Functional Improvement of Jeopardized Myocardium following Intracoronary Streptokinase Infusion in Acute Myocardial Infarction

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ABSTRACT The effect of reperfusion on regional left ventricular performance following acute myocardial infarction in man was determined. Intracoronary streptokinase was administered in 24 patients within 6 h of the onset of symptoms. 15 patients (62%) were successfully recanalized during the initial study. Mean percent radial shortening (%RS) in both the jeopardized and compensatory regions were determined using 23 radii from the centroid of diastolic and systolic angiographic silhouettes. Sequential measurements were obtained during repeat cardiac catheterization studies at 24 h in 19 patients and before discharge from the hospital (16±11 d) in 15 patients. At the time of the predischarge study, each acutely reperfused patient showed improvement in %RS in the jeopardized region (P = 0.01) with 56% returning to the normal range. Despite the uniform improvement in the contractile function of the jeopardized region in each reperfused patient, the global ejection fraction showed no improvement or a decrease at the time of the chronic study in 44%. This was due to a decrease in the compensatory wall motion in the uninvolved segments between the acute and chronic study in each case. Neither the %RS nor the ejection fraction changed significantly at the time of the chronic study in the patients who could not be acutely recanalized. These data indicate (*a*) significant salvage of jeopardized myocardium associated with recovery of contractile function in patients reperfused during the first 6 h of chest pain following acute myocardial infarction; (*b*) no improvement in regional or global left ventricular performance in patients who could not be reperfused acutely; and (*c*) the ejection fraction is strongly influenced by changes in the compensatory wall motion of the uninvolved segments and does not accurately reflect changes in the contractile function of the jeopardized myocardium.

INTRODUCTION

Several recent studies have shown that coronary recanalization can be accomplished in patients with acute myocardial infarction using intracoronary streptokinase (1–6). The ability to salvage significant amounts of jeopardized myocardium using this technique, however, has not yet been established. One study has shown improvement in thallium-201 uptake immediately following reperfusion, suggesting at least some cellular viability in the ischemic region (6). Other studies have concentrated on measuring changes in the overall ejection fraction (EF)[1] using either contrast ventriculography or nuclear angiography (1–4). These reports have demonstrated only a modest improvement in the EF between acute and chronic studies in patients who were successfully recanalized.

The global EF represents an average of the contractile performance of all segments of the left ventricular myocardium. While the EF may indicate impaired performance of the ischemic region, it also simultaneously reflects the compensatory motion of the remaining normal myocardium. As contractile function

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[1] *Abbreviations used in this paper:* EF, left ventricular ejection fraction (%); %RS, mean percent radial shortening.

is restored to the region of the jeopardized myocardium following reperfusion, it is likely that the initially hyperdynamic wall motion of the uninfarcted myocardium returns toward normal. This could result in an unchanged or a decreased overall EF despite significant functional improvement in the region of the injured myocardium.

The purposes of the present study were (*a*) to quantitatively analyze sequential changes over time in the regional wall motion of the ischemic segment following intracoronary streptokinase infusion in patients with acute myocardial infarction; (*b*) to evaluate simultaneous changes in the uninvolved compensatory regions; and (*c*) to compare changes in regional performance with effects on the overall EF.

METHODS

24 consecutive patients with acute myocardial infarction admitted to Duke University Medical Center or Durham Veterans Administration Hospital within 6 h of the onset of symptoms were studied. Informed consent was obtained from each patient for the administration of streptokinase according to a protocol approved by the Human Experimentation Committees of both institutions. There were 21 men and 3 women with a mean age of 55±10 yr (±SD). The diagnosis of acute myocardial infarction was determined by the presence of persistent ST segment elevation of >2 mm in two or more leads on the electrocardiogram associated with precordial pain typical of acute infarction. The following exclusion criteria for the administration of streptokinase were observed: (*a*) a history of gastrointestinal bleeding, recent cerebrovascular accident, surgery, or trauma; (*b*) a pericardial friction rub; (*c*) history of a bleeding diathesis; (*d*) diabetic retinopathy; (*e*) chronic congestive heart failure; or (*f*) age >75 yr.

All patients initially received supplemental oxygen, sublingual nitroglycerin, and morphine sulfate. Each patient was transported to the catheterization laboratory under continuous electrocardiographic monitoring following initiation of intravenous lidocaine therapy. An 8F introducer sheath was inserted into the right femoral artery and arterial pressure was continuously monitored. Biplane left ventriculography in the 30° right anterior oblique and 60° left anterior oblique projection was performed before initiation of streptokinase therapy in 12 patients (50%) and immediately following completion of the infusion in the remaining patients. All ventriculograms were recorded using a 35-mm camera at 60 frames/s following the power injection of 45 cm^3 of Renografin (66% diatrizoate meglumine and 10% diatrizoate sodium) into the left ventricle using a No. 7F pigtail catheter. The pigtail catheter was then removed and a No. 7F Judkins coronary catheter was introduced through the sheath and injection of the uninvolved vessel was performed. Injection of the involved vessel was then performed after exchange with another preformed No. 7F Judkins catheter. All patients demonstrated total occlusion of the proximal coronary artery that perfused the infarcted area with the exception of one patient who showed minimal passage of contrast past the obstruction and incomplete filling of the vessel. All patients showed a typical filling defect and persistent staining with contrast medium characteristic of intraluminal thrombus (7). Each patient received an intracoronary bolus of 300 μl of nitroglycerin followed by repeat injection with contrast to exclude focal spasm as the sole etiology of the transmural injury. Streptokinase (Kabikinase, Kabi AB, Stockholm, Sweden) was administered into the occluded coronary artery as a 20,000-U bolus over 2 min. This was followed by a constant infusion of 4,000 U/min until a total dose of 350,000 U was administered. Vessel patency was assessed every 15 min. The entire dose of 350,000 U of streptokinase was infused regardless of whether or not recanalization was established. If >6 h had elapsed from the onset of symptoms and recanalization had not occurred, the procedure was terminated after completion of the streptokinase infusion. Following the procedure, the catheters were removed and the femoral artery sheath was maintained under sterile conditions for later use.

