Thallium-201 myocardial imaging in patients with dilated and ischaemic cardiomyopathy

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SUMMARY Ischaemic cardiomyopathy and dilated cardiomyopathy may be clinically indistinguishable and cardiac catheterisation is often required to differentiate between them. We have described the thallium-201 scintigraphic appearances both on exercise and after redistribution in 13 patients with ischaemic cardiomyopathy and 11 patients with dilated cardiomyopathy and have assessed the usefulness of this non-invasive technique in distinguishing between the two groups.

All patients with ischaemic cardiomyopathy and seven of the 11 patients with dilated cardiomyopathy displayed perfusion defects. Reversible defects were equally common in the two groups, occurring in approximately 60% of patients. Reverse redistribution defects were confined to the group with ischaemic cardiomyopathy and were found in five patients, and fixed defects were also much more common in this group, being present in 92% compared with 27% of patients with dilated cardiomyopathy. In addition, fixed defects were much more extensive in the group with ischaemic cardiomyopathy and involved greater than 40% of the outer perimeter of the left ventricular image in 10 out of 12 of these patients compared with only one patient in the group with dilated cardiomyopathy.

We conclude that the finding of a reversible defect on thallium imaging is non-specific as to aetiology, and does not necessarily imply ischaemic heart disease. The presence, however, of either a fixed defect involving more than 40% of the outer left ventricular perimeter or a reverse redistribution defect strongly favours an ischaemic rather than a dilated cardiomyopathy.

Both dilated cardiomyopathy and ischaemic heart disease may have an identical clinical presentation with cardiomegaly, impaired left ventricular function, and congestive heart failure.^{1,2} Subjects with dilated cardiomyopathy have poor myocardial function associated with widely patent, non-obstructed coronary arteries, whereas when ischaemic heart disease is the underlying pathology, myocardial dysfunction results from severe atheromatous narrowing of the coronary arteries. The term ischaemic cardiomyopathy has been coined to describe this latter situation.¹ In view of the differing natural history, prognosis, and treatment of the two conditions accurate differentiation between them is important.

At present, coronary angiography is often necessary to make the distinction, but myocardial perfusion scintigraphy using thallium-201 (Tl) has been suggested by Bulkley *et al.*³ as a useful non-invasive alternative. These authors performed imaging only at rest but were able to differentiate correctly between dilated cardiomyopathy and ischaemic cardiomyopathy in the majority of patients studied.

The aim of the present study was to establish the Tl scintigraphic appearances on exercise and after redistribution in patients with dilated cardiomyopathy and to evaluate the usefulness of sequential imaging with Tl as a non-invasive means of distinguishing this group from patients with a similar clinical presentation secondary to ischaemic heart disease.

Subjects and methods

Twenty-four patients presenting to the Cardiac Department of St Thomas' Hospital were studied, 11 with dilated cardiomyopathy and 13 with ischaemic cardiomyopathy. The diagnoses were based on the results of cardiac catheterisation, which in each case involved both left ventricular cineangiography and selective coronary arteriography (including both left and right craniocaudal views of the left coronary artery). All subjects had both impaired left ventricular function (ejection fraction ≤ 0.50) in the absence of localised aneurysm formation and cardiomegaly (left ventricular end-diastolic volume index > 90 ml/m²). In addition those patients with dilated cardio-

myopathy had arteriographically normal coronary arteries while those with ischaemic cardiomyopathy had $\geq 70\%$ stenosis in at least one major coronary artery.

The aetiology was unknown in 10 of the 11 patients with dilated cardiomyopathy, but in one acromegaly was regarded as the underlying pathology. In two further patients, excessive alcoholic intake was thought to be relevant. No subject in either group had significant organic valvular heart disease.

Exercise and redistribution Tl scanning was performed in all cases using a sequential imaging technique. Initially, patients were exercised on an Avionics E16 programmable treadmill using the standard Bruce protocol⁴ which consisted of continuous three minute exercise stages. Heart rate and electrocardiogram were continuously monitored on an Avionics Exerstress 3000 electrocardiograph system. Maximal exercise performance was encouraged by adopting a symptomatic end-point of chest pain, dyspnoea, or fatigue.

At peak exercise 1.5 to 2.0 mCi of thallous chloride (Phillips Duphar, Holland) was administered intravenously and this level of exercise was continued for a further 30 to 60 seconds. Images were obtained five to 10 minutes later (exercise scan) using an Anger gamma camera (General Electric Maxi Camera II) fitted with a low energy, high resolution converging hole collimator (General Electric No. H2503 AD). A Varian Series 71 computer system with 64K of memory was interfaced to the gamma camera and images were acquired in static 64×64 word mode. A 25% energy window was centred on the 69 to 83 KeV Hg-201 X-ray peak and images containing 300K counts were obtained in each of the anteroposterior (AP), 45° left anterior oblique (LAO), and left lateral (LL) projections. Approximately three to four hours later, patients were reimaged in the same views (redistribution scan) without further administration of Tl.

