Residual Left Ventricular Pump Function After Acute Myocardial Infarction in NIDDM Patients

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OBJECTIVE — Left ventricular remodeling occurs immediately after MI, involving structural changes in noninfarcted segment. However, the residual left ventricular pump function in NIDDM patients after acute MI has not been clarified. The purpose of this study was to evaluate the difference in the process of left ventricular remodeling between NIDDM and nondiabetic patients.

RESEARCH DESIGN AND METHODS — Left ventricular regional EF images obtained by radionuclide angiography were investigated in 20 NIDDM and 29 nondiabetic patients the 3rd wk after acute MI.

RESULTS — Regional EF of the noninfarcted area and P/V had a significant hyperbolic relation with left ventricular EDV in both groups of patients. Despite no difference in the extent of myocardial necrosis and the number of coronary vessels diseased between NIDDM and nondiabetic patients, regional EF of the noninfarcted area and P/V were significantly lower when left ventricular EDV increased in NIDDM patients compared with nondiabetic patients.

CONCLUSIONS — Pathogenetic changes of the residual myocardium associated with NIDDM may adversely influence the process of left ventricular remodeling after MI, especially in patients with increased left ventricular EDV.

Prognosis after acute MI is related to residual left ventricular function and thus to the amount of damaged myocardium. Systolic impairment secondary to loss of contractile function of the infarcted myocardium results in a decreased systolic ejection, but left ventricular function is compensated by an increase in left ventricular EDV (1). An increased incidence of congestive heart failure with a comparable infarct size has been documented in NIDDM patients. Although pathogenesis of left ventricular dysfunction in NIDDM patients is not understood completely, some mechanisms proposed are metabolic disorder, microangiopathy of the heart (2–4), and reduction in aortic elasticity that increases left ventricular afterload. However, the residual left ventricular pump function after acute MI in NIDDM patients has not been clarified.

Radionuclide angiocardiography is advocated as a useful tool for assessing left ventricular function and wall motion abnormalities (5–8). Attempts have been made to assess left ventricular wall motion quantitatively with the regionally derived radionuclide left ventricular EF (5,9). The purpose of this study was to evaluate left ventricular regional EF of the noninfarcted area and its relation to left ventricular EDV in NIDDM and nondiabetic patients.

RESEARCH DESIGN AND METHODS

— Among 75 consecutive patients with acute Q-wave MI admitted to our Coronary Care Unit, 49 patients fulfilled the following criteria: *1*) aged 40 to 75 yr; 2) no prior history of MI; and 3) no evidence of hypertension (antihypertensive therapy previously prescribed, or ≥2 previous documented diastolic readings ≥95 mmHg, or ≥2 previous systolic readings ≥160 mmHg), valvular heart disease, atrial fibrillation, or intraventricular conduction defect. Twenty patients (13 men and 7 women with a mean age of 56 ± 8 yr) had NIDDM, and 29 patients (18 men and 11 women with a mean age of 59 ± 11 yr) were nondiabetic. Diagnosis of acute MI was made when the patients had *1*) typical chest pain lasting >30 min; 2) new Q-wave in serial electrocardiogram, and 3) at least twice a normal elevation in CK level with the MB isoenzyme of 5% or more. QRS score (Selvester's Complete 54-Criteria,

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NIDDM, NON-INSULIN-DEPENDENT DIABETES MELLITUS; EF, EJECTION FRACTION; MI, MYOCARDIAL INFARCTION; P/V, RATIO OF SYSTEMIC ARTERIAL SYSTOLIC PRESSURE TO LEFT VENTRICULAR END-SYSTOLIC VOLUME; EDV, END-DIASTOLIC VOLUME; CK, CREATINE KINASE; ESV, END-SYSTOLIC VOLUME; BMI, BODY MASS INDEX.

32-point QRS Scoring System) was obtained on the 14th hospital day (10,11). Blood samples for CK were obtained from the antecubital vein every 8 h for a period of 72 h after admission. Enzymatic activity of CK was measured by the method of Rosalki (12). QRS score and peak CK (13) were used as the index of infarct size. Patients were defined as having NIDDM if they were on medical treatment for diabetes mellitus (of adult-onset variety) at the time of hospitalization, or if they had abnormally high fasting blood glucose values (>120 mg/dl) for 3 days after hospitalization and still needed treatment (diet and/or oral hypoglycemic agents) at the time of the study.

BMI was used as an index of obesity and was calculated from the equation: BMI = weight (kg)/height (m^2) (14). Patients were divided into smokers or nonsmokers (who had never smoked). Blood samples for serum cholesterol, plasma triglyceride, blood glucose, and HbA_{1c} were taken during hospital days 11–14 after an overnight fast. HbA_{1c} was determined by high-performance liquid chromatography (normal range 4.3–6.3%).