Each patient was then transferred to the Coronary Care Unit. The femoral artery sheath was used to continuously monitor arterial pressure for 24 h. Intravenous heparin was begun at a rate of 1,000 U/h when the partial thromboplastin time fell to less than twice normal. 24 h after the initial study, cardiac catheterization including coronary arteriography and left ventriculography was repeated in 19 of the 24 patients. The indwelling femoral sheath was then removed. A repeat catheterization study was again performed from the opposite femoral artery before discharge from the hospital (mean±SD = 16±11 d; range = 10–53 d) in 15 patients. The coronary arteriograms from each catheterization study were reviewed by two cardiologists who agreed on the degree of luminal narrowing in each of the coronary arteries. The amount of obstruction was expressed as the percent narrowing of the diameter of the vessel.

Two patients were receiving propranolol at the time of the myocardial infarction, two at the 24-h study, and three at the chronic study. One patient was on digitalis at the time of the chronic study, and one was on dobutamine at the time of the 24-h study.

There were three episodes of ventricular tachycardia requiring cardioversion and two patients developed bradydysrhythmias requiring a temporary pacemaker during the acute study. None of the dysrhythmias occurred following acute reperfusion. One patient who could not be recanalized developed refractory ventricular fibrillation and could not be resuscitated. There were no significant dysrhythmias in any of the patients during the 24-h or chronic studies. Six patients developed local hematomas, one of which required surgical evacuation. One additional patient had an unexplained decrease in hematocrit requiring transfusion. All bleeding complications occurred while the patients were on full dose heparin therapy. All but one occurred more than 24 h after the streptokinase infusion (a length of time associated with a return of plasma fibrinogen levels to the normal range in most patients following administration of intracoronary streptokinase) (8).

Regional wall motion was analyzed in the right anterior oblique projection using a quantitative angiographic technique (9, 10) as modified in our laboratory (11, 12). The cineangiograms from all patients were coded and placed in random order. The left ventricular silhouette from each film was projected onto a rear projection screen and was traced onto clear plastic sheets at end-diastole and end-systole by a blinded observer. These tracings were then digitized by a second blinded observer using a sonic digitizing device interfaced to a PDP11/45 computer (Digital Equipment Corp., Marlboro, MA). This digitized information was then used to calculate the EF, according to the method of Kennedy et al. (13) using biplane ventricular volume determinations as described by Dodge et al. (14) and validated for oblique an-

giographic projections by Rogers et al. (15). Quantitative regional wall motion analysis was then performed using a previously described method employed in our laboratory (12). A longitudinal axis is constructed connecting the middle of the aortic valve plane and apex of the heart for both the end-diastolic and end-systolic silhouettes. The midpoint of this axis is then determined by the computer and radii are constructed from the midpoint to the edge of the ventricular silhouette at 15° intervals (Fig. 1). The percent shortening of each radius is calculated according to the formula: % shortening = (diastolic length − systolic length)/(diastolic length) × 100. Radial axes 1 and 21–23 were not included in the analysis because they overlie aortic and mitral valve structures. Normal values for radial shortening were derived from 58 patients studied in our laboratory with normal coronary arteriograms and left ventriculograms who had undergone cardiac catheterization because of atypical chest pain (12). Abnormal radial shortening in the study group was defined quantitatively as percent shortening greater than two standard deviations below the normal mean.

The ischemic zone (jeopardized region) in each patient was identified as the longest continuous asynergic segment found in any of the three studies as defined by abnormal radial shortening in the distribution of the occluded vessel. The remaining normal or hyperdynamic (>2SD above the normal mean) radii comprised the compensatory region.

Patients who underwent repeat cardiac catherization studies had gated radionuclide equilibrium angiograms performed at the time of the 24-h catheterization study (19 patients), and at the time of the chronic study (15 patients). Images were acquired using a Siemens low energy, mobile gamma camera (Siemens Corp., Iselin, NJ) in approximately a 45° left anterior oblique projection adjusted for ventricular separation and using caudal tilt. The data were acquired in a 64 × 64 matrix of 24 frames using a Medical Data Systems A^2 computer (Medical Systems Corp., Great Neck, NY) and an R wave triggered gate. The data were analyzed using a semiautomatic edge detection algorithm and a varying region of interest technique to generate time activity curves for measurement of EF. The patients were imaged using ^{99m}Tc pertechnetate and an in vivo erythrocyte-labeling technique.

All patients in the study developed evidence of transmural myocardial infarction with evolution of diagnostic Q waves in the distribution of the occluded vessel. All patients were found to have an elevation of total serum creatine phosphokinase and creatine phosphokinase MB isoenzyme on serial determination of serum enzymes.

