Left Ventricular Regional Function After Acute Anterior Myocardial Infarction in Diabetic Patients

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To elucidate the pathophysiological role of diabetes mellitus in determining the left ventricular regional function of the noninfarcted area, 55 patients with acute Q wave anterior myocardial infarction (MI) were studied. The regional ejection fraction of the noninfarcted area was obtained by radionuclide angiocardiography and was used to estimate the left ventricular regional function of the noninfarcted area. Multiple regression analysis was performed to determine the important variables contributing to the regional ejection fraction based on 10 clinical variables: age, sex, QRS score, diabetes mellitus, hypertension, smoking, postinfarction angina, body mass index, serum cholesterol, and coronary atherosclerosis. A high QRS score ($P < .001$) and the association of diabetes mellitus ($P < .05$) were the important factors contributing to regional left ventricular dysfunction. The regional ejection fraction and QRS score had an inverse linear relationship in the diabetic and nondiabetic groups, and the regional ejection fraction was significantly lower in diabetic patients at every QRS score ($P < .05$). The association of hypertension, severity of coronary atherosclerosis, serum cholesterol level, age, and body mass index did not differ between diabetic and nondiabetic patients, which indicates that diabetes mellitus was not mediated through these atherogenic traits. Thus, diabetes mellitus is another discrete cause of regional left ventricular dysfunction of the noninfarcted area after acute MI. *Diabetes Care* 12:630–35, 1989

An increased incidence of congestive heart failure and the resultant higher mortality rate during the course of acute myocardial infarction (MI) in diabetic patients has been reported (1–3). Generally, the size of myocardial necrosis is the major determinant of congestive heart failure and mortality after acute MI. Therefore, a more extensive infarction among diabetic patients is thought to be one of the explanations for the increased incidence of congestive heart failure (4). However, an increase in congestive heart failure with a comparable infarct size has also been documented in diabetic patients (1–3). Some form of cardiomyopathy in diabetes mellitus resulting from a metabolic disorder or microangiopathy in the heart, or higher prevalence of associated hypertension or coronary atherosclerosis is considered to affect left ventricular function in diabetic patients, but the role of diabetes mellitus in determining left ventricular function after acute MI is yet to be defined (5–7).

Radionuclide left ventriculography is advocated as a useful tool for assessing left ventricular function and left ventricular wall motion abnormalities (8,9). The prognostic value of the left ventricular ejection fraction has been established in patients with coronary artery disease (10,11). Recently, attempts have been made to quantitatively assess left ventricular wall motion with the regionally derived radionuclide ejection fraction (12,13), and an estimation of the regional ejection fraction of the noninfarcted area is considered to more favorably assess residual left ventricular function in acute MI than the global ejection fraction.

This study was designed to evaluate the left ventricular regional ejection fraction of the noninfarcted area and to elucidate the role of diabetes mellitus in determining the left ventricular regional ejection fraction after acute MI.

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RESEARCH DESIGN AND METHODS

We studied 55 patients with first acute Q wave anterior MI (anteroseptal, anterolateral, and extensive anterior infarction) who were admitted to the coronary care unit within 24 h from the onset of MI. Diagnosis of MI was made if the patient had ST-T wave changes with new Q waves in serial electrocardiograms with enzymatic confirmation. There were 45 men and 10 women aged 38–79 yr (mean ± SD age 58 ± 11 yr). Patients were defined as having non-insulin-dependent diabetes mellitus if diabetes (of adult-onset variety) had been documented and therapy initiated before the onset of MI. Patients without a previous diagnosis of diabetes mellitus were further examined by oral glucose tolerance test during their hospitalization and diagnosed according to the diagnostic criteria recommended by the World Health Organization Expert Committee (14).

Used as an index of obesity, body mass index was calculated from the equation body mass index = weight (kg) ÷ height^2 (m) (15). A history of hypertension was defined as antihypertensive therapy previously prescribed, ≥2 previous documented diastolic readings ≥95 mmHg, or ≥2 previous systolic readings ≥160 mmHg. Patients were divided into smokers or nonsmokers (who had never smoked). Blood samples for serum cholesterol and HbA_{1c} were taken during the third to seventh hospital day after an overnight fast. The infarct size was determined from a 12-lead electrocardiogram with a QRS scoring system developed by Selvester et al. (16) and modified by Hindman et al. (17) on the seventh hospital day. Patients did not have electrocardiographic evidence of conduction abnormalities. Postinfarction angina was diagnosed when a patient had complained of chest pain with ST-T wave changes on the 12-lead electrocardiogram compatible with ischemia.

