

Detection of the Viable Myocardium. A Perfusion Scintigraphic Study, Before and After Coronary Bypass Surgery in Myocardial Infarction Patients

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Objective - To compare single-photon-emission computed tomography (SPECT) imaging scans using ^{201}Tl and $^{99\text{m}}\text{Tc}$ -MIBI in detection of viable myocardium, in regions compromised by infarction.

Methods - Thirty-two (59.3 ± 9.8 years old and 87% male) myocardial infarction patients were studied. All had Q waves on the ECG and left ventricle ejection fraction of $<50\%$. They underwent coronary and left ventricle angiographies and SPECT before (including ^{201}Tl reinjection) and after coronary artery bypass surgery (CABG). Improvement in perfusion observed after surgery was considered the gold standard for myocardial viability.

Results - Among 102 studied regions of the heart, there were 40 (39.2%) areas of transient perfusion defects in the conventional protocol with ^{201}Tl and 52 (51.0%) after reinjection. Therefore, 12/62 (19.4%) more viable regions were identified by reinjection. Using $^{99\text{m}}\text{Tc}$ -MIBI, only 14 (13.7%) regions with transient defects were identified, all of which were seen also in ^{201}Tl protocols. After surgery, 49 of a total of 93 regions analyzed (52.7%) were viable. Sensitivity, specificity, accuracy, positive and negative prediction values were, respectively, ^{201}Tl SPECT scans - 65.3%, 90.9%, 77.4%, 88.9% and 70.2%, reinjection protocol with ^{201}Tl scans - 81.6%, 81.8%, 81.7%, 83.3% and 80.0%; $^{99\text{m}}\text{Tc}$ -MIBI SPECT scans - 20.4%, 90.9%, 53.8%, 71.4% and 50.6%. Logistic regression demonstrated that the reinjection protocol with ^{201}Tl was the best predictor of viability ($P < 0.001$).

Conclusion - Our data suggest the election of ^{201}Tl for viability studies, especially when using the reinjection protocol.

Keywords: myocardial viability, coronary artery disease, myocardial perfusion scintigraphy

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Ischemic cardiomyopathy is a frequent cause of hospitalization and death. In addition, patients with severe ischemic heart disease have high mortality, when treated medically, with about a 31% two-year survival rate¹. Cardiac transplantation is sometimes indicated for these patients^{2,3}.

Ischemic cardiomyopathy can be due to ventricular dysfunction caused by large areas of infarction or by hypokinetic regions caused by chronic hypoperfusion without necrosis. The presence of viable myocardium could favor the indication of myocardial revascularization, thus halting the evolution to larger necrotic areas with the consequent ventricular dysfunction and the need for heart transplantation⁴.

The correct identification of the state of myocardial viability constitutes an important element in the choice of the therapy subsequently adopted: myocardial revascularization, resection of aneurysms, or heart transplantation.

Often, clinical data, the electrocardiogram (ECG), coronary angiography and the analysis of regional wall motion at rest, are not enough for the distinction of fibrosis from viable myocardium.

Initially, postextrasystolic potentiation and infusion of inotropic agents were used to identify viable myocardium based upon the observation of the recovery of myocardial contraction using sensors placed directly on the epicardium under experimental conditions, or by ventricular wall motion analysis in conventional ventriculograms. Recently, echocardiography and gated radionuclide angiography with pharmacological stress (low dose dobutamine) were used for the same purpose.

Positron emission tomography is considered the most sensitive noninvasive technique for the identification of viability. It allows the evaluation of regional flow (nitrogen-13 labeled ammonia) and the myocardial carbohydrate metabolism (fluorine-18 labeled glucose) and lipids (carbon-11 labeled palmitate). However, its use is limited due to the high cost of the equipment required, the need for a multiprofessional team, and also to the extremely short half-life of the tracers.

Cardiac imaging techniques using myocardial perfusion scintigraphy (MPS), based on the study of myocardial perfusion and cellular membrane integrity, have achieved substantial success in the assessment of myocardial viability⁵.

Thus, the present work aimed to investigate the presence of viable muscle in myocardial infarction areas using single-photon-emission computed tomography (SPECT). For that purpose, both thallium-201 chloride (²⁰¹Tl) and 2-methoxy-isobutyl-isonitrile labeled with technetium-99m (^{99m}Tc-MIBI) were used. Improvement in perfusion of these areas after coronary artery bypass graft surgery (CABG) was used in the statistical calculations.

²⁰¹Tl is the radionuclide most often used as a myocardial perfusion marker in the assessment of myocardial viability. ^{99m}Tc-MIBI is frequently used for the diagnosis of coronary artery disease; however, there are insufficient data about its utility in the detection of the viable myocardium.

Methods

Thirty-two patients with a history of MI (of a total of 113 patients referred for viability studies) were selected. The patients fulfilled the following inclusion criteria: MI between 3 and 12 months prior; presence of Q waves (≤ 40 ms) on the ECG; angina and heart failure functional class ⁶ < III; global left ventricle ejection fraction (LVEF) < 50%; no absolute contraindications to the stress testing (ST). Patients were excluded for: clinical instability; the use of thrombolytic agents; coronary bypass surgery during an acute MI; bundle branch block on ECG; uncontrolled hypertension; valve disease, pericardial disease or other cardiac diseases.

All patients underwent cardiac catheterization and both rest and stress ²⁰¹Tl and ^{99m}Tc-MIBI scintigraphies, up to six months before CABG. Complete revascularization was confirmed⁷, and the patients repeated the radionuclide evaluation after approximately three months and the catheterization up to six months after the procedure. Thallium and technetium studies were performed a minimum of three and a maximum of seven days apart. Patients were under the same medication and doses during the follow-up.

