Ventricular Tachycardia and Psychiatric Depression in Patients With Coronary Artery Disease

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PURPOSE: **The purpose of this study was to examine the relationship between psychiatric depression and ventricular arrhythmias in patients with coronary artery disease (CAD). The hypothesis was that depressed patients with CAD would have a higher prevalence of ventricular tachycardia (VT) than nondepressed patients with CAD.**

PATIENTS AND METHODS: **One hundred three patients who were found to have significant CAD by elective diagnostic cardiac catheterization were administered a standardized psychiatric interview and underwent 24-hour Holter monitoring.**

RESULTS: **Twenty-one patients (20%) met the criteria for either major or minor depression. There were no significant differences between depressed and nondepressed patients with CAD in severity of CAD or in ventricular function. Five (23.8%) of the depressed patients and three (3.7%) of the nondepressed patients exhibited episodes of VT during 24 hours of Holter monitoring ($p < 0.008$). This difference remained significant even after controlling for relevant covariates.**

CONCLUSIONS: **We conclude that there is a higher prevalence of VT among patients with CAD and depression than among those CAD patients without depression. This may help to explain the increased risk for cardiac mortality in depressed patients with CAD.**

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Depressed mood and related symptoms such as hopelessness are very common among cardiac patients [1–5]. Psychiatric depression is also very common. The combined point prevalence of minor and major depressive disorders, using current diagnostic criteria, is 45% in patients with a recent myocardial infarction (MI) [6]. The prevalence of major depression alone is between 18% and 25% among patients with a recent MI [6,7], and 18% in patients without a history of MI, but with angiographically proven coronary artery disease (CAD) [8]. By contrast, the 6-month prevalence for major depression in a community sample of persons of comparable age and sex ratio is estimated to be approximately 3% [9].

The presence of depression is associated with an increased risk for mortality after acute infarction [10–17]. In addition, the mortality rate among patients who are depressed at the time of diagnosis and treatment of supraventricular and ventricular tachyarrhythmias or of syncope of unknown etiology is five times higher than among comparable nondepressed patients [18]. Furthermore, women may be particularly vulnerable to sudden cardiac death when depressed or bereaved [19–21].

The underlying mechanism for the association between depression and increased cardiac mortality is not well understood [5]. Since psychiatric depression is associated with elevated autonomic tone [22], one plausible mechanism is an increased prevalence or severity of ventricular arrhythmias. Increased sympathetic nervous system activity is known to trigger ventricular arrhythmias under certain circumstances [23–27]. The severity of ventricular arrhythmias has been shown to be an independent predictor of mortality after acute MI [28], and ventricular tachycardia precedes most sudden cardiac deaths [29–34]. In addition, ventricular arrhythmias are often associated with reduced left ventricular function, and, thereby, they may serve as a marker for an increased risk of nonsudden cardiac death as well.

Previous efforts to study the relationship between psychologic distress and ventricular arrhythmias in a variety of populations have produced mixed results [35–39]. To our knowledge, no study to date has examined the relationship between ven-

tricular arrhythmias and psychiatric depressive disorders as defined by current psychiatric diagnostic criteria. The present study assessed this relationship after diagnostic cardiac catheterization and angiography in a series of patients without previously identified rhythm disturbances.

PATIENTS AND METHODS

Patients

Patients undergoing elective diagnostic cardiac catheterization with coronary arteriography and left ventriculography for evaluation of CAD during a 12-month period at Barnes and Jewish Hospitals in the Washington University Medical Center, St. Louis, Missouri, were considered for inclusion in this study. Patients were eligible to participate if they were 75 years of age or younger, were without a history of arrhythmias of any kind, had no evidence or history of a recent (within 4 weeks) MI or other severe systemic illness, had never undergone coronary artery bypass surgery or coronary angioplasty, were without evidence of valvular heart disease other than mitral valve prolapse, had no evidence of cardiomyopathy, were found to have 50% or greater stenosis in one or more major coronary arteries, had never experienced cardiac arrest, and gave informed consent to participate. Patients undergoing emergency catheterization were excluded.

