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*Published in:*

Journal of the American College of Cardiology

*Publication date:*

2003

*Document Version*

Publisher's PDF, also known as Version of record

[Link to publication in Tilburg University Research Portal](#)

*Citation for published version (APA):*

Strik, J. M. H., Denollet, J. K. L., Lousberg, R., & Honig, A. (2003). Comparing symptoms of depression and anxiety as predictors of cardiac events and increased health care consumption after myocardial infarction. *Journal of the American College of Cardiology*, 42(10), 1801-1807.

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## Effect of Depression/Anxiety on Cardiac Events

# Comparing Symptoms of Depression and Anxiety as Predictors of Cardiac Events and Increased Health Care Consumption After Myocardial Infarction

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<b>OBJECTIVES</b>	We sought to compare symptoms of depression and anxiety as predictors of incomplete recovery after a first myocardial infarction (MI).
<b>BACKGROUND</b>	Depressive symptoms have been related to post-MI mortality and health care consumption, but little is known about the effect of anxiety. We wanted to examine the effect of emotional distress on health care consumption and whether depressive symptomatology is a better predictor of prognosis than anxiety.
<b>METHODS</b>	Subjects were 318 men (mean age 58 years) who completed the depression, anxiety, and hostility scales from the 90-item symptom check list after they survived a first MI.
<b>RESULTS</b>	After an average follow-up of 3.4 years, there were 25 cardiac events (fatal or non-fatal MI). Symptoms of both depression (hazard ratio [HR] 2.32, 95% confidence interval [CI] 1.04 to 5.18; $p = 0.039$ ) and anxiety (HR 3.01, 95% CI 1.20 to 7.60; $p = 0.019$ ) were associated with cardiac events, adjusting for age, left ventricular ejection fraction, and use of antidepressants. However, a multivariate analysis including all three negative emotions indicated that symptoms of anxiety (HR 2.79, 95% CI 1.11 to 7.03; $p = 0.029$ ) explained away the relationship between depressive symptoms and cardiac events. Regarding health care consumption, anxiety (OR 2.00, 95% CI 1.24 to 3.22; $p = 0.005$ ), but not depression/hostility, was a predictor of cardiac rehospitalization and frequent visits at the cardiac outpatient clinic.
<b>CONCLUSIONS</b>	Symptoms of depression and anxiety were associated with cardiac events. Anxiety was an independent predictor of both cardiac events and increased health care consumption and accounted for the relationship between depressive symptoms and prognosis. Symptoms of anxiety need to be considered in the risk stratification and treatment of post-MI patients. (J Am Coll Cardiol 2003;42:1801-7) © 2003 by the American College of Cardiology Foundation

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Negative emotions, such as depression and anxiety, have been related to coronary artery disease (CAD) (1-3) and a poor prognosis after myocardial infarction (MI) (4). Possible mechanisms linking negative emotions to the post-MI period include increased vulnerability to arrhythmias as a result of increased sympathetic tone (5) and increased platelet

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### See page 1808

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aggregation (6). It is unclear whether treatment of depression may lead to a decrease in post-MI mortality (7), but the findings of a recent study suggest that reducing emotional stress may improve the prognosis (8).

Depression is frequently studied and considered as a pathogenic factor in post-MI patients (9-12). Minor depression and depressive symptoms also have a negative effect on prognosis in cardiac patients (13). The increased risk of

cardiac events may extend to patients with symptoms of negative affect other than depression (14,15). In healthy populations, anxiety (1-3) and anger (16) have been associated with the incidence of cardiac events, but less is known about the role of anxiety and anger in post-MI patients. Some studies have found that symptoms of depression and anxiety (17,18) or anxiety alone (19) did not predict mortality in MI patients but did predict quality of life among those MI patients who lived to 12 months. Other studies reported that both depression and anxiety, independent of each other, predicted cardiac events (20) or CAD (21).

However, there has been a tendency to focus on only one negative emotion at a time (15). Hence, the question remains whether symptoms of depression play a specific role in the prognosis of post-MI patients or whether symptoms of other negative emotions such as anxiety and anger have a comparable adverse effect on recovery after MI. In psychiatric patients, anxiety and depression frequently co-occur, and co-morbid anxiety has been associated with a greater severity of depressive disorder and a poor response to anti-depressive treatment (22-27). In depressed post-MI patients, evidence suggests that co-morbid anxiety rather than pure depression may account for

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Manuscript received November 4, 2002; revised manuscript received June 30, 2003, accepted July 29, 2003.