This study was approved by the scientific committee of the Heart Institute and also by the ethics committee of our hospital. All patients agreed to participate in the study after informed consent.

ECG tracings were conventionally obtained on the same days of the scintigraphies. Myocardial regions affected by MI were classified as: septal, anterior, inferior, dorsal and lateral, according to the literature⁸.

Coronary lesions were classified according to the percentage of obstruction: occluded (100% of the lumen), severe lesions (>90% and <100%); critical lesion from 70% to 90%; and noncritical lesions (<70%). The presence of collateral circulation (Cc) was assessed as well as its origin and intensity⁹. Obstructed arteries were considered infarct-related arteries depending on the anatomical location of the

affected region, i. e., left anterior descending artery (LAD) for septal, anterior and apical regions; right coronary (RC) for inferior region; and circumflex (Cx) arteries for lateral and dorsal regions. When RC and Cx had a similar degree of obstruction, the dominant artery assumed to be responsible for the inferior region was the RC and for the dorsal region the Cx branch.

Ventricular wall motion analysis was performed using left ventriculography, in right anterior oblique (RAO) projection. Ventricular wall motion abnormalities were classified as follows: hypokinesia - discrete, moderate or accentuated diminished motion; akinesia - total absence of motion; dyskinesia - paradoxical systolic expansion of a given LV segment. Wall motion was graded arbitrarily ranging from zero to five, according to LV motion (0 = normal, 1 to 3 = discrete to accentuated hypokinesia; 4 = akinesia and 5 = dyskinesia). A change of at least one point was considered an improvement, when comparing parameters before and after the procedure.

Global LVEF was calculated by Dodge's uniplanar method¹⁰ modified by Kennedy¹¹.

Stress tests were conventionally performed¹², using the treadmill and the Ellestad's protocol¹³, with a 12-lead simultaneous recording.

The protocol of the ²⁰¹Tl scintigraphy included three phases: 1st, imaging was acquired immediately after radionuclide injection at peak exercise; the dose injected was 111 MBq (3mCi) and tomographic images obtained with the patient in the supine position; 2nd, after 4h the redistribution images, similarly acquired; 3rd, reinjection, performed after 24h, with an additional dose of thallium administered at rest and SPECT images acquired after 4h.

For ^{99m}Tc-MIBI studies, the entire procedure was performed in one day. Initially, images were obtained at rest, with a 296 to 370 MBq (8 to 10mCi) intravenous infusion, followed by the stress images. The radionuclide [888 to 1110 MBq (24 to 30mCi)] was injected at peak exercise, three times the resting dose. To acquire tomographic images, a Siemens scintigraphic camera, model Orbiter ZLC-Digitrac 750, coupled to a Maxdelta (Microvax - 3300) computer was used. Analog imaging was converted to digital in a 64x64, 64 projections with 20 s duration each, over a 180° arch, beginning from 45° RAO to 45° left posterior oblique LPO (step/shoot acquisition mode). The filter used was a Butterworth, with a cutoff frequency of 0.4 Ny (Ny-Nyquist frequency) for ²⁰¹Tl and 0.5 Ny for ^{99m}Tc-MIBI.

After image reconstruction, transverse slices every 6.09 mm, along the heart main axis, were obtained allowing the determination of sections corresponding to three plans mutually perpendicular to the coordinate system of the heart: coronal section or horizontal long axis (in the infero-anterior direction); oblique section or short axis (in the apex-base direction); sagittal section or vertical long axis (in the septolateral direction). The heart was divided into five regions: septal, anterior, inferior, apical and lateral (latero-dorsal) and, for each area an arbitrary value in a four-point grading system was given according to radionuclide con-

centration (0 = normal perfusion; 1 = mild perfusion defect, 3 = severe perfusion defect or tracer absence). A change of at least one point in the grade of a given region was considered as transient perfusion defects and was classified as partial when zero was not observed in the redistribution and/or reinjection images. Maintenance of perfusion values was indicative of persistent perfusion defects (fibrosis).

In this study, we analyzed only LV regions compromised by MI, as shown on the ECG. The apical region was considered as an extension of anterior and/or inferior involvement, when graded with values greater than zero. Areas of improvement in myocardial perfusion observed on the resting images were considered as true viable ones.

To accomplish the goals of this study, descriptive tables were constructed. Continuous variables were presented descriptively as mean and standard deviations. Comparisons before and after surgery were performed with Wilcoxon's (nonparametric) or Student (paired) *t* tests¹⁴. Agreement between methods for myocardial viability was analyzed using Kappa statistics¹⁵ (K). Values >0.75 represent excellent agreement, between 0.40 and 0.75 good agreement, and <0.40, poor agreement. Sensitivity (S), specificity

(E), accuracy (A), positive (PPV) and negative (NPV) predictive values were calculated. Viability confirmed after surgery was adjusted using a stepwise logistic regression model in which the other protocols were considered predictive factors.

The significance level used was 0.05. Calculations were made using the SAS system¹⁶. Intra and interobserver variability analysis was calculated by reevaluating a sample of 10 cases after at least 30 days.

Results

Studied population data are found in table I. The mean age was 59.3±9.8 years (ranging from 42 to 75 years), 28 (87.6%) males and 4 (12.4%) females. Patients were studied on average 8.14±3.29 months after MI.

