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Dipyridamole stress thallium-201 perfusion abnormalities in patients with hypertrophic cardiomyopathy

Relationship to clinical presentation and outcome

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Aims Thallium-201 perfusion abnormalities are common in patients with hypertrophic cardiomyopathy and may be associated with an adverse prognosis in the young. The aim of this study was to prospectively determine the relationship between thallium-201 defects during dipyridamole stress to clinical presentation and outcome in a large consecutive series of patients with hypertrophic cardiomyopathy.

Methods/Results Thallium-201 single photon computed tomography was performed in 216 patients with hypertrophic cardiomyopathy during dipyridamole stress ($0{\cdot}5$ mg . kg^{-1}). Fixed perfusion defects occurred in 25%, and reversible defects in 22%. A combination of defects was present in 7%. Fixed defects were associated with: a history of syncope (17 of 46 with, vs 36 of 170 without syncope, $P=0{\cdot}03$); larger left ventricular end-diastolic ($46{\cdot}9 \pm 7{\cdot}4$ mm vs $43{\cdot}3 \pm 6{\cdot}4$ mm; $P=0{\cdot}001$) and end-systolic dimension ($30{\cdot}2 \pm 8{\cdot}4$ mm vs $24{\cdot}5 \pm 5{\cdot}9$ mm, $P<0{\cdot}0001$); increased left atrial diameter ($46{\cdot}1 \pm 8{\cdot}1$ mm vs $40{\cdot}5 \pm 7{\cdot}7$ mm, $P<0{\cdot}0001$); lower fractional shortening ($35{\cdot}9 \pm 10{\cdot}4\%$ vs $43{\cdot}8 \pm 8{\cdot}6\%$, $P<0{\cdot}0001$); and lower maximal exercise oxygen consumption ($24{\cdot}2 \pm 8{\cdot}1$ ml . min^{-1} . kg^{-1} vs $29{\cdot}4 \pm 8{\cdot}8$ ml . min^{-1} . kg^{-1}, $P<0{\cdot}0003$). Reversible defects did not correlate with symptomatic status, but were associated with: larger left atrial dimensions ($44{\cdot}5 \pm 8{\cdot}1$ mm vs $41{\cdot}0 \pm 8{\cdot}0$ mm; $P=0{\cdot}009$) and greater maximal left ventricular wall thickness ($24{\cdot}0 \pm 7{\cdot}0$ mm vs $20{\cdot}6 \pm 7{\cdot}0$ mm, $P=0{\cdot}003$). The mean follow up time was 41 ± 21 months, range 0·6–124. There was no association between any thallium-201 abnormality and disease related death in young or adult patients.

Conclusion The present study shows that fixed thallium-201 perfusion defects detected during dipyridamole stress in patients with hypertrophic cardiomyopathy are associated with syncope, larger left ventricular cavity dimensions and reduced exercise capacity. Although the event rate was relatively small, there was no evidence for an association between thallium-201 defects and survival.
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Key Words: Thallium-201, hypertrophic cardiomyopathy, prognosis.

Introduction

Patients with hypertrophic cardiomyopathy frequently complain of exertional angina despite angiographically normal coronary arteriograms[1]. Pathological and clinical evidence suggests that myocardial ischaemia may be the underlying cause[2–5], but the clinical evaluation of chest pain in patients with hypertrophic cardiomyopathy remains problematic. Several reports have shown that reversible perfusion abnormalities are common in patients with disease[6–11], and recently it has been suggested that they are associated with an adverse prognosis in the young[12]. However, with the exception of a single study[10], no report has demonstrated a correlation between a history of exertional angina and the presence of reversible thallium-201 perfusion defects. The aim of this study was to prospectively test the hypothesis that thallium-201 perfusion abnormalities are

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related to clinical presentation, markers of sudden death risk (exercise blood pressure response, non-sustained ventricular tachycardia, syncope and family history) and outcome using dipyridamole stress in a large consecutive series of patients with hypertrophic cardiomyopathy.