#### Abbreviations and Acronyms

ASAT	= aspartate aminotransferase
AZM	= Academic Hospital Maastricht
CAD	= coronary artery disease
CHD	= coronary heart disease
CI	= confidence interval
HR	= hazard ratio
LVEF	= left ventricular ejection fraction
MI	= myocardial infarction
OR	= odds ratio
SCL-90	= 90-item Symptom Check List

reduced heart rate variability as a cardiotoxic factor (28). Of note, pharmacologic treatment of anxiety may also decrease the risk of major depression (27).

Most studies investigating the relationship between psychological factors and prognosis after MI focus on mortality and new cardiac events (29–31). Negative emotions may also have an adverse effect on other “softer” end points such as angina, quality of life, and incomplete recovery (32). The effect of depression on angina and re-hospitalization is even more strongly established than its effect on mortality (33). This is reason for concern because adverse outcomes also represent increased health care costs (34).

The purpose of the present study was twofold. First, we wanted to examine whether depression is a better predictor of incomplete recovery after MI than anxiety. Second, we wanted to examine the effect of emotional distress not only on major cardiac events but also on re-hospitalization and increased health care consumption.

## METHODS

**Patients.** Between May 1994 and September 1999, a total of 407 eligible male patients were admitted to the First Heart Aid of the Academic Hospital of Maastricht (AZM) with acute MI. Inclusion criteria of the present study were male gender, first MI, clinical picture and electrocardiographic signs typical of acute MI, and a maximum value of the enzyme aspartate aminotransferase (ASAT) of at least 80 U/l (twice above the upper limit) (35). Patients were excluded who had a major psychiatric disorder other than affective disorders (e.g., schizophrenia, dementia, present psychotic episode). Additionally, patients who were unable to communicate reliably (e.g., because of cognitive dysfunction or not speaking Dutch) or with a co-morbid life-threatening disease were excluded. The local ethics committee approved this study.

Of the 407 eligible patients, 89 (21.9%) refused to participate and 318 (78.1%) gave written, informed consent before inclusion. A refusal rate of 21.9% is comparable to other studies in which MI patients were screened for depression (12,29). Of the 318 patients, 14 were treated in a randomized, placebo-controlled trial of fluoxetine during 25 weeks (36). After the trial, they were offered further treatment at the mood disorder clinic of AZM if necessary.

Furthermore, another 11 patients were treated with antidepressants by the general practitioner or at the mood disorder clinic of AZM.

**Assessment of emotional distress.** The 90-item Symptom Check List (SCL-90), which is a well-validated and widely used self-assessment scale (37,38), was used to measure emotional distress. Each of the items of the SCL-90 ranges from 0 to 4, with 0 indicating no complaint and 4 maximal complaint. Patients filled out the SCL-90 one month after MI at home or during the first post-MI visit at the outpatient clinic of the Department of Cardiology. The scales of “depression” (16 items), “anxiety” (10 items), and “hostility” (6 items) from the SCL-90 were scored for the purpose of the present study. These scales were conceptualized as markers of emotional distress. In previous research, we evaluated the SCL-90 depression scale in patients with post-MI depression and found it to be a valid instrument, with a sensitivity of 81.1% and a specificity of 83.5%. In comparison, the Beck Depression Inventory had a sensitivity of 83.8% and a specificity of 71.7% (39).

**End points.** The end points in this study were major cardiac events and health care consumption during an average follow-up period of 3.4 years (range 1 to 70 months). Major cardiac events were defined as cardiac death or recurrent MI, as diagnosed by the attending cardiologist. Increased health care consumption was defined as cardiac rehospitalization and/or frequent visits (>6 visits during follow-up) at the cardiac outpatient clinic. Patients without cardiac events during the follow-up period and with an average number of visits at the cardiac outpatient clinic were considered to be “event free.”

