Improvement of Cardiac Neuronal Function After Carvedilol Treatment in Dilated Cardiomyopathy: A ^{123}I-MIBG Scintigraphic Study

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Carvedilol can induce important clinical and hemodynamic improvements in patients with chronic heart failure resulting from severe left ventricular (LV) dysfunction. This study examines the impact of carvedilol on cardiac neuronal function using ^{123}I-metaiodobenzylguanidine (MIBG) scintigraphy in dilated cardiomyopathy. **Methods:** Twenty-two patients with chronic heart failure (19 men, 3 women; mean age, 54 y; age range, 34–64 y) assessed as New York Hospital Association (NYHA) class II or III and with initial resting radionuclide LV ejection fractions (LVEF) < 0.40 were enrolled in the study. Patients had long histories of symptomatic LV dysfunction despite optimal diuretics and angiotensin-converting enzyme inhibitor treatment. Over a 6-mo period, 50 mg/day carvedilol was administered to these patients. Planar ^{123}I-MIBG scintigraphy provided measurements of cardiac neuronal uptake (as heart-to-mediastinum count activity ratio [HMR]), 4h after intravenous injection of 185 MBq MIBG. Hemodynamic, clinical, radionuclide LVEF and HMR data measured at the outset and after 6 mo of carvedilol were compared. **Results:** Resting heart rate decreased from 81 ± 13 to 71 ± 9 bpm (P = 0.003). After carvedilol therapy NYHA functional classification for these patients improved from 2.6 ± 0.5 to 2.3 ± 0.5 (P = 0.04), LVEF improved from 22% ± 9% to 30% ± 13% (P = 0.005), and HMR improved from 145% ± 23% to 170% ± 25% (P = 0.0001). **Conclusion:** Carvedilol induces improvements of clinical symptoms and cardiac neuronal and systolic functions in patients with dilated cardiomyopathy and chronic optimal treatment.

Key Words: carvedilol; cardiac neuronal function; dilated cardiomyopathy; metaiodobenzylguanidine; scintigraphy

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Adrenergic activation in chronic heart failure appears to have adverse effects on myocardial function (*1*). β-blockers may improve hemodynamic function in patients with heart failure caused by idiopathic cardiomyopathy (*2–4*).

Carvedilol is a potent, mildly β1-selective β-blocking agent with vasodilator and antioxidant properties related to α1-receptor blockade (*5*). A small trial of carvedilol suggested that this agent was well tolerated and improved exercise tolerance and left ventricular (LV) function (*6*). In several controlled trials of carvedilol (*6–8*), patients with heart failure caused by ischemic or idiopathic cardiomyopathies improved in New York Hospital Association (NYHA) functional class assessment, exercise tolerance, LV ejection fraction (LVEF), quality of life, and survival times (*9*).

In congestive heart failure the sympathetic nervous system is activated, as reflected by the increase in the concentration of plasma norepinephrine (NE). In addition, in the failing myocardium, neuronal uptake of noradrenaline is impaired (*10,11*). Both the enhanced release of noradrenaline and the altered cardiac neuronal uptake may be responsible for the observed downregulation of adrenoreceptors in patients with heart failure (*12*).

We applied a scintigraphic method of assessing cardiac adrenergic innervation in chronic heart failure. ^{123}I-metaiodobenzylguanidine (MIBG), an analog of NE, concentrates in adrenergic nerve endings in various regions including the heart (*13–15*). It is possible to assess myocardial presynaptic adrenergic uptake in heart diseases (myocardial infarction [*16*], idiopathic dilated cardiomyopathy [DCM] [*17,18*], pheochromocytoma [*19*], acute myocarditis [*20*], and ventricular arrhythmia [*21*]). A report from our laboratory showed that exercise rehabilitation can improve cardiac neuronal function without negative effects on systolic function in patients with ischemic cardiomyopathy and DCM (*22*).

Fukuoka et al. (*23*) showed that regional myocardial assessment using MIBG SPECT imaging can predict the functional improvement of LVEF in patients with DCM treated with metoprolol for 1 mo. In addition, Suwa et al. (*24*) showed that cardiac MIBG uptake provided a useful index of whether patients with DCM could respond to bisoprolol therapy.