Methods

Patient characterization

Two hundred and sixteen consecutive patients (125 men, mean age 36 ± 15 years, range 11–88), referred to the cardiomyopathy clinic at St. George's Hospital were prospectively studied. One hundred and eighty two patients fulfilled strict WHO criteria for hypertrophic cardiomyopathy[13] with a maximal left ventricular wall thickness greater than or equal to 1·5 cm in the absence of any other cardiac or systemic cause of hypertrophy. The remaining 34 patients had lesser degrees of hypertrophy (1·2 ± 0·2 cm), but all had an abnormal baseline electrocardiogram, a parent and/or sibling with an established diagnosis of hypertrophic cardiomyopathy and abnormal diastolic function (i.e. slow and prolonged isovolumic relaxation, reduced rate of rapid filling, increased left ventricular 'stiffness', and/or altered atrial contribution to stroke volume).

Fifty-five patients (25%) had a family history of premature (<55 years) sudden death due to hypertrophic cardiomyopathy. Five patients had been successfully resuscitated from out-of-hospital ventricular fibrillation prior to study. Eighty-nine (41%) patients had dyspnoea, New York Heart Association class II–IV and 46 (21%) had experienced two or more episodes of unexplained syncope whilst performing normal daily activities within the previous 5 years. A history of exertional angina pectoris was present in 77 (36%) patients and atypical pain (i.e. pain at rest or more than 30 min in duration, in the absence of infarction) in 46 (21%) patients. Twenty-eight patients had both atypical and exertional angina. Coronary arteriography was performed in 21(18%) patients (out of 116 patients over the age of 35) with coronary risk factors and other clinical markers suggestive of coronary artery disease. Minor single vessel disease (<20% diameter stenosis) was detected in one patient.

Thirty-four patients received amiodarone therapy during the follow-up period for supraventricular arrhythmia (n = 10) and/or sudden death prophylaxis (n = 24).

Echocardiography

Two dimensional and M-mode echocardiography was performed using conventional techniques[14]. Left ventricular wall thickness was recorded, where possible, at mitral valve and papillary muscle level in the anterior and posterior septum, and in the lateral and posterior left ventricular wall using short-axis, two-dimensional images. Ejection fraction was calculated using the Teicholz method[15]. The mean maximal left ventricular wall thickness was 21·4 ± 7·1 mm. Mean maximal thicknesses in each ventricular segment were: anterior septum, 20·1 ± 7·0 mm; posterior septum, 17·7 ± 6·6 mm; posterior left ventricular wall, 12·3 ± 3·5 mm; and lateral wall, 15·4 ± 5·2 mm. Mean left ventricular end-diastolic and end-systolic dimensions were 44·1 ± 6·8 mm and 25·8 ± 7·0 mm, respectively. Mean left ventricular fractional shortening and calculated ejection fraction were 42·0 ± 9·6% and 66·5 ± 11·4%, respectively. The mean left atrial diameter was 41·8 ± 8·1 mm. Fifty-two patients had a resting peak outflow gradient of >30 mmHg (0–144 mmHg, mean 21·2 ± 33·5 mmHg).

Ambulatory electrocardiographic monitoring

One hundred and ninety five (90%) patients underwent 48 h ambulatory electrocardiographic monitoring off cardioactive medications whilst performing unrestricted daily activities. Recordings were made using the Marquette (Marquette Electronics Inc., Diagnostic Division, Milwaukee, U.S.A.) Holter recording system on two channels; CM5 on channel 1 and V_2 on channel 2. Computer-assisted analysis was performed using the Marquette Series 8000 Laser Holter and Laser Holter XP system. Fifty (26%) patients had one or more episodes of paroxysmal atrial fibrillation or atrial tachycardia. Fifty-six (29%) had one or more runs of non-sustained ventricular tachycardia (i.e. three or more consecutive ventricular extrasystoles with a mean rate of 120 beats . min^{-1}, lasting for less than 30 s). No patients had a sustained (> = 30 s) ventricular tachycardia.