All group data are expressed as mean±SD. Differences between and changes within each group of patients were determined using the nonparametric Wilcoxon rank sum and Wilcoxon signed rank tests, respectively. Limits for defining statistical significance were adjusted when making multiple comparisons within each group according to the formula: $P = 0.05/n$ (where n is the number of comparisons performed).

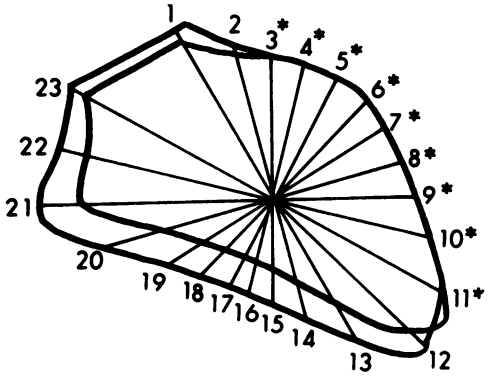

FIGURE 1 Superimposed diastolic and systolic ventriculographic outlines showing the 23 radii and the centroid of each silhouette. Abnormal wall motion, defined as percent radial shortening of >2 SD below the normal mean, is indicated with an asterisk.

RESULTS

Clinical and hemodynamic data recorded during the acute infarction are listed for all patients in Tables I and II. 12 had anterior and 12 had inferior wall infarctions. 9 had single vessel disease, and 15 had multivessel involvement. 15 patients (62%) were reperfused during the initial study within 6 h of the onset of symptoms. Among the patients who were not successfully recanalized, one died following streptokinase infusion before left ventriculography could be performed. Five patients who were shown to have coronary occlusion at the end of the acute study were found to be recanalized at the time of the 24-h study; four were restudied before discharge from the hospital and two were found to have reocclusion. One patient was reperfused during the acute study but reoccluded before the chronic study. One patient demonstrated persistent occlusion during each of the three studies. The mean time from the onset of symptoms to the infusion of streptokinase was 4.4±1.2 h. Among the patients who were recanalized acutely, the mean time from the onset of symptoms to reperfusion was 4.8±0.9 h. The average time from the beginning of the infusion to successful recanalization was 34±18 min with a range of 15–75 min.

The initial EF was not significantly different in patients with single vessel compared to those with multivessel disease ($P = 0.3$). There was also no difference in the mean radial shortening in the ischemic region ($P = 0.7$). The mean radial shortening in the compensatory region, however, was 39% in patients with single vessel involvement compared with 23% ($P = 0.05$) in patients who also had significant lesions in the vessels supplying portions of the compensatory region.

Angiographically evident collateral vessels to the jeopardized region were demonstrated before streptokinase infusion in three of the acutely reperfused patients and in three of the patients who were not successfully reperfused. Acute and chronic cardiac catheterization studies were available in five of these patients (three reperfused and two nonreperfused pa-

TABLE I
Patient Data

Patient	Age/Sex	Studies performed	Location of infarct	Site of occlusion	Other vessel involvement	Previous infarct	Hours to infusion	Hours to reperfusion
1	52/M	1, 2	AMI	LAD	—	N	5.5	6
2	38/F	1, 2, 3	AMI	LAD	—	N	3.5	4
3	47/M	1, 2, 3	AMI	LAD	—	N	3	3.5
4	62/M	1, 2	AMI	LAD	75% LM 95% RCA 95% CIRC	N	4.5	5.25
5	46/M	1, 2, 3	AMI	LAD	75% RCA	N	5.5	6.5
6	61/F	1, 2, 3	AMI	LAD	—	N	3.75	4.0
7	37/M	1, 2	AMI	LAD	95% × 2 RCA 95% × 2 CIRC	Y-IMI	5.75	6.25
8	64/M	1, 2, 3	AMI	LAD	—	N	4.0	NRA
9	64/M	1, 3	AMI	LAD	100% RCA	Y-IMI	6.0	NRA
10	70/M	1, 2	AMI	LAD	75% × 2 CIRC	N	4.5	NRA
11	56/M	1, 2, 3	AMI	LAD	75% CIRC 75% MARG	N	7.25	NRA
12	63/M	1	AMI	LAD	95% RCA	N	4.5	NRA
13	34/F	1, 2	IMI	LCA	—	N	4.0	5.0
14	56/M	1, 2, 3	IMI	RCA	—	N	4.75	5.0
15	58/M	1, 2, 3	IMI	LCA	—	N	3.25	4.5
16	52/M	1, 2, 3	IMI	RCA	95% LAD	N	4.75	5
17	50/M	1, 3	IMI	RCA	—	N	4.75	5
18	61/M	1, 2, 3	IMI	RCA	95% LAD	N	3.5	4
19	59/M	1, 2	IMI	RCA	100% LAD 95% × 4 CIRC	Y-AMI	2.0	2.5
20	60/M	1, 3	IMI	RCA	100% LCA	N	3.5	4 (Reclosed)
21	52/M	1, 2, 3	IMI	RCA	99% LCA	Y-IMI	3.0	NRA
22	59/M	1, 2, 3	IMI	LCA (L Dom)	100% PD	N	3.5	NRA
23	56/M	1, 2	IMI	RCA	95% LAD 95% × 2 CIRC	N	5.0	NRA
24	67/M	1	IMI	RCA	95% LAD 95% CIRC	Y-IMI	3.5	NRA