Carvedilol (a third-generation β-blocker), then, might induce changes in the sympathetic nervous system in patients with heart failure caused by idiopathic DCM.

The aim of the study was to assess noninvasively the effect of 6 mo of carvedilol treatment on cardiac adrenergic function in patients with DCM, using ^{123}I-MIBG scintigraphy.

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MATERIALS AND METHODS

Study Design

The study was approved by the local Research Ethics Committee and compared patients with DCM and congestive heart failure at 2 times: baseline (t0) and after 6 mo (t6) of carvedilol treatment. The nuclear physicians conducting the scintigraphic protocol were unaware of the clinical status of the patients and also unaware of the imaging sequence.

Procedure of Carvedilol Therapy

Inclusion of Patients. Patients 18–80 y old were eligible for inclusion in the study if they had symptomatic but stable heart failure (NYHA functional class II [n = 10] or III [n = 12]) caused by DCM (as evidenced by normal coronary arteriography and endomyocardial biopsy) and a radionuclide LVEF < 0.40. Patients had histories of heart failure averaging 16 mo (range, 6–24 mo). Twenty-two consecutive patients (19 men, 3 women; mean age, 54 y; age range, 34–64 y) gave their informed consent for participation in this study. Patients were excluded if they had valvular heart disease as the cause of LV dysfunction, active myocarditis, active angina, a documented history of sustained ventricular tachycardia, symptomatic nonsustained ventricular tachycardia not adequately controlled by antiarrhythmic drugs, or second- or third-degree atrioventricular block unless equipped with a permanent pacemaker. Patients with symptomatic peripheral vascular disease, chronic obstructive lung disease, bronchial asthma, diabetes mellitus, long-term alcohol or drug abuse, or chronic renal, hepatic, hematologic, neurologic, or collagen vascular disease were excluded. Medications that could interfere with myocardial MIBG uptake, such as β-blockers, digoxin, calcium channel blockers, monoamine oxidase inhibitors, tricyclic antidepressant agents, β-agonists, reserpine, guanethidine, and antihypertensive medications were excluded (*25*).

Concomitant Medications. Permissible concomitant medications included diuretic drugs (furosemide, n = 22), angiotensin-converting enzyme (ACE) inhibitors (n = 22), anticoagulant agents (n = 4), antiplatelet agents (n = 10), nitrates (n = 4), and amiodarone (n = 6). Adjustment of cardiac medication doses was not permitted during the screening or baseline phases but was permitted when clinically indicated during the remainder of the study. All patients had optimal but tolerated doses of furosemide and ACE inhibitors within the period of 6 mo. Therefore, no significant changes in body water space that could affect the volume of distribution of MIBG occurred during the period of medication. Other noncardiac medications were administrated when appropriate.

Treatment Phases with Carvedilol

Based on the different studies described in the literature (*7–9*), medication was initiated in Hospital of Trouville-sur-mer at a dose equivalent to 6.25 mg orally every 12 h. Each time dosages were changed, vital signs were monitored for at least 2 h after the first dose was administrated. At each weekly clinic visit, patients were evaluated for symptoms and signs of worsening heart failure, hypotension, or other adverse effects possibly related to β-blocker therapy. If no adverse effects were observed, doses of carvedilol were then titrated upward at weekly intervals until either a maximal tolerated dose or the maximal allowed dose was reached. The maximal allowed dose was 25 mg twice a day for 20 patients weighing <75 kg and 50 mg twice a day for 2 patients weighing >75 kg. The maximal attained dose of study medication was then continued for a fixed-dose maintenance period of 6 mo.

During the final week of the fixed-dose maintenance period, noninvasive isotopic variables were measured again.

MIBG Imaging Procedure

Radiopharmaceuticals. The pharmacologic precursor, metaiodobenzyl guanidium sulfate, was obtained commercially (CIS Biointernational, Gif/Yvette, France). The specific activity of MIBG was 37 MBq/mL. The radiochemical purity of the radioisotope was guaranteed to exceed 99.8% by the manufacturer at the time of delivery. Thin-layer chromatography showed that the radiopharmaceutical purity of each dose exceeded 90%.