Exercise testing

All patients underwent symptom-limited maximal exercise testing using the Bruce (n = 193), modified Bruce (n = 21), Cleveland (n = 1) and Naughton (n = 1) protocols under standardized conditions. Respiratory gases were collected using a tightly fitting facemask. Gas analysis was performed using a dedicated metabolic cart (Marquette Electronics Inc, WI, U.S.A.) and a mass spectrophotometric gas analyser, according to established methodology[16]. Oxygen consumption was determined using a temperature-controlled polarographic sensor and an on-board microprocessor. The age-predicted maximal oxygen consumption (V_{O_2}) was calculated using established formulae[17,18]. Arterial blood pressure was determined using a mercury sphygmomanometer and auscultation of the Korotov sounds at the brachial artery at rest, every minute during exercise and every 15 s during the initial 5 min of the recovery period. Blood pressure responses were classified as normal, flat (i.e. a systolic blood pressure rise of less than 20 mmHg above the resting value during the

whole exercise period) or hypotensive (a continuous fall throughout exercise of >20 mmHg from baseline or an initial increase in systolic blood pressure with a subsequent fall of >20 mmHg compared to the peak pressure)[19]. Mean maximal oxygen consumption at peak exercise was $28{\cdot}1 \pm 8{\cdot}9$ ml . min^{-1} . kg^{-1}. The mean calculated percentage of predicted maximum oxygen consumption was 68 ± 19%. Thirty-five (16%) patients had a flat and 24 (11%) a hypotensive blood pressure response during exercise. ST segment analysis was performed in 196 (91%) of patients. Of these, 74 (38%) patients had 0·1 mV horizontal or downsloping ST segment depression (from baseline) at 60 ms after the J point at peak exercise.

Thallium-201 single photon emission tomography

All cardioactive medications, with the exception of amiodarone, and drugs or beverages containing theophylline or caffeine were discontinued for at least 48 h or five half-lives before thallium-201 imaging. A loading dose of dipyridamole (0·5 mg . kg^{-1} . 4 min^{-1}) was administered intravenously to all patients and was combined with 3 min straight leg raising[20]. This was followed by injection of 74 MBq of thallium-201 chloride. Imaging was commenced within 10 min of thallium injection and repeated 3 h later. A wide field-of-view gamma camera (General Electric 400AT or Elscint SP6) was rotated 180° from the 45° left posterior oblique to the 45° right anterior oblique view. Thirty-two images were acquired on the General Electric 400 AT system and 30 on the Elscint SP6 system. All images were of 45 s duration. Image reconstruction and washout analysis were performed using the General Electric Star system or the Elscint APEX. Filtered back projections were obtained using a Hanning filter with a cut-off of 0·5 cycle/pixel with a pixel size of 6·25 mm. No attenuation or scatter correction was used. A slice width of 1 cm was used for image reconstruction. The distribution of thallium uptake was analysed qualitatively in standard orthogonal tomographic imaging planes: septal, apical and lateral regions in the horizontal long-axis (transaxial) view, anterior, apical and inferior in the vertical long-axis (sagittal) view, and anterior, septal, inferior and lateral regions in the short-axis (oblique) view. Stress and delayed images were normalized to the region with the maximal myocardial activity in each image. Four consecutive representative slices of each view were displayed simultaneously for interpretation. The images were scored by two experienced observers, blinded to clinical details using a 4 point scale: 3 (markedly reduced/absent activity); 2 (moderately reduced); 1 (mildly reduced) and 0 (normal). Each region was classified according to the lowest score obtained in all tomographic slices and views. Defects with a score of 1 or more were considered to be significant perfusion abnormalities. 'Reversible' perfusion was defined by a change in the defect score of 1 from the stress to the redistribution study.

