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Asymmetry of cardiac [^{123}I] meta-iodobenzylguanidine scans in patients with ventricular tachycardia and a "clinically normal" heart

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Abstract

***Objective*—Patients with exercise induced ventricular tachycardia associated with a "clinically normal" heart may have an abnormality of the regional distribution of the cardiac sympathetic nerve supply. In this study the regional distribution of the myocardial nerve supply in patients with ventricular tachycardia (VT) and control subjects was examined by [^{123}] meta-iodobenzylguanidine (MIBG) scanning.**

***Patients and design*—Eight patients with exercise induced VT and seven patients with VT unrelated to exercise with "clinically normal" hearts were studied and compared with a control group of six subjects with atrioventricular reentrant tachycardia not related to exercise and eight patients with angiographically normal left ventricular function and normal coronary anatomy who had thallium scans without evidence of ischaemia or fixed perfusion deficits.**

***Methods*—Single photon emission computed tomography gamma scanning was performed in patients three hours after intravenous injection of MIBG. The left ventricular MIBG uptake data was processed into bull's-eye target plots. The inferior portion of the scan frequently showed artefact due to uptake of MIBG in the liver or spleen and was not used for statistical analysis. Asymmetry of uptake was defined as a ratio of uptake exceeding 1·25 in the upper quadrants (posterior (anterolateral free wall)/anterior (anteroseptal region)) of the MIBG scan.**

***Results*—Patients with VT had a higher proportion of asymmetrical MIBG scans (47%) than subjects in the control groups (0%) and this was particularly obvious in the patients with exercise induced VT (62·5%). This suggests that patients with VT may have relative denervation in the septal portion of the left ventricle leading to an imbalance of the sympathetic supply to the myocardium and locally imbalanced sympathetic or parasympathetic interactions. Considerable evidence from animal experiments suggests that imbalance of the sympathetic supply to the myocardium is important in the genesis of ventricular arrhythmia.**

***Conclusions*—These results support the hypothesis that selective denervation of the human myocardium may be an important mechanism in the genesis of VT in "clinically normal" hearts.**

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The regional integrity and function of the cardiac sympathetic nervous system has been difficult to determine in vivo. Radiolabelled [^{123}I] meta-iodobenzylguanidine (MIBG) is an analogue of noradrenaline[1] and shares the same uptake, storage and release mechanisms.[2] It is not metabolised by catechol-*o*-methyl transferase or monoamine oxidase and has an affinity for the adrenal medulla and adrenergic nerves.[3] Meta-iodobenzylguanidine has therefore been used as an imaging agent for the localisation of chromaffin tumours, including phaeochromocytoma[4 5] and neuroblastoma.[6] The heart has a dense innervation of adrenergic nerves and MIBG is of potential value as an imaging agent for the cardiac sympathetic innervation. The first measurement of the concentration of MIBG in the rat, dog and monkey myocardium was in 1981.[7] Kleine *et al* used this agent to obtain images of the human heart.[8] Since these reports, several investigators have suggested that the uptake and storage of MIBG by adrenergic nerves is responsible for the scintigraphic visualisation of the heart.[9 11] This method therefore offers an opportunity to study the regional cardiac adrenergic innervation in disease conditions where adrenergic innervation is thought to be disordered.

Ventricular tachycardia (VT) in most patients has detectable underlying cardiac pathology such as coronary artery disease, cardiomyopathy, and valvar or congenital heart disease. A few patients (5%-10%), however, have no detectable abnormality as suggested by invasive and non-invasive assessment of left and right ventricular function and coronary anatomy and are therefore described as "clinically normal" hearts.[12 14] Ventricular tachycardia in these patients is frequently induced either during exercise or in the recovery phase after exercise.[15 18] Tachycardia is usually difficult to start by programmed stimulation, but is frequently started by infusion of isoprenaline or its induction is facilitated by infusion of isoprenaline.[19] The myocardium therefore shows a sensitivity to endogenous or exogenous catecholamines in patients with this form of tachycardia. This suggests that there may be an anatomical derangement of the cardiac sympathetic innervation contributing to insta-

bility, although it is possible that there may be a functional abnormality of the sympathetic nervous system without definable anatomical abnormalities. Examination by MIBG scanning allows a direct method of studying the regional cardiac sympathetic innervation that can be applied to this condition.