Planar Imaging Protocol. All sympathomimetic medicines that could potentially interfere with the uptake of MIBG were discontinued for at least 5 half-lives before the scintigraphic examination. In addition, patients with diabetes and chronic renal failure were excluded because of possible interference with cardiac MIBG uptake (*26,27*). Patients were pretreated with 30 drops of Lugol's solution in a cup of water 2 d before and 4 d after administration of the radiopharmaceutical. There was no pretreatment wih clonidine. One hundred eighty-five MBq ^{123}I-MIBG were administrated. Scanning was performed 4 h later for evaluation of cardiac MIBG uptake (*18,22*). Energy discrimination was provided by a 20% window centered on the 159-keV photopeak of ^{123}I. An anterior thoracic view using a γ camera equipped with a low-energy, all-purpose, large-field-of-view, parallel-hole collimator. Images were acquired using a dedicated nuclear medicine computer. The anterior view acquisition lasted for 10 min.

The uptake of MIBG to the heart was semiquantified with a region of interest (ROI) automatically drawn in each subject. The ROI was placed in the cardiac area, and an ROI of the same size was placed over the upper mediastinum to standardize cardiac uptake, as previously described (*18,22*). The mediastinum ROI was placed in the middle of the top of the lungs. The ROI was 24 × 24 pixels and the matrix frame 128 × 128. When there was cardiac inhomogeneous uptake, the ROI was placed using chest radiography. In addition, a similar amount of activity of MIBG was injected (185 ± 8 MBq) at t0 and t6.

A control value of cardiac MIBG uptake was determined in 10 healthy volunteers matched in age (mean age, 46 ± 11 y) with the group of patients. The healthy volunteers showed no sign of cardiac disease after clinical, electrocardiographic, and echocardiographic examinations.

Radionuclide LVEF Imaging

After in vivo red-blood-cell labeling with 925 MBq ^{99m}Tc, gated blood-pool scans were acquired with the same γ camera in the left anterior oblique 30°–50° view and 5°–10° caudal tilt to provide the best separation between both ventricles and atria. The cardiac cycle was divided into 24 segments. The matrix size format was 64 × 64. Five million counts per view were collected. Data were stored on a magnetic disk for subsequent analysis. LVEF was measured with semiautomatic edge detection, and counts technique was measured with a varying ROI. Fourier phase and amplitude images were generated to help trace ROIs. MIBG imaging was performed 48 h after the LVEF imaging.

Assessment of Reproducibility

We determined the interobserver and intraobserver reproducibilities of cardiac MIBG scintigraphic data. The time between the 2 evaluations was 1 wk.

Statistical Analysis

The Student t test for paired data and the Kendall τ rank correlation were used on relative differences between t6 and t0. All tests were 2-tailed.

RESULTS

Twenty-two patients were enrolled in the study. All patients completed the full study period. During the 6-mo period of carvedilol treatment, none of the patients showed any immediate adverse cardiac effects to therapy. These patients remained clinically stable during the course of the study. All patients were classified as having DCM. Drug treatment did not change during the 3 mo before study or during the study in any subject who completed the study. All patients were taking diuretics and ACE inhibitors.

The NYHA functional class improved significantly from 2.6 ± 0.5 to 2.3 ± 0.5 ($P = 0.04$) in DCM patients. Resting heart rate (mean, 81 bpm; range, 60–109 bpm) decreased significantly after carvedilol (mean, 71 bpm; range, 53–92 bpm; $P = 0.003$). However, resting systolic blood pressure did not change significantly after carvedilol therapy (mean, 109 mm Hg; range, 85–137 mm Hg, versus mean, 107 mm Hg; range 83–130 mm Hg; P = not significant [NS]). Resting diastolic blood pressure did not change significantly after carvedilol therapy (mean, 71 mm Hg; range, 69–89 mm Hg, versus mean, 69 mm Hg; range, 60–75 mm Hg; P = NS). Therefore, resting rate pressure product did not change significantly (mean, 8,688 bpm/mm Hg 10^{-3}; range, 5,871–11,882, versus mean, 8,566; range, 5,210–12,112; P = NS).

