p=0.01). No significant differences were found between the HAMD/HAMA/HAMP A scores and the patients who underwent coronary angiography or PCI.

**Table 3. Depression, anxiety, and panic agoraphobia scores among diabetic and non-diabetic patients**

Psychological symptom scales	Presence of DM	n	Mean± SD	p*
Hamilton Depression Rating Scale	yes	17	21.05 ± 7.72	0.02
	no	65	15.10 ± 7.3	
Hamilton Anxiety Rating Scale	yes	17	19.17 ± 9.5	0.03
	no	65	12.96 ± 7.77	
Hamilton Panic Agoraphobia Rating Scale	yes	17	16.52 ± 7.89	0.26
	no	62	12.45 ± 7.44	
*- unpaired t test DM- diabetes mellitus				

**Table 4. Depression, anxiety, and panic agoraphobia scores in patients with and without hypercholesterolemia**

Psychological symptom scales	Hypercholesterolemia	n	Mean ± SD	p*
Hamilton Depression Rating Scale	yes	47	18.1±8.23	0.02
	no	35	13.97±6.38	
Hamilton Anxiety Rating Scale	yes	47	15.74±8.75	0.11
	no	35	12.25±7.79	
Hamilton Panic Agoraphobia Rating Scale	yes	45	14.66±7.39	0.11
	no	34	11.55±7.8	
*- unpaired t test				

## Discussion

Our study demonstrated that female patients had higher scores of depression, anxiety, and panic agoraphobia. Many studies have also demonstrated that women have higher depression and anxiety levels in their daily life or following ACS; however, these levels were not as high as those we have found in present study (1113). Our finding is important because there is a greater association between depression and higher coronary risk in women following ACS (14).

The association of diabetes mellitus with higher HAMD and HAMA scores has also been demonstrated. Of 17 diabetic patients (9 females, 8 males), HAMD scores equal to and greater than 14, which fall within the range of moderate and major depression on the scale, were found in all 9 (100%) of the female patients and in 3 (37.5%) of the male patients. In many other studies, depression was also frequently found in diabetics (15, 16). Diabetes mellitus may place patients at risk for a depressive disorder through a biological mechanism linking the metabolic changes of this disease to changes in brain structure and function (17). Use of serotonergic antidepressants (e.g., fluoxetine) to treat depression in diabetics has been found to reduce hyperglycemia, normalize glucose homeostasis, and increase insulin sensitivity (18). Therefore, the relationship between depression and diabetes mellitus is a bidirectional phenomenon. We believe that diabetes mellitus may also be regarded as a risk factor for depression and anxiety disorder following ACS.

Depression scores were also found to be higher in our patients with a previous history of CVD. Hackett et al. (19) showed that 33% of all stroke survivors experience depression. Patients with elevated depression scores at baseline were >2 times as likely to have carotid plaque at the 10-year followup (20). However, in this sample, elevated HAMD scores were not associated with prior CHD. We think that prior CHD had no additional effect on the HAMD score after ACS. On the other hand, prior CVD seems to have an additional effect on depression score after ACS treatment. Thus, it appears that a recent coronary event, namely ACS, seems to be much more related to the HAMD score.

Interestingly, our findings also indicated that a relationship exists between hypercholesterolemia and depression scores, however, we do not know the exact mechanism of this phenomenon. Many studies have investigated this association. Ledochowski et al. (21) showed that hypercholesterolemia may not necessarily increase the risk of depressive mood; conversely, increased intake of fat and carbohydrates by individuals with depressive mood may increase cholesterol levels. There are also controversies surrounding the possible relationship between hypercholesterolemia and depression (22). For example, one study indicated that long-term cholesterol lowering therapy has different effects on serotonin transmission. This finding suggests that within this period some patients could be vulnerable to depression, violence, or suicide (23). Statin usage (47.5% of all patients) was not associated with increased depression scores in our patients who exceeded the first month of statin therapy.

Depression and anxiety scores were surprisingly found to be significantly lower in patients who had undergone CABG. We think that CABG might have positively affected the psychological status of our patients, which may be related to the surgical procedure itself. In their prospective study of patients who underwent CABG, Boudrez et al. (24) demonstrated a clear overall improvement in patients' psychological status over the first year, more specifically during the first 6 months after CABG. According to their findings, patients were less anxious, less depressed, and less exhausted, and experienced a more subjective wellbeing. In our study, we assessed the psychological status of patients (who had been previously treated for ACS) 6 to 15 months after undergoing PCI or CABG. The lower scores of depression and anxiety in patients who underwent CABG may be related to improved quality of life and reduced rate of restenosis after CABG.