Our study examines the regional cardiac innervation in patients with and without exercise induced VT but with "clinically normal" hearts and two groups comprising patients with supraventricular tachycardia without a sympathetic component (atrioventricular reentrant tachycardia) and controls (patients with normal left ventricular function on cineangiography and normal coronary anatomy) without arrhythmia shown on MIBG scanning.

The study was approved by the hospital ethics committee and informed consent was given by each patient before the examination.

Patients and methods

PATIENTS WITH VENTRICULAR TACHYCARDIA

Two groups of patients with ventricular tachycardia in "clinically normal" hearts were studied, including patients with VT related to exercise and those with VT unrelated to exercise. All patients showed ventricular tachycardia on multiple electrocardiographic leads either during a spontaneous episode or exercise test. These patients had no history of ischaemic heart disease, cardiomyopathy, or congenital cardiac abnormality and had a normal clinical cardiovascular examination, normal chest radiograph (cardiothoracic ratio < 50%), and normal resting electrocardiogram although minor T wave abnormalities were present in the precordial leads of some patients. No patient had evidence of intraventricular conduction abnormalities, left or right ventricular hypertrophy, or prolongation of the QT interval. All patients aged over 30 years had diagnostic cardiac catheterisation. No patient had angiographic evidence of coronary artery disease, reduced ejection fraction of the left ventricle, or abnormality of regional wall motion during left ventricular cineangiography. All patients had treadmill exercise tests with the Bruce protocol.[20] Patients also had detailed echocardiographic examination including right heart views, signal averaged electrocardiograms, and right ventricular cardiac biopsies. Details of these procedures have been published previously.[21 22]

Patients with exercise induced VT

Patients had a history of palpitation related to exercise and all had ventricular tachycardia induced by at least one exercise test either at peak exercise or during the early phases of recovery (n = 8). Ventricular tachycardia was defined as the presence of five or more consecutive ventricular extrasystoles at a rate > 120 beats/min occurring during or after exercise and was considered sustained if it lasted 30 seconds or longer. Five patients had sustained tachycardia and three patients had non-sustained tachycardia at exercise. All patients had programmed ventricular stimulation (Wellens protocol) after insertion of two to four multipolar electrode catheters.[23] Intracardiac electrograms and the surface electrocardiograms were displayed simultaneously on a multichannel oscilloscope and recorded on a multichannel inkjet recorder at paper speeds of 25–100 mm/s. Ventricular tachycardia of the same morphology and axis as the spontaneous tachycardia was inducible in five patients. If the initial study did not induce the VT, isoprenaline was infused at a rate of 1–4 μg/min to increase the sinus rate by at least 30% or to 120 beats/min (whichever was less), and the programmed ventricular stimulation was repeated. Two patients had VT spontaneously during isoprenaline infusion, and five had VT induced more easily after isoprenaline infusion (that is at a less aggressive stage of the programmed ventricular stimulation protocol) but did not develop VT during isoprenaline infusion alone.

Patients with ventricular tachycardia not related to exercise

Seven patients with VT which did not seem to have an adrenergic component were also studied in the same manner as patients with exercise-induced VT. All patients had documented episodes of VT, but in these patients, the history of episodes of VT was not related to exercise and the tachycardia was not induced by exercise stress testing. Furthermore, the induction of the tachycardia was not facilitated by isoprenaline during programmed ventricular stimulation. Non-inducible VT was not made inducible by isoprenaline; nor was inducible VT made more easily inducible at a lower stage of the Wellens protocol. None of the patients had spontaneous tachycardia during the infusion of isoprenaline.

PATIENTS WITH NORMAL CORONARY ANATOMY

Eight patients attending for diagnostic coronary angiography were also studied. These patients had presented with atypical chest pain and all had treadmill exercise testing. The tests had been reported as equivocal for evidence of myocardial ischaemia in three patients and normal in five patients. None of the patients had hypertension, diabetes, or evidence of left ventricular hypertrophy. Patients were investigated further by coronary angiography. All subjects had left ventricular angiograms and selective coronary angiograms. Left ventricular function and the anatomy of the coronary arteries were reported as normal in all patients when cineangiograms were reviewed by two independent observers. All these patients also had thallium scintigraphy that did not show any fixed or reversible perfusion defects (see MIBG scanning).