Follow-up data

Follow-up data were obtained from patients, family members and attending physicians in all subjects up to November 1995. The end-points were defined as: sudden death (witnessed, instantaneous collapse leading to death within minutes), resuscitated cardiac arrest, progressive cardiac failure and cardiac transplantation.

Statistical analysis

Data were expressed as mean ± 1 standard deviation. Statistical analysis was performed using a two-tailed Student t-test and Fishers Exact test where appropriate. A P value of $<0{\cdot}05$ was considered significant. Simple and multiple linear regression analysis was performed using standard techniques (Statview® v4.1, Abacus Concepts Inc, Berkeley, CA, U.S.A. and SPSS® v6.0, SPSS Inc. Chicago, Illinois, U.S.A.). Kaplan Meier plots and Cox linear regression were used to study cumulative survival and its relation to clinical and scintigraphic variables. A cut-off of 21 years was used to examine age related differences.

Results

Thallium-201 scintigraphy was performed in all patients without complication. Regional perfusion defects were identified in 86 (40%) patients. Fifty three patients (25%) had one or more fixed defects and 48 patients (22%) had one or more reversible defects. Fixed defects were most commonly detected in the anterior segment (n=36) followed by inferior (n=21), lateral (n=7) and septal (n=5) regions. The number of reversible defects in each region was: anterior: 28, inferior: 11, septal: 9, and lateral: 5.

Fixed defects

Fixed defects were more common in patients with a history of syncope (17 (37%) of 46 patients with syncope vs 36 (21%) of 170 individuals without syncope, $P=0{\cdot}03$), but were not associated with any other symptom or clinical risk factor (i.e. non-sustained ventricular tachycardia, a family history of sudden death or abnormal exercise blood pressure response). Patients with fixed defects had larger mean left ventricular end-diastolic ($46{\cdot}9 \pm 7{\cdot}4$ mm vs $43{\cdot}3 \pm 6{\cdot}4$ mm; $P=0{\cdot}001$) and end-systolic ($30{\cdot}2 \pm 8{\cdot}4$ mm vs $24{\cdot}5 \pm 5{\cdot}9$ mm, $P<0{\cdot}0001$) dimensions. Fixed perfusion abnormalities were associated with larger left atrial dimension ($46{\cdot}1 \pm 8{\cdot}1$ mm vs $40{\cdot}5 \pm 7{\cdot}7$ mm, $P<0{\cdot}0001$) and lower

Table 1 Relationship between age, clinical characteristics and reversible defects. Values are mean ± SD

	<=21 n=40				*P*	>21 n=176				*P*
	RD(−) n=29	(%)	RD(+) n=11	(%)		RD(−) n=139	(%)	RD(+) n=37	(%)	
Age (years)	16 ± 3		18 ± 3			40 ± 12		42 ± 15		
Gender (male)	15	(52)	8	(73)	ns	83	(60)	19	(51)	ns
FHSD	10	(34)	5	(45)	ns	32	(23)	8	(22)	ns
Angina	8	(28)	4	(36)	ns	48	(35)	17	(46)	ns
Dyspnoea (II-IV)	12	(41)	5	(45)	ns	56	(40)	16	(43)	ns
Syncope	5	(17)	1	(9)	ns	32	(23)	8	(22)	ns
LA	38·9 ± 6·0		41·5 ± 9·2		ns	41·5 ± 8·3		45·5 ± 7·7		0·01
LVED (mm)	42·5 ± 6·5		45·1 ± 6·6		ns	44·7 ± 7·0		43·0 ± 6·5		ns
LVES (mm)	23·4 ± 6·4		26·8 ± 7·9		ns	26·7 ± 7·2		24·2 ± 5·6		ns
MLVWT (mm)	20·9 ± 8·1		27·5 ± 9·5		0·03	20·5 ± 6·7		22·9 ± 5·8		ns
FS (%)	45·5 ± 9·6		41·2 ± 11·0		ns	40·9 ± 9·4		43·4 ± 9·3		ns
EF (%)	70·5 ± 10·4		65·5 ± 12·3		ns	65·3 ± 11·7		68·2 ± 10·7		ns
Grad >30 mmHg	3	(10)	3	(27)	ns	20	(14)	9	(24)	ns
n*	(26)		(11)			(124)		(34)		
SVT	4	(15)	1	(9)	ns	36	(29)	9	(26)	ns
NSVT	2	(8)	2	(18)	ns	41	(33)	11	(32)	ns
Vo_2 (ml . min^{-1} . kg^{-1})	31·0 ± 9·5		28·5 ± 7·7		ns	28·0 ± 9·3		26·2 ± 6·7		ns
% pred Vo_2	59·9 ± 14·9		53·7 ± 12·9		ns	69·7 ± 20·0		70·2 ± 16·2		ns