Seventy-eight myocardial regions of fibrosis were studied. They were divided into: 23 (29.5%) septal, 23 (29.5%) anterior, 21 (26.9%) inferior, 10 (12.8%) lateral and 1 (1.3%) dorsal regions.

Catheterization (data are displayed in table II) was performed a mean of 2.79±2.73 months before surgery. Single vessel disease occurred in one (3.1%) patient; double

Table I - Population Data

No	Name	Age (years)	Gender	Weight (kg)	Height (Cm)	BMI (kg/m ²)	HBP	DM	HC	HT	S	FH	ECG - areas					Time (months)	FC AP	FC HF
													S	A	I	L	P			
1	GAL	61	M	88	1.75	28.7	YES	NO	NO	NO	YES	NO	S	A	I		3.8	I	III	
2	CABG	42	M	79	1.70	27.3	YES	NO	NO	NO	YES	YES	S	A		L	10.3	III	III	
3	MIS	61	M	102	1.78	31.9	NO	YES	YES	NO	NO	YES			I		12.0	III	III	
4	OVA	47	M	92	1.79	28.7	YES	NO	NO	NO	YES	YES	S	A	I		3.8	III	II	
5	ACGD	49	M	63	1.62	24.0	YES	YES	YES	NO	NO	NO	S	A	I		6.8	II	III	
6	SS	65	M	67	1.65	24.6	YES	YES	NO	NO	NO	NO			I	L	12.0	II	II	
7	TI	55	M	68	1.70	23.5	YES	NO	YES	NO	YES	NO	S	A	I		4.3	III	III	
8	AOA	74	M	63	1.72	21.3	NO	NO	NO	NO	YES	NO	S	A	I		6.9	III	III	
9	PSS	72	M	86	1.72	29.1	YES	YES	NO	NO	YES	YES	S	A		L	11.7	III	III	
10	PL	65	M	60	1.60	23.4	NO	NO	NO	NO	YES	NO			I	L	11.7	I	III	
11	CP	48	M	86	1.74	28.4	NO	NO	NO	NO	YES	YES	S	A		L	4.6	I	II	
12	MTM	67	M	81	1.66	29.4	NO	YES	NO	NO	YES	NO			I		3.1	II	II	
13	OF	63	M	70	1.70	24.2	NO	NO	YES	NO	YES	YES	S	A			12.0	III	II	
14	BM	72	M	65	1.80	20.1	NO	YES	NO	NO	YES	NO	S	A			3.3	II	III	
15	DCA	63	M	68	1.73	22.7	NO	YES	NO	NO	NO	NO	S	A	I		11.6	I	III	
16	PAAG	65	M	79	1.77	25.2	YES	YES	NO	NO	YES	NO	S	A			11.1	I	III	
17	JMP	54	F	51	1.58	20.4	YES	NO	YES	NO	YES	NO	S	A			12.0	III	II	
18	NCP	65	F	66	1.56	27.1	YES	YES	YES	NO	NO	YES	S	A	I		4.2	III	II	
19	JBS	56	M	73	1.54	30.8	YES	NO	NO	NO	YES	NO	S	A	I		8.7	I	II	
20	JMB	74	M	75	1.60	29.3	YES	NO	NO	NO	YES	NO			I	L	P	11.7	I	III
21	FP	56	M	66	1.55	27.5	YES	YES	YES	NO	NO	NO			I	L		11.8	III	I
22	NGS	42	F	52	1.46	24.4	NO	YES	YES	NO	NO	NO	S	A	I		5.5	III	III	
23	JB	61	M	70	1.70	24.2	YES	NO	NO	NO	YES	YES			i		11.6	III	III	
24	GMS	63	M	70	1.70	24.2	NO	NO	NO	NO	YES	NO	S	A	I	L	12.0	I	III	
25	SAC	67	M	72	1.72	24.3	NO	NO	NO	NO	YES	YES			I	L	11.1	III	III	
26	JMC	52	M	85	1.73	28.4	YES	YES	NO	NO	YES	YES	S	A	I		12.0	I	III	
27	SAA	44	M	71	1.58	28.4	NO	NO	YES	NO	YES	NO	S	A			3.4	I	III	
28	GDS	75	M	81	1.72	27.4	NO	NO	NO	NO	YES	NO			I	L	5.7	II	III	
29	AM	65	M	82	1.71	28.0	YES	YES	YES	NO	NO	NO	S	A			3.3	III	III	
30	JCNN	45	M	78	1.80	24.1	YES	YES	NO	NO	YES	NO	S	A	I		3.3	III	III	
31	GTB	62	M	56	1.63	21.1	NO	NO	NO	NO	NO	NO	S	A			11.9	III	III	
32	MFL	49	F	90	1.60	35.2	YES	NO	YES	NO	NO	YES	S	A	I		3.7	III	III	

BMI - body mass index kg/m²; HBP- high blood pressure; DM- diabetes mellitus; HC- hypercholesterolemia, HT- hipertriglyceridemia; S- smoking; FH- coronary artery disease family history; ECG- pathologic Q waves or QS complex; Time MI - CABG time interval, CABG- coronary artery bypass graft; FC - functional class (New York Heart Association); AP- angina pectoris, HF- heart failure; S- septal; A- anterior; L- lateral; I- inferior; P- posterior.

vessel disease in 7 (21.9%), most frequently the LAD and RC combination (71.4%); triple vessel disease in 24 (75.0%). Collateral circulation was observed in 24 (75.0%) patients. Regional motion could be studied in the anterior, inferior and apical LV wall, making a total of 96 regions. Changes found were: 61 (63.4%) regions with hypokinesis, 23 (24%) with akinesis and 11 (11.6%) with dyskinesis. Global LVEF observed in all patients was $34.9 \pm 10.2\%$. The 3 patients who died in the immediate postoperative (PO) period had LVEF of 20%, 30% and 43%.