Cardiac Catheterization and Angiography

Left heart catheterization, hemodynamic studies, and left ventricular and selective coronary angiography were performed according to standard techniques. Coronary arteriograms and left ventriculograms were interpreted independently by experienced angiographers who were unaware of the results of the psychiatric interview or Holter monitor. CAD was defined as 50% or greater reduction in the luminal diameter of one or more major coronary arteries or branches. Left ventricular ejection fraction was calculated using the area-length method. All other pertinent medical information was obtained from medical records with the use of a standardized data log.

Psychiatric Interview

On the day of catheterization, a modified version of the National Institute of Mental Health Diagnostic Interview Schedule (DIS) [40] was administered to determine the presence of psychiatric disorders. Modifications of the DIS included the addition of questions assessing the recency of each symptom and its temporal relationship to symptoms believed to reflect the patient's medical condition, including chest discomfort and dyspnea. Interviews were carried out by research assistants with extensive prior training and experience in administering psychiatric diagnostic interviews. Diagnoses of either major depression, based on the DSM-IIIR criteria of the American Psychiatric Association [41], or of minor depression, based on the Research Diagnostic Criteria (RDC) [42], were derived from the results of this interview independently by two senior diagnosticians who initially agreed in 97% of the cases. The remaining interviews were subsequently reviewed jointly and consensus was reached in every case. Psychiatric diagnoses were made without knowledge of the angiographic or Holter findings.

Ambulatory Monitoring

All patients received a standard 24-hour Holter electrocardiographic (ECG) recording during the day after catheterization. Patients were monitored during hospitalization instead of at home in order to control for the potential confound between depression and physical activity level. Consequently, physical exertion and exertion-related arrhythmic events were minimized in both the depressed and nondepressed groups. Holter ECG recordings were scanned by a Delmar Avionics (Irvine, CA) 9000A Trendsetter with supplemental software for calculating heart rate variability. ECG variables of interest included salvos of ventricular tachycardia (VT), defined as three or more consecutive ventricular beats at a cycle length less than 600 milliseconds, the occurrence and frequency of ventricular couplets and triplets, the mean premature ventricular contraction frequency per hour, and the mean heart rate and heart rate variability. Heart rate variability was defined as the standard deviation of all normal R-to-R cycle lengths occurring during the recording period. All ectopic beats and nonsinus rhythms were excluded from the analysis. In addition, the number of episodes and cumulative duration of myocardial ischemia, defined as spontaneous occurrences of greater than 60 seconds of greater than 1-mm horizontal or downsloping ST-segment depression 60 milliseconds after the J point, with or without associated chest discomfort, were recorded.

Statistical Methods

When appropriate, the χ^2 statistic was used to test univariate associations between categoric variables; Fisher's exact test was used whenever the assumptions of the χ^2 test were not met. An unconditional multiple logistic regression of VT on depression was performed, using the sequential backward elimination technique to control for the effects of covariates [43]. Two-tailed t-tests were used for comparisons of continuous variables. The α value was set at 0.05 per comparison.

TABLE I

Demographics and Medical History of Study Patients by Presence of Depression*

	Depressed (n = 21)	Nondepressed (n = 82)	p Value
Age (y)	57.3 ± 10.0	60.3 ± 7.9	0.14
Male	66.7% (14)	85.4% (70)	0.05
Married	66.7% (14)	89.0% (73)	0.01
Smokers	45.0% (9)	23.5% (19)	0.05
History of MI	42.9% (9)	35.4% (29)	0.68
No. of vessels with ≥50% stenosis	2.3 ± 0.9	2.1 ± 0.9	0.44
LVEF	60.7 ± 17.1	63.2 ± 13.7	0.48
Potassium (mEq/L)	4.0 ± 0.3	4.1 ± 0.3	0.28

LVEF = left ventricular ejection fraction.
*Continuous variables are reported as means ± standard deviations; categoric variables are listed as column-wise percentage (cell size).

TABLE II

Cardiac Medications by Presence of Depression*

	Depressed (n = 21)	Nondepressed (n = 82)	p Value
β Blockers	14.3% (3)	45.1% (37)	0.01
Nitrates	61.9% (13)	37.8% (31)	0.05
Calcium antagonists	61.9% (13)	51.2% (42)	0.38
Diuretics	14.3% (3)	9.8% (8)	0.55
ACE inhibitors	4.8% (1)	11.0% (9)	0.39
Digoxin	4.8% (1)	4.9% (4)	0.98
Antidepressants	4.8% (1)	2.4% (2)	0.57
Anxiolytics	4.8% (1)	7.3% (6)	0.68

ACE = angiotensin-converting enzyme.
*Categoric variables are listed as column-wise percentage (cell size).

