REVIEW ARTICLE

Ischemic Cardiomyopathy: A Clinical Nuclear Cardiology Perspective

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Ischemic cardiomyopathy results from severe extensive coronary artery disease, which is associated with left ventricular dysfunction and also, in many cases, with significant left ventricular dilatation. Mortality is high, especially in patients who satisfy myocardial viability criteria but who have not undergone revascularization. Although age, exercise capacity, and comorbidity influence survival, the most important prognostic factors are the extent of the ischemia, myocardial viability, and left ventricular remodeling, all of which can be successfully evaluated by gated myocardial perfusion single-photon emission computed tomography (SPECT).

Key words: *Cardiomyopathy. Coronary disease. Nuclear medicine. Revascularization. Prognosis.*

La miocardiopatía isquémica desde la perspectiva de la cardiología nuclear clínica

La miocardiopatía isquémica es consecuencia de una enfermedad coronaria severa y extensa que conlleva una disfunción del ventrículo izquierdo y, en muchas ocasiones, una importante dilatación de éste. Su mortalidad es elevada, sobre todo en los pacientes con criterios de viabilidad miocárdica que no son revascularizados. Si bien la edad, la capacidad de ejercicio y las comorbilidades influyen en la supervivencia, la isquemia, la viabilidad miocárdica y el remodelado ventricular son variables pronósticas importantes y todas ellas pueden valorarse adecuadamente mediante la *gated*-SPECT de perfusión miocárdica.

Palabras clave: *Miocardiopatía. Enfermedad coronaria. Medicina nuclear. Revascularización. Pronóstico.*

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INTRODUCTION

Coronary artery disease is the most frequent cause of cardiovascular mortality in Europe, with almost 2 million deaths per year.[1] Within this context, ischemic heart disease with moderately or severely decreased systolic function (ejection fraction ≤35%-40%), ie, ischemic cardiomyopathy (IC), involves very high rates of cardiac mortality (CM): nineteen percent during an average follow-up of 22 (14) months.[2] Contractile dysfunction may be caused by necrosis or by so-called viable myocardium. This term refers to living myocardium in the presence of severe contractile abnormalities and can indicate myocardial stunning or hibernation. Stunning is a form of myocardial contractile dysfunction caused by a transitory ischemic episode or reperfusion injury. Such contractile dysfunction can persist for hours or days, but, providing reperfusion recovers, then contractile activity recovers. Myocardial hibernation is another type of contractile dysfunction, but is found within the framework of chronic ischemic heart disease. Unlike stunned myocardium, in which contractile activity spontaneously reverts, myocardial hibernation requires coronary revascularization (CR) to recover ventricular function.

In our experience,[3,4] patients with IC present a history of infarction in 84% of cases and multivessel disease has a prevalence of 78%. Around 70% of the patients have scintigraphic criteria of myocardial viability (MV) in 3 or more of the segments with severe contractile abnormalities. This corresponds to 17.6% of the 17 segments into which the left ventricle (LV) is divided for the purposes of imaging techniques, as recommended. When a challenge test can be performed, using exercise or drugs, scintigraphic ischemia can be observed in more than half of the cases.

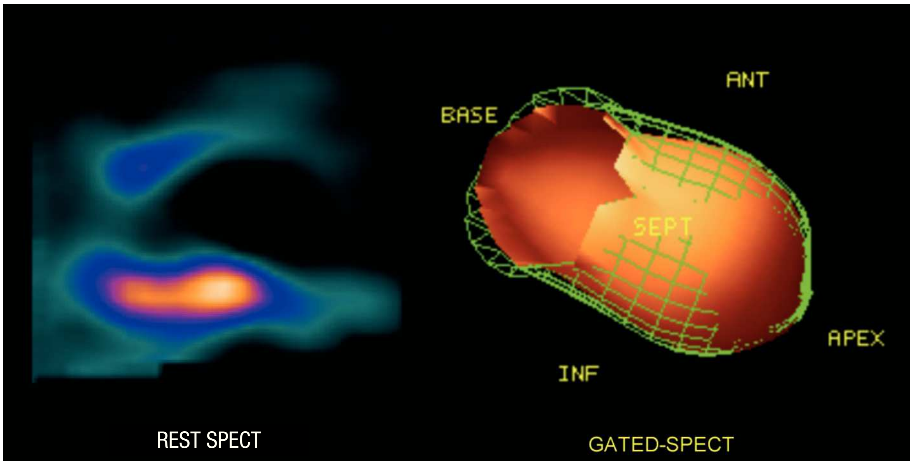

Figure. 1. Left: divergent left ventricular pattern (transversal diameter at the apical level > transversal diameter at the basal level in vertical long-axis view) and absence of anteroapical uptake in myocardial perfusion SPECT at rest in a patient with anterior infarction. These criteria are highly specific for myocardial nonviability. Right: gated-SPECT of the same patient in whom anterior akinesia and septal and apical dyskinesia can be observed. End-diastolic volume, 248 mL; end-systolic volume, 203 mL; ejection fraction, 18%. Ant indicates anterior; Inf, inferior; SPECT, Single-Photon Emission Computed Tomography.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of IC basically focuses on idiopathic dilated myocardiopathy. The definitive technique for differential diagnosis continues to be coronary angiography, but despite this, different noninvasive techniques, such as echocardiography, radionuclide angiography, magnetic resonance imaging, and computed tomography, can provide orientative criteria for one type of myocardiopathy or another.[5-18]

In gated myocardial perfusion Single-Photon Emission Computed Tomography (SPECT) studies using thallium 201 (^{201}Tl) or technetium compounds (^{99m}Tc-tetrofosmin and ^{99m}Tc-methoxyisobutyl isonitrile), different variables have been observed that are hallmarks of IC, such as the presence of extensive myocardial perfusion abnormalities at rest,[6-8] the complete absence of segmental uptake,[9] abnormalities in segmental wall motion,[10] summed stress perfusion score,[11] the extent of stress perfusion defect,[12,13] and the presence of myocardial ischemia.[12,14] In our opinion, when using gated myocardial perfusion SPECT with technetium compounds, the most specific criteria (although having low sensitivity) for IC are the presence of at least 1 wall segment with grade 4 perfusion (absence of uptake) at rest and a divergent pattern of the LV (apical transverse diameter > transverse diameter) (Figure 1).