There were no significant differences in the main clinical, electrocardiographic, hemodynamic and metabolic stress test variables. Mean maximal heart rates were: 132 ± 20.6 bpm and 130.5 ± 18.6 bpm; systolic blood pressure, 159.5 ± 30.5 mmHg and 153.7 ± 23.2 mmHg; and double product 21159.2 ± 5676.1 and 20063.0 ± 4125.9 ($p=ns$). The tracers were injected in similar conditions during both SPECT studies.

Every artery with lesions $\geq 50\%$ was bypassed. Follow-up period after MR surgery was 15.16 ± 10.17 months. Three (9.4%) patients died soon after operation due to cardiogenic shock. Another patient died suddenly after four months. Angina and CHF symptoms were evaluated in twenty-nine (90.6%) patients to determine functional class before and after CABG (fig. 1), and statistical analyses showed significant ($p < 0.001$) improvement in both parameters analyzed.

Coronary angiographic studies after surgery could be performed in 23 patients (4.98 ± 1.09 months postoperatively). All grafts were patent. There was wall motion improvement in 48 (69.6%) regions and no change in 21 (30.4%) myocardial regions, when compared with the preoperative studies ($p < 0.001$). Mean global LVEF also increased ($46.4 \pm 13.5\%$; $p < 0.001$; fig. 2).

For the detection of viable myocardium using scintigraphy, 102 myocardial regions affected by MI were analyzed. ^{201}Tl , conventional protocol (comparing stress and 4h redistribution imaging) showed 40 (39.2%) reversible

regions and 62 (60.8%) nonviable ones (fixed defect); the reinjection protocol (stress and 24 h reinjection imaging) showed 52 (51.0%) and 50 (49%) myocardial regions to be reversible and irreversible, respectively. Therefore, reinjection identified 12 additional reversible regions (19.4%) initially classified as irreversible by the conventional study. With the conventional $^{99\text{m}}\text{Tc-MIBI}$ protocol (stress and rest imaging) there were 14 (13.7%) reversible regions and the remaining 88 (86.3%) were considered nonviable (tab. III).

After surgery, 29 of 32 patients were able to undergo scintigraphy, except for the three cases of death in an early postoperative phase. Therefore, 93/102 (91.2%) regions were analyzed: 21 (22.6%) septal, 21 (22.6%) anterior, 22 (23.7%) apical, 19 (20.4%) inferior and 10 (10.7%) latero-dorsal. 49 (52.7%) regions were classified as truly viable, in 41 (44.1%) there was agreement between scintigraphies and

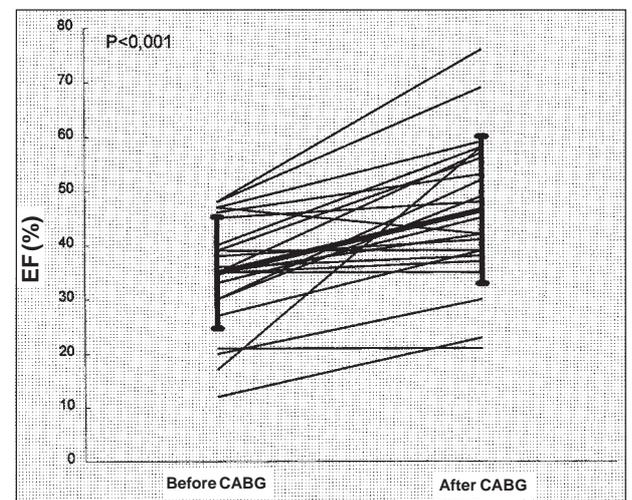


Fig. 2 - Left Ventricle ejection fraction distribution, before and after Coronary Artery Bypass Graft. N = 23 patients; EF = Global Left Ventricle Ejection Fraction; CABG = Coronary Artery Bypass Graft Surgery