*n: of 195 patients who underwent ambulatory electrocardiography (see text).
RD = reversible thallium-201 defect; FHSD = family history of sudden death; dyspnoea (II-IV) = New York Heart Association functional classification; LA = left atrial dimension; LVED = left ventricular end-diastolic dimension; LVES = left ventricular end-systolic dimension; MLVWT = maximum left ventricular wall thickness; FS = fractional shortening; EF = left ventricular ejection fraction; Grad > 30 mmHg = left ventricular outflow gradient greater than 30 mmHg; SVT = supraventricular tachycardia; NSVT = non-sustained ventricular tachycardia; Vo_2 = maximum exercise oxygen consumption; %pred Vo_2 = percent of maximum exercise oxygen consumption predicted for age, sex, height and weight.

fractional shortening (35·9 ± 10·4% vs 43·8 ± 8·6%, $P<0·0001$). Of the 12 patients with a calculated ejection fraction of <50%, nine (75%) had fixed defects ($P=0·0001$). There was no relationship between peak resting left ventricular outflow gradient and fixed defects. Maximal exercise oxygen consumption was significantly lower in patients with fixed defects (24·2 ± 8·1 ml . min^{-1} . kg^{-1} vs 29·4 ± 8·8 ml . min^{-1} . kg^{-1}, $P<0·0003$). The percentage of the age-predicted exercise oxygen consumption was also lower in patients with fixed defects (62·1 ± 18·1% with fixed defects vs 69·3 ± 19·0% without, $P=0·017$). There was no relation between fixed defects and ST segment depression during exercise.

Reversible defects

There was no relationship between reversible defects, symptoms or recognised clinical risk markers. Patients with reversible defects had larger left atrial dimensions (44·5 ± 8·1 mm vs 41·0 ± 8·0 mm; $P=0·009$) and greater maximal left ventricular wall thickening (24·0 ± 7·0 mm vs 20·6 ± 7·0 mm, $P=0·003$). There was no relationship between reversible defects and the presence of a resting left ventricular outflow gradient >30 mmHg. Left ventricular cavity dimensions were similar in patients with and without reversible defects. There was no relation between reversible defects and actual or predicted exercise oxygen consumption, or ST segment depression.

Age-related differences

The relationship between clinical variables, thallium-201 defects and age are shown in Tables 1 and 2. The numbers of patients with fixed and reversible defects were not significantly different in patients greater or less than 21 years of age. In the young, the only significant associations were between syncope and fixed defects ($P=0·0008$), and reversible defects and maximal left ventricular wall thickness ($P=0·03$).