Studies performed: 1, acute study; 2, 24-h study; 3, predischarge study.
AMI, anterior myocardial infarction; IMI, inferior myocardial infarction; NRA, not reperfused acutely; LAD, left anterior descending coronary artery; LCA, left circumflex coronary artery; RCA, right coronary artery; L Dom, left dominant circulation; LM, left main coronary artery; PD, posterior descending coronary artery.

tients). The degree of improvement in regional contraction, mean percent radial shortening in the jeopardized region (Δ% RS Jeop = +7%) or EF (ΔEF = 0%) between the acute and chronic studies among the reperfused patients with collateral vessels was no greater than in reperfused patients without collaterals (Δ%RS Jeop = +10%, ΔEF = +5%). Similarly, the Δ%RS in the jeopardized region and the ΔEF was −4% and −7% respectively in the nonreperfused patients with collaterals, and −4 and −6% in the nonreperfused patients without evidence of collateral vessels. Collateral vessels that were initially present in the reperfused patients were no longer evident in any of the subsequent catheterization studies following initial recanalization. Collateral vessels initially identified in the two nonreperfused patients were unchanged during subsequent catheterization studies.

A total of four patients died, all within the first week following the acute infarction. Three of the patients died in cardiogenic shock and one patient who was not reperfused died of refractory ventricular fibrillation. All had multivessel disease and three had a history of previous myocardial infarction. Two of the patients were successfully reperfused acutely and two were not. Angiography was performed in three of the patients all of whom had EF of <21%. The mean radial

TABLE II
Hemodynamic Data During Acute Myocardial Infarction

Patient	EF	EDP	MSAP	HR	%RS Jeop	%RS Comp	Collateral vessels present	Survival
	%	mmHg		beats/min				
1	35	13	77	72	3	46	N	Y
2	44	9	95	80	9	43	N	Y
3	50	28	83	75	5	53	N	Y
4	13	25	90	90	1	6	N	Y
5	38	20	83	72	8	25	N	Y
6	29	26	92	81	−1	36	N	Y
7	18	32	74	100	2	6	N	N
8	41	25	87	69	6	56	N	Y
9	17	18	93	90	8	7	N	Y
10	38	12	87	72	8	28	N	Y
11	47	24	93	94	11	32	N	Y
12	20	20	71	128	2	17	N	N
13	32	21	83	81	5	24	N	Y
14	47	12	75	69	12	37	Y	Y
15	42	30	93	90	9	30	N	Y
16	52	15	90	65	10	48	Y	Y
17	58	15	83	72	13	36	Y	Y
18	46	17	72	90	13	24	N	Y
19	21	18	82	64	16	15	N	N
20	50	25	88	72	8	43	Y	Y
21	36	18	73	67	12	26	Y	Y
22	38	21	97	72	13	26	N	Y
23	43	6	86	72	13	26	Y	Y
24	NA	18	80	90	NA	NA	N	N

EDP, left ventricular end diastolic pressure; MSAP, mean systemic arterial pressure; HR, heart rate; %RS Jeop, mean percent radial shortening in the jeopardized region; %RS Comp, mean percent radial shortening in the compensatory region; NA, not available; Y, yes; N, no.

shortening was below the normal range in both the jeopardized region (7±8%) and the compensatory region (13±6%).

To validate the accuracy of the contrast angiographic EF using an independent technique, the contrast studies were compared with gated equilibrium radionuclide EF. The mean±SD radionuclide EF in all patients who underwent cardiac catheterization at 24 h was 40±8% compared with 39±6% using contrast angiography. The mean radionuclide EF for all patients with chronic catheterization studies was 45±11% compared with 43±10% using contrast angiography.

Patients who were successfully reperfused at the time of the initial study showed significant improvement in the mean radial shortening of the involved segment as well as a decrease in the amount of compensatory wall motion at the time of the 24-h study (Table III, top). The EF did not change significantly, but tended to follow the directional change of the compensatory wall motion. The heart rate decreased significantly at the time of the 24-h study ($P = 0.01$), but there was no change in mean systemic arterial ($P = 0.2$) or left ventricular end-diastolic ($P = 0.9$) pressures between the two studies. Patients who were not reperfused acutely had a significant decrease in the segmental function of the jeopardized myocardium. The degree of compensatory wall motion, EF, heart rate ($P = 0.34$), and the left ventricular end-diastolic ($P = 0.5$), or mean systemic arterial ($P = 0.29$) pressures did not change.

Angiography was performed immediately following streptokinase infusion in 11 patients and just before streptokinase infusion in 12 patients. The changes in EF and mean radial shortening in the ischemic segment between the acute and 24-h study were compared in all patients who were successfully recanalized. There was no difference in the amount of change in either the EF ($P = 0.4$) or the mean radial shortening in the jeopardized region ($P = 0.9$) in patients with angiography before compared with those with angiography performed immediately after successful reperfusion.

The mean data for all patients with both acute and chronic studies are shown in the bottom panel of Table

TABLE III
Global and Regional Left Ventricular Performance

Acute vs. 24-h study

	EF*			%RS: Jeop*			%RS: Comp*		
	Acute	24 h	*P*	Acute	24 h	*P*	Acute	24 h	*P*
Opened (n = 13)	38±14	34±12	0.40	7±5	9±4	0.05	31±15	26±13	0.02
Closed (n = 6)	40±4	39±5	0.75	10±4	5±4	0.04	32±12	32±11	0.6

Acute vs. chronic study

	EF*			%RS: Jeop*			%RS: Comp*		
	Acute	Chronic	*P*	Acute	Chronic	*P*	Acute	Chronic	*P*
Opened (n = 9)	45±8	48±5	0.35	9±4	17±4	0.01	37±10	34±10	0.06
Closed (n = 6)	37±11	33±9	0.18	10±3	6±2	0.06	32±17	27±10	0.58

* Abbreviations as in Table II.