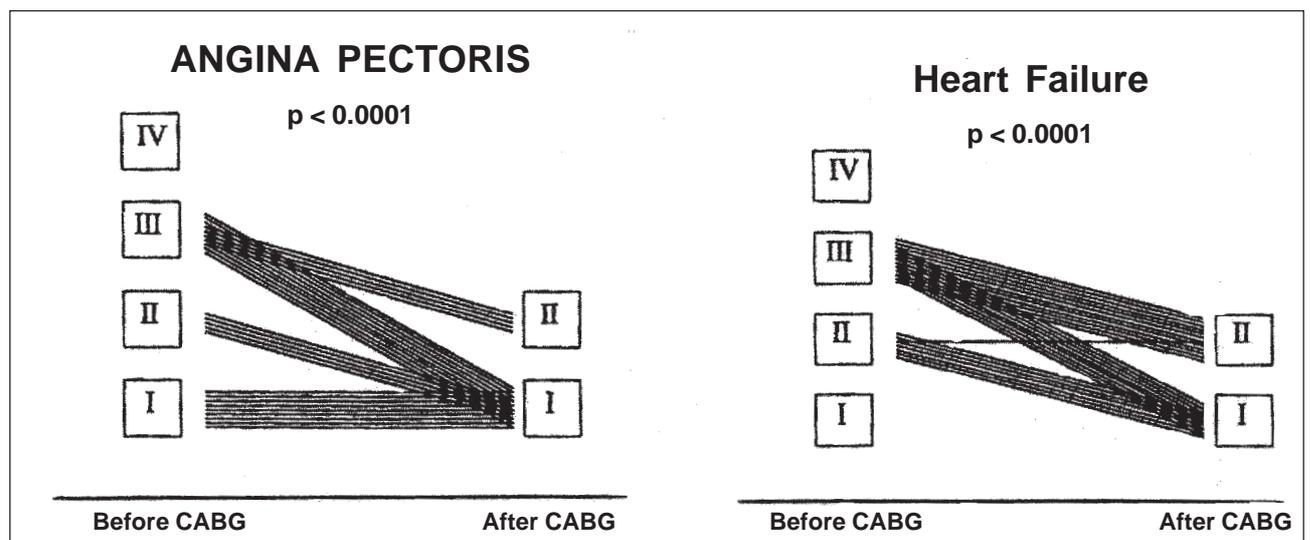


Fig. 1 - Functional Class, before and after Coronary Artery Bypass Graft Surgery. N = 29 patients; CABG = Coronary Artery Bypass Graft Surgery.

of the remaining 8.4 (4.3%) were viable according to ^{201}Tl and 4 (4.3%) according to $^{99\text{m}}\text{Tc}$ -MIBI; the other 44 (47.3%) regions were truly nonviable (tab. III). There was agreement in 85 (91.4%) regions, which is significant ($p < 0.001$) with excellent reproducibility ($k = 0.828$).

Figures 3 and 4 show an MPS example with tomographic slices of the oblique axis of a patient with MI and viable muscle.

Calculations of operating variables S, E, A, PPV and NPV in the entire population were, respectively: 65.3%, 90.9%, 77.4%, 88.9% and 70.2% for the conventional proto-

col with ^{201}Tl ; and 81.6%, 81.8%, 81.7%, 83.3% and 80.0% for reinjection one; 20.4%, 90.9%, 53.8%, 71.4% and 50.6% for the conventional protocol with $^{99\text{m}}\text{Tc}$ -MIBI. It is concluded that there is an underestimation of viable myocardium by the conventional protocol with $^{99\text{m}}\text{Tc}$ -MIBI. The increased perfusion, observed after revascularization of myocardial regions with MI and fibrosis but still viable areas, was shown better by ^{201}Tl SPECT, notably with the reinjection protocol. It could be confirmed, using logistic regression analyses, that the reinjection protocol was the best predictor of viability ($p < 0.001$).