In magnetic resonance imaging studies, the presence of late gadolinium enhancement at subendocardiac or transmural levels strongly indicates IC.[19,20] Cardiac catheterization,[21,22] and more recently, coronary angiography by multidetector computed tomography,[23,24] which has a very high negative predictive value, are the techniques of choice for differential diagnosis.

CRITERIA FOR VIABILITY AND DIAGNOSTIC EFFICACY OF GATED-SPECT AND GATED-PET

The most suitable isotopic technique for the study of MV is gated-Positron Emission Tomography (PET), which offers the possibility of assessing contractile function, using ECG synchronization, perfusion and glucose and fatty acid metabolism. The so-called mismatch pattern (or perfusion-metabolism mismatch) is the basic criterion for the diagnosis of MV (Figure 2). Despite this, in the clinical context, and for reasons of cost-efficiency, the most used technique is gated-SPECT which, at present, is more often performed with technetium compounds than with ^{201}Tl, since image quality is superior using the former techinque.[25]

The MV study should be conducted in regions or segments with severe myocardial wall motion abnormalities. The administration of nitrates prior to radionuclide administration is advisable, since it increases test sensitivity. Electrocardiographic synchronization (gated-SPECT) enables the evaluation of myocardial excursion and wall thickening. The criteria for MV using gated-SPECT are based on the degree of uptake of the radionuclide compared to the maximum LV uptake at rest or after reinjection of the radionuclide in the case of ^{201}Tl, when objectifying myocardial thickening and the presence of stress-rest reversibility. When using gated-SPECT and technetium compounds, our experience-based criteria[3,4] are perfusion with a score of 0-2 out of a total of 4 (>30%-40% uptake compared to maximum uptake) (Figure 3) and preserved wall thickening (score 0-2) (Figure 4). Whenever possible, a stress test or drug challenge is recommended, because the presence of stress-rest reversibility, ie, ischemia, indicates viability (Figure 5).

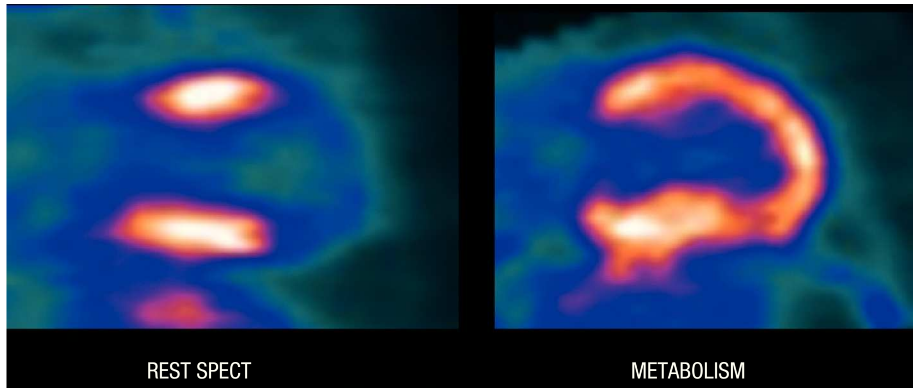

Figure 2. Example of anteroapical myocardial viability in PET images in vertical long-axis view: mismatch pattern or disagreement between the perfusion image with abnormal rubidium-82 uptake (left) and that of preserved metabolism with ^{18}F-deoxyglucose (right). PET indicates Positron Emission Tomography.

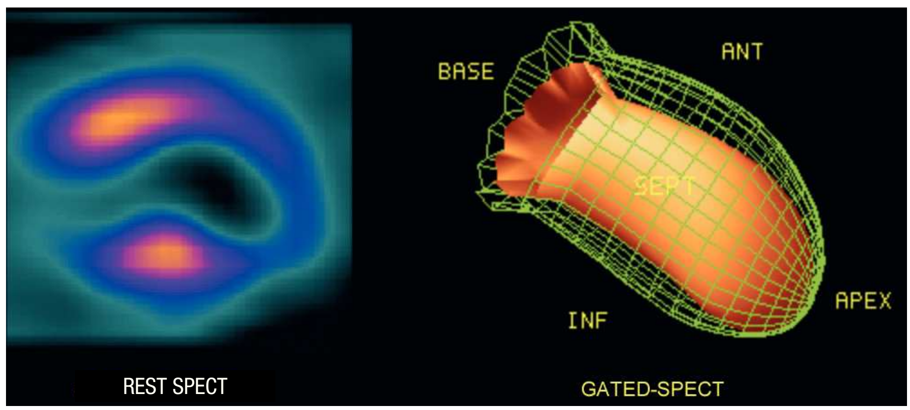

Figure 3. SPECT images of myocardial perfusion at rest (vertical long-axis view) of a patient with anterior infarction and criteria of myocardial viability. The apical akinesia region (right) indicates to moderate (grade 2) perfusion uptake defect (left). End-diastolic volume, 123 mL; end-systolic volume, 81 mL; ejection fraction, 34%. Ant indicates anterior; Inf, inferior; SPECT, Single-Photon Emission Computed Tomography.