It was necessary to use the chest radiograph to locate the heart in 2 cases. Table 1 showed results for LVEF and cardiac MIBG uptake after 6 mo of carvedilol in all patients with DCM. LVEF increased in 16 patients, decreased in 4 patients, and remained the same in 2 patients. Cardiac MIBG uptake increased in 20 patients, decreased in 1 patient, and remained the same in 1 patient.

Carvedilol significantly increased LVEF by +30% (−37, +218; $P = 0.005$) and cardiac MIBG uptake by +10% (−9, +46; $P = 0.0001$).

Cardiac MIBG uptake was significantly lower in patients at both t0 and t6 than in healthy volunteers (145% ± 23% and 170% ± 25% versus 221% ± 15%, respectively; P = 0.001). Myocardial MIBG uptake was significantly lower before carvedilol (mean, 145%; range, 111%–186%), as described in chronic heart failure. However, myocardial MIBG uptake was higher at t6 (mean, 170%; range, 128%–220%) and increased significantly by 10% (−37, +218; $P = 0.0001$) after the 6-mo period of carvedilol treatment.

No significant correlations were observed between LVEF and cardiac MIBG uptake at time t0 ($r = 0.4$; $P = 0.087$) and time t6 ($r = 0.35$; $P = 0.098$). No significant correlation was observed when studying variations of relative values (Δ LVEF at t0 − LVEF at t6 versus Δ MIBG at t0 − MIBG at t6; $P = 0.5$). As an example, the effects of carvedilol on cardiac MIBG uptake in a 54-y-old patient with DCM are shown in Figures 1A and B.

TABLE 1
Scintigraphic Data for Patients at Outset (t0) and After 6 Months (t6) of Carvedilol Therapy

Patient age (y)	Sex	LVEF (%)		HMR (%)	
		t0	t6	t0	t6
63	M*	10	13	144	157
49	M	21	19	136	157
63	M*	30	19	161	176
58	M	33	39	141	205
34	M	15	29	163	176
46	M	19	23	114	154
54	M*	13	36	111	162
64	M	11	35	132	152
58	M*	23	37	141	169
50	M	39	54	184	202
50	M	31	40	167	171
62	M	25	26	155	215
53	M	19	33	125	131
57	M*	13	18	186	186
49	M	40	40	174	220
41	M	32	49	132	144
54	M*	34	57	178	191
46	M	11	08	123	128
54	M	24	31	146	180
58	M	13	19	184	168
46	F	17	13	135	157
57	F	27	25	159	175
Mean ± SD		22 ± 9	30 ± 13	145 ± 23	170 ± 25

*Patients taking amiodarone.

In the 22 patients with DCM, the intraobserver correlation for the calculation of cardiac MIBG uptake was $r = 0.99$ and the interobserver correlation was $r = 0.96$ at both t0 and t6.

DISCUSSION

We used ^{123}I-MIBG scintigraphy to assess the response of cardiac neuronal uptake to carvedilol treatment in patients with DCM. Our data suggest that cardiac neuronal uptake of ^{123}I-MIBG is significantly improved after carvedilol in patients with heart failure.

The sympathetic nervous system plays an important role in the development and progression of heart failure (*28*). Heart failure is accompanied by an increase of circulating noradrenaline concentrations, an increased neuronal release, and a reduced neuronal uptake of noradrenaline (*8,9,28*). These alterations result in an increased noradrenaline concentration in the synaptic cleft and are responsible for the myocardial β adrenoreceptor downregulation (*12*).

Cardiac MIBG Uptake in DCM

Presynaptic neuronal activity is sometimes altered with advancing age (if subjects are >65 y old) (*29*). Thus, the heart-to-mediastinum ratios seen at baseline can be affected by this physiologic mechanism and can be accounted for in assessment of MIBG uptake. However, both our volunteer