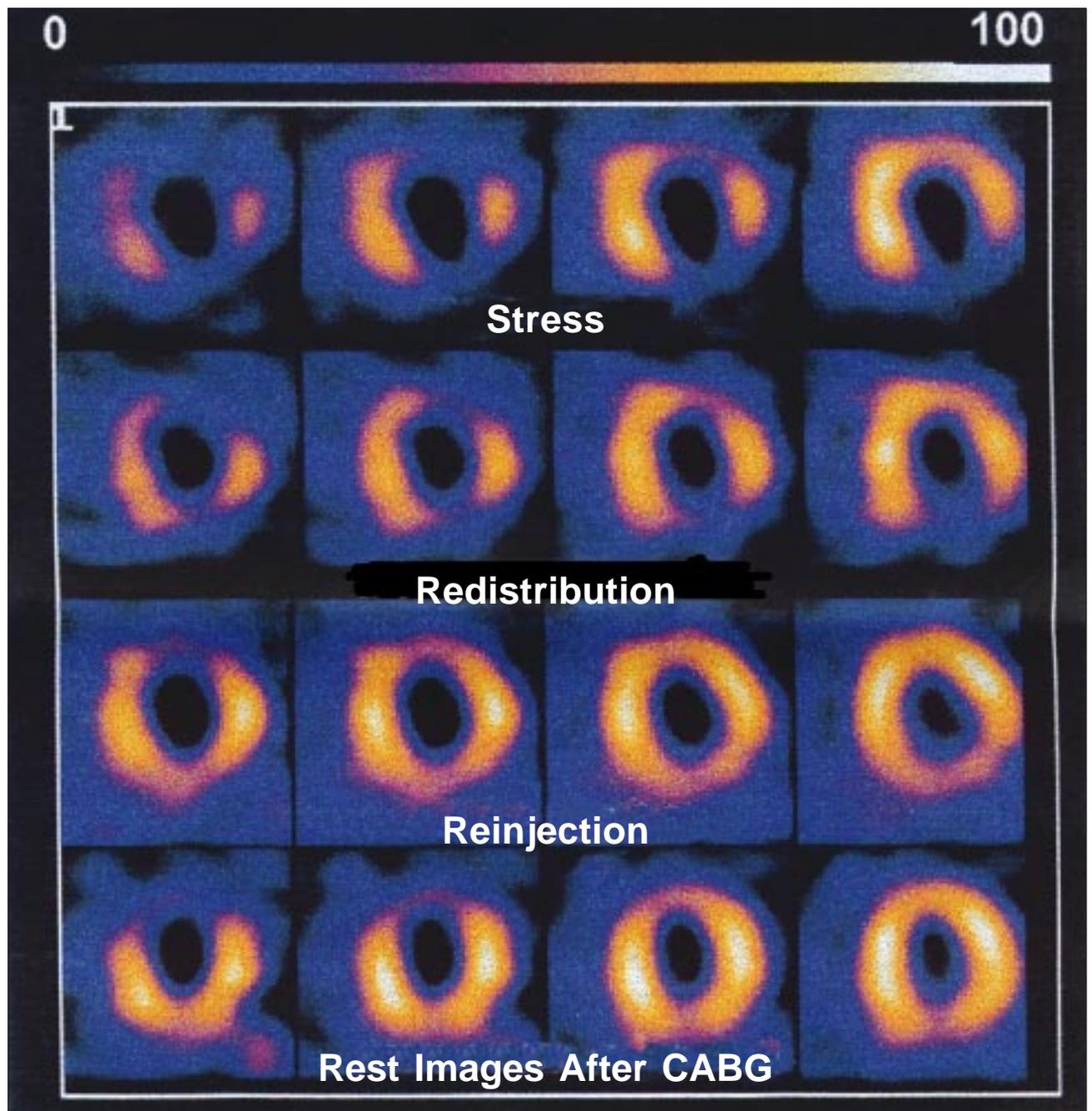


Fig. 3 - Myocardial perfusion scintigraphy with ^{201}Tl and tomographic slices in the oblique plan. Redistribution images suggest viability in the anterior and lateral regions; reinjection suggest viability of the inferior wall.

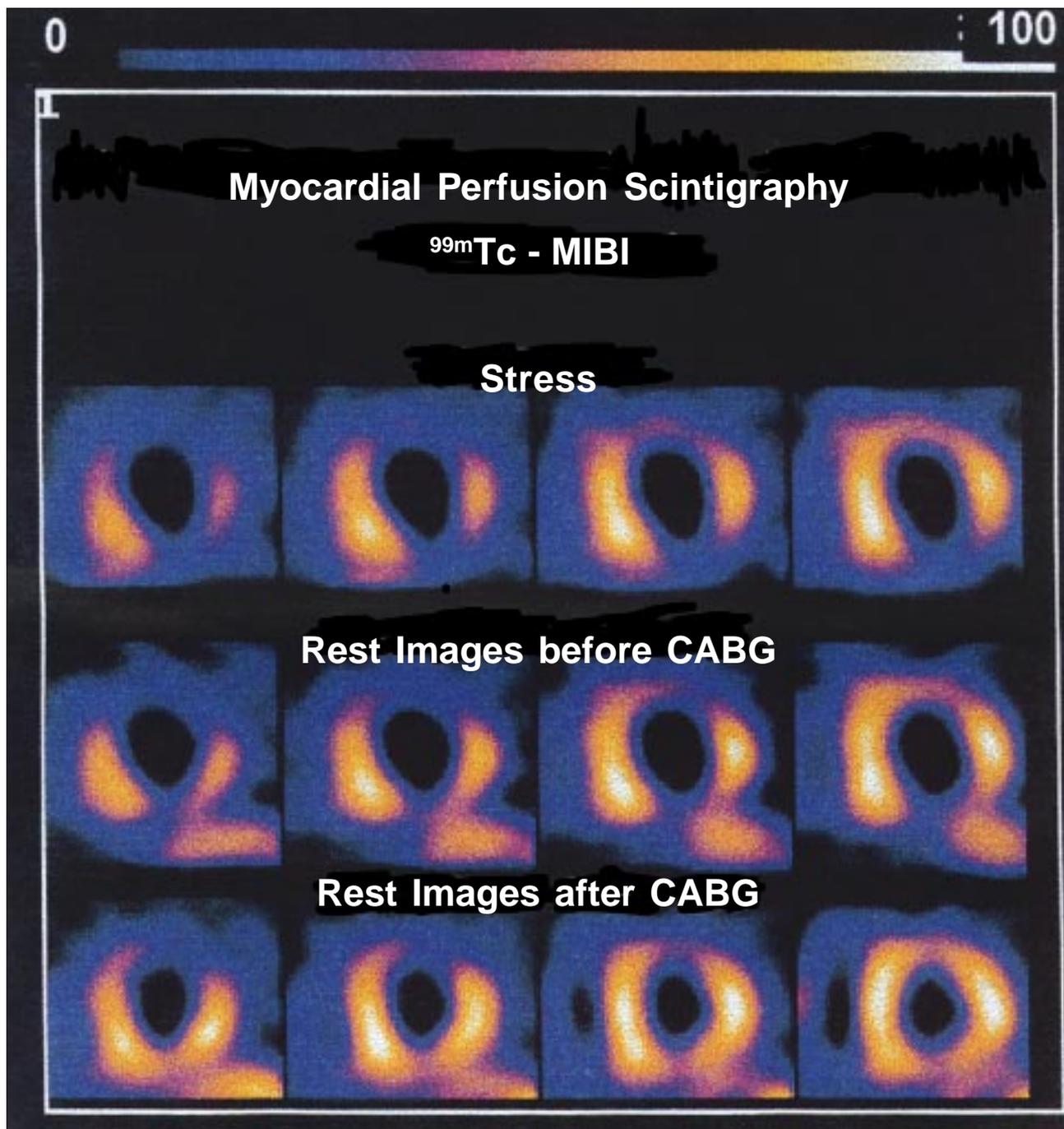


Fig. 4 - Myocardial perfusion scintigraphy with ^{99m}Tc-MIBI and tomographic slices in the oblique plan. Conventional protocol imaging shows persistent defects in the anterior, inferior and lateral regions. After CABG, images confirmed that these persistent defects contained viable muscle. CABG - Coronary artery bypass graft.