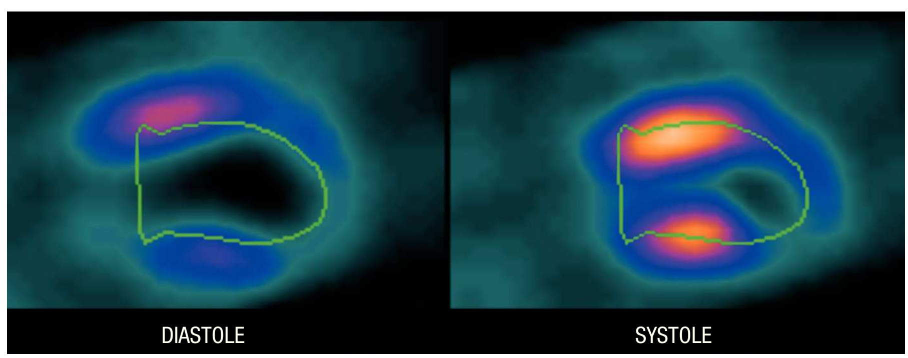

Figure 4. Images in diastole and systole using gated-myocardial perfusion SPECT at rest (vertical long-axis view) of the same patient referred to in Figure 3. A moderate alteration (degree 2) in thickening can be observed in the anteroapical region. SPECT indicates Single-Photon Emission Computed Tomography.

Tables 1-3[26-65] show the scintigraphic criteria for MV and Table 4 and Figure 6 present a summary of the efficiency of PET, SPECT, echocardiography, and magnetic resonance imaging in predicting improved systolic function after CR.[27,28,35,41-44,46,48,51,64,66-73] As can be seen, the negative predictive value of all these tests is higher than the positive predictive value, which means that in clinical practice these may be more reliable when predicting regions that are not going to recover following revascularization.

Although the diagnostic criteria for MV are quite clear regarding wall segments, there is no consensus on what quantity of viable tissue is needed such that the LV significantly improves its general function after revascularization. In our series, we considered that a patient has scintigraphic criteria of viability when viable myocardium is found in 3 or more of the segments with severe contractile abnormalities. This corresponds to 18% of the total area of the LV.[3,4] This cut-off value is related to those found in PET studies in which a mismatch pattern ≥18% demonstrated significant benefit after a CR procedure.[74]

COURSE OF LEFT VENTRICULAR SYSTOLIC FUNCTION AFTER REVASCULARIZATION

In IC patients, improved ejection fraction (EF) may often be observed during medical treatment due its anti-ischemic effects, as well as spontaneous

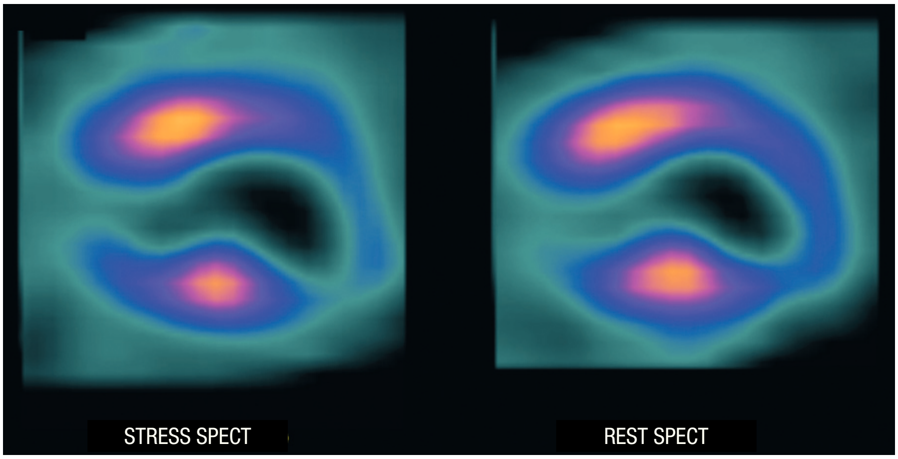

Figure 5. Residual ischemia after infarction in the anteroapical region in vertical long-axis view myocardial perfusion SPECT images of the same patient referred to in Figures 3 and 4. Reversibility can be observed between the uptake during stress and at rest. SPECT indicates Single-Photon Emission Computed Tomography.

TABLE 1. Criteria of Myocardial Viability by ^{201}Tl Myocardial Perfusion SPECT

	Techniques	Criteria of Myocardial Viability
Dreyfus et al[26]	^{201}Tl G-SPECT, 18FDG-PET	Normal uptake or moderate abnormality. Extent ≥2 regions
Arnese et al[27]	^{201}Tl SPECT, Echo with dobutamine	Improved thickening with dobutamine
Bax et al[28]	^{201}Tl SPECT + dobutamine	Normal uptake. Reversibility
Gioia et al,[29] Pagley et al,[30]	201Tl SPECT, rest/redistribution	Uptake 50%. Reversibility
Petretta et al,[31] Petretta et al,[32] Kubo et al[33]		
Bax et al[34,35]	^{18}FDG SPECT, 201Tl SPECT, Echo with dobutamine	Normal perfusion
Cuocolo et al[36]	^{201}Tl SPECT, Rad ang, Echo	Uptake ≥50%
Chan et al,[37] Petretta et al,[31]	^{201}Tl SPECT,	Reversibility >10% uptake in the redistribution images.
Morse et al[38]	rest-redistribution-reinjection	Extent: total number of viable segments/total number of evaluated segments >0.5.
Pasquet et al,[39] Roelants et al,[40]	201Tl SPECT, stress-redistribution-reinjection	Uptake >50%. Extent >50%
Simoes et al[41]		
Castell-Conesa et al[42]	^{201}Tl SPECT	Uptake >30%
Piscione et al[43]		Uptake ≥65%
Bax et a[l44]	^{201}Tl SPECT, Rad ang, PET, Echo + dobutamine	Extent >8 segments

Echo indicates echocardiography; FDG, fluorodeoxyglucose; G-SPECT, gated-Single Photon Emission Computed Tomography; MIBI, methoxyisobutyl isonitrile; PET, Positron Emission Tomography; SPECT, Single Photon Emission Computed Tomography; Rad ang, radionuclide angiography.