Long-acting nitrates, Ca^{2+} antagonists, and anticoagulants were continued after the onset of MI, but all medications were discontinued for at least 24 h before the radionuclide angiographic study. Patients who were on β-blocking agents, and angiotensin converting enzyme inhibitors were not included in this study. None of the patients had an intervening clinical event after the onset of acute MI, such as orthostatic hypotension, critical arrhythmias, postinfarction angina, recurrent MI, percutaneous transluminal coronary angioplasty, or coronary artery bypass grafting.

Radionuclide data acquisition and analysis

Radionuclide angiography was conducted the 3rd wk after acute MI. Left ventricular EDV and ESV were determined by the first-pass method with a computerized multicrystal camera (Baird-Atomic System 77) in the anterior projection under the same conditions (i.e., fasting state and in upright position). In preparation for the procedure, each patient had a short 18-gauge Teflon catheter placed percutaneously into an external jugular or antecubital vein. For each radionuclide acquisition, 15 mCi of ^{99m}Tc pertechnetate was injected as a bolus, and counts were recorded at 25 msec intervals with a multicrystal γ-camera. After correction for background activity and electronic data time, data from 3–6 individual beats were combined to produce an average or representative cardiac cycle. The left ventricular EF was determined from the background-corrected representative cardiac cycle as follows: (end-diastolic counts − end-systolic counts)/end-diastolic counts × 100. Left ventricular EDV and left ventricular ESV were calculated by the area-length method of Dodge et al. (15), with the ellipse of revolution modified for the single anterior plane projection as $0.85 \times A^2/L$ (where A is the area obtained by planimetry, and L is the longest diameter measured from the aortic valve to the apex of the left ventricle). Reliability and reproducibility of this method have been reported (16). P/V was calculated by dividing the cuff-determined systolic blood pressure by left ventricular ESV index (17). Regional wall motion was assessed with static images of the end-diastolic and end-systolic perimeters that were outlined by the computer program at the 23% isocount contour of the end-diastolic image. In addition, regional function was evaluated with a regional EF 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 EF. Background-corrected activity in the region at the base of the heart was low even in healthy, nondiabetic subjects, probably resulting from inclusion of adjacent structures into the region. Therefore, this region was not included in the subsequent analysis of the regional EF. From this left ventricular regional EF image, wall motion was subjectively categorized as normal, hypokinetic, akinetic, or dyskinetic by three mutually blinded experienced observers who were unaware of the patients' clinical status. Akinetic and dyskinetic zones were defined as infarcted areas. The remaining categories were defined as noninfarcted areas, and a mean regional EF was calculated for each area. The reliability and reproducibility of this method have been reported (18). In addition, single-photon emission computed tomography was performed in all patients at rest within 3 days of radionuclide angiographic study. Based on the site and extent of MI by thallium-201 scintigraphy, infarcted and noninfarcted areas were confirmed.

Coronary angiography

Coronary angiographic studies were performed within 2 days of radionuclide angiographic study. The severity of coronary atherosclerosis in the vessels supplying noninfarcted segments of the left ventricle was stratified with the scoring system developed by Gensini (19) with some modification (i.e., obstructions of infarct-related coronary artery and its distal lesions were not included in the analysis).

Statistical analysis

Results are reported as means ± SD. Students t test and χ^2 analysis were used to test the significance of variables between NIDDM and nondiabetic patients. Hyperbolic regression models ($1/y = a\chi + b$) were derived for the regional EF of the noninfarcted area and left ventricular EDV relationship. The difference between NIDDM and nondiabetic groups was analyzed with analysis of covariance. $P < 0.05$ was considered significant.

Table 1—*Clinical profile of 20 NIDDM patients*

	PATIENTS (*N*)
DURATION OF NIDDM (YR)	
≤5	6
6–10	11
≥11	3
THERAPY ON ADMISSION	
DIET	14
ORAL HYPOGLYCEMIC AGENTS	6
THERAPY AT DISCHARGE	
DIET	7
ORAL HYPOGLYCEMIC AGENTS	13
HbA_{1c} (%)	
≤6.3	5
>6.3	15

RESULTS

Clinical and hemodynamic variables

Clinical profiles of NIDDM patients with MI are shown in Table 1. Blood glucose ranged from 82 to 96 mg/dl (92 ± 8 mg/dl), and HbA_{1c} ranged from 4.6 to 6.2% (5.1 ± 0.4%) in nondiabetic patients. When 10 clinical variables were compared between NIDDM and nondiabetic patients, no significant differences were observed between the two groups in age, sex distribution, location of MI, extent of necrosis (Selvester' QRS scoring system and peak CK), BMI, serum cholesterol and triglyceride levels, and history of smoking (Table 2). Of the 49 patients who underwent coronary arteriography, 14 had single-vessel and 6 had double-vessel disease in NIDDM patients; and 21 had single-vessel and 8 had double-vessel disease in nondiabetic patients. No significant differences were noted in the severity of coronary atherosclerosis and number of coronary vessels diseased between NIDDM and nondiabetic patients.