Fig. Segmentation of the left ventricular images in the anteroposterior, 45° left anterior oblique, and left lateral views.

IMAGE ANALYSIS

The raw images underwent both a single nine point smooth and empirical background subtraction. They

were then displayed on a colour television with a 15-step colour scale. In each view the myocardium was segmented as in the figure and correlation with the number of diseased vessels was based on the work of Lenaers *et al.*⁵ Consequently, the anterolateral (AP view), anteroseptal (LAO view), and the anterior (LL view) segments were equated with left anterior descending artery disease; the inferior segment (all views) with right coronary artery disease; and the posterolateral segment with circumflex disease. A perfusion defect was defined as an area with a count density <75% of the maximum in that view and such regions were recognised by displaying a 75% contour line superimposed on the image. Equivocal areas were clarified by a region-of-interest analysis. Perfusion abnormalities present on both exercise and redistribution images were defined as fixed defects, those present on exercise but infilling to normal (or almost normal) after redistribution as reversible defects, and those appearing for the first time or getting much more extensive on the redistribution image were defined as reverse redistribution defects.⁶ Finally, the percentage of the outer perimeter of the left ventricular myocardium, excluding valve planes, involved in the perfusion defect was calculated in each view and the largest one used in the study.

Results

The clinical and catheter data on the 13 patients with ischaemic cardiomyopathy are detailed in Table 1. There were 12 men and one woman; age range 36 to 65 years (49.2 ± 8.7 years, mean ± 1 standard deviation). In the group with dilated cardiomyopathy (Table 2) all patients were male and their ages ranged from 18 to 65 years (47.0 ± 15.0 years; mean ± 1 standard deviation). No significant difference ($p > 0.05$) existed between the two groups in either mean left ventricular end-diastolic volume index (121.3 v 169.1 ml/m²) or mean ejection fraction (0.40 v 0.28), for ischaemic and dilated cardiomyopathy respectively.

Good quality images were obtained in all patients both on exercise and after redistribution and the results of image analysis are summarised in Tables 3 and 4.

(a) ISCHAEMIC CARDIOMYOPATHY

All 13 patients displayed at least one perfusion abnormality (Table 3). Fixed defects occurred in 12 patients. Reversible abnormalities were found in combination with fixed ones in seven and alone in one patient. Reverse redistribution defects occurred in five patients.

The fixed defects tended to be very large (Table 4). In 10 of the 12 patients (83%) with such

Table 1 Clinical details and catheter data on 13 patients with ischaemic heart disease

Case no.	Age/sex	Clinical details		Catheter data		
		NYHA	Chest pain	LVEDI (ml/m ²)	EF	CAD
1	47/M	2	+	92	0.50	LAD, Cx, RCA
2	54/M	4	—	120		LAD, Cx, RCA
3	62/M	3	+	93	0.40	LAD
4	65/M	3	+	132	0.20	LAD, Cx, RCA
5	40/M	3	+	123	0.30	LAD, Cx
6	50/M	2	+	103	0.30	LAD, RCA
7	37/M	1	—	103	0.50	LAD, RCA
8	52/M	3	+	173	0.50	LAD, RCA
9	52/M	2	—	154	0.45	LAD, Cx, RCA
10	48/M	2	+	103	0.25	LAD, Cx, RCA
11	44/M	2	+	113	0.45	LAD, Cx, RCA
12	52/M	2	+	121	0.50	RCA
13	36/F	2	+	147	0.40	LAD, Cx, RCA

LVEDI, left ventricular end-diastolic volume index; EF, ejection fraction; CAD, coronary artery disease; LAD, left anterior descending; Cx, circumflex; RCA, right coronary artery.

Table 2 Clinical details and catheter data on 11 patients with dilated cardiomyopathy

Case no.	Age/sex	Clinical details		Catheter data		
		NYHA	Chest pain	LVEDI (ml/m ²)	EF	Added procedure
14	18/M	4	—	390	0.10	LV biopsy lactate
15	35/M	1	+	168	0.25	LV biopsy
16	48/M	2	—	125	0.25	LV biopsy lactate
17	61/M	2	—	201	0.25	LV biopsy
18	33/M	1	+	94	0.25	
19	60/M	2	—	189	0.20	
20	35/M	1	+	134	0.50	
21	51/M	1	+	93	0.50	
22	50/M	3	—	197	0.10	
23	61/M	3	+	111	0.50	
24	65/M	2	—	158	0.20	Lactate

LVEDVI, left ventricular end-diastolic volume index; EF, ejection fraction.