PATIENTS WITH ATRIOVENTRICULAR REENTRANT TACHYCARDIA

Six patients with atrioventricular tachycardia due to Wolff-Parkinson-White syndrome were studied. All patients, except for one, had Wolff-Parkinson-White syndrome diagnosed on the surface electrocardiogram and all had symptomatic palpitation. All patients underwent

detailed electrophysiological studies with at least four multipole electrode catheters inserted through the subclavian vein and femoral vein. Stimuli were delivered through a Medtronic programmable stimulator (Medtronic, Minneapolis, USA) and intracardiac electrograms and the surface electrocardiograms were recorded on a multichannel inkjet recorder at 100 mm/s. All patients had the site of the pathway mapped at electrophysiological study and this was the left free wall in four patients (concealed in one) and left posteroseptal in two patients. In none of the patients were the symptoms consistently related to exercise and in none was the use of isoprenaline necessary for the induction of atrioventricular reentrant tachycardia by programmed stimulation.

MIBG SCANNING

Thyroidal uptake of iodine was blocked by prior administration of potassium iodide. The patient fasted on the morning of the scan and was positioned supine within the gamma camera ring. A peripheral intravenous line was sited and the electrocardiogram was monitored continuously during the procedure. The patient began exercise by straight leg raising for two minutes or until the heart rate had doubled and [^{123}I] MIBG (370 MBq/1·73 m^2 of body surface) was injected as an intravenous bolus. The subject then awaited the scan. The radiation exposure to the patient from the scan is about 6·5 mSv (some 28% of that from routine thallium 201 scintigraphy (23 mSv)).

Single photon emission computed tomographic images of the myocardium were taken with an IGE STAR gamma camera with a medium energy parallel hole collimator three hours after the MIBG injection. A single 180° pass of 32 steps with 45 s/step (64 × 64 matrix), was taken starting at a 45° lateral posterior oblique projection and going anticlockwise. The tomographic image raw counts were analysed by the STAR computer system and tomographic slices were reconstructed after visually identifying the long axis of the left ventricle. Slices were generated parallel to the short axis of the ventricle and neither scatter nor absorption corrections were applied. Sixteen tomographic slices starting from the left ventricular apex to the base of the heart were reconstructed. These were then used to generate bull's-eye target plots to display the data using the Emory University program as implemented in the IGE STAR system. The uptake from the apex formed the centre of the bull's-eye target and subsequent slices were superimposed as successive rings of the target. This allows the large amount of information acquired to be presented in a single image. All the patients in the control group with normal coronary anatomy were scanned with thallium-201 three days before or after the MIBG scan. The procedure was exactly as for the MIBG scan except that 1 MBq/kg of body weight of thallous chloride was used instead of the MIBG and immediate and delayed (three hour redistribution) images were acquired. In a pilot study, five patients with VT associated with a "clinically normal" heart also underwent thallium-201 scanning and the data for these is in the results.

STATISTICAL ANALYSIS

Figure 1 shows the bull's-eye image was divided into four equal quadrants. In all scans, the data in the inferior quadrants were not used due to the frequent presence of artifact (see results). The ratio of the counts in the superior two quadrants (posterior (representing the anterolateral free wall) / anterior (representing the anteroseptal region)) was calculated. The mean ± 2SD of the ratio of counts was 0·99 and 1·24 in the control group of patients and therefore levels of 0·98 and 1·25 were used as the cut off values for a normal ratio defining a symmetrical distribution of emission counts. Differences between the groups were examined by the Fisher exact test and *t* tests as appropriate.