It was observed that, through severe lesions (obstruction >90% lumen), coronary and Cc in the same territory were responsible for perfusion of 24/49 (49.0%) viable regions and of 26/44 (59.0%) nonviable ones (p=ns). However, the semiquantified analysis of collateral circulation intensity of +++/++++ was more frequent in viable regions (60%) and of +/+ in nonviable ones (78.6%). These differences were significant (p=0.004, tab. IV).

Forty-nine myocardial regions (of a total of 69) evaluated after revascularization were MI related. There was regio-

nal wall motion improvement in 36/49 (73.5%) after CABG (p<0.001, fig. 5).

The relationship between perfusion and systolic function recovery could be observed in 49 myocardial regions, 34 of which (69.4%) were in agreement, and 25 (51.%) improved both perfusion and regional motility, but 9 (18.4%) did not. The results were contradictory in 15 (30.6%) regions. There was an improvement in motion in 11 (22.4%) and in perfusion in 4 (8.2%). However, the improvement in regional perfusion was significantly related (p=0.011) to the improvement in wall motion.

Myocardial Segments	Collateral Circulation				P	Total
	+ / ++		+++ / ++++			
	N	%	N	%		
Viable	10	40.0	15	60.0	0.004	25
Non Viable	22	78.6	6	21.4		28
Total	32	60.4	21	39.6		53

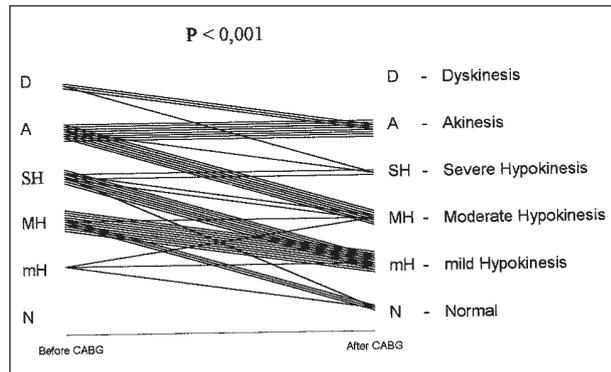


Fig. 5 - Regional motility before and after revascularization of the regions affected by myocardial infarction. D- dyskinesis; A- akinesis; HA- accentuated hypokinesis; HM- moderate hypokinesis; HD- discrete hypokinesis; N- normal.

Discussion

In patients with CAD and LV dysfunction, CABG surgery has been shown to have a positive impact on survival. In the present study, survival was 96.6% during a follow-up period of 15.2 ± 10.2 months. Only one of 29 patients discharged (3.4%) died suddenly.

The presence of viable myocardium is not the only factor to indicate the need for CABG, but also the size of the area at risk, which once recovered, will lead to changes both in the clinical condition and in the natural history after revascularization. In this sense, surgical benefits could be confirmed by symptoms of angina and heart failure.

The study has also shown an in-hospital survival of 90.6%. No patient with $EF < 20\%$ died in this phase. 19 patients had $EF \geq 20\%$ and $< 40\%$, of whom two died in the immediate postoperative period. Therefore, hospital survival for these patients was 89.5% (17/19 patients), similar to that observed in the literature. Hochberg et al¹⁷ studied 466 patients with CAD and $LVEF < 40\%$ who underwent CABG and followed them for 36 months. Hospital survival (up to 30 days after surgery) for patients with $LVEF \geq 20\%$ and $\leq 30\%$ was 89%. The CASS study¹⁸ observed significant surgical benefit in a subgroup of patients with CAD in the three main coronary vessels and $LVEF$ between 35% and 50%. They also observed increased survival after surgery in patients with LV dysfunction, particularly those with $LVEF \leq 25\%$, concluding that the presence of severe heart failure does not constitute a specific contra indication for surgery.

These data of increased survival, and the clinical improvement observed, favor the indication for surgery in patients with different degrees of left ventricular dysfunction and CAD. However, the improvement observed after MR represents a complex interaction between compensatory mechanisms, coronary anatomy, surgical results and patient selection.

The later the evaluation - two to three months after surgery - the more correct the interaction between recovery of perfusion and function, perioperative injury and graft patency will be.

In the conventional protocol, there were perfusion scans with ^{201}Tl showing 40/102 (39.2%) regions of reversibility. After reinjection 52/102 (51.0%) regions were viable. Therefore, from 62/102 irreversible regions by the conventional protocol, 12/62 (19.4%) regions were shown to be viable after reinjection. This figure is smaller than that in the literature. Several studies show that the reinjection protocol, as compared with conventional scans with ^{201}Tl , lowers the number of defects considered fixed by about 31 to 49%¹⁹⁻²¹. In the present study, the smaller overestimation of the degree of fibrosis could be justified by the method used, because the redistribution images of the conventional protocol were performed later than in the studies quoted above.

Overestimation of the degree of fibrosis (persistent perfusion defects) by the conventional protocol, when compared with that of ^{201}Tl reinjection, is dependent on the redistribution phenomenon. Soon after the initial ^{201}Tl uptake by the myocardium, there is a continuous exchange of this univalent ion with the blood that determines its redistribution. ^{201}Tl is continuously released from normal myocardium and replaced by recirculating ^{201}Tl , from residual activity in the blood. Although its initial biodistribution is similar to K^+ , compartment redistribution presents a different velocity of exchange between the intra- and extracellular milieu. ^{201}Tl uptake by the cells is dependant on regional availability, as well as on membrane and Na^+/K^+ pump integrity. However, ischemia-related metabolic changes alter the extraction rate and the exchange with the extracellular medium. In contrast to fibrotic cells, viable myocardium maintains a slow metabolism that preserves the basic cellular structure, making possible the recovery of its original functions. This complex protective mechanism may be detected by nuclear medicine and allows observation, using the dynamic biodistribution of the radionuclide in cardiac muscle. The smaller accumulation and slow washout of ^{201}Tl in the ischemic areas result in the perfusion defects. This process, based upon redistribution, is only possible if myocardium is viable, with an intact cellular membrane²²⁻²⁴.