III. In the patients who were acutely reperfused, there was a significant improvement in the region of the jeopardized myocardium, although there was no change in the EF. In the patients who were not initially reperfused, there was no improvement in the EF, the segmental function of the ischemic zone, nor was there a decrease in the amount of compensatory wall motion. There was no significant change in heart rate, mean systemic arterial pressure, or left ventricular end-diastolic pressure in either the reperfused or nonreperfused groups between the acute and chronic studies.

Table IV shows the mean data for patients with all three studies. In patients who were acutely reperfused, there was no significant change between the acute and 24-h studies in either the EF or the fractional shortening of the ischemic or compensatory regions. However, there was a marked increase of the mean radial shortening in the region of the jeopardized myocardium into the normal range between the 24-h and chronic studies. Among the patients who were not reperfused acutely, there was no significant change in either the EF or the segmental function of the jeopardized or compensatory regions between the acute and 24-h study. There was also no significant change between the 24-h and the chronic studies in these patients.

Table V shows the data in patients with acute and chronic studies who were successfully reperfused during the acute study. Among these patients the time to reperfusion ranged from 3.5 to 6.5 h. The degree of residual stenosis at the site of previous occlusion ranged from 25 to 95% narrowing at the time of the chronic study. Patients with anterior infarction are shown on the left and those with inferior infarction are shown on the right. The size of the jeopardized region is indicated by the number of radii involved and was found

TABLE IV
Global and Regional Left Ventricular Performance: Patients with All Studies

	EF*			*P* value		%RS: Jeop*			*P* value		%RS: Comp*			*P* value	
	1st	2nd	3rd	1 vs. 2	2 vs. 3	1st	2nd	3rd	1 vs. 2	2 vs. 3	1st	2nd	3rd	1 vs. 2	2 vs. 3
Opened (n = 8)	44±7	40±8	48±6	0.07	0.03	8±4	8±3	18±5	0.52	0.01‡	37±10	32±8	35±9	0.07	0.72
Closed (n = 4)	41±5	38±6	35±5	0.58	0.58	10±3	5±4	5±2	0.10	1.0	36±14	34±13	29±3	0.85	0.71

1st, Acute; 2nd, 24 h; 3rd, Chronic.
* Abbreviation as in Table II.
‡ P = <0.025.

TABLE V

Angiographic Data in Reperfused Patients with Acute and Chronic Studies

Anterior infarction					Inferior infarction				
Patient*	No. radii jeop region	Δ Angio EF	Δ No. Inv Seg	Δ% RS Jeop	Patient*	No. radii jeop region	Δ Angio EF	Δ No. Inv Seg	Δ% RS Jeop
					14	6	+7	−3	+6
2	13	+11	−10	+18	15	7	0	+1	+5
3	11	−8	−3	+8	16	6	0	−6	+12
5	10	+5	−1	+6	17	5	−6	0	+3
6	12	+16	−5	+18	18	9	+5	−2	+2
Mean±SD	12±1	6±10	−5±4	12±4	Mean±SD	7±2	1±5	−2±3	6±4

* Numbers correspond to patient numbers in Table I and II.

No. radii jeop region, number of abnormal radii defining the jeopardized region, Δ Angio EF, change in angiographic EF between acute and chronic study, Δ No. Inv Seg, change in the number of abnormal radii in the involved segment; Δ% RS Jeop, change in the mean percent radial shortening in the jeopardized region.

to be higher (≥10) in the patients with anterior infarction than in the patients with inferior infarction (<10). The patients with anterior infarction showed a greater improvement in EF and mean radial shortening as well as a greater decrease in the size of the jeopardized region as indicated by a larger decrease in the number of abnormal radii in the involved segment. There was no positive association found between the reduction in size of the jeopardized region or the improvement in regional or global function in patients with earlier reperfusion or smaller residual stenoses.

All acutely reperfused patients who showed improvement in EF (≥5%) between the acute and chronic studies are shown in Fig. 2 *A*. The radial shortening