RESULTS

One hundred three patients met the study enrollment criteria and agreed to participate. Twenty-one (20.4%) were subsequently found to meet either the DSM-IIIR criteria for major depression (n = 11) or the RDC criteria for minor depression (n = 10). Medical and demographic comparisons between these groups are presented in **Table I.** Depressed patients were more likely to be female, less likely to be presently married, and more likely to be current smokers than the nondepressed patients. There were no other significant differences in medical or demographic variables between these groups.

Patients in both groups were taking a variety of cardiac medications during the time of study. Depressed patients were less likely to be taking β blockers and more likely to be taking nitrates than were nondepressed patients, as shown in **Table II.**

Five (23.8%) of the depressed patients and three (3.7%) of the nondepressed patients had episodes of VT (Fisher's exact test, p <0.008) during Holter monitoring. There was no difference in the rate of VT between patients with major (two) and minor (three) depression. The relative risk for VT among the depressed patients was 8.2 (95% confidence bounds: 2.14 to 31.70). There were no other significant differences between depressed and nondepressed patients (**Table III**).

In order to determine whether depression is associated with VT after controlling for sex, current cigarette smoking, β blockers, and nitrates, multiple logistic regression was performed. A significant model was obtained (score $\chi^2 = 10.83$, p = 0.05). As shown in **Table IV,** there was a significant association between depression and VT after adjusting for the covariates. None of the covariates were significantly associated with VT.

TABLE III

Electrocardiographic Results by Presence of Depression*

	Depressed (n = 21)	Nondepressed (n = 82)	p Value
Ventricular tachycardia	23.8% (5)	3.7% (3)	0.008
Episodes of ST depression	28.6% (6)	17.1% (14)	0.24
Ventricular couplets	33.3% (7)	23.2% (19)	0.33
Ventricular triplets	23.8% (5)	12.2% (10)	0.18
Mean PVCs/h	24.9 ± 100.4	38.8 ± 137.0	0.60
Mean heart rate (beats/min)	70.1 ± 11.0	65.5 ± 11.7	0.10
Heart rate variability (ms)	81.8 ± 38.6	93.5 ± 29.9	0.14

PVCs = premature ventricular contractions.
*Continuous variables are reported as means ± standard deviations; categoric variables are listed as column-wise percentage (cell size).

Comparisons of selected variables between the depressed and nondepressed patients with VT are presented in **Table V.** Depressed patients were found to have significantly fewer diseased coronary vessels than nondepressed patients. There were nonsignificant trends suggesting more severe VT in the depressed patients.

COMMENTS

Twenty percent of the patients studied were found to meet either the DSM-IIIR criteria for major depression or the RDC criteria for minor depression. The depressed patients were significantly more likely than nondepressed patients to experience one or more episodes of VT during 24 hours of Holter monitoring. There was no difference in the

TABLE IV

Logistic Regression of Ventricular Arrhythmia on Depression and Covariates

Variable	Parameter Estimate	Standard Error	χ^2	p Value
Intercept	−3.22	0.83	15.09	0.00
Gender	−1.21	1.19	1.04	0.31
Current smoking	0.39	0.74	0.27	0.60
β Blocker	0.14	1.00	0.02	0.89
Nitrates	−0.36	0.87	0.17	0.68
Depression diagnosis	2.38	0.93	6.49	0.01

TABLE V

Depressed Versus Nondepressed Patients With Ventricular Tachycardia*

	Depressed (n = 5)	Nondepressed (n = 3)	p Value
VT runs	13.8 ± 18.9	2.0 ± 1.0	0.33
Maximum VT heart rate (beats/min)	158.6 ± 15.3	136.7 ± 27.2	0.14
Age (y)	59.4 ± 7.7	60.0 ± 1.0	0.90
Male	80.0% (4)	100.0% (3)	0.41
Married	100.0% (5)	100.0% (3)	1.00
Smoker	60.0% (3)	33.3% (1)	0.47
History of MI	40.0% (2)	100.0% (3)	0.09
No. of vessels with ≥ 50% stenosis	1.8 ± 0.8	3.3 ± 0.6	0.03
LVEF	52.6 ± 15.3	50.3 ± 18.5	0.85
Potassium	4.3 ± 0.3	4.3 ± 0.3	0.95
Heart rate (beats/min)	76.8 ± 12.8	63.3 ± 8.5	0.16
Heart rate variability (ms)	61.4 ± 30.2	94.3 ± 30.0	0.18
Episodes of ST depression	60.0% (3)	33.3% (1)	0.47
Duration of VT (beats)	10.2 ± 12.8	8.7 ± 3.5	0.80