TABLE 2. Criteria of Myocardial Viability by Myocardial Perfusion SPECT With Technetium Compounds and With PET

	SPECT	Criteria of Myocardial Viability
Gonzalez et al,[45] Zafrir et al[46]	^{99}mTc-MIBI G-SPECT, Echo	Uptake >40%-50%. Reversibility. Preserved thickening
Castell-Conesa et al[42]	^{99}mTc-MIBI SPECT	Uptake >30%
Sciagrá et al[47,48]	^{99}mTc-MIBI SPECT + nitrates	Uptake ≥65%. Increase in the >10% with nitrates
Casáns et al[49]	^{99}mTc-tetrofosmin, G-SPECT	Reversibility. Extent >8%
Romero-Farina et al[50]		Perfusion uptake or thickening 0-2
Romero-Farina et al[3]		Extent ≥3 segments (18%)
Candell-Riera et al[4]		
Leoncini et al[51]	^{99}mTc-MIBI G-SPECT, dobutamine and nitrates	Uptake ≥50%. Increase >1 degree of contractility with dobutamine
	PET	
Di Carli et al[52,53]	^{13}N ammonia and FDG PET	Mismatch pattern
Santana et al,[2] Tarakji et al,[54]	^{82}Rb and FDG PET	Mismatch pattern. Extent >15%
Santana et al[55]		

Echo indicates echocardiography; FDG, fluorodeoxyglucose; G-SPECT, gated-Single Photon Emission Computed Tomography; MIBI, methoxyisobutyl isonitrile; SPECT, Single Photon Emission Computed Tomography.

TABLE 3. **Criteria of Myocardial Viability in Joint Protocols: Echocardiography, SPECT, PET, and MRI**

	Technique	Criteria of Myocardial Viability
Vom Dahl et al[56]	^{99m}Tc-MIBI SPECT ^{18}FDG PET	MIBI uptake 51%-70% without mismatch mismatch pattern: MIBI ≤70% with >20% FDG or MIBI minimum activity with moderate FDG uptake
Beanlands et al[57]	^{99m}Tc-MIBI SPECT, ^{18}FDG PET	FDG uptake > MIBI perfusion uptake
Bax et al[58]	^{18}FDG SPECT ^{201}Tl SPECT, Echo	^{201}Tl uptake ≥60% Mismatch pattern: ^{201}Tl uptake <60% + preserved FDG metabolism
Gunning et al[59]	^{201}Tl SPECT, ^{99}mTc-tetrofosmin SPECT, MRI	Visual: ^{201}Tl score ≥2 + MRI motility score ≤1 (MRI or G-SPECT). Quantitative: perfusion uptake ≥55% + motility score ≤1 (MRI or G-SPECT)
Cuocolo et al[60]	^{201}Tl-MIBI SPECT, Rad ang, Echo	Uptake >60%. Extent ≥4 viable segments
Zhang et al[61]	^{99m}Tc-MIBI SPECT ^{18}FDG PET, Echo	Mismatch pattern: perfusion abnormality with preserved FDG metabolism Extent: >2 segments with mismatch pattern
Schinkel et al[62]	^{99m}Tc-tetrofosmin SPECT, ^{18}FDG PET, Rad ang, Echo with dobutamine	^{99m}Tc-tetrofosmin uptake <80% + preserved FDG uptake
Kühl et al[63]	^{99m}Tc-tetrofosmina SPECT, ^{18}FDG PET, MRI	Tetrofosmin uptake ≥50%. Mismatch pattern: tetrofosmin uptake <50% and preserved metabolism
Heiba et al[64]	^{201}Tl SPECT + dobutamine, ^{99m}Tc-MIBI SPECT, ^{18}FDG PET	Uptake ≥50%
Wu et al[65]	FDG, ^{201}Tl SPECT, MRI	^{201}Tl uptake ≥50%. Mismatch pattern: ^{201}Tl uptake <50% + preserved metabolism (FDG uptake ≥50%)

Echo indicates echocardiography; FDG, fluorodeoxyglucose; G-SPECT, gated-Single Photon Emission Computed Tomography; MIBI, methoxyisobutyl isonitrile; MRI, magnetic resonance imaging; Rad ang, radionuclide angiography.

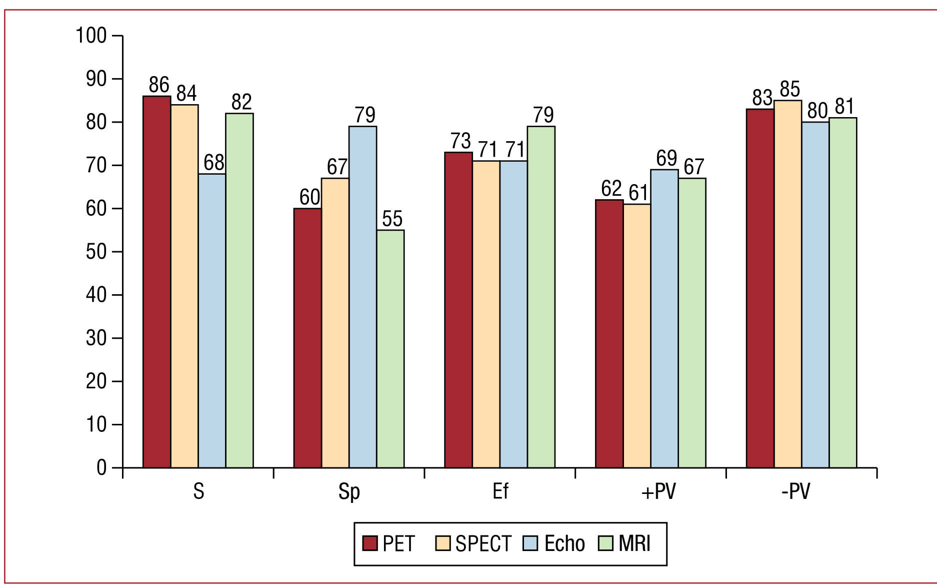

Figure 6. Total mean percentages of sensitivity (S), specificity (Sp), efficacy (Ef), and predictive values (PV) of different imaging techniques for the diagnosis of myocardial viability.[27,28,35,42,41-44,46,48,51,64,66-73]
ECHO indicates echocardiogram; MRI, magnetic resonance imaging; PET, Positron Emission Tomography; SPECT, Single-Photon Emission Computed Tomography.