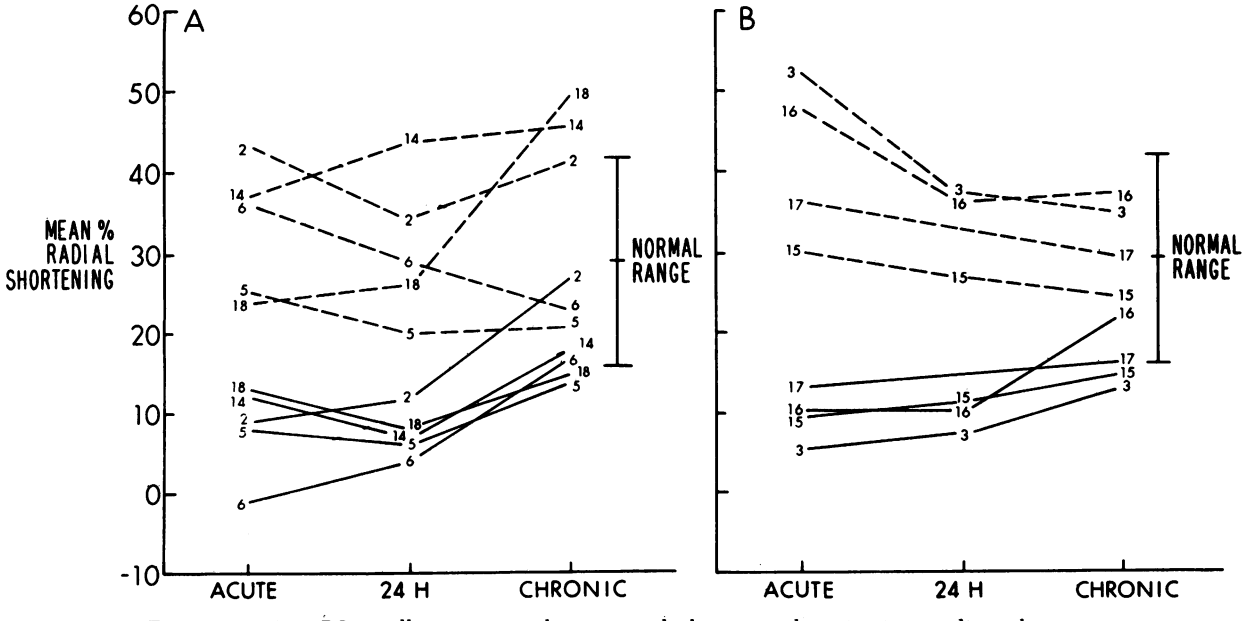

FIGURE 2 (*A*) %RS in all patients with acute and chronic catheterization studies who were initially reperfused and who showed a significant (≥5%) improvement in angiographic EF between the acute and chronic study. Changes in the %RS in the jeopardized region are shown using solid lines while changes in the compensatory region are shown using interrupted lines. The numbers correspond to the patient numbers in Table I. The normal range (mean±2SD) for %RS in 58 normal patients is shown on the right. (*B*) %RS in patients with acute and chronic catheterization studies who were initially reperfused and who showed no change or a decrease in the EF between the acute and chronic studies.

in the ischemic segment is plotted using solid lines. There is improvement in contractile function between the acute and chronic study in the region of the jeopardized myocardium in each patient. The mean radial shortening in the compensatory region is shown for each patient using interrupted lines.

Patients who were reperfused but who showed no improvement or a decrease in the EF between the acute and chronic study are shown in Fig. 2 *B*. A uniform improvement in the region of the jeopardized myocardium is again demonstrated despite the absence of improvement in the EF. There was a decrease in the degree of compensatory wall motion in the uninvolved region in each patient between the acute and chronic study.

The radial shortening data in the ischemic zone among the patients who were not successfully recanalized during the acute study are shown using solid lines in Fig. 3. The patency status during each study is indicated using a circle around the patient number to indicate opening of the infarct-related coronary artery. There was no improvement in contractile function of the jeopardized myocardium in any of these patients despite the frequent occurrence of late spontaneous recanalization. The mean radial shortening in the compensatory region is shown for each patient using interrupted lines.

DISCUSSION

The salvage of jeopardized myocardium during an acute myocardial infarction has been the subject of extensive investigation in recent years. Much of this interest stems from evidence indicating that infarct size is a major determinant of both early and late morbidity and mortality (16, 17). Recent studies describing the efficacy of streptokinase for intracoronary thrombolysis have demonstrated that myocardial reperfusion is clinically feasible (1–6). The ability to salvage significant amounts of jeopardized myocardium resulting in a re-

