Ischemic cardiomyopathy: lack of clinical applicability of the WHO/ISFC classification of cardiomyopathies

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Background. **The classification of cardiomyopathies proposed by the WHO/ISFC Task Force defines ischemic cardiomyopathy as "a dilated cardiomyopathy with impaired contractile performance not explained by the extent of coronary disease or ischemic damage". The aim of this study was to verify the clinical applicability of the WHO/ISFC definition of ischemic cardiomyopathy.**

Methods. **Retrospective analysis of the clinical characteristics of patients with a left ventricular ejection fraction < 40%, in whom coronary angiography showed a) stenosis ≤ 50% of a main coronary artery and/or b) stenosis > 50% of a distal portion of a main coronary artery or of a secondary branch. The patients with a clinical diagnosis of previous myocardial infarction were excluded.**

Results. **Fourteen patients with the angiographic characteristics listed above were identified. Twelve patients were males, mean age 59 years. They represented 3.8% of all the patients with left systolic ventricular dysfunction who underwent coronary angiography in the same period. The left ventricular end-diastolic volume was 170 ± 45 ml/m^2 and the ejection fraction was 27 ± 6%. The cause of systolic left ventricular dysfunction was systemic arterial hypertension in 3 patients, diabetes mellitus in 2, a combination of these diseases in 4, chronic alcohol abuse in 1, a previous clinically silent myocardial infarction in 1, and idiopathic dilated cardiomyopathy in 3.**

Conclusions. **In conclusion, in all our patients with severe left ventricular dysfunction which was not explained by the extent of coronary artery disease, at least one possible cause of impaired contractile performance could be identified. Thus the definition of ischemic cardiomyopathy according to the new WHO/ISFC classification of cardiomyopathies appears to be of scarce utility on clinical grounds and should be redefined and if necessary reclassified.**

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Introduction

Coronary artery disease is the most common cause of heart failure[1]. This clinical situation, which is usually a consequence of severe systolic left ventricular dysfunction, is popularly defined as "ischemic cardiomyopathy"[2-4]. Following the classification of cardiomyopathies proposed by the World Health Organization/ International Society and Federation of Cardiology (WHO/ISFC) Task Force in 1980, the term "cardiomyopathy", however, should be limited only to myocardial disease of unknown origin[5] thus excluding coronary artery disease. An opportune update[6] of this classification, which defines cardiomyopathy simply as "disease of the myocardium associated with cardiac dysfunction"[7] and lists ischemic cardiomyopathy among specific cardiomyopathies by defining it as "a dilated cardiomyopathy with impaired contractile performance not explained by the extent of coronary artery disease or ischemic damage"[7] was proposed in 1996. To date, no series of patients with ischemic cardiomyopathy as defined above has been reported in the literature. The definition itself has been a matter of debate[8].

The aim of this study was to verify the applicability of this new definition of ischemic cardiomyopathy. A series of patients characterized by non-critical and/or distal coronary artery disease associated with dilation and reduced systolic performance of the left ventricle has been evaluated.

Methods

We analyzed the files of all patients who underwent left ventricular cineangiography and coronary arteriography at our Institution between January 1995 and December

1998 to identify the patients with a left ventricular ejection fraction < 40% in whom coronary arteriography showed: a) stenosis ≤ 50% of a main coronary artery and/or b) stenosis > 50% of the distal portion of a main coronary artery or of a secondary branch. Those patients with a clinical diagnosis of previous myocardial infarction were excluded from the study. The hospital records of all patients so identified were reviewed and the following data were considered: sex, age, NYHA functional class, history of heart failure, systemic arterial hypertension, and diabetes mellitus. The patients had undergone diagnostic cardiac catheterization in order to identify the cause of left ventricular dysfunction. All patients underwent left ventricular cineangiography at the 30° right anterior oblique projection and selective coronary arteriography in multiple projections. The left ventricular end-diastolic volume and ejection fraction were calculated and the regional wall motion was evaluated to identify the presence of diffuse hypokinesis or segmental abnormalities. The localization and severity of the coronary artery stenosis were re-evaluated by two independent observers. A right ventricular endomyocardial biopsy was performed in 8 patients using the long sheath technique via the femoral vein. At least three endomyocardial samples were processed for routine histologic analysis.