Radionuclide angiography

No significant differences were observed in heart rate, systolic blood pressure, global EF, regional EF of the infarcted area, and left ventricular EDV between NIDDM and nondiabetic patients. But, left ventricular ESV was significantly larger, and regional EF of the noninfarcted area and P/V ratio were significantly lower in NIDDM patients compared with nondiabetic patients (Table 3).

To obtain the regional EF of the noninfarcted area-left ventricular EDV relation, the regional EF of the noninfarcted area was plotted against the corresponding left ventricular EDV. The regional EF of the noninfarcted area (Fig. 1) and the P/V ratio (Fig. 2) had negative nonlinear relations with left ventricular EDV. The slopes of the regional EF of the noninfarcted area-left ventricular EDV relation and P/V ratio-left ventricular EDV relation in NIDDM patients were significantly steeper compared with nondiabetic patients ($P < 0.05$ and $P < 0.05$, respectively): the regional EF of the noninfarcted area and P/V ratio were lower, because left ventricular EDV increased in NIDDM patients compared with nondiabetic patients.

CONCLUSIONS

Immediate consequences of MI are initial reduction in total myocardial force generated by the left ventricle and a decrease in cardiac output as a result of the loss of contractile myocardium (1). Previous research has demonstrated that the extent of necrosis is the principal factor determining the degree of left ventricular dysfunction after MI (20–22). Hsia and Starling (23) indicated that contractile indexes have a significant curvilinear relationship with left ventricular EDV. In our study, regional EF of the noninfarcted area and P/V had a curvilinear relation with left ventricular EDV. Despite a nearly identical extent of necrosis, severity of coronary atherosclerosis, and number of diseased coronary vessel between NIDDM and nondiabetic patients, we found that regional EF of the noninfarcted area and P/V ratio were significantly lower, because left ventricular EDV increased in NIDDM patients.

Early cavitary enlargement tends to restore normal or nearly normal left ventricular systolic function, but a further increase in ventricular cavity size

Table 2—*Comparison of seven variables between NIDDM and nondiabetic patients*

	NONDIABETIC (*N* = 29)	NIDDM (*N* = 20)
AGE (YR)	57 ± 12	55 ± 10
SEX		
MALE	21 (72)	16 (80)
FEMALE	8 (28)	4 (20)
LOCATION OF MI		
ANTERIOR	19 (66)	13 (65)
INFERIOR	10 (34)	7 (35)
QRS SCORE	9.4 ± 3.7	8.5 ± 3.4
PEAK CK (U/L)	2672 ± 1490	2380 ± 1375
SEVERITY OF CORONARY ATHEROSCLEROSIS	12.9 ± 13.8	14.6 ± 14.2
CHOLESTEROL (MG/DL)	216 ± 51	235 ± 37
TRIGLYCERIDE (MG/DL)	122 ± 48	134 ± 41
BMI (KG/M^2)	24.2 ± 3.2	25.2 ± 2.3
SMOKING		
POSITIVE	24 (86)	15 (75)
NEGATIVE	5 (14)	5 (25)

Values are means ± SD or number of patients, with percentages in parentheses. Differences were not significant.

Table 3—*Comparison of hemodynamic indexes between NIDDM and nondiabetic patients*

	NONDIABETIC (N = 29)	NIDDM (N = 20)	P VALUE
HEART RATE (BEATS/MIN)	67 ± 10	65 ± 11	NS
SYSTOLIC BLOOD PRESSURE (MMHG)	116 ± 13	114 ± 14	NS
GLOBAL EF (%)	45.4 ± 17.8	40.2 ± 15.3	NS
REGIONAL EF OF NONINFARCTED AREA (%)	58.1 ± 15.6	46.1 ± 15.8	<0.05
LEFT VENTRICULAR EDV (ML)	135.0 ± 62.4	129.4 ± 41.2	NS
LEFT VENTRICULAR ESV (ML)	62.3 ± 20.2	84.0 ± 25.3	NS
P/V RATIO	3.1 ± 1.9	1.9 ± 1.1	<0.05