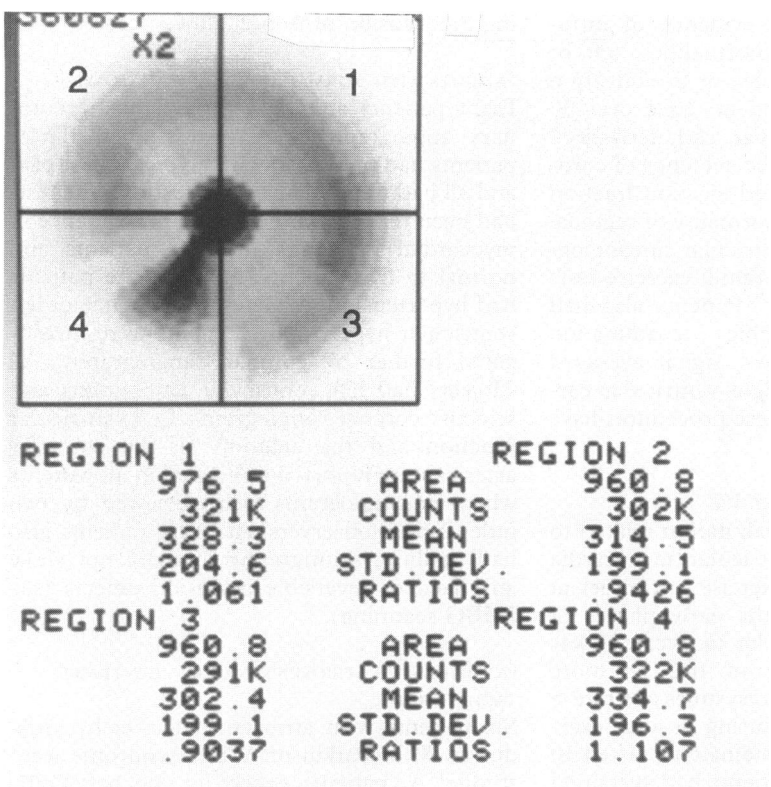

Figure 1 Subdivision of the bull's-eye target plot into 4 quadrants (patient 12, control group, table 3). A scale that represents increasing counts with increasing darkness is shown on the left in this and in all subsequent scans.

Results

Tables 1, 2 and 3 give the clinical details of the patient groups studied. The MIBG images from the subjects with Wolff-Parkinson-White syndrome and patients with normal coronary arteries showed the following features. The MIBG scan was not homogeneous in all segments and there was reduced uptake in the inferior segments unless these were occupied by high intensity artifacts from spleen or liver

Table 1 Patient details, results of exercise tests, influence of isoprenaline infusion, and cardiac MIBG distribution in patients with VT related to exercise

Patient	*Age*	*Sex*	*Spontaneous VT configuration/ axis*	*Exercise induction*	*Isoprenaline effect*	*Q1*	*Q2*	*Q3*	*Q4*	*Ratio Q1/Q2*	*Comment*
1	49	M	LBBB/I	NS	Enhanced ind	62	37	36	44	1·69	—
2	37	F	LBBB/I	S	Enhanced ind	124	80	89	145	1·55	L/S
3	30	M	LBBB/I	NS	Spontaneous ind	198	121	112	142	1·63	L/S
4	29	M	LBBB/I	S	Enhanced ind	292	255	248	309	1·15	L/S
5	43	F	LBBB/I	S	Enhanced ind	1108	789	1206	1056	1·40	L/S
6	30	M	LBBB/Sup	S	Enhanced ind	127	117	105	113	1·09	L/S
7	44	F	RBBB/Sup	S	Non-ind	134	142	138	179	0·95	L/S
8	45	F	LBBB/I	NS	Spontaneous ind	133	95	125	133	1·40	—

LBBB, left bundle branch block; RBBB, right bundle branch block: I, inferior; Sup, superior; NS, non-sustained; S, sustained; Enhanced ind, ventricular tachycardia inducible with a less aggressive stimulation protocol; Spontaneous ind, ventricular tachycardia induced during or shortly after the end of infusion of isoprenaline; non-ind, not inducible before and after isoprenaline. Q1, Q2, Q3, Q4, the counts in the quadrants (× 1000); L/S, artefact from liver or spleen uptake in the inferior quadrants.

Table 2 As table 1 in patients with VT not related to exercise

Patient	*Age*	*Sex*	*Spontaneous VT configuration/ axis*	*Exercise induction*	*Isoprenaline effect*	*Q1*	*Q2*	*Q3*	*Q4*	*Ratio Q1/Q2*	*Comment*
1	49	M	RBBB/I	—	Non-ind	97	86	77	78	1·14	—
2	44	M	LBBB/I	—	Non-ind	84	64	47	62	1·31	—
3	28	M	LBBB/I	—	Non-ind	2089	1329	892	1573	1·57	—
4	53	M	RBBB/Sup	—	No effect	227	190	202	172	1·20	L/S
5	17	M	RBBB/I	—	Non-ind	244	221	224	254	1·10	L/S
6	65	M	RBBB/I	—	Non-ind	191	195	114	128	0·98	L/S
7	51	F	LBBB/I	—	Non-ind	2062	1715	1614	1904	1·20	L/S

Non-ind, VT non-inducible. See footnote to table 1 for other abbreviations.