Increasing evidence indicates that psychological factors may adversely affect the outcome of CHD. Therefore, the diagnosis and treatment of some coexisting psychiatric diseases should be considered of importance following the onset of ACS (25, 26). A previous study reported finding depressive symptoms and major depression in 90% and in 35% of patients, respectively, following ACS treatment in a similar population (27). These results were similar to those found in other populations (2830). Use of antidepressant treatment in depressed patients who experience an acute MI has been shown to reduce subsequent cardiovascular morbidity and mortality (31). In the present study, patients were advised to visit a psychiatrist after our first evaluation to prevent the adverse effects of these psychological factors (11, 32). However, most of the patients included our study remained untreated for depression and/or anxiety disorder one year after receiving this advice, which was mostly associated with health policy.

### Limitations of the study

It is known that depression is a natural reaction to events, such as suffering from severe diseases that have not been overcome. If followed, half of the cases of depression diagnosed after MI spontaneously go into remission. For that reason, we included patients who had been treated for ACS and were discharged from hospital at least 6 months ago (6 to 15 months). Anxiolytic drugs, which are usually ordered during the hospitalization period for ACS, also disturb psychological evaluation. We tried to avoid overestimated and incorrect values in our study by conducting our patient assessments at least 6 months following hospitalization. Assessing the psychological status of patients may be best carried out at admission and throughout the followup period.

Because our study sample is small, it is difficult to draw definitive conclusions from the results. Therefore, conducting a study with a larger sample size should be considered in the future.

In addition, a trained psychologist usually measured the scores of depression in this study. Although the cardiologists involved in this study were informally trained in measuring depression scores, they successfully measured depression and anxiety scores under the supervision of the experienced psychologist and psychiatrist.

## Conclusion

Higher scores of depression, anxiety, and panic agoraphobia estimated by the psychological symptom scales following ACS treatment were associated with some prehospital factors, such as the presence of diabetes or hypercholesterolemia, and a history of CVD. Depression and anxiety disorder are prevalent in patients with CHD, indicating a causal relationship between psychological and physiological factors for development and prognosis of CHD. We believe that patients with diabetes mellitus, hypercholesterolemia, and CVD should be carefully followed for the diagnosis of depression and anxiety disorder; the treatment of which may improve the prognosis of ACS. Interestingly, patients who underwent CABG after ACS treatment showed significantly lower depression and anxiety scores. These data should be evaluated further.