Values are means ± SD.

has a detrimental effect on ventricular performance (24,25). Grossman (26) and McKay et al. (1) have reported that the left ventricular remodeling occurs immediately after MI involving structural changes in both infarcted and noninfarcted segments. Systolic impairment secondary to loss of contractile function of the infarcted myocardium results in a decreased systolic ejection and a secondary increase in ventricular volume. The increase in left ventricular EDV mobilizes the Frank-Staring mechanism and restores stroke volume, but the increased left ventricular wall stress, which is induced by the increased left ventricular EDV, causes a decrease in subendocardial coronary flow. This leads to the imbalance between myocardial oxygen demand and supply, which further depresses overall left ventricular function. In this left ventricular remodeling process, diabetes mellitus may play an important role. The diabetic heart lesion has been viewed from the point of microangiopathy, but the possible role of metabolic disturbances in diabetic myocytes also has been indicated. Blumenthal et al. (27) found more proliferative lesions in arterial branches of all sizes, increased extracellular collagen deposition, and abnormality of calcium transport in the sarcoplasmic reticulum, individually or in combination in NIDDM compared with nondiabetic patients. In our previous study (28), impaired left ventricular systolic function was observed in diabetic patients with retinopathy. Although a contribution of long disposure to metabolic disorder on left ventricular dysfunction cannot be totally excluded, considering the diffuse nature of small vessel disease in NIDDM patients, the microcirculator deterioration of myocardium based on microvascular alterations was the factor contributing to the left ventricular dysfunction, especially in patients with increased left ventricular EDV. In addition, the reduction in aortic elasticity in NIDDM patients increases the load seen by the recovering heart and may be another candidate affecting residual left ventricular function. Our findings suggest that microangiopathy in NIDDM patients could lead to further reduction in left ventricular systolic function after MI and therefore responsibility for the lower regional EF of the noninfarcted area and P/V ratio when the left ventricular EDV increased. Thus,

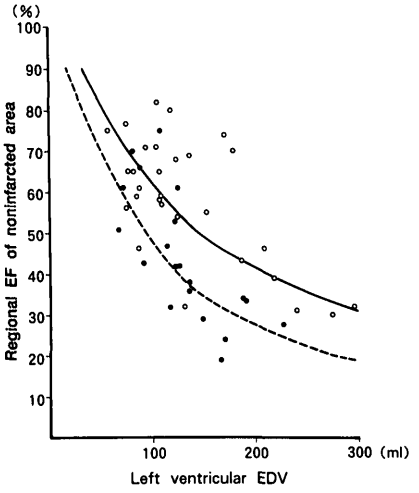

Figure 1—*Regional EF of the noninfarcted area and left ventricular EDV relationship in NIDDM and nondiabetic patients. (●), NIDDM patients; (○), nondiabetic patients; (———), regression equation obtained from nondiabetic patients; (– – – –), NIDDM patients, the equations for which were: 1/regional EF of noninfarcted area = 0.00013 × left ventricular EDV + 0.00816 in diabetic patients (r = 0.67, P < 0.001); 1/regional EF of the noninfarcted area = 0.00008 × left ventricular EDV + 0.00847 in nondiabetic patients (r = 0.75, P < 0.001).*

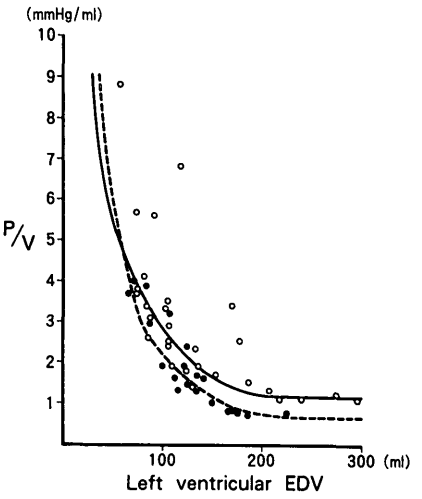

Figure 2—*Systolic blood pressure/left ventricular ESV (P/V ratio) and left ventricular EDV relationship in diabetic and nondiabetic patients. (●), NIDDM patients; (○), nondiabetic patients; (———), regression equation obtained from nondiabetic patients; (– – – –), NIDDM patients, the equations for which were: 1/P/V ratio = 0.00768 × left ventricular EDV − 0.2938 in diabetic patients (r = 0.85, P < 0.001); 1/P/V ratio = 0.00299 × left ventricular EDV + 0.01702 in nondiabetic patients (r = 0.82, P < 0.001).*

pathogenetic changes in diabetes mellitus may adversely influence the left ventricular remodeling process after MI.

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