The redistribution phenomenon is, however, highly influenced by serum concentration of the tracer and by cellular washout. Redistribution may occur later in situations in which there is resting low blood flow due to severe coronary stenosis, absence of hyperemia after stress, long-lasting metabolic abnormalities and low serum concentration of the tracer^{22,25}. Slow redistribution, observed in ischemic (viable) areas, makes the 3 to 4 hour images depen-

dent on limitations in the differentiation of viable from fibrotic myocardium.

The conventional protocol using ^{99m}Tc -MIBI showed only 14/102 (13.7%) viable regions; ^{201}Tl conventional scans identified 26 (25.5%) additional viable regions; and after reinjection, 38 (37.3%) more regions, when compared with the ^{99m}Tc -MIBI scans. Therefore, protocols with ^{201}Tl were superior in detecting reversible defects in areas affected by MI. This is similar to findings in the literature.

Cuocolo et al²⁶ studied 20 patients with CAD and LV dysfunction (EF of $30\% \pm 8\%$) using ^{201}Tl and ^{99m}Tc -MIBI scans, comparing conventional protocols with reinjection protocols. 122 regions had permanent defects in the conventional protocol with ^{201}Tl ; 57 (47%) of them had transient defects in the reinjection protocol. Using the protocol with ^{99m}Tc -MIBI, there were 22 (18%) regions of transient defects. Thus, ^{99m}Tc -MIBI did not identify 35 (29.0%) regions when compared with the reinjection protocol. Dilsizian et al²⁷, using similar methodology, observed an underestimation in the protocol with ^{99m}Tc -MIBI of 36% when compared with the reinjection protocol. Reinjection imaging with ^{201}Tl identifies a greater number of viable myocardial regions when compared with ^{99m}Tc -MIBI.

Clinical and experimental observations showed that, in normal tissue, soon after initial uptake, ^{99m}Tc -MIBI fixes in the myocardial cell, having minimal redistribution later. When depolarization of cell membranes and mitochondria occurs, as during ischemia, there is some difficulty in the storage and uptake of the tracer^{28,29}. Possibly, more intense metabolic changes diminish the passive transport of ^{99m}Tc -MIBI. On the other hand, Na^+/K^+ ATPase activity, an important factor in cell survival, would hardly interfere with ^{201}Tl extraction (active transport).

The statistical analysis demonstrated that the reinjection protocol was the best approach for detecting viable myocardium, and there was an important depreciation of ^{99m}Tc -MIBI when compared with ^{201}Tl for myocardial viability identification.

Positron emission tomography³⁰ (PET) is considered the most sensitive noninvasive technique for identifying viable myocardium and has been used for comparison with other methods. Several studies^{20,31} showed that ^{201}Tl positivity after reinjection is as sensitive as PET imaging with 18-F-deoxyglucose (FDG) in viability detection. Agreement between methods was 88% in the 1st study and 85% in 2nd. Other studies^{19,29,32-34} showed similar predictive values, using recovery of wall motion observed after revascularization as the gold standard: PPV of 78% to 85% for PET and 73% to 87% for the reinjection protocol; NPV of 80% to 92% for PET and 75% to 100% for the reinjection protocol. In the present study the reinjection protocol had

similar predictive values: positive of 83.3% and negative of 80.0%, using perfusion recovery assessed by greater myocardial uptake after surgical revascularization.

A significant relationship was found between myocardial perfusion recovery and regional wall motion recovery ($p=0.011$) after revascularization in myocardial infarction areas.

These data are relevant to the observation that the metabolic abnormalities due to inappropriate perfusion recovery after coronary flow restoration. The presence of chronic myocardial contractile dysfunction is not enough to indicate revascularization. The extent of the area potentially recoverable - viable myocardium - allied to proper coronary anatomy, could lead to change in the clinical condition of a patient after revascularization.

Probably due to the lack of other more objective and precise methods for CAD identification, coronary angiography, despite its limitations, has been used to evaluate the diagnostic precision of the methods used for studying myocardial ischemia. Angiography also has a number of problems related to the possibility of underestimation or overestimation of coronary lesions³⁵. Quantitative coronary angiography³⁶ seems to be more objective than visual estimation but also there are divergences among the several methods used (i.e. density against geometric method), especially when analyzing unstable and eccentric plaques. There is the possibility that the degree of anatomic stenosis does not express the real coronary flow in specific situations such as during cardiac stress^{37,38}.

Evaluations of perfusion and LV contractile function have some limitations, especially because of the absence of a precise and of a practical quantitative method. The best quantification method currently available in practice is the semiquantitative scoring system. Therefore, the method is observer-dependant, causing intra and interobserver variability common to most diagnostic methods.

In this study, intra and interobserver variability were, respectively, 4.6% and 7% for coronary angiography; 3% and 4% for left ventriculography; 2% and 4% for the stress test; and 4% and 5.1% for the myocardial perfusion scintigraphy.

Despite these limitations, intra and interobserver variabilities were acceptable. Myocardial perfusion scintigraphy and coronary angiography with visual quantification are accepted and performed routinely in most medical centers.

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