**Cardiac variables.** Left ventricular ejection fraction (LVEF) was recorded one month after MI as a measure of disease severity. Data on intervention at the time of MI (thrombolysis, percutaneous transluminal coronary angioplasty, coronary artery bypass graft surgery), medication (beta-blockers, platelet aggregation inhibitors, angiotensin-converting enzyme inhibitors), and cardiovascular risk factors (smoking, hypertension, hypercholesterolemia, diabetes) were taken from the patients’ records.

**Analyses.** All data were entered into a computerized data base and analyzed using SPSS version 6.0 (SPSS Inc., Chicago, Illinois) standard software. According to the results of follow-up, patients were classified into one of three groups: patients with a major cardiac event; patients with increased health care consumption; and event-free patients. To determine the prognostic power of emotional distress, scores on the depression, hostility, and anxiety subscales were dichotomized according to the cut-off values for high-risk psychopathology (38): 23 for depression; 12 for anxiety; and 7 for hostility. The LVEF was dichotomized at 50%, using standards of a former publication on CAD patients (8). A median split was used to dichotomize patients according to age (median 58 years) and the number of visits at the outpatient cardiology clinic (median 6 visits). Differences in baseline characteristics between the three

groups were tested by the independent *t* test for continuous variables and the chi-square test for all dichotomous variables. Fisher exact probabilities were calculated when they were expected.

Multivariate Cox regression analysis was used to examine the SCL-90 depression, anxiety, and hostility subscales separately as predictors of major cardiac events. To select appropriate co-variables for statistical control, all baseline variables were dichotomized (at predetermined points). Those variables significantly related to major cardiac events in the univariate Cox regression models were entered into the multiple Cox regression analysis, followed by the addition of the SCL-90 depression, anxiety, and hostility subscales. Because anti-depressive agents can flaw the impact of depression on cardiac prognosis, we also included the use of antidepressants as a co-variate in our model. Finally, a stepwise multivariate Cox regression analysis, including all three negative emotions (SCL-90 subscales of depression, anxiety, and hostility), was used to examine these emotions as independent predictors of major cardiac events.

Regarding analysis of SCL-90 depression, anxiety, and hostility subscales as predictors of health care consumption, univariate logistic regressions were first performed. Those baseline variables significantly related to health consumption were entered in a multivariate logistic regression model, followed by the addition of the SCL-90 subscales. Finally, multivariate logistic regression with all three negative emotions was used. A two-tailed *p* value  $\leq 0.05$  was considered to be significant.

## RESULTS

**Patients.** The average ( $\pm$ SD) age of the 318 included men was  $58 \pm 11$  years, and the mean LVEF and maximum ASAT scores were  $51 \pm 9.8\%$  and  $247 \pm 182$  U/l, respectively. There were no differences between the participating and non-participating groups with respect to age, maximum ASAT, or LVEF. Of the 318 participants, 91.9% were prescribed platelet aggregation inhibitors, 58.2% beta-blockers, 45.2% lipid-lowering drugs, 36.2% angiotensin-converting enzyme inhibitors, 9% diuretics, and 5.7% oral antidiabetic agents. Fifty-four percent of patients were smoking before MI, 20.4% were known to have hypercholesterolemia, 8.5% had diabetes, and 28% had hypertension. Next, we evaluated whether not only age and LVEF but also medication and risk factors for CAD were associated with the distress variables of depression, anxiety, and hostility (Table 1). Age under 58 years was associated with patients with depressive symptoms ( $p = 0.031$ ), as was smoking ( $p = 0.003$ ). Diabetes, prescription of oral antidiabetic agents, and platelet aggregation inhibitors were associated with symptoms of anxiety ( $p = 0.043$ ,  $0.047$ , and  $0.026$ , respectively). Hyperlipidemia was associated with symptoms of hostility ( $p = 0.022$ ), as was smoking ( $p = 0.026$ ). According to the psychological assessment one month after MI, 47.1% of the patients scored above the cut-off value of the

SCL-90 depression subscale, 59.5% above the anxiety subscale, and 62.1% above the hostility subscale.

**Cardiac events.** One hundred forty-four patients (45.2%) were event-free during follow-up, whereas 25 (7.9%) had experienced a major cardiac event. On univariate Cox regression analyses (Table 2), LVEF  $\leq 50\%$  was significantly associated with cardiac death or recurrent MI ( $p = 0.031$ ). There was also a trend for age  $>58$  years ( $p = 0.066$ ). The other cardiovascular variables (i.e., beta-blockers, invasive intervention, smoking, hypercholesterolemia, hypertension, and diabetes) were not associated with cardiac events (Table 2) or health care consumption (Table 3).