Table 3 Details in control group

Patient	*Age*	*Sex*	*Diagnosis*	*Site of pathway*	*Thallium*	*Q1*	*Q2*	*Q3*	*Q4*	*Ratio Q1/Q2*	*Comment*
1	43	M	WPW	Left free wall	—	2031	1925	1463	1430	1·06	—
2	27	M	WPW	Left posteroseptal	—	278	262	242	231	1·06	L/S
3	28	F	WPW	Left free wall(c)	—	2214	1902	1872	2117	1·16	11o'clock
4	23	M	WPW	Left posteroseptal	—	141	125	140	132	1·13	L/S
5	21	M	WPW	Left free wall	—	307	274	227	253	1·12	—
6	35	F	WPW	Left free wall	—	237	190	211	248	1·24	L/S
7	50	M	Normal	—	Normal	244	204	180	208	1·20	L/S
8	59	M	Normal	—	Normal	121	100	75	66	1·22	11 o'clock
9	53	M	Normal	—	Normal	198	192	143	163	1·03	—
10	57	M	Normal	—	Normal	227	198	205	265	1·15	L/S
11	48	F	Normal	—	Normal	445	372	320	359	1·12	11 o'clock
12	45	F	Normal	—	Normal	321	302	291	332	1·06	L/S
13	53	F	Normal	—	Normal	208	196	191	259	1·06	L/S
14	59	F	Normal	—	Normal	87	79	84	85	1·11	L/S

WPW, Wolff-Parkinson-White syndrome; 11 o'clock, a reduction of counts in this region of the bull's-eye plot. See footnote to table 1 for other abbreviations.

uptake. Because of the high incidence of artifacts in this area (in 18 patients, 62%), these quadrants were not used for further analyses in any of the scans. The wall of the superior anterior and posterior quadrants showed roughly equal MIBG uptake in normal patients (figure 2). In ten of the normal group of patients, there was an area of reduced uptake at roughly 11 o'clock on the bull's-eye plot. The reasons for this area of reduced uptake are not clear, but the papillary muscles receive a rich supply of sympathetic terminals and the intermediate area that has less sympathetic innervation would therefore appear less intense. The important finding seems to be a balanced sympathetic supply around this area of lower uptake in the normal patients and the ratio of the counts in the superior segments was in the range 0·98–1·25 in all the patients of the control group. The apex and the base of the heart had a less intense MIBG uptake than the intermediate portions of the heart as reported in previous studies.[11]

In the patients with exercise induced VT, a high proportion of patients (75·0%) showed an asymmetrical sympathetic supply to the myocardium with the counts being higher in the posterior wall and reduced on the septal surface (fig 3) in all patients except one who showed evidence of reduced counts on the posterior surface. This imbalanced supply was also found in 28·6% of patients with non-exercise induced VT. The prevalence of asymmetrical scans was statistically greater in patients with exercise induced VT when compared with control patients (Fisher's exact test