improvement if dysfunction is due to myocardial stunning.[75-77] After a CR procedure, a significant increase (≥5%) can be observed in 29%[42] to 65%[78] of patients, although the greatest benefit is found in patients with criteria of viability or myocardial ischemia providing it is associated with a moderate or severe reduction in EF, especially if CR is not delayed.[79,80] Between 59% and 92% of IC patients present improved symptoms of heart failure after CR.[75,81] Hibernating myocardium is usually associated with alterations in LV volume and shape that can also revert after successful CR.[82,83] In gated myocardial perfusion SPECT studies, left ventricular remodeling finds its greatest expression when there is a divergent pattern of the left ventricle.[3,84] The greater the interval between acute myocardial infarction and gated-SPECT, the greater the prevalence of LV remodeling.

TABLE 4. **Efficacy of SPECT, PET, Echocardiography, and Magnetic Resonance Imaging in Predicting Improved Left Ventricular Systolic Function After Coronary**

	Criteria of Improved Systolic Function Following CR	Technique	S, %	Sp, %	Efficacy, %	PPV, %	NPV, %
Gropler et al[66]	Contractile recovery	^{11}C-acetate PET	–	–	–	67	69
		FDG				52	81
Tamaki et al[67]	Improved contractility	Rest PET perfusion ^{13}N	92	35	58	48	87
		Rest PET perfusion-stress ^{13}N	84	68	75	65	87
		PET FDG	88	82	85	76	92
Arnese et al[27]	Improved segmental wall motion	SPECT + ^{201}Tl	89	48	–	33	94
		ECHO + LDD	74	95	–	85	93
Bax et al[28]	Increased EF ≥5%	SPECT + ^{201}Tl reinjection	93	43	58	40	93
		FDG + SPECT ^{201}Tl reinjection	89	77	80	62	94
		ECHO + LDD	85	63	67	49	91
Castell-Conesa et al[42]	Increased EF ≥5%	SPECT + MIBI	79	40	53	39	80
		SPECT + ^{201}Tl	80	46	58	43	82
Martínez et al[68]	Reduced ESV, improved thickening	MRI + nitroglycerin	97	64	89	89	88
		Dobutamine echo	93	42	79	86	71
Pace et al[69]	Increased EF ≥5%	ECHO + LDD	53	88	76	72	77
		^{201}Tl SPECT	72	86	81	74	85
Gerber et al[70]	Increased EF ≥5%	PET	79	55	–	–	–
Sciagrà et al[48]	Increased EF ≥5%	SPECT + MIBI	67	79	72	–	–
		SPECT + MIBI + nitrates	81	69	75	–	–
Bax et al[35]	Increased EF ≥5%	SPECT + FDG	86	92	–	90	89
Leoncini et al[51]	Increased EF ≥5%	Gated-SPECT MIBI + LDD	79	78	78	–	–
Simoes et al[41]	Improved wall motion	Gated-^{201}Tl SPECT	93	50	69	59	90
		LDD	71	94	84	91	81
Piscione et al[43]	Increased EF ≥5%	Gated-^{201}Tl SPECT	77	65	72	75	67
		ECHO-LDD	64	62	63	70	56
		Collateral circulation	74	27	55	58	43
		Joint SPECT-ECHO	53	79	64	78	55
Bax et al[44]	Increased EF ≥5%	^{201}Tl SPECT	95	57	72	–	–
		ECHO-LDD	63	89	79	–	–
		Both strategies	89	89	89	–	–
		SPECT + FDG	89	86	87	–	–
Zafrir et al[46]	Improved wall motion	Gated-SPECT MIBI ≥50%	93	59	77	73	87
		Gated-SPECT MIBI ≥50% + LDD	96	58	79	74	93
		Gated-SPECT MIBI ≥60%	70	86	77	86	70
		Gated-SPECT MIBI ≥60% + LDD	85	78	82	82	81
Heiba et al[64]	Improved contractile reserve	Perfusion (^{201}Tl, MIBI, FDG)	73	82	76	92	52
		Contractile reserve with LDD	52	85	60	91	38
		Joint methods	86	75	83	91	65
Krittayaphong et al[71]	Improved wall motion ≥1 degree	MRI: delayed enhancement	74	83	–	63	81
		Diastolic wall thickness	70	55	–	50	74
Potter et al[72]	Improved strain	MRI + LDD: principal strain	81	55	–	–	–
		Circumferential strain	79	54	–	–	–
		Radial strain	80	30	–	–	–
Saraste et al[73]	Improved systolic function	MRI >90[a]	26-68[a]	–	–	–	

CR indicates coronary revascularization; ECHO, echocardiogram; EF, left ventricular ejection fraction; ESV, end-systolic volume; LDD, low-dose dobutamine; MRI, magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value; S, sensitivity; Sp, specificity.
[a]General values contributed by review article.