Table 3 Incidence and type of perfusion defects present on Tl myocardial scintigraphy

	No. (%) defect	Fixed (%)	Reversible (%)	Fixed and reversible (%)	Reverse redistribution (%)
Ischaemic cardiomyopathy (n=13)	0	12 (92)	8 (62)	7 (54)	5 (38)
Dilated cardiomyopathy (n=11)	4 (36)	3 (27)	7 (64)	3 (27)	0

Table 4 Size of scintigraphic defects

% of outer LV circumference	Fixed		Reversible		Reverse redistribution	
	Ischaemic cardiomyopathy (n=12)	Dilated cardiomyopathy (n=3)	Ischaemic cardiomyopathy (n=8)	Dilated cardiomyopathy (n=7)	Ischaemic cardiomyopathy (n=5)	Dilated cardiomyopathy (n=0)
1-20	0	2	4	0	1	0
21-40	2	0	3	3	3	0
>40	10	1	1	4	1	0

abnormalities, the maximum defect in any projection on the exercise or redistribution scan was $\geq 40\%$ of the outer left ventricular perimeter and in the remaining two patients it lay between 20 and 40%. Reversible and reverse redistribution defects were more variable in size (Table 4), the majority (11 out of 13; 85%) involving less than 40%.

In all 13 subjects, the T1 defects involved myocardial segments supplied by more than one coronary artery suggesting double vessel disease in 11 and triple vessel disease in the remaining two patients.

(b) DILATED CARDIOMYOPATHY

The perfusion scans were entirely normal in four of the 11 patients (36%) but in the remaining seven (64%) at least one perfusion defect was present (Table 3). Fixed defects were found in three patients (27%) and reversible ones in seven (64%). No reverse redistribution defects were noted. The fixed defects tended to be small and in only one patient did the maximum defect in any view exceed 40% of the outer left ventricular perimeter (Table 4). Reversible defects were again variable in size with four out of seven (57%) exceeding 40% and three out of seven (43%) lying between 20 and 40% of the left ventricular perimeter.

Perfusion abnormalities did not involve as many different myocardial segments in each patient as they did in the ischaemic group. In three patients they were limited to a single myocardial segment, in a further three patients they involved segments supplied by two different coronary arteries, and in the remaining patient involved segments supplied by all three coronary arteries.

Discussion

Dilated cardiomyopathy can usually be distinguished from ischaemic heart disease on clinical grounds. Both may produce an identical picture, however, consisting of impaired left ventricular function, cardiomegaly, and often congestive cardiac failure.¹ The true aetiology may remain obscure clinically since coronary artery disease need not be associated with chest pain or electrocardiographic evidence of myocardial infarction.^{7,8} Conversely, patients with dilated cardiomyopathy may have chest pain or electrocardiographic abnormalities suggesting infarction without accompanying pathological evidence of necrosis.⁹

At present, when doubt exists clinically, cardiac catheterisation and coronary angiography are used to differentiate between the two conditions. A non-invasive alternative is clearly desirable, and both electrocardiograph-gated blood pool scanning and myocardial perfusion scintigraphy using thallium-201

have been reported³ to be useful in this context. Bulkley *et al.*³ performed T1 scintigraphy at rest but not on exercise in 13 patients with ischaemic cardiomyopathy and in eight patients with primary dilated cardiomyopathy. All patients in the former group were found to have a defect occupying $>40\%$ of the outer left ventricular perimeter in any one projection. On the other hand, all but one patient with dilated cardiomyopathy demonstrated either normal perfusion (four patients; 50%) or a defect amounting to $<20\%$ of the left ventricular circumference (three patients; 38%). Using this criterion of the presence of a defect exceeding 40%, the authors blindly re-evaluated the scans and were able to differentiate correctly between the two conditions in all but one patient.