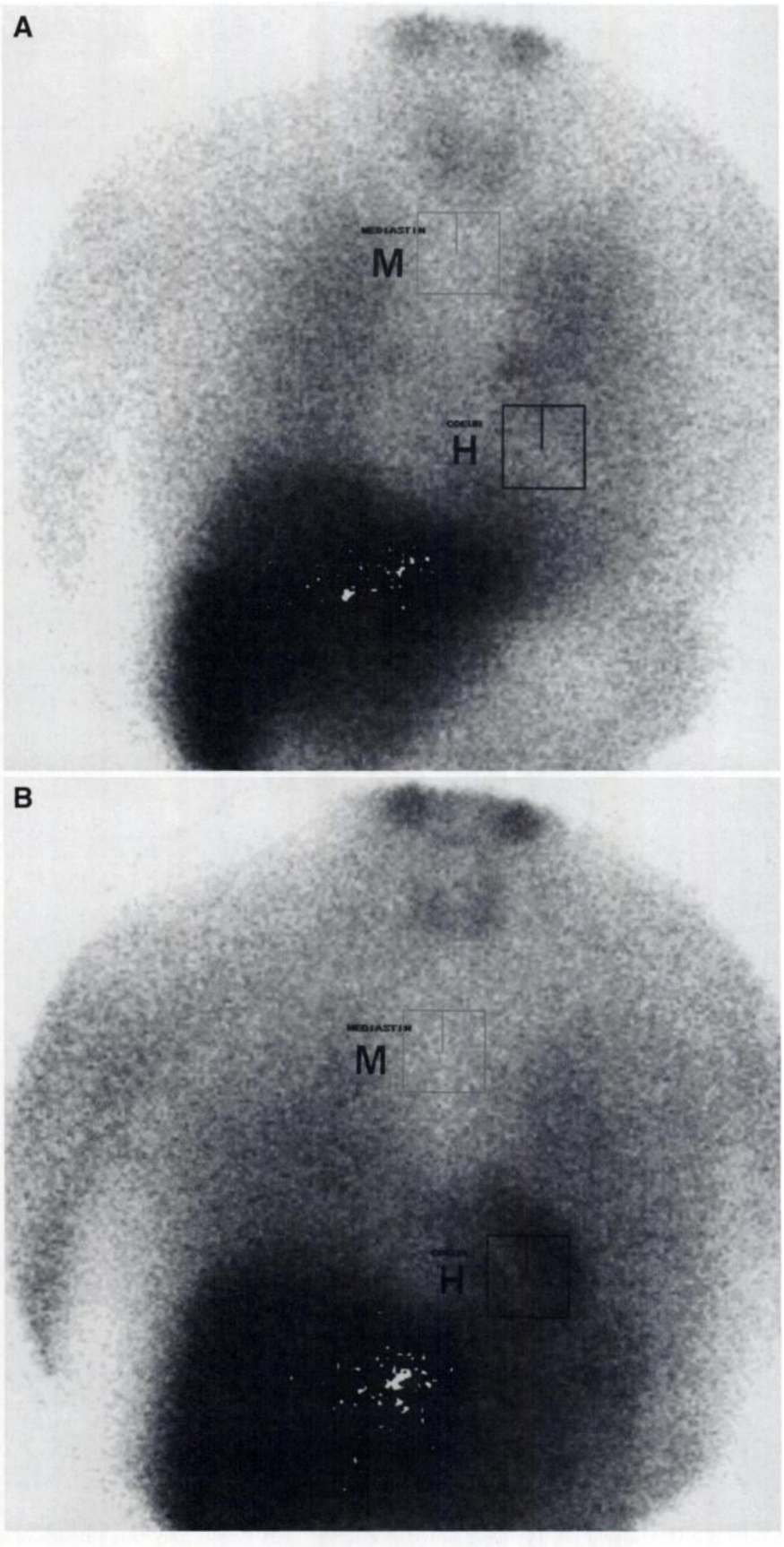

FIGURE 1. (A) Planar scintigraphic image of anterior view of chest of 54-y-old man 4 h after ^{123}I-MIBG intravenous injection and before carvedilol (t0). Heart (H) and mediastinum (M) were selected as shown to measure heart-to-mediastinum ratio activity (HMR). HMR was evaluated as 111%. (B) Planar scintigraphic image of anterior view of chest 4 h after ^{123}I-MIBG intravenous injection after carvedilol (t6). Significant increase in cardiac MIBG uptake was observed (HMR = 162%).

and our patient populations were younger than 65 y, and the decrease of cardiac MIBG uptake is the result of heart failure and not related to the age of patients.