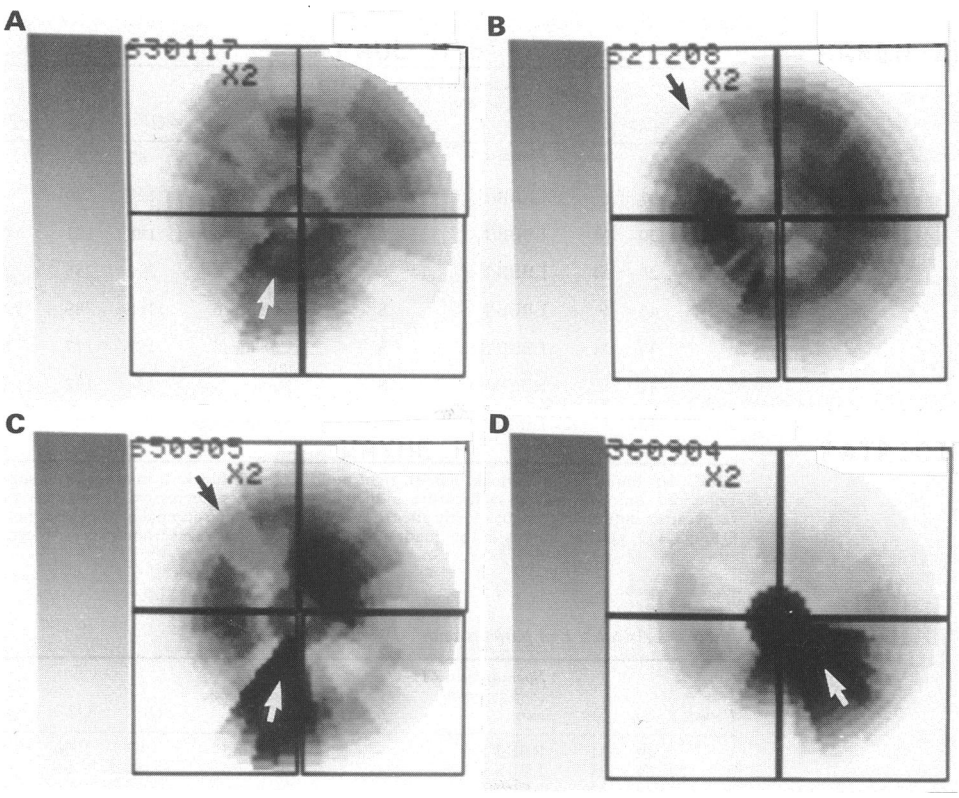

Figure 2 Four typical MIBG scans from patients in the control group (patients 2, 3, 4 and 13, control group, table 3). The scans (A, C and D) show artefact (white arrow) in the lower portion of the reconstruction that is due to liver uptake in scans A and C and spleen uptake in scan D. Uptake in the 10 o'clock region (black arrow) is also reduced in scans A and D. All scans show symmetry of uptake in the septal and posterior wall of the left ventricle.

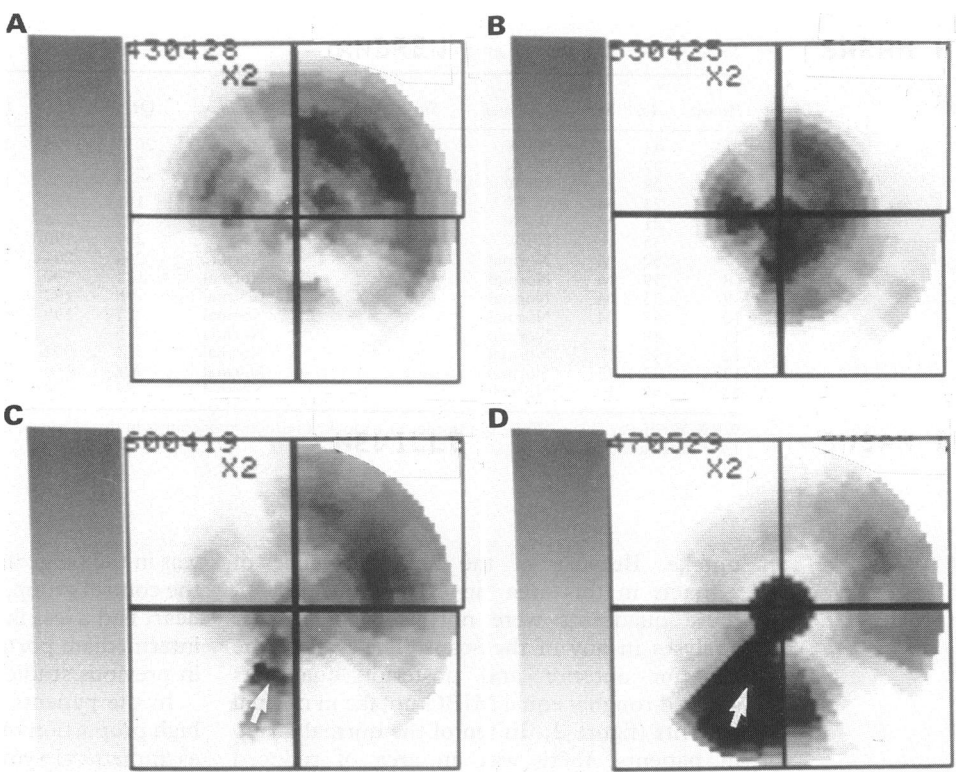

Figure 3 Four typical MIBG scans from patients with ventricular tachycardia (patients 2, 3 and 5, table 1; patient 2, table 2). The asymmetry of the sympathetic supply to the septal and posterior portion of the left ventricle is apparent in all scans. The white arrows indicate the liver artefact in scans C and D.

