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THE RELATIONSHIP BETWEEN HEART RATE, HEART RATE VARIABILITY AND DEPRESSION IN PATIENTS WITH CORONARY ARTERY DISEASE

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Abstract—Seventy-seven patients undergoing elective cardiac catheterization were administered a diagnostic psychiatric interview and their mean heart rates and heart rate variability were determined from the results of a 24 hr ambulatory ECG. The mean heart rate for depressed patients with coronary artery disease (CAD) was significantly higher than for nondepressed CAD patients, independent of the patient's age, smoking status, and beta blocker therapy. Heart rate variability was lower in depressed patients but did not achieve significance. With the exception of smoking, which was more common in depressed patients, there were no significant differences between the depressed and nondepressed patients on any other medical or demographic variable assessed. It is concluded that elevated heart rate may represent increased sympathetic tone in depressed CAD patients, and may help to explain the increased morbidity and mortality reported in these patients.

INTRODUCTION

DEPRESSION is a common psychiatric complaint in patients with coronary artery disease. Point prevalence estimates for clinical depression in post myocardial infarction patients have been reported to be between 20 and 30% [1–3], and as many as 40% of patients with ischemic heart disease may be clinically depressed [4]. Not only do these patients experience the suffering and despair associated with a clinical depression, but they are also at increased risk for further morbidity and mortality due to their heart disease.

Between 33 and 50% of patients who die from an initial myocardial infarction may be significantly depressed for some time prior to the infarction [5, 6]. Psychiatric patients with depression have higher rates of myocardial infarction than patients with other psychiatric illnesses [7], and nearly two times the expected mortality due to cardiovascular diseases [8]. Depression in the first twelve months after myocardial infarction has been associated with increased mortality and medical morbidity [3, 9], and patients with a clinical depression have been found to be at increased risk for mortality during and after cardiac surgery [10, 11]. Thus, there is much evidence that depression is associated with increased mortality and morbidity in patients with cardiovascular disease, and a significantly higher proportion of patients with depression die of cardiovascular disease relative to nondepressed individuals, including those with other psychiatric disorders.

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There are many possible mechanisms which may explain the relationship between depression and mortality in CAD patients. Antidepressant medications may have undesirable side effects in CAD patients [12]. However, it has been observed in many studies that patients with coronary artery disease and depression frequently are not identified as having depression, and the majority of these patients are not treated [4]. Furthermore, as Rabins and his colleagues note, the association between increased mortality and depression was reported long before the use of any psychiatric medications for depression [8]. Another possible mechanism concerns the increased autonomic activity observed in persons who are clinically depressed [13]. Medically well, depressed psychiatric patients have been found to have significantly higher resting heart rates than controls [14–16], and elevated resting heart rate has been shown to predict mortality in patients at risk for myocardial infarction or sudden death [17–20]. The purpose of this study is to determine whether the presence of depression in patients with coronary artery disease is associated with increased heart rate and decreased heart rate variability.

METHODS

Subjects

Eighty-two patients undergoing elective cardiac catheterization for evaluation of suspected coronary artery disease during a four month period were asked to participate in the study. Patients were excluded if they were over 70 yr of age, had a recent myocardial infarction (< 4 weeks), previous bypass surgery or coronary angioplasty, valvular heart disease other than mitral valve prolapse, or known or suspected cardiomyopathy. Three patients refused to participate and two patients did not complete the psychiatric interview. Thus, complete data were collected on 77 patients. On the day prior to catheterization, details of the study were discussed with the patient and informed consent was obtained.

Psychiatric interview

A modified version of the Diagnostic Interview Schedule (DIS) [21] was used to assess the presence of major symptoms of depression. The modifications included the addition of questions to determine the recency and duration of each symptom, as well as the temporal relationship of depression symptoms to those symptoms believed to reflect the patient's medical condition, such as chest pain, breathlessness, etc. Diagnoses based on DSM–III criteria [22] are easily derived from the results of this interview.

The interview was carried out on the day before catheterization by two Master's level psychologists, both of whom have had experience and training in psychiatric diagnostic interviews. DSM–III diagnoses for Major Depressive Disorder were made independently by two raters with 95% agreement.

Medical assessments

All patients were administered a standard 24 hr ambulatory ECG recording prior to cardiac catheterization. Ambulatory ECG recordings were scanned by Avionics 9000A Trendsetter with supplemental software for calculating heart rate and heart rate variability. Heart rate variability was defined as the standard deviation of the mean R–R cycle length over consecutive 5 min intervals during the recording period. All ectopic beats and non-sinus rhythms were excluded from the analysis, as were 5 min intervals in which there were fewer than 30 evaluable sinus beats.

Cardiac catheterization and coronary angiography were performed, and all coronary cineangiograms were analyzed independently by one of the authors (MWR). Significant CAD was defined as a 50% or greater stenosis in one or more major coronary arteries or branches. Left ventricular ejection fraction was calculated using the area-length method.

Medical history and demographic information were obtained from the patient or from the patient's chart. Functional class, psychiatric diagnosis, ambulatory ECG recordings, and catheterization findings were assessed independently without knowledge of the results of the other assessments.