Symptoms of anxiety, but not depression, were associated with cardiac events on univariate analysis (Fig. 1). After adjusting for age, LVEF, and the use of antidepressants, symptoms of both depression and anxiety were associated with cardiac events ( $p = 0.039$  and  $0.019$ , respectively) (Table 4). There was no relation with hostility.

**Increased health care consumption.** Of the 318 male patients with a first MI, 149 (46.9%) had increased health care consumption (i.e., frequent visits to the outpatient cardiac clinic or rehospitalizations due to cardiac events) up to six years after MI. On univariate analyses (Table 3), there were no cardiovascular variables related to increased health care consumption, although there was a trend for LVEF  $\leq 50\%$  to be related to increased health care consumption ( $p = 0.069$ ).

Regarding emotional distress as a determinant, depressive and anxious symptoms at baseline were associated with increased health care consumption during follow-up ( $p = 0.047$  and  $0.004$ , respectively) (Table 3). After adjusting for age, LVEF, and the use of antidepressants, anxiety was the only negative emotion that was significantly associated with the secondary end point (odds ratio [OR] 2.00, 95% confidence interval [CI] 1.23 to 3.26;  $p = 0.006$ ) (i.e., frequent cardiac outpatient visits and rehospitalizations due to cardiac events) (Table 4). Hostility was not related to increased health care consumption.

**Independent predictors of end points.** A multivariate analysis including all three negative emotions indicated that symptoms of anxiety (hazard ratio [HR] 2.79, 95% CI 1.11 to 7.03;  $p = 0.029$ ) (Table 5) explained away the relationship between depressive symptoms and cardiac events. This stepwise multivariate Cox regression also retained LVEF  $<50\%$  (HR 2.29, 95% CI 1.01 to 5.21;  $p = 0.047$ ) and age  $>58$  years (HR 2.44, 95% CI 1.01 to 5.88;  $p = 0.047$ ) as independent predictors of major cardiac events (Table 5, top). Neither depression ( $p = 0.44$ ) nor hostility ( $p = 0.39$ ) predicted major cardiac events in this multivariate model. Regarding increased health care consumption, a stepwise logistic regression model again retained anxiety (OR 2.00, 95% CI 1.24 to 3.22;  $p = 0.005$ ) as an independent predictor of frequent visits to the outpatient cardiac clinic or rehospitalizations due to cardiac events (Table 5, bottom). Neither depression ( $p = 0.65$ ) nor hostility ( $p = 0.93$ ) predicted increased health care consumption. In other

**Table 1.** Baseline Demographic Data, Medications, and Coronary Artery Disease Risk Factors and Their Univariate Relationship With Depression, Anxiety, and Hostility

Cross Tabulations	Depression		Anxiety		Hostility	
	n/N	p Value	n/N	p Value	n/N	p Value
Age >58 yrs						
Yes	64/156		84/155		93/155	
No	83/156	0.031	101/156	0.058	100/156	0.456
LVEF ≤50%						
Yes	67/141		84/141		81/140	
No	80/171	0.897	101/170	0.977	112/171	0.167
Beta-blockers						
Yes	87/185		109/184		121/184	
No	60/127	0.969	76/127	0.915	72/127	0.105
PAI						
Yes	133/285		164/284		174/284	
No	7/15	0.999	13/15	0.026	12/15	0.145
ACE inhibitors						
Yes	46/109		58/109		64/108	
No	94/190	0.225	119/189	0.099	121/190	0.449
Diuretics						
Yes	10/26		12/26		14/25	
No	127/269	0.393	163/268	0.146	168/269	0.525
Lipid-lowering drugs						
Yes	62/135		79/135		82/135	
No	75/160	0.871	96/159	0.746	100/159	0.705
Oral antidiabetics						
Yes	10/17		14/17		13/17	
No	126/277	0.284	160/276	0.047	168/276	0.199
Invasive intervention						
Yes	57/137		82/137		82/137	
No	90/175	0.085	103/174	0.907	111/174	0.477
Smoking						
Yes	93/170		108/170		115/170	
No	54/142	0.003	77/141	0.111	78/141	0.026
Hypercholesterolemia						
Yes	33/63		43/63		47/63	
No	114/249	0.349	142/248	0.112	146/248	0.022
Hypertension						
Yes	43/89		54/89		58/89	
No	104/223	0.789	131/222	0.787	135/222	0.474
Diabetes						
Yes	15/27		21/27		21/27	
No	132/285	0.358	164/284	0.043	172/284	0.078