Survival analysis

The mean follow-up period following thallium-201 scintigraphy was 41 ± 21 months, range 0·6–124. Thirteen patients died: eight suddenly; three from progressive heart failure; one from an intra-cerebral haemorrhage and one from acute mesenteric ischaemia. Two additional patients underwent orthotopic cardiac transplantation and one patient was successfully resuscitated from spontaneous out-of-hospital ventricular fibrillation in the follow-up period. Survival analysis was performed in those patients with sudden or disease-related cardiac

Table 2 Relationship between age, clinical characteristics and fixed defects. Values are mean ± SD

	≤21 n=40				*P*	>21 n=176				*P*
	FD(−) n=35	(%)	FD(+) n=5	(%)		FD(−) n=128	(%)	FD(+) n=48	(%)	
Age (years)	17 ± 3		16 ± 2			40 ± 13		42 ± 12		
Gender (male)	21	(60)	2	(40)	ns	77	(60)	25	(52)	ns
FHSD	14	(40)	1	(20)	ns	31	(24)	9	(19)	ns
Angina	10	(29)	2	(40)	ns	46	(36)	19	(40)	ns
Dyspnoea (II-IV)	14	(40)	3	(60)	ns	49	(38)	23	(48)	ns
Syncope	2	(6)	4	(80)	0·0008	27	(21)	13	(27)	ns
LA	39·9 ± 7·2		37·4 ± 4·8		ns	40·7 ± 7·9		47·1 ± 7·8		<0·0001
LVED (mm)	43·0 ± 6·4		45·3 ± 9·0		ns	43·4 ± 6·5		47·0 ± 7·3		0·003
LVES (mm)	23·8 ± 6·7		29·3 ± 7·5		ns	24·7 ± 5·7		30·3 ± 8·6		<0·0001
MLVWT (mm)	22·6 ± 9·3		24·2 ± 6·8		ns	21·1 ± 6·7		21·0 ± 6·4		ns
FS (%)	45·3 ± 10·0		35·5 ± 5·9		ns	43·4 ± 8·1		35·9 ± 10·8		<0·0001
EF (%)	70·2 ± 10·9		59·6 ± 8·4		ns	68·5 ± 9·1		58·8 ± 14·4		<0·0001
Grad >30 mmHg	6	(17)	0	(0)	ns	18	(14)	11	(23)	ns
n*	(32)		(5)			(117)		(41)		
SVT	5	(16)	0	(0)	ns	28	(24)	17	(41)	0·04
NSVT	3	(9)	1	(20)	ns	35	(30)	17	(41)	ns
Vo_2 (ml . min^{-1} . kg^{-1})	31·2 ± 8·9		24·6 ± 9·1		ns	28·9 ± 8·7		24·2 ± 8·1		0·002
% pred Vo_2	59·2 ± 13·9		51·4 ± 18·3		ns	72·3 ± 19·2		63·2 ± 17·8		0·006

For abbreviations see footnote to Table 1.

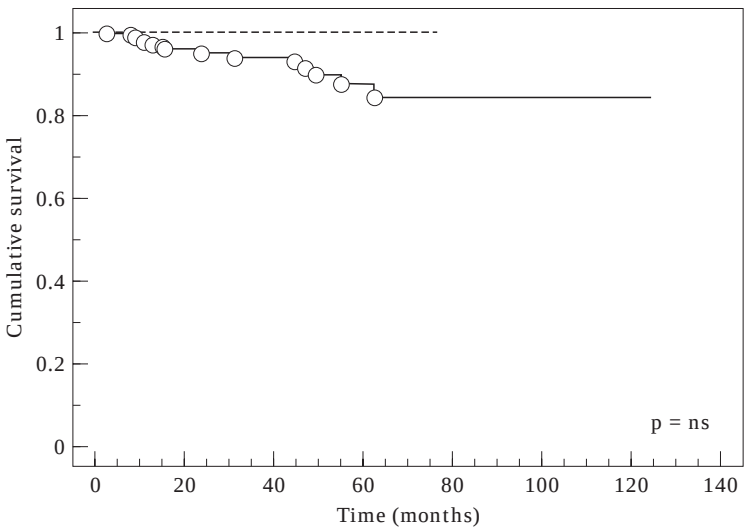

Figure 1 **Kaplan–Meier survival plot demonstrating cumulative survival in patients with (□) and without (○) reversible thallium-201 perfusion defects.**