RESULTS

Fifty-two (67.5%) were found to have significant coronary artery disease (CAD). Based on the results of the psychiatric interview, the patients were classified as

TABLE I.—CHARACTERISTICS OF CAD PATIENTS BY PRESENCE OF DEPRESSION

	Depressed $N = 9$	Non depressed $N = 43$	
Age	58.2 ± 7	54.3 ± 10	NS
Sex (males)	56%	77%	NS
NYHA (functional class)	2.3 ± .9	2.7 ± .5	NS
Total serum cholesterol (mg/dl)	233 ± 61	232 ± 52	NS
Hypertension	22%	42%	NS
Diabetes mellitus	33%	26%	NS
Cigarette smoking	89%	53%	≤ 0.05
Family history of heart disease	56%	56%	NS
Beta blockers	44%	58%	NS

TABLE II.—AMBULATORY ELECTROCARDIOGRAPHIC AND CATHETERIZATION DATA FOR STUDY PATIENTS

	CAD		
	Depressed $N = 9$	Non depressed $N = 43$	
HR	73.1 ± 7	66 ± 6	≤ 0.05
HRV	77.5 ± 22	92 ± 25	≤ 0.10
LVEF	59.1 ± 22	63.4 ± 14	NS
Severity of stenosis			
One vessel disease	33%	41%	NS
Two vessel disease	22%	28%	NS
Three vessel disease	44%	31%	NS

currently depressed or nondepressed. Baseline characteristics of the patients are presented in Table I. Portions of these baseline data have been presented previously [23]. All data are expressed as per cent, or mean ± standard deviation. Two-tailed t tests were used for the comparison of interval data and Chi Squares or Fisher's Exact Tests were used to make the remaining comparisons. With the exception of smoking, which was more prevalent in depressed patients, baseline characteristics were not different between groups.

Table II summarizes data obtained from the ambulatory electrocardiograms and cardiac catheterization. The mean heart rate for depressed CAD patients was 73.1 (± 7.1), compared to 66 (± 6) for nondepressed CAD patients ($t = 2.14$, df = 50, $p \leq 0.05$) (Table II). The mean heart rate variability for depressed CAD patients was found to be 77.5 msec (± 22.3), compared to 92 msec (± 25) for nondepressed CAD patients ($t = 1.83$, df = 50, $p \leq 0.10$). There were no differences between depressed and nondepressed CAD patients on the extent of coronary artery disease or on left ventricular function.

Smoking may be associated with increased heart rate, and there was a disproportionately higher percentage of depressed patients who were smokers. Furthermore, although not statistically significant, more nondepressed (58%) than depressed patients (44%) were on beta blocker therapy at the time of testing. In order to determine whether depression made an independent contribution to heart rate, a hierarchical linear multiple regression was performed [24]. Age, smoking status, and beta blocker therapy were first entered into the equation followed by depression

status. The multiple regression produced an $R^2 = 0.59$ ($p \leq 0.001$). Semipartial correlations for each of the three predictor variables was $r = 0.01$ for age ($p \leq 0.05$), $r = 0.03$ for smoking ($p \leq 0.05$), $r = 0.46$ for beta blocker therapy ($p \leq 0.001$), and $r = 0.27$ ($p \leq 0.05$) for depression. Thus, depression was significantly associated with heart rate after controlling for the effects of the other predictor variables. As heart rate variability did not quite meet significance, no comparable analysis was conducted.

DISCUSSION

Heart rate was significantly higher in depressed patients with coronary artery disease compared to the nondepressed CAD patients. This effect was independent of the patient's age, sex, smoking status, and beta blocker therapy. Heart rate variability was lower for the depressed patients in the sample, but did not quite achieve significance. These findings cannot be explained by the degree of functional impairment, presence of other disease processes or medication, extent of coronary disease, or abnormalities of ventricular function. Thus, the increased heart rates cannot be attributed to the presence of more severe medical illness.

Depression in nonmedically ill patients has been associated with increased levels of plasma cortisol [25, 26], elevated plasma catecholamines [14, 27–29], and various electrophysiologic indices of autonomic arousal [15, 16, 29]. At least three studies have documented that non-medically ill patients with depression have elevated heart rates compared to nondepressed controls [14, 15, 16]. In the present study, depression was associated with increased HR and decreased HRV in CAD patients, suggesting the possibility of increased sympathetic tone.

Previous studies [17–20] have shown that increased heart rate is a significant predictor of mortality in patients at risk for myocardial infarction or sudden death. With effective beta blockade, morbidity and mortality following acute MI is decreased [31–35], and this effect has been shown to be best predicted by significant reduction in HR [36]. Furthermore, decreased heart rate has been shown to be associated with reduced atherosclerosis in animals [37]. Elevated sympathetic activity in depressed patients with CAD, as suggested by elevated heart rate, may promote increased manifestations of ischemic heart disease, lethal arrhythmias, or increased atherosclerosis and thus may lead to a higher rate of mortality and morbidity.

An unexpected finding in the present study was that significantly more depressed patients smoked than nondepressed patients. Specifically, 89% of the depressed CAD patients smoked at the time of study, in contrast to 53% of nondepressed CAD patients ($p \leq 0.05$). Although increased heart rate in depressed patients was independent of the effects of smoking, this finding is of interest in that smoking is a known risk factor for heart disease. In a recent study, Hughes and his colleagues [38] reported that psychiatric outpatients with depression are more likely to be smokers (50%) than nonpsychiatric controls (33%). Thus, the increased risk for mortality and morbidity associated with depression and other psychiatric disorders may be related to some extent to the presence of cigarette smoking. Future epidemiologic studies relating depression and other psychiatric disorders to heart disease must control for this variable.

In conclusion, the presence of depression in CAD patients is associated with a significantly higher heart rate than is found in nondepressed CAD patients, independent of the use of beta blockers, age, sex, and smoking status. Elevated heart rate may represent increased sympathetic tone associated with depression in nonmedically ill patients, and this factor may help to explain the increased risk for morbidity and mortality in CAD patients when depression is present.

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