First-pass radionuclide angiocardiography was performed 4 wk after the onset of MI. In preparation for the procedure, each patient had a short 18-gauge Teflon catheter placed percutaneously into an external or antecubital vein. For each radionuclide acquisition, 15 mCi of ^{99m}Tc pertechnetate was injected as a bolus, and counts were recorded at 25-ms intervals with a multicrystal gamma camera (Baird Atomic System Seventy-Seven) (18,19). After correction for background activity and electronic dead time, data from 3 to 6 individual beats were combined to produce an average or representative cardiac cycle. Regional wall motion was assessed with static images of the end-diastolic and end-systolic perimeters that were outlined by computer program at the 23% isocount contour of the end-diastolic image. In addition, regional function was evaluated with a regional ejection fraction image that was generated by subtracting end-systolic counts from end-diastolic counts for each of the 21 × 14 crystals in the left ventricular image. Differences in regional function were displayed with a 16-color coded image, each color representing a 6.25% difference in the regional ejection fraction. From this left ventricular regional ejection fraction image, wall motion was subjectively categorized as normal, hypokinetic, akinetic, or dyskinetic by three experienced observers. Akinetic and dyskinetic zones were defined as infarcted areas and the remaining categories were defined as noninfarcted areas, and a mean of the regional ejection fraction was calculated for each area. Background-corrected activity in the region at the base of the heart was low even in healthy subjects, probably resulting from inclusion of adjacent structures into the region. Therefore, this region was not included in the subsequent analysis of the regional ejection fraction.

Single-photon emission computed tomography was performed in all patients. After injection of 2 mCi of thallium-201, tomograms were obtained by a tomographic system (Toshiba GCA-90B). A large field-of-view gamma camera with a high-resolution parallel-hole collimator was rotated 180° around the long axis of a patient. Thirty views every 6° were obtained for 20 s from the 60° left posterior oblique to the 30° right anterior oblique. After correction for nonuniformity and center of rotation, images were reconstructed into long- and short-axis cuts. Definite perfusion defect on the tomograms was visually defined as an infarcted area by three experienced observers, which was referred to qualitatively assess the site and extent of the infarct in determining the regional ejection fraction of the noninfarcted area.

Coronary angiographic studies were also performed 4 wk after the onset of MI. The severity of coronary atherosclerosis present in vessels supplying noninfarcted segments of the left ventricle was stratified with the scoring system developed by Gensini (20) with some modification, i.e., obstructions of infarct and its distal lesions were not included in analysis.

Results are reported as means ± SD. Multiple regression analysis (forward stepwise-selection method) was performed to evaluate the factors related to the left ventricular regional ejection fraction of the noninfarcted area. Categorical variables were subdivided as follows: sex (male or female), postinfarction angina, and risk factors (absent or present). Student's t test and χ^2-analysis were used to test the significance of variables between diabetic and nondiabetic patients. Linear regression models were derived for the regional ejection fraction of the noninfarcted area and QRS score relationship in the diabetic and nondiabetic groups, and its difference was analyzed with analysis of covariance. $P < .05$ was considered significant.

RESULTS

Of the 55 patients, 17 had diabetes mellitus. Clinical profiles of diabetic patients are shown in Table 1. One patient had background retinopathy. Duration of smoking was 32 ± 11 yr (range 10–60 yr) and frequency was 32 ± 22 (5–100) cigarettes per day among smokers.

TABLE 1
Clinical profiles of 17 diabetic patients

	Patients (*n*)
Duration of diabetes mellitus (yr)	
≤5	11
6–10	4
≥11	2
Therapy on admission	
Diet	13
Oral hypoglycemic agents	4
Therapy at discharge	
Diet	7
Oral hypoglycemic agents	10
Admission HbA_{1c} (%)	
≤6.3	5
>6.3	12
Retinopathy	
Negative	16
Positive	1

Multiple regression analysis was performed with 10 variables (age, sex, QRS score, diabetes mellitus, hypertension, smoking, postinfarction angina, body mass index, serum cholesterol, and severity of coronary atherosclerosis) to determine the important variables related to the left ventricular regional ejection fraction of the noninfarcted area in patients with acute MI (Tables 2 and 3). As a result, QRS score ($P < .001$) and diabetes mellitus ($P < .05$) were identified as significant variables.

When nine clinical variables were compared between diabetic and nondiabetic patients, there were no significant differences in age, sex distribution, QRS score, association of hypertension, history of smoking, episode of postinfarction angina, body mass index, serum cholesterol level, and severity of coronary atherosclerosis between the two groups (Table 4).