## References

1. Ferketich AK, Schwartzbaum JA, Frid DJ, Moeschberger ML. Depression as an antecedent to heart disease among women and men in the NHANES I study National Health and Nutrition Examination Survey. *Arch Intern Med* 2000; 160: 1261–8.
2. Barefoot JC, Schroll M. Symptoms of depression, acute myocardial infarction, and total mortality in a community sample. *Circulation* 1996; 93: 197680.
3. Kaufmann MW, Fitzgibbons JP, Sussman EJ, Reed JF 3rd, Einfalt JM, Rodgers JK, et al. Relation between myocardial infarction, depression, hostility, and death. *Am Heart J* 1999; 138: 54954.
4. Lesperance F, FrasureSmith N, Talajic M, Bourassa MG. Fiveyear risk of cardiac mortality in relation to initial severity and oneyear changes in depression symptoms after myocardial infarction. *Circulation* 2002; 105: 1049–53.
5. Ziegelstein RC. Depression after myocardial infarction. *Cardiol Rev* 2001; 9: 4551.
6. Musselman DL, Evans DI and Nemeroff CB. The relationship of depression to cardiovascular disease: epidemiology, biology, and treatment. *Arch Gen Psychiatry* 1998; 55: 580–92.
7. Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol* 1959; 32: 505.
8. Akdemir A, Turkcapar MH, Orsel SD, Demiregi N, Dag I, Ozbay MH. Reliability and validity of the Turkish version of the Hamilton Depression Rating Scale Compr *Psychiatry* 2001; 42: 1615.
9. Yazıcı MK, Demir B, Tanrıverdi N, Karaağaoğlu E, Yolaç P. Hamilton Anksiyete Değerlendirme Ölçeği, değerlendiriciler arası güvenilirlik ve geçerlilik çalışması. *Türk Psikiyatri Derg* 1998; 9: 1147.
10. Karasar N. Bilimsel araştırma yöntemi. Ankara; Nobel Yayınları: 1999.
11. Blazer II DG. Mood Disorders: Epidemiology. In: Sadock BT, Sadock VA, editors. *Comprehensive Textbook of Psychiatry*. 7th ed. Philadelphia; Lippincott Williams and Wilkins: 2000. p. 1298308.
12. Naqvi TZ, Naqvi SS, Merz CN. Gender differences in the link between depression and cardiovascular disease. *Psychosom Med* 2005; 67 (Suppl 1): 158.
13. Perez GH, Nicolau JC, Romano BW, Laranjeira R. Depression and acute coronary syndromes: genderrelated differences. *Arq Bras Cardiol* 2005; 85: 31926.
14. Chrysohoou C, Panagiotakos DB, Pitsavos C, Kokkinos P, Marinakis N, Stefanadis C, et al. Gender differences on the risk evaluation of acute coronary syndromes: the CARDIO2000 study. *Prev Cardiol* 2003; 6: 717.
15. Gülseren L, Hekimsoy Z, Gülseren Ş, Bodur Z, Kültür S. Diabetes mellituslu hastalarda depresyon, anksiyete, yaşam kalitesi ve yeti yitimi. *Türk Psikiyatri Dergisi* 2001; 12: 8998.
16. Bruce DG, Davis WA, Starkstein SE, Davis TM. A prospective study of depression and mortality in patients with type 2 diabetes: the Fremantle Diabetes Study. *Diabetologia* 2005; 48: 25329.
17. Jacobson AM, Samson JA, Weinger K, Ryan CM. Diabetes, the brain, and behavior: is there a biological mechanism underlying the association between diabetes and depression? *Int Rev Neurobiol* 2002; 51: 45579.
18. McIntyre RS, Soczynska JK, Konarski JZ, Kennedy SH. The effect of antidepressants on glucose homeostasis and insulin sensitivity: synthesis and mechanisms. *Expert Opin Drug Saf* 2006; 5: 15768.
19. Hackett ML, Yapa C, Parag V, Anderson CS. Frequency of depression after stroke: a systematic review of observational studies. *Stroke* 2005; 36: 133040.
20. Haas DC, Davidson KW, Schwartz DJ, Rieckmann N, Roman MJ, Pickering TG, et al. Depressive symptoms are independently predictive of carotid atherosclerosis. *Am J Cardiol* 2005; 95: 54750.
21. Ledochowski M, Murr C, SpernerUnterweger B, Neurauder G, Fuchs D. Association between increased serum cholesterol and signs of depressive mood. *Clin Chem Lab Med* 2003; 41: 8214.
22. Terao T, Whale R. High serum cholesterol and suicide risk. *Am J Psychiatry* 2001; 158: 8245.
23. Vevera J, Fisar Z, Kvasnicka T, Zdenek H, Starkova L, Ceska R, et al. Cholesterollowering therapy evokes timelimited changes in serotonergic transmission. *Psychiatry Res* 2005; 133: 197203.
24. Boudrez H, Backer G. Psychological status and the role of coping style after coronary artery bypass graft surgery. Results of a prospective study. *Qual Life Res* 2001; 10: 3747.
25. Vural M, Basar E. Impact of psychological factors on development and course of coronary heart disease: should be negative psychological factors altered? *Anadolu Kardiyol Derg* 2006; 6: 559.
26. Taylor CB, Youngblood ME, Catellier D, Veith RC, Carney RM, Burg MM, et al. Effects of antidepressant medication on morbidity and mortality in depressed patients after myocardial infarction. *Arch Gen Psych* 2005; 62: 7928.
27. Vural M, Acer M. Preliminary results of the study to determine depression prevalence in patients who had been treated as acute coronary syndrome in Kirsehir: prevalence ratios are higher than expected values. *Anadolu Kardiyol Derg* 2005; 5: 2278.
28. Lesperance F, FrasureSmith N, Talajic M. Major depression before and after myocardial infarction: its nature and consequences. *Psychosom Med* 1996; 58: 99110.
29. Robins LN, Reiger DA. *Psychiatric disorders in America*. New York: Free press. 1991.
30. Stewart RA, North FM, West TM, Sharples KJ, Simes RJ, Colquhoun DM, et al. Depression and cardiovascular morbidity and mortality: cause and consequence? *Eur Heart J* 2003; 24: 202737.
31. Taylor CB, Youngblood ME, Catellier D, Veith RC, Carney RM, Burg MM, et al. Effects of antidepressant medication on morbidity and mortality in depressed patients after myocardial infarction. *Arch Gen Psych* 2005; 62: 7928.
32. Vural M, Satiroglu O, Acer M. Shortcomings in the psychiatric treatment of major depression in patients with acute coronary syndrome and recommendations for amelioration. *Türk Kardiyol Dern Arş* 2006; 34: 2656.