Results

The angiographic characteristics listed above were identified in 20 patients, 6 of whom had a history of previous myocardial infarction and were consequently excluded from the study. The remaining 14 patients, who are the object of this paper, represented 3.7% of 378 patients with a left ventricular ejection fraction < 40% and who underwent coronary arteriography in the same period. Twelve patients were males (mean age 59 years). Two patients were in NYHA functional class I, 10 in class II, and 2 in class III. Nine patients showed, or had shown in the past, signs of overt heart failure. All patients were treated with angiotensin-converting enzyme inhibitors, 13 with digitalis, 12 with diuretics, and 3 with beta-blockers. Nine patients had a history of arterial hypertension and/or diabetes. One patient had a background of chronic alcohol abuse. Electrocardiography showed left bundle branch block in 7 patients and pathologic Q waves in 1. Hemodynamic and cineangiographic data are summarized in table I. The mean left ventricular end-diastolic volume was markedly increased in all patients (170 ± 45 ml/m^2) and the mean ejection fraction was 27 ± 6%. Left ventricular cineangiography showed homogeneously reduced wall motion in 7 patients and segmental alterations in 7. Coronary arteriography showed a stenosis > 70% of the distal portion of the anterior descending coronary artery in 2 patients. In case 6 it was associated with stenosis of both the circumflex and right coronary arteries and, in case 5, with a proximal obstruction of a very thin circumflex artery and with mild stenosis of a largely dominant right coronary artery. Stenosis < 50% of at least one main coronary artery was observed in 11 patients, 2 of whom with associated stenosis of a secondary branch. Isolated stenosis of the branch of the obtuse

Table I. Cardiac catheterization data and cause of left ventricular dysfunction.

	Age (years)	Sex	PAP (mmHg)	PCP (mmHg)	CI (l/min/m^2)	LVEF (%)	LVEDV (ml/m^2)	RWMA	Coronary artery stenosis (%)				EMB	LVD cause
									LAD	Cx	RC	SB		
1	51	M	20	12	2.7	34	158	+	0	30 II	40 II	0	+	H
2	58	M	20	12	2.0	18	177	+	0	0	40 II	0	+	H
3	83	M	25	18	2.9	19	174	0	30 I	0	0	0	-	H
4	64	M	45	27	2.1	22	212	0	0	0	50 II	0	+	DM
5	72	M	16	10	2.2	20	190	+	70 III	100 I*	20 I	0	-	DM
6	56	M	20	10	2.0	29	129	0	80 III	80 II	50 II	0	-	H-DM
7	59	M	35	22	2.9	19	174	+	50 II	30 II	50 III	80 DP	-	H-DM
8	57	M	25	18	3.1	33	161	0	40 II	0	0	0	-	H-DM
9	59	M	35	22	1.3	31	164	+	10 I	40 II	0	0	-	H-DM
10	56	M	16	8	2.4	25	136	0	0	0	30 I	0	+	IDC
11	45	M	8	4	2.9	26	277	0	30 I	0	40 II	0	+	IDC
12	60	F	15	5	3.6	37	126	0	0	0	0	60 D	+	IDC
13	40	M	32	20	2.5	25	223	+	50 II	0	50 II	90 OM	+	Alcohol
14	62	F	13	8	1.8	34	106	+	50 II	0	0	0	+	MI
Mean ± SD			24 ± 11	15 ± 8	2.5 ± 0.7	27 ± 6	170 ± 45							