death (including transplantation) (n=14). Cumulative survival at 5 years for the whole population was 90%. None of the patients who died had a reversible defect, and five had fixed defects. Cumulative survival at 5 years was 100% in patients with reversible defects (*P*=ns) and 91% in patients with fixed defects (*P*=ns), Figs 1 and 2. Fixed defects were significantly more common in patients who experienced syncope and/or ventricular fibrillation prior to or following thallium-201 scintigraphy (n=47), (18 (38%) of 47 patients with vs 35 (21%) of 169 patients without, *P*=0·02).

No independent variable, including the administration of amiodarone at any point during follow-up, was predictive of cardiac death in any age group (Cox stepwise linear regression). There were no differences in the proportion of patients with reversible or fixed defects treated with amiodarone. Three patients were taking amiodarone at the time of death; two had sudden death and one died from progressive heart failure. An additional patient was successfully resuscitated from ventricular fibrillation, and one other received a cardiac transplant. Of these five patients with cardiac endpoints

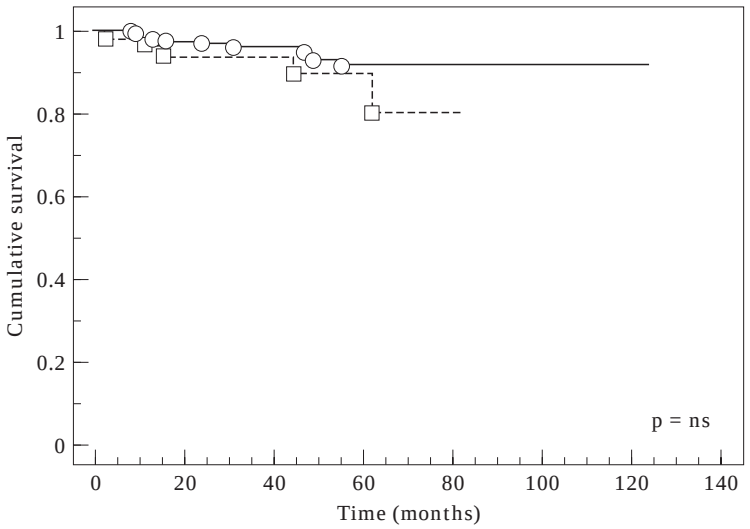

Figure 2 **Kaplan–Meier survival plot demonstrating cumulative survival in patients with (□) and without (○) fixed thallium-201 perfusion defects.**

on amiodarone therapy, none had reversible defects and two had fixed defects.

Discussion

This study demonstrates that thallium-201 perfusion abnormalities are common in patients with hypertrophic cardiomyopathy, and that specific types of defect relate to particular clinical features. In contrast to the findings in a recent study[12], there was no relation between reversible regional scintigraphic abnormalities, recognised clinical risk markers and cumulative survival in young or adult patients.

Thallium-201 defects and clinical features

The present investigation expands on findings reported previously in a number of smaller studies in patients with hypertrophic cardiomyopathy[6–11]. In particular, the demonstration of a relationship between fixed defects and left ventricular cavity dimensions, shortening fraction and maximum exercise oxygen consumption supports the hypothesis that fixed thallium-201 perfusion abnormalities in patients with hypertrophic cardiomyopathy represent areas of myocardial fibrosis[6,7]. It should be noted, however, that the majority of patients with fixed defects in the present study had ejection fractions in excess of 50%, underlining the complexity of the mechanisms responsible for functional limitation in hypertrophic cardiomyopathy.