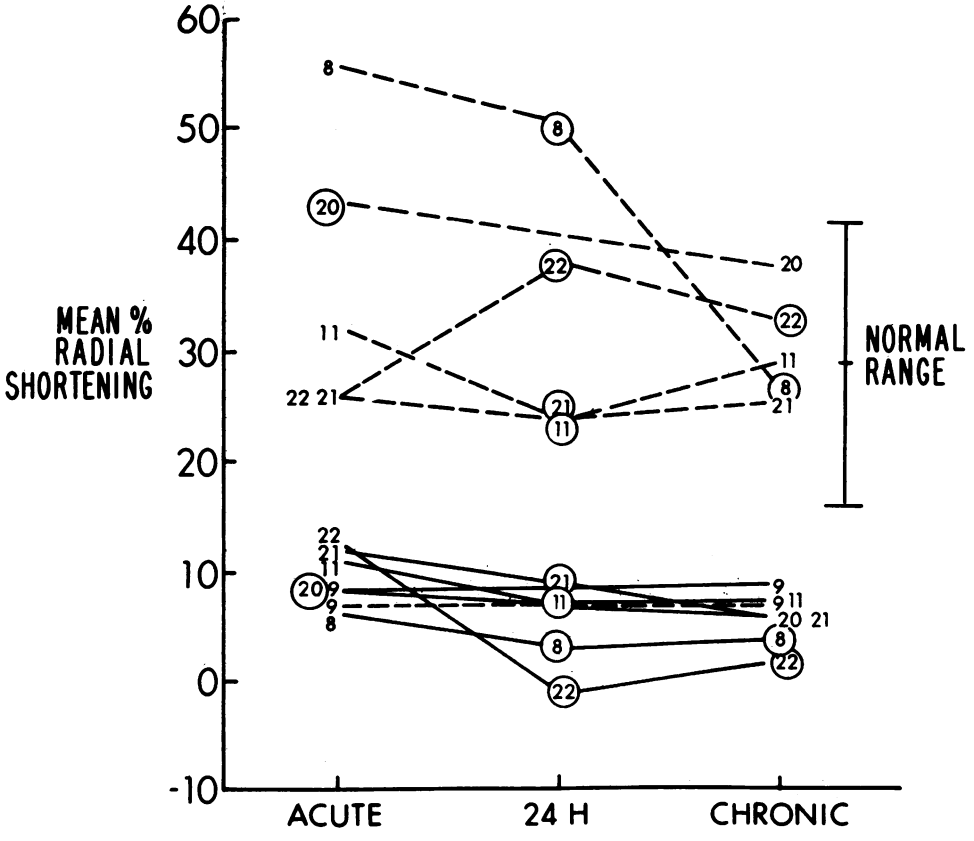

FIGURE 3 %RS in all patients with acute and chronic catheterization studies who were not reperfused during the acute study or who later reoccluded after initial recanalization. A circle around the patient number indicates that the infarct-related vessel was open at the end of that study. Changes in the %RS in the jeopardized region are shown using solid lines while changes in the compensatory region are shown using interrupted lines.

duction of infarct size using this technique has not yet been established.

This study was specifically designed to quantitatively analyze the function of the jeopardized myocardium over time. Changes in the regional performance of the remaining compensatory segments and the net effect on the overall EF were also analyzed.

The technique used in this study for quantitative analysis of regional wall motion utilizes multiple radii that sample segmental wall motion at 15° intervals around the ventricular silhouette. This method determines the systolic and diastolic radial lengths independently and thus corrects for heart motion artifact with the possible exception of cardiac rotation occurring with ventricular contraction. The normal range of fractional shortening for each radius was determined using a large number of normal patients who were shown to have no evidence of heart disease at cardiac catheterization (12).

Gated equilibrium radionuclide scans confirmed the accuracy of the angiographically determined EF. The radionuclide EF are measured using the percent change in counts during the cardiac cycle and therefore do not depend on assumptions regarding left ventricular geometry in the presence of major wall motion abnormalities.

The results of this study show that all patients with acute and chronic studies who were reperfused within 6 h of the onset of symptoms uniformly improved the mean radial shortening in the region of the jeopardized myocardium. In 56% of these patients, the segmental function in the jeopardized region returned to the normal range by the time of the chronic catheterization study. Despite this improvement in each patient, however, 44% of the reperfused patients showed either no improvement or a decrease in EF between the acute and chronic studies. The failure of the EF to improve despite a significant return of function in the jeopardized region was due to a decrease in the amount of compensatory wall motion in the uninvolved region in each patient within 24 h after reperfusion.

There was no improvement of segmental function in the ischemic region of acutely reperfused patients at 24 h in the group of patients with all three studies. There was evidence of a mild but significant improvement at 24 h in the larger group of all acutely reperfused patients with both acute and 24-h studies. The main improvement in regional and global performance, however, occurred between the 24-h and chronic studies.

Previous experimental studies have also found a delayed functional recovery within the borders of the jeopardized myocardium. Theroux et al. (18) studied segmental function following a 2-h temporary occlusion using ultrasonic crystals in awake dogs. These investigators showed that there was a delayed functional improvement at 2–4 wk both at the center and particularly at the margins of the ischemic zone. Puri (19) found a 60% recovery of segmental function at 2 wk in dogs following a 3-h occlusion. The mechanism of delayed functional recovery following reperfusion is not known. One explanation could be that some of the myocytes in the region of the jeopardized myocardium become intensely ischemic but are able to survive in the absence of blood flow until the time of reperfusion. Restoration of blood flow into the infarcted area could possibly promote hypertrophy of these cells allowing partial functional recovery of the involved region. Another explanation could be delayed recovery of myocardial ATP stores in the ischemic region or prolonged abnormalities in local calcium activity (20). The number of surviving cells could also be modified by the presence or absence of effective collateral circulation to the region of the jeopardized myocardium.

During our early experience with streptokinase therapy we were concerned about possible deleterious effects of contrast angiography on infarct size in patients who had not yet been recanalized. We therefore performed angiography immediately following streptokinase infusion in the first 11 patients in our series. We reasoned that if an improvement in regional performance was apparent between acute studies performed immediately after reperfusion and the chronic studies, then any possible functional improvement not recorded in the short time between reperfusion and angiography could only serve to further support a conclusion of functional improvement following reperfusion. As the study progressed, it soon became apparent that patients who had not been successfully recanalized were able to tolerate angiography without increased chest pain or evidence of hemodynamic compromise. We elected to change our protocol so that angiography was performed immediately before streptokinase therapy in the remaining half of our patients, so that any immediate improvement following reperfusion could be detected. We then compared the amount of change in both segmental function and EF at 24 h in the acutely reperfused patients who were studied before streptokinase therapy with those studied immediately after streptokinase infusion. We found no difference in the amount of change in either the EF or the mean radial shortening in the jeopardized region between the two groups. The timing of left ventricular angiography relative to the streptokinase infusion was of little consequence in patients who were not successfully recanalized since reperfusion did not occur. These data are consistent with a previous study by Reduto et al. (2), which showed no change in EF measured before and immediately after streptokinase infusion in patients who were successfully reperfused.

Although the number of patients with angiographically demonstrable collateral vessels in the present study was small, the presence of collateral vessels did not appear to improve the regional or global left ventricular performance in either the reperfused or the nonreperfused patients. However, the precise role of collaterals in preserving the viability of jeopardized myocardium will require further studies. For example, it is possible that the presence of adequate collateral vessels could extend the upper limits of time available for successful reperfusion to be accomplished.