CI = cardiac index; Cx = circumflex coronary artery; D = diagonal branch; DM = diabetes mellitus; DP = descending posterior branch; EMB = endomyocardial biopsy; H = systemic hypertension; IDC = idiopathic dilated cardiomyopathy; LAD = left anterior descending coronary artery; LVD = left ventricular dysfunction; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; MI = myocardial infarction; OM = branch of the obtuse margin; PAP = mean pulmonary artery pressure; PCP = mean pulmonary capillary pressure; RC = right coronary artery; RWMA = regional wall motion abnormality; SB = secondary branch; I-II-III = first, second and third portion of the coronary artery. * = very thin coronary artery.

margin was present in 1 patient. Endomyocardial biopsy showed non-specific histologic features (hypertrophy and attenuation of myofibers, varying degrees of nuclear abnormalities and fibrosis) and therefore it ruled out myocarditis or specific cardiomyopathies. In patient 14, who underwent heart transplantation, direct examination of the excised heart revealed a larger fibrous scar in the left ventricular anterior wall consistent with a previous myocardial infarction. The possible cause of systolic left ventricular dysfunction was systemic arterial hypertension in 3 patients, diabetes mellitus in 2, a combination of these diseases in 4, chronic alcohol abuse in 1, a previous clinically silent myocardial infarction in 1, and idiopathic dilated cardiomyopathy in 3.

Discussion

Our results demonstrate the difficulty in identifying patients who fit the diagnosis of ischemic cardiomyopathy as defined by the new WHO/ISFC classification[7], namely severe systolic left ventricular dysfunction which cannot be explained by the degree of coronary artery disease. The definition of ischemic cardiomyopathy according to the WHO/ISFC classification also includes patients in whom left ventricular dysfunction is not explained by the extent of previous ischemic myocardial damage[7,9]. This latter patient category was not taken into consideration in the present study.

In all our patients the impairment of the left ventricular function might have been secondary to a known cause and therefore these clinical conditions could be otherwise classified. In 9 patients the impairment of the left ventricular function could be attributed to systemic arterial hypertension and/or diabetes mellitus which *per se* can induce an impairment in systolic performance[10-12]. Therefore, these patients seem to more properly fit the definition of hypertensive or diabetic cardiomyopathy as stated by the new WHO/ISFC classification of cardiomyopathies[7]. In 3 patients, the clinical and angiographic presentation as well as the histologic features of the myocardium at biopsy and the presence of very mild or peripheral coronary artery stenosis were all consistent with idiopathic myocardial disease and therefore better classified as idiopathic dilated cardiomyopathy with incidental coronary artery disease[7]. In 1 patient, the heavy alcohol intake could explain the impaired left ventricular function[13] and therefore the most correct diagnosis should be alcoholic cardiomyopathy, which is also included in the new WHO/ISFC classification among the sensitivity and toxic reactions[7]. In the last patient, a previous myocardial infarction could account for the reduction in the left ventricular ejection fraction[14]. This event was a silent one and the diagnosis was confirmed by post-transplant examination of the heart. According to the recent WHO/ISFC classification of heart muscle diseases, even this case cannot be defined as ischemic cardiomyopathy. In the other 13 patients, although the pathogenetic role of myocardial ischemia remains questionable, it cannot be excluded. Therefore in these patients the impairment of the left ventricular function could be the result of the interplay of two or more causes.

On the basis of our data, the value of the definition of ischemic cardiomyopathy as proposed by the WHO/ISFC classification, is debatable not only from a theoretical point of view[8] but also in clinical practice, at least for the patients in whom the left ventricular dysfunction cannot be explained by the severity of coronary artery disease.

The lack of clinical applicability of the definition of ischemic cardiomyopathy proposed by the new WHO/ISFC classification is confirmed by the fact that even in recent papers[15-20], the term ischemic cardiomyopathy was used as popularly defined[2-4].

In conclusion, in all our patients with severe left ventricular dysfunction which was not explained by the extent of coronary artery disease, at least one possible cause of impaired contractile performance could be identified. Thus, the definition of ischemic cardiomyopathy according to the new WHO/ISFC classification of cardiomyopathies appears to be of scarce utility on clinical grounds and should be redefined and if necessary reclassified.

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