In IC patients, chronic angina, when present at least 30 days before infarction, can significantly influence the extent of necrosis, the diagnosis of MV and ventricular remodeling. Observational data indicate a prevalence of 21% of chronic angina prior to infarction, offering a protective effect against IC characterized by a smaller necrotic area, less left ventricular remodeling and a greater percentage of patients with scintigraphic criteria of MV.[76]

TABLE 5. **Predictors of Improved Left Ventricular Function After Coronary Revascularization**

	N	Techniques	EF1, %	EF2, %	CR-EF2 Interval	Predictor Variables	S	Sp
Rozanski et al[85]	53	^{201}Tl planar, Rad ang	52	56	–	Improved motility after immediate stress	–	–
Vom Dahl et al[86]	37	18FDG and ^{13}N PET	34	36	13 wk	Mismatch pattern	–	–
Yamaguchi et al[87]	20	Catheterization	26	32	28 d	EDV ≤100 mL	–	–
Nagueh et al[88]	80	^{201}Tl SPECT, contrast Echo,	38	45	≤6 wk	Uptake ≥60%	91	43
		and dobutamine Echo						
Christian et al[89]	86	Rad ang	39	38	6 mo	–	–	–
Qureshi et al[90]	34	Dobutamine Echo,	39	–	≥6 wk	2-phase response	74	89
		^{201}Tl-SPECT				^{201}Tl uptake ≥60%	90	56
Meza et al[91]	39	Echo + contrast				Viability	84	23
		Dobutamine	25	31	3 mo	Contractile reserve	80	33
		Both				Ischemic response	92	49
Castell-Conesa et al[42]	116	^{99m}Tc-MIBI and ^{201}Tl SPECT	41	41	4.5 mo	Uptake >30%	79	40
Kitsiou et al[92]	24	^{201}Tl SPECT				Reversible defect	–	–
		MRI Rad ang	30	58	8 mo			
Bax et al[58]	42	^{201}Tl SPECT	37	39	3.5 mo	Mismatch pattern	–	–
		^{18}FDG SPECT						
Pace et al[69]	31	Dobutamine ECHO	31	–	40 d	Viability	72	86
Candell-Riera et al[93]	82	^{99m}Tc-MIBI SPECT Rad ang	41	41	3-6 mo	Reversible perfusion pattern	–	–
						Rest uptake >30%		
Pasquet et al[94]	66	Rest-dipyridamole	28	–	10 wk	↑ EF with LDD. Viability	–	–
		^{82}Rb PET and ^{18}FDG PET						
		and LDD-atropine Echo						
Gerber et al[70]	178	^{18}FDG PET	38	43	–	FDG uptake >45% ≥3 s		
Koch et al[95]	46	^{18}FDG PET	–	–	–	Unipolar ECG amplitude >7.5 mV	91	71
		^{99m}Tc-MIBI SPECT				Myocardial viability by PET and SPECT	82	86
		Electroanatomic mapping						
Dellegrottaglie et al[96]	26	^{201}Tl SPECT				≥3 s with viable contractile reserve	37	47
		Echo + LDD	37	51	12 mo	in ^{201}Tl images		
Knuesel et al[97]	19	^{18}FDG PET and MRI			11 mo	FDG >50% + diastolic thickness		
						>4.5 mm MRI		
Bax et al[79]	85	Dobutamine echo	28	40	10.5 mo	Early coronary revascularization	–	–
						(≤1 month)		
Khoury et al[98]	70	Dobutamine echo and 3D Echo	–	–	40 wk	EF <38%	–	–
Schinkel et al[99]	118	Dobutamine echo	29	–	4.5 mo	ESV ≤140 mL	68	65
Slart et al[100]	38	^{18}FDG PET and MRI	32	39	>3 mo	FDG uptake >50%	93	85
						Wall thickness ≥10%	89	78
Romero-Farina et al[50]	30	^{99m}Tc-tetrofosmin G-SPECT	30	39	<2 mo	EDV <190 mL	71	69
						ESV <148 mL	88	61
						Sum of the SDP ≥4	65	99
Penicka et al[101]	54	18FDG PET, MRI, and	30	–	>6 mo	Positive pre-ejection velocity in	93	60
		tissue Doppler ultrasound				≥5 dysfunctional segments		
Mandegar et al[102]	85	Echo	27	39	6 mo	Extent of myocardial viability	–	–
						>6 s (35%), ESV <145 mL		
Takeda et al[103]	15	MRI (delayed enhancement)	20	31	30 mo	Extent of necrosis	–	–

CR indicates coronary revascularization; Echo, echocardiogram; LDD, low-dose dobutamine; EDV, end-diastolic volume; ESV, end-systolic volume; FE1, mean ejection fraction prior to CR; FE2, ejection fraction after revascularization; MRI, magnetic resonance imaging; S, sensitivity; SDP, summed differential perfusion score; Sp, specificity.

VARIABLES PREDICTIVE OF IMPROVED LEFT VENTRICULAR SYSTOLIC FUNCTION AFTER REVASCULARIZATION

Table 5 presents a summary of the predictors of improved LVEF in echocardiographic, magnetic resonance imaging, and radionuclide angiography studies.[42,50,58,69,70,79,85-103] These variables are direct or indirect markers of ischemia, viability, and LV remodeling. In our experience,[50] patients with a increase of EF ≥5% after surgery are characterized by having a greater prevalence of left main coronary artery disease and, as assessed by scintigraphy, greater ischemic burden. SPECT imaging indicates that a summed differential stress-rest perfusion score ≥4 is predictive of a significant increase of EF. However, left ventricular dilatation (end-systolic volume >145 mL or end-diastolic volume >190 mL) is the most significant variable showing that EF does not undergo improvement in the presence of MV. Other authors have observed that in patients with less than 6 viable segments (35% of the LV) and an end-systolic volume >145 mL, the probability of increasing EF post-CR is very limited.[102]

In the presence of myocardial hibernation, post-CR contractile recovery usually occurs relatively early.[104] Patients who in earlier dobutamine studies present greater contractile reserve recover the function at rest; however, those who do not present recovered function at rest, despite having contractile reserve, tend to present greater myocardial ischemia prior to revascularization. Dobutamine echocardiography studies are very accurate for predicting the recovery of ventricular function, but can underestimate the degree of late recovery.[105]

PROGNOSTIC VALUE OF GATED-SPECT AND GATED-PET

The prognostic variables that have been described in IC patients are presented in Table 6.[24,52,55,106-115] In our experience, the most important variables are age, the inability to perform the stress test, exercise capacity, MV, myocardial ischemia, left ventricular remodeling and CR.[3,4,116,117]

Myocardial viability is significantly associated with cardiac mortality and its prognostic value increases even more when it is associated with myocardial ischemia. For this reason, it is advisable to adopt, whenever the patient can tolerate it, stress-rest protocols with the aim of preserving information on the presence and severity of myocardial ischemia, either in the same region as the necrosis or at a distance.