= 8·6, p < 0·001), but did not differ in patients with VT unrelated to exercise (Fisher's exact test = 1·9, p = 0·18). The mean ratio of counts in the superior quadrants was higher in patients with exercise induced VT (1·36 (0·27)) when compared with controls (2·22 (0·065)), (t = 3·4, p < 0·001), and was also higher in patients with VT unrelated to exercise (1·21 (0·19)) when compared with controls (t = 1·99, p = 0·03). It is notable that the pattern

of septal reduction of counts was found only in patients with VT of left bundle branch block - like configuration with an inferior axis suggesting that these arise from the right ventricular outflow tract. The one patient with reduction of counts in the posterior quadrant had VT of right bundle block-like configuration with a superior axis. There was no obvious relation between the presence of asymmetrical scans and the presence of histological abnormalities of the right ventricle. In five patients from the patients with ventricular tachycardia associated with a "clinically normal" heart who had had thallium scans performed, none was abnormal (table 1, patient 6, ratio 1·12; patient 7, ratio 1·12; table 2, patient 5, ratio 1·16; patient 6, ratio 1·18, and patient 7, ratio 1·11). The MIBG scans were also normal in these patients.

Discussion

This study shows evidence of an abnormality of the cardiac sympathetic nerve supply in patients with VT in "clinically normal" hearts. This asymmetry is present particularly in patients with exercise induced VT and in patients with left bundle branch block-like configuration VT with an inferior axis. Our data differ from that of Wharton *et al* who studied seven patients with VT in "clinically normal" hearts where two had exercise induced VT, and only one patient had an abnormal MIBG scan.[24] This difference may result from differences in selection of the patients or interpretation of the MIBG scans. Certainly, the proportion of patients with exercise induced VT was lower than our study. There has been one report of a patient with VT associated with a "clinically normal" heart in whom there was a very abnormal scan, but the increased uptake was in the septal region.[25]

The generation of arrhythmias in cardiac muscle seems to depend on three basic mechanisms[26]: enhanced automaticity,[26-28] triggered automaticity[29] and re-entry.[30] There is evidence that sympathetic activity enhances automaticity,[31 32] triggered activity,[27 33] and the occurrence of re-entry,[34] potentiating the possibility of arrhythmias.

These mechanisms for arrhythmogenesis seem to depend upon the presence of an underlying myocardial disease such as myocardial fibrosis and disarray. In many circumstances, a localised area of cardiac tissue seems to be responsible for the genesis and maintenance of the arrhythmia and this has been regarded as the arrhythmogenic substrate. In patients after myocardial infarction, this is often in the border zone of the infarction and is characterised by islands of relatively viable muscle interspersed between bands of fibrosis. This leads to fragmentation of the activation wave front due to slowed inhomogeneous conduction.[35] Normally the regionally slowed conduction is insufficient to give rise to VT and further factors (triggers) may be required to initiate the arrhythmia. It is thought that single or multiple beats possibly initiated at a remote site are important in the initiation of re-entrant arrhythmia. Many patients with VT associated with a "clinically normal" heart show evidence of histological abnormality of the myocardium, including fibrosis and fatty infiltration suggesting an underlying substrate for the arrhythmia.[21] A recent study suggests that histological abnormalities of the myocardium may occur in the outflow tract of the right ventricle even in the presence of normal histology of cardiac biopsy in the rest of the right ventricle.[36]

There is considerable evidence that the sympathetic and parasympathetic systems interact with this underlying substrate and have important roles in the genesis of ventricular arrhythmia. Most information exists for the occurrence of ventricular fibrillation. Electrical stimulation of the brain results in ventricular arrhythmias mostly mediated by activation of the sympathetic nervous system.[37-40] Decreases in the ventricular fibrillation threshold can be induced in vagotomised animals and by direct stimulation of the cardiac nerves suggesting that these were sympathetically mediated.[41-43] Cardiac sympathetic denervation by unilateral stellectomy, however, gives paradoxical results. Left stellectomy is accompanied by an increase in the ventricular fibrillation thresholds, whereas right stellectomy results in a fall in the ventricular fibrillation threshold (that is increased vulnerability).[44-47] The sympathetic nervous system seems to be of particular importance in exercise induced cardiac arrhythmias. In dogs performing submaximal exercise, some arrhythmias occurred in intact animals and those with left stellectomy and arrhythmias were absent after bilateral stellectomy.[47] Arrhythmias were increased in dogs with a right stellectomy where the left stellate ganglion was intact and where the myocardium was denervated with the exception of the ventrolateral cardiac nerve (from the left stellate ganglion).[48] Patients who had undergone stellectomy for Raynaud's phenomenon have also been studied by exercise stress testing. Arrhythmias were uncommon in patients with left stellectomy and those with intact ganglia, whereas arrhythmias were common in those with a right stellectomy.[49] These data suggest that imbalance of the regional myocardial sympathetic nerve supply is of importance in the genesis of ventricular arrhythmias.[50] Previous studies have shown that the nerves from the left stellate ganglion supply the posteroventral surface of the left ventricle, whereas those from the right stellate ganglion supply the septal and superior surfaces.[51] Data from our MIBG scans would suggest that many patients with VT have an unbalanced, asymmetrical sympathetic nerve supply to the myocardium and this is particularly obvious in subjects with exercise induced VT. The decrease in the MIBG uptake is usually on the septal surface, which would correspond to the area supplied by the right stellate ganglion. It is not possible from this study to tell whether this is due to a loss of sympathetic terminals in the myocardium or within the stellate ganglion, although the recent data suggesting a high prevalence of histological abnormality in the