ACE = angiotensin-converting enzyme; LVEF = left ventricular ejection fraction; PAI = platelet aggregation inhibitors

words, anxiety accounted for the relationship between depression and cardiac events, and anxiety was the only significant predictor of increased health care consumption in survivors of acute MI.

## DISCUSSION

The findings of the present study showed that symptoms of both depression and anxiety were associated with an increased risk of adverse cardiac events. However, anxiety was an independent predictor of cardiac events and increased health care consumption and accounted for the relationship between depression and prognosis. These findings support the notion that psychological factors are related to a poor prognosis after MI (1-3) and indicate that symptoms of anxiety need to be considered in the risk stratification and treatment of post-MI patients.

The fact that anxiety was a stronger predictor of cardiac outcome in MI patients than depressive symptomatology is a novel finding. A recent review of negative emotions and the onset of coronary heart disease (CHD) in initially healthy individuals also concluded that research should not ignore the risk associated with anxiety (40). The present study focused on patients with established CHD to examine the relative impact of symptoms of depression and anxiety on prognosis. Although most previous research focused on either anxiety (1-3) or depression (4) as single risk indicators, these negative emotions were investigated simultaneously in the present study. Although there was a trend for depressive symptoms to predict cardiac outcome on univariate analysis, anxiety explained away this association on multivariate analysis. In fact, anxiety was associated with a more than twofold increased risk (HR 2.79, 95% CI 1.11 to

**Table 2.** Cardiac Events During Follow-Up as a Function of Age and Cardiovascular Variables at Baseline

	Major Cardiac Events			
	% n/N	HR	95% CI	p Value*
Age >58 yrs				
Yes	19 (18/94)	2.27	0.95-5.44	0.066
No	9 (7/75)			
LVEF ≤50%				
Yes	25 (16/72)	2.46	1.08-5.57	0.031
No	8 (9/97)			
Beta-blockers				
Yes	16 (15/100)	1.33	0.58-3.0	0.501
No	15 (10/69)			
Invasive intervention†				
Yes	12 (8/74)	0.57	0.25-1.33	0.197
No	18 (17/95)			
Smoking				
Yes	11 (10/90)	0.59	0.26-1.30	0.187
No	20 (15/79)			
Hypercholesterolemia				
Yes	9 (3/35)	0.62	0.19-2.09	0.441
No	17 (22/134)			
Hypertension				
Yes	21 (9/47)	1.73	0.76-3.92	0.193
No	13 (16/122)			
Diabetes				
Yes	14 (2/14)	0.94	0.22-4.0	0.933
No	15 (23/155)			

\*Two-tailed level of significance (univariate Cox regression analyses). †Invasive intervention: percutaneous transluminal coronary angioplasty or coronary artery bypass graft surgery.

CI = confidence interval; HR = hazard ratio; LVEF = left ventricular ejection fraction.

7.03;  $p = 0.029$ ) of cardiac death or recurrent MI after controlling for disease severity (i.e., LVEF ≤50%; HR 2.29, 95% CI 1.01 to 5.21;  $p = 0.047$ ) and age (HR 2.44, 95% CI 1.01 to 5.88;  $p = 0.047$ ). The fact that anxiety, but not depression, was retained as an independent predictor of cardiac outcome is in line with the findings of a recent study by Watkins et al. (28), who found that high levels of anxiety, measured 6 ± 3 days after MI, but not depression, were independently associated with reduced vagal control in post-MI patients. Previous research in our own group also indicated that anxiety was a significant predictor of clinical depression in a sample of 206 post-MI patients (39). Hostility was not associated with cardiac prognosis or increased health care consumption in the present study.