Another variable of prognostic value is the degree of LV remodeling. Gated-PET studies using fluorodeoxyglucose have reported an end-systolic volume ≥200 mL or end-diastolic volume ≥260 mL[2] as predictors of cardiac mortality. In the presence of MV, a divergent pattern of the LV as assessed by scintigraphy—a sign of apical aneurysm—is associated with mortality in general and cardiac mortality due to heart failure.[3,118,119]

In our experience,[4] during a follow-up of 2.3 (1.2) years of 167 patients with IC, cardiac mortality was 17.4% and the scintigraphic criterion of MV was an independent predictor of cardiac mortality using gated-SPECT at rest (P=.027; HR=5.1; 95% confidence interval [CI], 1.2-21.4). In the 137 patients who could undergo stress gated-SPECT, the predictors were ischemia + scintigraphic viability (P=.026; HR=3.6; 95% CI, 1.16-11.2) and an exercise duration of ≤5 min (P=.04; HR=2.7; 95% CI, 1.01-7.36). The variables derived from coronary angiography—performed in 111 patients—did not significantly modify the prognosis of the noninvasive variables (Figure 7).

In a metaanalysis which included SPECT, PET, and echocardiographic studies, a close association was observed between MV and a significant improvement in survival after a CR procedure; this was not the case among patients without criteria for MV.120 We obtained similar outcomes in our series of IC patients who were studied using gated myocardial perfusion SPECT, observing greater CM in the patients with criteria for MV who did not undergo revascularization (Figure 8).[116,117]

In clinical practice, therapeutic decision-making is based on symptoms, myocardial ischemia, ventricular function, MV, coronary anatomy, and comorbidities. Patients who have undergone coronary angiography are in general more symptomatic, have a more depressed LV systolic function and a greater degree of myocardial ischemia as assessed by gated myocardial perfusion SPECT.

In practice, we believe that the decision to indicate coronary angiography and CR is based more on the demonstration of ischemia in the SPECT images, together with less LV remodeling, than on the presence of MV. The main reason for coronary angiography in the patients without myocardial viability is scintigraphic ischemia in non-necrotic regions, that is, ischemia at a distance. Revascularization procedures are more frequent in patients in whom SPECT is performed prior to cardiac catheterization, probably because coronary angiography is often no longer indicated when no criteria of MV or ischemic criteria are observed according to SPECT or PET.

The other therapeutic option in IC patients is cardiac resynchronization therapy. It has been shown that the phase analysis of ECG-gated SPECT myocardial perfusion imaging and ECG-gated PET myocardial perfusion imaging enables the assessment of LV dyssynchrony and the selection of potential candidates for resynchronization.[121-127] Resynchronization therapy does not lead to improved symptoms or ventricular function in approximately 40% of the patients undergoing this procedure.[125] It has been observed that patients with lateral scar tissue have a lower probability of response to resynchronization therapy.[128-131]

CONCLUSIONS

Ischemic cardiomyopathy is a disease with high mortality and whose prognosis is basically influenced

TABLE 6. **Predictors of Cardiac Mortality in Patients With Ischemic Cardiomyopathy**

	No.	Techniques	Predictor Variables	Effect Measures
Técnicas isotópicas				
Di Carli et al[52]	93	PET	Mismatch pattern	–
			Severe angina without myocardial viability	–
Santana-Boado et al[2]	99	Gated-PET	End-diastolic volume ≥260 mL	RR=2.7; *P*=.014
			End-systolic volume ≥200 mL	RR=2.5; *P*=.021
Santana-Boado et al[55]	104	Gated-PET	Mismatch pattern	HR=0.29; *P*=.01
			Maximum percentage FDG match/mismatch	HR=0.23; *P*=.005
Morishima et al[106]	106106	Gated-SPECT	ESV >97 mL/m²	RR=3.44; *P*=.039
			EDV 145 mL/m²	RR=3.96; *P*=.011
			Amiodarone prescribed	RR=5.09; *P*=.003
			Perfusion defect volume = 47.5 mL	RR=6.34; *P*=.005
Romero-Farina et al[3]	156	Gated-SPECT	Divergent pattern + myocardial viability	HR=3.1; *P*=.028
Evangelista et al[107]	164	SPECT	Myocardial viability	–
Candell-Riera et al[4]	167	Gated-SPECT	Age ≥65 y	HR=3.6; *P*=.002
			Inability to perform stress test	HR=3.4; *P*=.002
			Duration of exercise ≤5 min	HR=2.8; *P*=.037
			Charge <70 W	HR=2.5; *P*=.048
			At least 3 segments with myocardial viability[a]	HR=5.7; *P*=.017
			Viability + ischemia[a]	HR=4.1; *P*=.012
Tio et al[108]	480	PET	Myocardial perfusion reserve	–
Non-radionuclide techniques				
Chow et al[109]	768	ECG	Microvoltage T wave alternans	HR=2.29; *P*=.049
Schinkel et al[110]	1781	Dobutamine echo	Myocardial ischemia	–
			Contractile reserve	
Rizzello et al[111]	128	Dobutamine echo	Multivessel disease[a]	HR=0.21; *P*<.0001
			Baseline EF	HR=0.90; *P*=.0001
			Motion score at rest	HR=4.02; *P*=.0006
			Motion score with LDD[a]	HR=7.01; *P*=.0001
			Motion score with HDD	HR=4.62; *P*=.0001
			Extent of myocardial scarring	HR=1.39; *P*=.0001
			CR in >25% of dysfunctional segments[a]	HR=0.34; *P*=.02
Yokota et al[112]	86	MRI	Scarring volume and percentage of scar tissue	–
Iler et al[113]	337	ECG	Age	HR=1.03; *P*=.04
			No ACEI	HR=2.17; *P*<.02
			Duration of QRS	HR=1.50; *P*=.01
Antonini et al[114]	105	ABPM	Low prognostic index[b] <220[a]	HR=4.8; *P*=.0001
Niizeki et al[115]	112	Blood analysis	NYHA functional class	HR=1.85; *P*=.0008
			Natremia[a]	HR=0.74; *P*=.04
			Creatinemia	HR=1.29; *P*=.034
			Glomerular filtrate[a]	HR=0.66; *P*=.01
			BNP[a]	HR=1.45; *P*=.003
			HSP 60[a]	HR=1.37; *P*=.008