outflow tract of the right ventricle would indicate that this is a local myocardial problem.[36] The limited number of thallium scans in the patients with VT associated with a "clinically normal" heart implies that a local perfusion deficit is unlikely. We cannot, however, completely exclude this possibility as we did not have thallium scans in patients who showed abnormalities on MIBG scanning. Certainly, the presence of an asymmetrical sympathetic supply did not correspond to the presence of histological myocardial abnormalities on cardiac biopsy or the presence of late potentials that are usually associated with underlying myocardial abnormality, as evaluated in our patients.

The mechanism by which relative denervation leads to an increased propensity to arrhythmogenesis (particularly exercise induced VT) is not known. Both animal and human studies, however, show that sympathetic denervation of the myocardium results in an increase in the number of β adrenoceptor sites,[52] leading to a hypersensitivity to circulating catecholamines. This would result in areas of decreased MIBG uptake having increased receptor density and therefore being hypersensitive to endogenous or exogenous catecholamines. It is interesting to note that the area of relative denervation is on the septal surface of the ventricle. Most of the patients had left bundle branch block-like morphology VT and many of these can be mapped to the outflow tract of the right ventricle.[17] This area would correspond well with the area of relative denervation and therefore of hypersensitivity to catecholamines. This pattern was also found, however, in patients with VT unrelated to exercise, so this mechanism may also be important in this form of tachycardia.

The balance between the sympathetic and parasympathetic systems also seems to be important in the genesis of VT, but the data on the role of the parasympathetic system are less clear. Kent and Epstein found that vagal stimulation increased the threshold for ventricular fibrillation in normal and ischaemic myocardium.[53] Lown and Verrier report, however, that the vagus exerts a protective action when sympathetic activity is increased and is almost without action when sympathetic action is prevented by β adrenoceptor blockade.[54] Conversely in dogs during the arrhythmia free phase of myocardial infarction, vagal activity, or acetylcholine infusion elicited VT, an effect that was rate dependent, as it was abolished by removal of the vagally induced bradycardia.[55] There is more recent evidence that after myocardial infarction, patients who develop late arrhythmias have decreased variability in heart rate.[56] As the major component of variability of heart rate originates from parasympathetic tone, it is likely that differential changes in sympathetic and parasympathetic supply to the myocardium in the region of the infarct cause predisposition to VT. MIBG scanning performed in patients after myocardial infarction suggests that the area of sympathetic denervation extends beyond the region of the infarct and the periinfarct ischaemic region as seen by thallium scanning.[57] These data would suggest that a balanced sympathetic supply, and preservation of the sympathetic to parasympathetic relation is of importance in the maintenance of normal conduction within the myocardium. Loss of this balance, when acting upon an underlying substrate, is of importance in the genesis of tachycardia.

We have attempted to find physiological evidence of abnormality of autonomic control of the myocardium in our patients. Although the QT interval, QT_c and QT interval dynamics during exercise do not seem to differ in patients with and without exercise induced VT in "clinically normal" hearts,[58] there was some evidence of excess parasympathetic tone in patients with exercise induced VT where non-spectral measures of heart rate variability from 24 hour Holter recordings were used.[59]

We conclude that asymmetry of myocardial sympathetic nerve supply is often found in patients with VT and "clinically normal" hearts. These abnormalities seem to be more prevalent in patients with exercise induced VT. This implies that VT which originates from catecholamine sensitivity may be due to an imbalance in the sympathetic supply to the myocardium. It remains to be seen whether abnormalities of the MIBG scan are of any potential prognostic importance in this group of patients.

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