In the present study, we performed scintigraphy on exercise and after redistribution since in clinical practice patients are likely to undergo this sequence of investigations. We also wished to characterise the type of perfusion abnormality which occurs. In the group with ischaemia perfusion defects were widespread, involving the territories of two or three coronary arteries. Reversible defects suggestive of myocardial ischaemia¹⁰ were found in about 60% of these patients but fixed defects indicative of myocardial infarction, fibrosis, or scarring¹⁰ occurred in 92% and tended to be extensive, involving $>20\%$ of the outer left ventricular perimeter in all cases and $>40\%$ in 83% of cases. Reverse redistribution defects⁶ in which the perfusion abnormality first appears or gets much worse in the delayed (redistribution) scan were less common and were confined exclusively to the group with ischaemia. In the group with dilated cardiomyopathy, reversible perfusion defects were again common (64% of patients) but they tended to be more localised, being limited to the territory of one or two coronary vessels only. Fixed defects, however, occurred much less commonly than in the group with ischaemic cardiomyopathy being found in only three patients (27%), and in addition tended to be smaller, $<20\%$ of the left ventricular circumference.

In the context of ischaemic heart disease, fixed perfusion defects have been shown to correlate with epicardial scar formation at the time of operation in approximately 80% of cases¹¹ and with the presence of segmental wall motion defects on left ventricular angiography in all cases studied by Bodenheimer *et al.*¹² Furthermore, the latter authors showed that fixed defects did not occur in any myocardial segments supplied by significantly ($\geq 75\%$ luminal narrowing) diseased coronary arteries which displayed normal contraction patterns on ventriculography. Massie *et al.*¹³ also compared angiographic wall motion and T1 scintigraphy in 27 patients without electrocardiographic or clinical evidence of previous

myocardial infarction. In only two of 100 (2%) myocardial segments with normal contraction were fixed perfusion defects found. In addition, they showed that the incidence of perfusion defects was closely related to the degree of coronary artery narrowing, being much commoner in vessels with $\geq 90\%$ compared with those with 70 to 90% stenoses. Hence, the finding of a fixed perfusion defect in a patient with known ischaemic heart disease strongly indicates severe coronary narrowing, segmentally impaired left ventricular contraction and epicardial scar formation caused by infarction and/or fibrosis.

The results of the present study, however, indicate that in patients presenting with impaired left ventricular function and cardiomegaly, fixed perfusion defects are non-specific occurring in both ischaemic and dilated cardiomyopathy and thus in no way exclude the latter diagnosis. None the less the presence of either a reverse redistribution defect or a fixed defect which involves more than 40% of the left ventricular perimeter in any view is strongly in favour of ischaemic heart disease and may be used to differentiate such patients from those with dilated cardiomyopathy. Using these criteria in the present study, only one patient would have been misdiagnosed. At catheterisation this subject had a uniformly dilated left ventricle (end-diastolic volume index 111 ml/m^2), anterolateral hypokinesia, and normal coronary arteries. Tl scanning showed a large fixed anterolateral and apical defect involving approximately 50% of the left ventricular circumference, thus indicating on the above criteria the incorrect diagnosis of ischaemic heart disease. The cause of the wall motion abnormality and Tl defect in this subject is unclear. It is possible that he belongs to the group of patients with myocardial infarction and normal coronary arteries. The matching nature of the abnormalities suggests that some myocardial damage is likely in this region and probably accounts for the clinical picture of impaired left ventricular function.

The causative mechanism underlying the production of perfusion defects in patients with dilated cardiomyopathy remains obscure though a number of possibilities exists. Firstly, true myocardial ischaemia may be present. In three of our patients, however, metabolic studies were performed during catheterisation (Table 2) and in none did myocardial lactate extraction fall below 10% even on pacing. An ischaemic aetiology for the obvious perfusion abnormalities which they displayed on Tl scanning is thus unlikely. Secondly, foci of interstitial or replacement fibrosis are known to occur¹⁴ in dilated cardiomyopathy and their presence was postulated by Bulkley *et al.*³ as the possible cause of defects found in such patients. Again, however, our results tend to contradict this hypothesis since we found reversible

defects to be more common than the fixed ones normally associated with myocardial fibrosis.¹⁰ In addition, we performed left ventricular myocardial biopsies during catheterisation in four of our 11 patients with dilated cardiomyopathy (Table 2) and found histological fibrosis of varying degree in three. All of these displayed reversible Tl defects but none had fixed defects suggestive of fibrosis. Lastly, a primary abnormality at the myocardial cell membrane level, perhaps impairing Tl extraction, may exist at rest or be induced by exercise and so produce perfusion defects in the image.

In conclusion, this study has shown that localised reversible segmental perfusion defects are common in patients with dilated cardiomyopathy. In the context of patients presenting with poor left ventricular function and congestive heart failure the finding of such defects does not help in the differentiation between ischaemic heart disease and dilated cardiomyopathy. The presence of a reverse redistribution defect or a fixed perfusion defect involving $>40\%$ of the outer left ventricular perimeter, however, strongly favours ischaemic heart disease and using these criteria, Tl scanning may provide useful information when clinical doubt exists.

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