The regional ejection fraction of the noninfarcted area had an inverse linear relationship with QRS score (Fig. 1), the equations for which were: regional ejection fraction of the noninfarcted area = $-3.74 \times$ QRS score + 81.1 in diabetic patients ($P < .005$), and regional ejection fraction of the noninfarcted area = $-2.91 \times$ QRS score + 81.9 in nondiabetic patients ($P < .001$). When the regional ejection fraction of the noninfarcted area and QRS score relationship in the two groups were compared, the regional ejection fraction was significantly lower in diabetic patients at every QRS score ($P < .05$).

DISCUSSION

We evaluated the left ventricular regional ejection fraction of the noninfarcted area and elucidated the important factors associated with left ventricular regional dysfunction after acute MI. Of the 10 clinical variables, a high QRS score and association of diabetes mellitus were the important factors related to regional left ventricular dysfunction of the noninfarcted area in patients with acute MI. Because there was no significant difference between diabetic and nondiabetic groups in the remaining 9 clinical variables, diabetes mellitus was considered to be an independent factor contributing to the lower regional ejection fraction of the noninfarcted area.

Radionuclide left ventriculography is used as an estimation of left ventricular function, and the left ventricular ejection fraction has been widely used to predict the prognosis in patients with coronary artery disease (8–11). Because the global left ventricular ejection fraction is affected by the extent of infarct mass, attempts have been made to quantitatively assess left ventricular wall motion with the regionally derived radionuclide ejection fraction, and this regional ejection fraction of the noninfarcted area is considered to more favorably assess residual left ventricular function after MI than the global ejection fraction (12,13).

The QRS score had an inverse relationship with the regional ejection fraction of the noninfarcted area. The QRS scoring system has been shown to quantify the amount of myocardial necrosis (16,17,21–23). The QRS score correlates well with postinfarction left ventricular function and also is a good predictor of mortality after

TABLE 2
Correlation coefficient matrix

Sex	QRS score	Hypertension	Diabetes mellitus	Smoking	Postinfarction angina	Coronary atherosclerosis	Body mass index	Cholesterol	Regional ejection fraction	Variables
.33	.05	.09	−.08	−.36	.08	.18	−.11	−.24	−.03	Age
	.02	.08	−.11	−.59	.05	−.03	.04	.17	.01	Sex
		−.04	−.13	−.30	−.02	.00	−.29	−.04	−.69	QRS score
			−.01	−.18	.05	.20	.19	.17	.02	Hypertension
				.03	−.04	.08	.11	.22	−.14	Diabetes mellitus
					.00	−.27	.15	−.19	.19	Smoking
						.01	.07	−.08	.05	Postinfarction angina
							−.06	−.13	−.16	Coronary atherosclerosis
								.42	.29	Body mass index
									.06	Cholesterol

TABLE 3
Relationship between clinical variables and regional ejection fraction

Variables	Partial regression coefficient	Standard partial regression coefficient*	Partial *t* value†	*P*
Constant	73.127			
QRS score	−3.163	−0.725	−6.47	<.001
Diabetes mellitus	−8.213	−0.245	−2.34	<.05
Severity of coronary atherosclerosis	−0.187	−0.172	−1.54	NS
Body mass index	0.708	0.112	0.94	NS
Smoking	−4.754	−0.133	−0.88	NS
Sex	−3.511	−0.087	−0.65	NS
Postinfarction angina	1.663	0.028	0.28	NS
Hypertension	−0.393	−0.013	−0.12	NS
Age	0.012	0.008	0.07	NS
Cholesterol	0.002	0.006	0.05	NS

*R = 0.75; †R^2 = 0.57.

MI (24,25). In this study, we included only patients with anterior infarcts because the QRS score correlates with infarct size and left ventricular function better in anterior than inferior infarcts (21,22,26). The fundamental pathological alteration underlying left ventricular dysfunction in acute MI is the loss of functioning segments of myocardium and is directly related to the extent of left ventricular damage (27). If the infarct is of sufficient size, it depresses overall left ventricular function and stroke volume falls. The failing left ventricle is compensated by an increase in preload, i.e., it dilates the normally functioning portion of the left ventricle. Because Laplace's law dictates that the dilated ventricle must develop a higher wall tension, intramyocardial pressure rises. Increased intramyocardial pressure by cardiac dilation causes a decrease in subendocardial coronary flow and a resultant imbalance between myocardial oxygen demand and supply (28,29). Lengthening of the noninfarcted segment also appears to occur with adaptive hypertrophy, which may undergo a transition with ultimate impairment of contractile function (30). Our results from multiple regression analysis are in keeping with previous findings suggesting that larger infarct mass is associated with regional left ventricular dysfunction of the noninfarcted area.