Our findings confirm studies which concluded that depression and anxiety may be predictors of cardiac events after MI (20,21). The follow-up period (1 year) in studies that could not confirm a relationship between depression/anxiety and cardiac events (17,18) was considerably shorter than the follow-up period in the present study (average 3.4 years). It may be that cardiac events related to affective dysregulation after MI tend to occur more in long-term periods. The timing of the assessment may also be important. In a study reporting that both depression and anxiety did not predict outcome at three years after MI (41), the depression and anxiety symptoms were assessed in the

**Table 3.** Increased Health Care Consumption as a Function of Age, Cardiovascular Variables, and Emotional Distress at Baseline

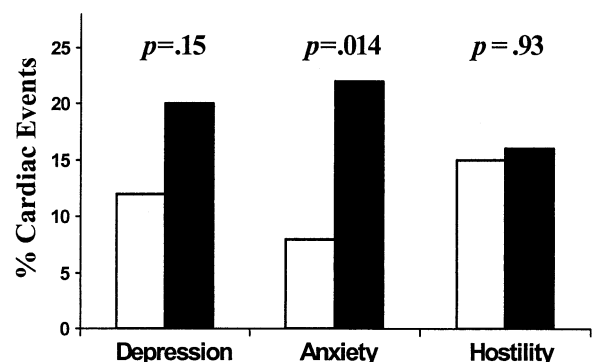
	Increased Health Care Consumption			
	% n/N	OR	95% CI	p Value
Age >58 yrs				
Yes	55 (81/148)	0.74	0.47-1.17	0.200
No	47 (68/144)			
LVEF ≤50%				
Yes	57 (72/126)	1.54	0.97-2.46	0.069
No	46 (77/166)			
Beta-blockers				
Yes	50 (85/169)	1.07	0.67-1.71	0.769
No	52 (64/123)			
Invasive intervention†				
Yes	50 (64/129)	1.11	0.70-1.76	0.667
No	52 (85/163)			
Smoking				
Yes	51 (82/162)	0.96	0.61-1.53	0.876
No	52 (67/130)			
Hypercholesterolemia				
Yes	48 (30/62)	0.87	0.50-1.53	0.640
No	52 (119/230)			
Hypertension				
Yes	53 (42/79)	1.12	0.67-1.89	0.657
No	50 (107/213)			
Diabetes				
Yes	52 (13/25)	1.04	0.46-2.37	0.919
No	51 (136/267)			
Depression				
Yes	58 (77/133)	1.61	1.00-2.57	0.047
No	46 (71/154)			
Anxiety				
Yes	59 (98/166)	2.02	1.25-3.25	0.004
No	42 (50/120)			
Hostility				
Yes	54 (96/178)	1.31	0.81-2.11	0.271
No	47 (51/108)			

\*Two-tailed level of significance (univariate Cox regression analyses). †Invasive intervention: percutaneous transluminal coronary angioplasty or coronary artery bypass graft surgery.

OR = odds ratio; other abbreviations as in Table 2.

hospital. In the present study, these symptoms were assessed at one month after MI.

**Study limitations.** The limitations of this study include the relatively small number of cardiac events, the exclusion of



**Figure 1.** Cardiac events during follow-up as a function of emotional distress at baseline. Open bars = low score; solid bars = high score.

**Table 4.** Poor Outcome as a Function of One Negative Emotion at a Time, Adjusting for Age, Left Ventricular Ejection Fraction, and Use of Antidepressants

	Cardiac Events*		
	HR	95% CI	p Value†
Depression	2.32	1.04-5.18	0.039
Age >58 yrs	2.06	0.86-4.96	0.107
LVEF ≤50%	2.14	0.94-4.87	0.070
Use of antidepressants			0.979
Anxiety	3.01	1.20-7.60	0.019
Age >58 yrs	2.22	0.93-5.36	0.073
LVEF ≤50%	2.09	0.92-4.75	0.078
Use of antidepressants			0.979
Hostility	1.03	0.46-2.30	0.950
Age >58 yrs	1.94	0.80-4.70	0.142
LVEF ≤50%	2.18	0.96-4.97	0.064
Use of antidepressants			0.978