ABPM indicates ambulatory blood pressure monitoring; BNP, brain natriuretic peptide; CR, contractile reserve; ECG, electrocardiogram; EDV, end-diastolic volume; EF, left ventricular ejection fraction; ESV, end-systolic volume; HDD, high-dose dobutamine; HR, hazard ratio; HSP, heat shock protein; LDD, low-dose dobutamine; MRI, magnetic resonance imaging; PET, Positron Emission Tomography; RR, relative risk; SPECT, Single-Photon Emission Computed Tomography.
[a]Significant variables in the multivariate analysis.
[b](120–age) + (mean diastolic blood pressure + mean systolic blood pressure recorded over 24 h).

by exclusively cardiac variables, such as ischemia and myocardial viability, the degree of ventricular remodeling and exercise tolerance. Gated-SPECT and gated-PET techniques are very suitable tools for studying these patients, as they provide information on perfusion and myocardial metabolism, systolic function, remodeling, and ventricular synchrony.

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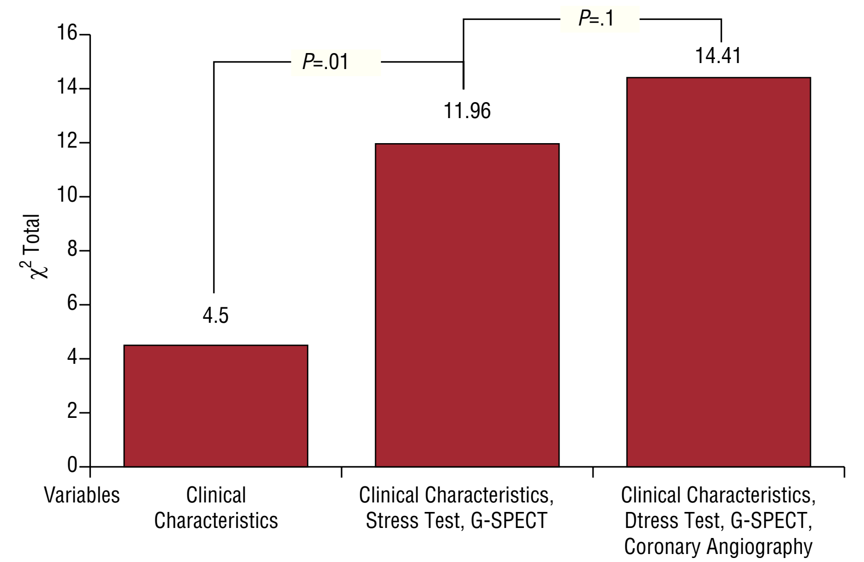

Figure 7. Incremental prognostic value of cardiac death according to the independent variables obtained in the multivariate analysis: clinical characteristics (age >65 years, inability to perform a stress test), of gated-SPECT during stress (duration of exercise <5 min, scintigraphic ischemia + viability) and coronary angiographies (proximal coronary stenosis).4 SPECT indicates Single-Photon Emission Computed Tomography.

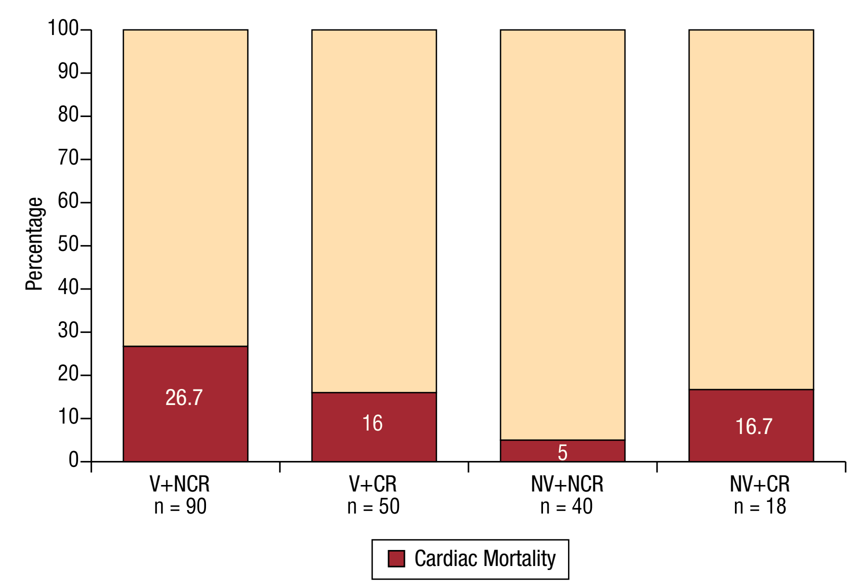

Figure 8. Cardiac mortality is significantly higher in the patients with scintigraphic criteria of viability who did not undergo revascularization than in the patients with viability who underwent revascularization and in the patients without criteria for viability.[116] CR indicates coronary revascularization; NCR, no coronary revascularization; NV, non-viable; V, viability.

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