In this study, a significant effort was made to avoid the use of any drugs that could alter regional or global left ventricular performance. However, because of the severity of illness present among many of the patients included in this study, there were occasions when the use of such drugs were deemed necessary. Despite successful recanalization, one of the patients (patient 7, Table II), who had been in cardiogenic shock before initiation of streptokinase therapy, required a dobutamine infusion to maintain adequate arterial pressure at the time of the 24-h study. Despite a slight improvement in the region of the jeopardized myocardium at 24 h, there had been a major decrease in compensatory wall motion in the uninvolved segments resulting in a fall in EF from 18 to 11%. These results are consistent with changes seen in the first 24 h in several other successfully reperfused patients in our series. The patient subsequently died before the chronic catheterization study. Another patient (patient 9, Table II), who required digitalis therapy before the predischarge catheterization study, was in congestive heart failure with recurrent episodes of atrial fibrillation. This patient was not successfully recanalized acutely. Even with the addition of digitalis, this patient showed no improvement in left ventricular performance between acute and chronic studies. Three patients required propranolol for control of recurrent angina pectoris at the time of the chronic study. Two patients (patient 5 and 21, Table II) were already on propranolol at the time of the acute infarction. One was successfully recanalized and the other was not. Discontinuing propranolol in these patients would have resulted in a potentially greater effect on left ventricular performance than allowing them to continue on the drug. The final patient (patient 15, Table II) requiring propranolol therapy had been weaned to only 20 mg q6h by the time of the chronic study and had been successfully recanalized during the acute study. He showed the same improvement in regional function as other recanalized patients despite the presence of low dose propranolol therapy (% RS Jeop = 9% acutely and 14% chronically, EF = 42% acutely and 42% during the chronic study). Thus, the requirement for positive and negative inotropic drugs in the specific instances in which they were used would not be expected to influence the conclusions of this study.

The present study was designed to compare changes in global and segmental function between patients who were acutely reperfused and those who either could not be reperfused within 6 h of the onset of symptoms or who demonstrated late reocclusion of the infarct-related vessel. The patients who were not acutely reperfused do not represent an ideal control group. It is possible that the pathophysiology of the coronary occlusion and subsequent myocardial infarction in these patients differs from that of patients who respond to thrombolytic agents. In addition, the patients in this study who were not initially reperfused demonstrated a wide spectrum of late recanalization as well as late reocclusion of the infarct-related coronary artery. Despite these limitations, the functional changes in the region of the ischemic myocardium within the group were consistent and differed markedly from the changes in the patients who were acutely reperfused.

There was no improvement in the mean radial shortening in the region of the jeopardized myocardium at 24 h or at the time of the chronic catheterization study in any of the patients who could not be recanalized within 6 h of the onset of symptoms. Among the patients who had acute and 24-h studies, there was a significant decrease in the %RS in the jeopardized region at 24 h. This occurred despite the fact that five out of the six patients were shown to have late recanalization of the infarct-related vessel at the time of the 24-h study. The EF tended to fall during the same period but this change was not significant. In the smaller group of patients with all three studies, the decrease in % RS of the ischemic region and the EF were not significant between either the acute and the 24-h studies or the 24-h and the chronic studies. There was also no significant reduction in the degree of compensatory wall motion between the acute and 24 h, or the 24-h and chronic studies. Two of the patients who had late recanalization remained patent at the time of the chronic study and two demonstrated reocclusion. None of the four showed improvement in segmental function in the ischemic region compared with the acute study. These data suggest that late reperfusion does not result in significant salvage of segmental function in the region of the jeopardized myocardium. This is consistent with previous histologic studies in dogs that showed little or no salvage of ischemic myocardium following 3–6 h of temporary occlusion (21, 22). This study however, was not designed to determine the upper limit of time available before reperfusion was of no further benefit. Because of differences in species, mechanism of occlusion, and degree of collateral flow, the length of time available for successful reperfusion in man may differ from the dog model.

Four patients in this series died within the first week following their acute myocardial infarction. One of the four patients (patient 24, Table II) was suffering from recurrent ventricular fibrillation during the initial hours of acute infarction, refractory to all available antidysrhythmic medications. Two other patients (patients 7 and 12, Table II) were in cardiogenic shock before the initial catheterization study. The final patient developed a second myocardial infarction in the contralateral wall 4 d following his initial infarction and immediately developed cardiogenic shock and died. It is unlikely that streptokinase or acute cardiac catheterization negatively influenced the outcome in these patients since two of these patients were in cardiogenic shock before cardiac catheterization and the final patient did well for several days following the catheterization procedure until he developed a new myocardial infarction in the opposite wall.

Previous studies that have evaluated the effects of reperfusion using streptokinase have relied mostly on the global EF obtained during the acute infarction to evaluate subsequent changes in left ventricular performance (1–5). The results of this study indicate that the EF is strongly influenced by the compensatory wall motion in the uninvolved segments and does not accurately reflect changes in the ischemic region in the first 24 h after acute infarction. The degree of compensatory response is highly variable and is strongly influenced by the presence of multivessel disease or previous infarction in the compensatory region.

The present study shows that there is a quantitative improvement in the contractile function of the jeopardized myocardium following reperfusion within 6 h of the onset of symptoms. No improvement was found in patients who were not initially reperfused. The clinical significance of the functional improvement following early reperfusion in terms of late prognosis and left ventricular performance must await further long-term studies.

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