Diabetes mellitus was another significant factor contributing to the lower regional ejection fraction of the noninfarcted area after acute MI. Previous studies indicate that diabetic patients are likely to be at high risk for congestive heart failure after acute MI, but these studies were based on clinical findings during the course of

TABLE 4
Comparison of nine variables between diabetic and nondiabetic patients

	Patients	
	Nondiabetic	Diabetic
n	38	17
QRS score	9.6 ± 3.7	8.5 ± 3.4
Age (yr)	58 ± 11	56 ± 11
Sex		
Male	30 (79)	15 (88)
Female	8 (21)	2 (12)
Severity of coronary atherosclerosis	11.9 ± 14.6	14.4 ± 14.1
Cholesterol (mg/dl)	212 ± 51	235 ± 37
Body mass index (kg/m^2)	23.5 ± 2.8	24.1 ± 1.7
Postinfarction angina		
Positive	3 (8)	1 (6)
Negative	35 (92)	16 (94)
Hypertension		
Positive	16 (42)	7 (41)
Negative	22 (58)	10 (59)
Smoking		
Positive	28 (74)	13 (76)
Negative	10 (26)	4 (24)

Data are means ± SD or *n*, with percentages in parentheses. *P* was not significant.

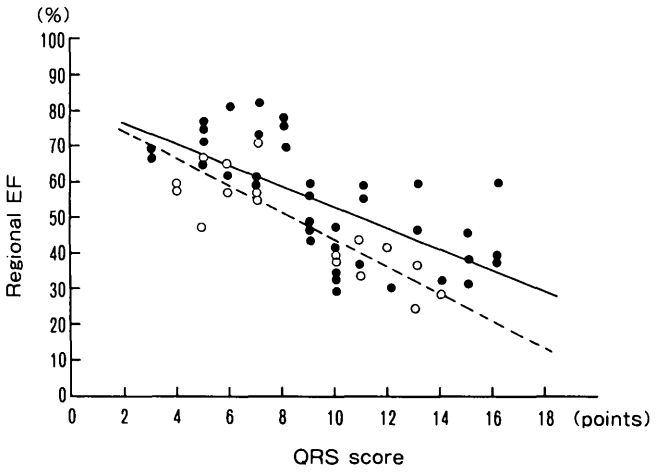

FIG. 1. Regional ejection fraction (regional EF) and QRS score relationship in diabetic and nondiabetic patients. ○, Diabetic patients; ●, nondiabetic patients. *Solid line* represents regression equation obtained from nondiabetic patients and *dashed line* represents diabetic patients.

acute MI and did not further elucidate the difference in the actually measured left ventricular function between diabetic and nondiabetic patients (1,2). Our data that used the regionally derived ejection fraction indicate that diabetes mellitus was an independent factor contributing to regional left ventricular dysfunction which was not influenced by the extent of myocardial necrosis.

The pathogenesis of left ventricular dysfunction in diabetic patients is not completely understood. Association of hypertension, accelerated coronary atherosclerosis, high serum cholesterol levels, advanced age, and obesity are considered risk factors for congestive heart failure, but the effect of diabetes was not mediated through these atherogenic traits in our results. Kannel et al. (31) analyzed the influence of treatment in the development of congestive heart failure and revealed that the subgroup of subjects treated with insulin sustained a significant increased risk of congestive heart failure and speculated that only insulin-dependent diabetes mellitus implicated and promoted cardiac decompensation. Our study included only subjects treated by diet or orally administered drugs, but it is speculated that even diabetic subjects treated without insulin potentially have a risk of cardiac decompensation when an extra burden is placed on the heart after MI.

Blumenthal et al. (7) found more proliferative lesions of arterial branches of all sizes in diabetic patients compared with nondiabetic patients. Therefore, in the noninfarcted but dilated portion of the myocardium after acute MI, the decrease of subendocardial coronary flow will be more severe in diabetic patients than in nondiabetic patients. The heart normally derives most of its energy for contraction from free fatty acids (32–34). When the heart is associated with limited subendocardial flow or exposed to hypoxia, the use of free fatty acids is depressed and glycolytic metabolism must be fallen back on for energy. This places the myocardium of the diabetic heart in jeopardy because the use of glucose is also faulty in such patients. Thus, these mechanisms (microangiopathy and metabolic disorder) could be responsible for regional left ventricular dysfunction of the noninfarcted area after acute MI in diabetic patients. Our data indicate that diabetes mellitus is another discrete cause of left ventricular dysfunction after acute MI as well as a risk factor for coronary heart disease.

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