	Health Care Consumption‡		
	OR	95% CI	p Value
Depression	1.55	0.96-2.52	0.076
Age >58 yrs	0.79	0.49-1.28	0.339
LVEF ≤50%	1.57	0.97-2.53	0.065
Use of antidepressants	1.00	0.42-2.35	0.994
Anxiety	2.00	1.23-3.26	0.006
Age >58 yrs	0.81	0.50-1.31	0.395
LVEF ≤50%	1.57	0.97-2.55	0.067
Use of antidepressants	1.07	0.46-2.51	0.881
Hostility	1.33	0.81-2.16	0.257
Age >58 yrs	0.75	0.47-1.24	0.245
LVEF ≤50%	1.60	0.99-2.58	0.055
Use of antidepressants	0.90	0.39-2.09	0.804

\*Using a Cox regression model. †Two-tailed level of significance. ‡Using a logistic regression model.  
Abbreviations as in Tables 2 and 3.

female patients, and the lack of information on depression treatment during the course of follow-up. However, as yet, it is not clear whether treatment of post-MI depression can improve the prognosis (42). Another limitation concerns the use of only one instrument to assess specific symptoms of depression and anxiety. Undoubtedly, measures of depressive symptoms may yield significant prognostic information in post-MI patients (40). At the present time, we do not know what elements of depression predict cardiac mortality. However, the present findings suggest that, in addition to assessing depressive symptomatology, it is equally important to assess other negative emotions, including anxiety.

Apart from a cardiac prognosis, the present study also examined the prognostic role of emotional distress on health care consumption. Depression not only precedes cardiac death and recurrent MI but also may predict morbidity (33). We found that anxiety was an independent predictor of frequent visits to the outpatient cardiac clinic or rehospitalizations due to cardiac events. There was a trend for symptoms of depression to also be related to increased health care consumption, but once again, anxiety accounted for this association in the multivariate model. Hence, it is also important to detect and treat emotionally distressed patients from an economic point of view, given the fact that

**Table 5.** Independent Predictors of Major Cardiac Events and Health Care Consumption

	Cardiac Events*		
	HR	95% CI	p Value†
Anxiety	2.79	1.11-7.03	0.030
Age >58 yrs	2.44	1.01-5.88	0.047
LVEF ≤50%	2.29	1.01-5.21	0.047
Variables not in the equation			
Depression			0.447
Hostility			0.392
Use of antidepressants			0.137

	Health Care Consumption‡		
	OR	95% CI	p Value†
Anxiety	2.00	1.24-3.22	0.005
Variables not in the equation			
Depression			0.645
Hostility			0.929
Age >58 yrs			0.494
LVEF ≤50%			0.089
Use of antidepressants			0.937

\*Using a Cox regression model. †Two-tailed level of significance. ‡Using a logistic regression model.  
Abbreviations as in Tables 2 and 3.

increased health care consumption entails a significant increase in health care costs among patients with CHD (34).

These findings have implications for clinical research and practice. First, biobehavioral research on CHD has largely focused on depression and depressive symptoms (9-12). It is timely to also include other psychological factors such as anxiety (40). Second, the identification of CHD patients who experience anxiety may lead to more accurate risk estimates in clinical practice. Compared with the Beck Depression Inventory, total Hospital Anxiety and Depression Scale (combination of the anxiety and depression subscale) proved to be more sensitive and specific to depression after MI than the subscales separately (39). This appears to be in line with the results of the present study (i.e., the fact that symptoms of anxiety were predictive of cardiac events in addition to symptoms of depression). Third, as yet, it is not clear whether pharmacologic (36) or behavioral (42,43) treatment of depression can influence the prognosis of post-MI patients (7,44). The present study indicated that besides depression, anxiety is also important in the prediction of cardiac outcome. This finding may help to explain why an intervention that was specifically designed to treat depression (37) failed to improve the prognosis of post-MI patients (44). A more comprehensive approach to treatment, including exercise training and individualized treatment of a wide variety of psychological factors, may be more successful in improving the cardiac prognosis (8).

**Conclusions.** We found that anxiety was an independent predictor of cardiac events and increased health care consumption after controlling for disease severity and age. Moreover, anxiety accounted for any associations between depressive symptoms and prognosis. These findings support the notion that symptoms of emotional distress are related

to the cardiac prognosis after MI. Yet, they also indicate that, apart from depressive symptoms, other symptoms of emotional distress must be considered to optimize risk stratification and treatment.

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