We and others have shown that myocardial ischaemia occurs in patients with hypertrophic cardiomyopathy and abnormal thallium scans[4–6]. There are numerous potential mechanisms for myocardial ischaemia in hypertrophic cardiomyopathy, including small vessel narrowing[2,3], raised intracavitary pressures[4], and the effects of left ventricular hypertrophy on metabolic demand[21], coronary vascular resistance, and capillary density[22]. In the present study, we demonstrated an association between reversible defects and the severity of left ventricular thickening. However, as has been observed in most previous studies in patients with hypertrophic cardiomyopathy, the correlation between angina and reversible thallium-201 perfusion defects was poor. While it is suggested that this intriguing paradox might be explained by a high prevalence of 'silent ischaemia' or non-ischaemic chest pain[6–7], the consistent disparity between symptoms and reversible perfusion defects raises two important questions. First, how often does significant myocardial ischaemia occur in patients with hypertrophic cardiomyopathy and normal thallium scans, and secondly, is a reversible increase in the heterogeneity of regional thallium-201 uptake always indicative of significant myocardial ischaemia? With regard to the first query, it has already been shown that a proportion of patients with hypertrophic cardiomyopathy and normal thallium-201 scans have metabolic evidence of myocardial ischaemia[5,6,11]. This phenomenon might be explained in several ways. Studies using positron emission tomography have shown that, in some patients with hypertrophic cardiomyopathy, coronary flow reserve is globally reduced, i.e. coronary vasodilatation is impaired in hypertrophied and non-hypertrophied myocardial segments[23]. As thallium-201 perfusion defects result from relative differences in myocardial thallium-201 uptake, it is possible that a relatively homogeneous reduction in coronary vasodilator reserve might not be detected by qualitative analysis of thallium-201 perfusion images[24]. Secondly, and of particular relevance to a study using dipyridamole, subendocardial hypoperfusion is known to be an important mechanism of ischaemia in hypertrophied ventricles.

Thus, the limited resolution of conventional thallium-201 scanning might hamper reliable detection of subendocardial hypoperfusion in patients with hypertrophic cardiomyopathy[25,26]. The answer to the second question of whether qualitative differences in regional thallium uptake in patients with hypertrophic cardiomyopathy always equate with myocardial ischaemia, is less certain. However, regional differences in tracer concentration secondary to factors such as variable myocardial thickness (i.e. partial volume effect) are more likely in hypertrophic cardiomyopathy. Thus, in contrast to the situation in patients with coronary artery disease, the sensitivity and specificity of thallium-201 imaging in hypertrophic cardiomyopathy remains uncertain and requires further study.

Thallium-201 abnormalities and prognosis

The present investigation is the first large prospective study, in an unselected population, to examine the prognostic implications of thallium-201 perfusion abnormalities in patients with hypertrophic cardiomy opathy. In a recent cross-sectional study of 23 young individuals, Dilsizian *et al*.[12] demonstrated that reversible thallium-201 defects were significantly more common in patients with a history of cardiac arrest or syncope. When patients with a history of ventricular fibrillation and syncope were considered as a separate cohort in the present study, there was an association with fixed but not reversible defects. These findings might be explained by a number of factors, including the different stresses used in the two studies, the clinical characteristics of the respective patient populations, and referral bias at the recruiting institutions. The use of a reinjection protocol by Dilsizian *et al*.[12] is also important as this may have detected some areas of reversible perfusion that would have been coded as fixed using the conventional stress-redistribution technique employed in the present study[27]. Notwithstanding this potential limitation, it is unlikely that this factor alone explains the lack of association between any type of defect and cumulative survival in the present study.

In the present study, there was no relationship between reversible defects and the administration of amiodarone. This, together with the fact that none of the patients that died suddenly had a reversible defect, makes it very unlikely that amiodarone treatment explains the relation between survival and thallium-201 perfusion.

Conclusions

Patients with hypertrophic cardiomyopathy have abnormalities of thallium-201 uptake during dipyridamole stress that are associated with morphological and functional abnormalities. As yet there is no prospective evidence that perfusion abnormalities are of prognostic significance, although it is acknowledged that the follow-up period in this study was relatively short and the event rate was relatively small. Long-term follow-up is continuing and more information on this aspect will become available in the future.

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