LVEF = left ventricular ejection fraction.
*Continuous variables are reported as means ± standard deviations; categoric variables are listed as column-wise percentage (cell size).

prevalence of VT between patients with major versus minor depression. None of the other ECG variables differed significantly between the depressed and nondepressed groups. There were also no differences between groups with respect to the severity of coronary stenosis, ventricular function, or other medical variables. The depressed patients were significantly less likely to be taking β blockers, more likely to be taking nitrates, and more likely to be current smokers than were the nondepressed patients. There were no differences in the proportions of depressed versus nondepressed patients taking any of the other cardiac medications, including diuretics. The relationship of depression to VT was found to be independent of current smoking status and β-blocker therapy. Despite the small sample size, depressed patients with VT were found to have significantly less severe CAD than the nondepressed patients with VT. There were no other significant differences between these groups.

The major limitation of the present study was the small number of patients who presented with VT. This limited the statistical power of the major analyses, particularly those addressing potential confounds or possible mechanisms. One of the potential confounds was the difference in the proportion of depressed and nondepressed patients who were prescribed β blockers at the time of study. It is unclear why depressed patients were less likely to be prescribed β-blocker therapy. It is possible that some of them had been treated with β blockers, but then these medications were discontinued after an increase in associated central nervous system symptoms. Although there is evidence that β blockers do not generally cause a major depressive episode, they are associated with depression-like symptoms, including fatigue and dysphoric mood [44,45]. Such side effects could be more difficult for a depressed patient to tolerate. Clearly, more study of the relationship among the effects of β blockers, prescription decisions, and depression is warranted. Nevertheless, in this study, depressed patients were more likely than nondepressed patients to have episodes of VT, even after controlling for the potential effects of β blockers and other confounds.

The patients in this study with episodes of VT all had normal ventricular function, and, therefore, the occurrence of VT was not immediately life-threatening. However, the increased prevalence of VT in these depressed patients with CAD may place them at greater risk for cardiac-related death during the course of their illness, particularly in the context of reduced ventricular function.

The increased prevalence of VT in depressed patients may be related to dysregulation of the sympathetic nervous system and of hypothalamic-pituitary-adrenal axis activity. Increased sympathetic tone has been documented in depressed psychiatric patients [22], and there is substantial evidence that increased sympathetic nervous system activity may result in VT and even ventricular fibrillation [23–27]. Elevated sympathetic activity in depressed patients with CAD may, therefore, trigger malig-

nant cardiac arrhythmias or sudden cardiac death. This explanation is better supported in patients with major rather than minor depression, because major depression has been more consistently associated with altered autonomic function and hypercortisolism. Nevertheless, alterations in these systems may occur more commonly in patients with minor depression than in nondepressed subjects [46]. Clearly, the role of autonomic tone in the occurrence of ventricular arrhythmias in depressed cardiac patients deserves further study.

Other mechanisms have also been suggested to explain the relationship between depression and increased morbidity and mortality. For example, smoking is a well-known independent risk factor for cardiac disturbances, and poor social support has been found to be an independent risk factor in recent studies [47,48]. In the present study, as in our previous studies [49], depressed patients were more likely than nondepressed patients to smoke cigarettes and to be unmarried. Smoking was not associated with VT in this sample, and all depressed and nondepressed patients with VT were married. Nevertheless, it is possible that these or other features of depression may increase the risk for medical morbidity and mortality. The relationships among depression, social support, smoking, and other risk factors, and medical morbidity and mortality are presently unclear and warrant further study.

In conclusion, depression may be associated with an increased risk for VT. A higher prevalence of VT may explain why depression is a risk factor for cardiac mortality. This finding does not rule out alternative explanations, however, and the relationship of depression to VT, as well as the role of other known and potential risk factors associated with depression, should be studied further.

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