In patients with DCM, assessment of the myocardial distribution of ^{123}I-MIBG might be used as a relatively noninvasive means of evaluating the severity of altered adrenergic innervation in the heart (*30*). The myocardial kinetics of ^{123}I-MIBG can be classified into adrenergic neuronal compartments (intravesicular accumulation) and extraneuronal compartments (extravesicular accumulation) (*31*). One study has suggested that the extraneuronal uptake does not play a role in the human heart, because there is no accumulation of ^{123}I-MIBG on either early or delayed images in the transplanted heart (*32*).

Meredith et al. (*28*) suggested that the marked increase in NE spillover from the heart in heart failure results largely from an increase in sympathetic nerve firing and neuronal release of NE and not from a failure to recapture NE.

The ^{123}I-MIBG myocardial concentration, especially the heart-to-mediastinum ratio count activity, has been shown to correlate with myocardial NE concentration and LVEF (*17*). Because MIBG shares many transport properties with NE, ^{123}I-MIBG can be used to assess cardiac adrenergic nervous system disintegrity in human heart failure (*32*). Imamura et al. (*30*) have shown that the heart-to-mediastinum activity ratio of ^{123}I-MIBG decreases in severe heart failure, and myocardial washout of ^{123}I-MIBG is accelerated in proportion to the severity of heart failure.

In heart failure, reduction of cardiac MIBG uptake may result from several causes. Increased circulating catecholamines may be competing at the NE uptake sites for MIBG in patients with heart failure (*31*). Several authors showed that in patients with DCM, heart-to-mediastinum MIBG ratio decreased with increasing plasma catecholamine levels (*17,18*). Indeed, in patients with pheochromocytoma, Nakajo et al. (*33*) found that the cardiac MIBG accumulation at 24 and 48 h after injection was inversely related to plasma concentrations and urinary excretion rate of catecholamine. In our study, plasma catecholamine concentrations were not determined. Plasma NE did not reflect cardiac sympathetic activity, because cardiac NE spillover accounts for less than 3% of total body NE release (*34*). Merlet et al. (*18*) showed that MIBG uptake decreased with normal circulating NE concentrations in patients with moderate heart failure. This finding suggested that an increase of circulating NE concentrations was not the only factor involved in the decrease of cardiac MIBG uptake.

Others causes of nonvisualization of the heart may be drugs such as labetalol or propranolol that interfere with the uptake of ^{123}I-MIBG in the heart (*25*). No patient was taking medications that might have interfered with cardiac MIBG uptake (other β-blockers, such as atenolol or metoprolol).

Myocardial MIBG uptake was measured within a long period of time without any change in the clinical situation and treatment of each patient. Therefore, it can be assumed that the condition under which MIBG uptake was measured remained the same during the course of the study.

Carvedilol and Cardiac MIBG Uptake in DCM

Carvedilol induces a significant improvement in cardiac neuronal function assessed by MIBG scintigraphy. Chizzola et al. (*35*) showed in the preliminary and randomized double-blind study that carvedilol improved cardiac adrenergic function and LVEF in patients with DCM as assessed at early (3 mo) and late (6 mo) follow-up. Different mechanisms can be involved in this finding.

Carvedilol may improve cardiac neuronal uptake of NE by increasing the ratio of NE uptake to release or increasing uptake and reducing release. However, the metabolic pathway is not well defined and remains unclear. This local effect may result in a reduced exposure of the myocytes to NE and a subsequent upregulation of the myocardial β adrenoreceptors in patients with chronic heart failure.

No isotopic method using monophotonic tracers can really evaluate directly and noninvasively both cardiac parasympathetic and sympathetic systems. Few PET studies have quantitated cardiac presynaptic activity (*36,37*). In fact, PET is probably the optimal way that the effect of carvedilol on regional myocardial sympathetic function can be evaluated.

MIBG delivery to the myocardium is largely flow limited, as is the case for several of the PET NE analogs. Improved myocardial blood flow, as a result of improved cardiac output from the carvedilol, improved ventricular function. The fact that these subjects had no coronary artery disease eliminated the possibility of differential regional delivery which might confound the issue. Also, data suggest that endothelial function in DCM is abnormal and may account for altered delivery globally. However, it is difficult to explore in vivo the endothelial function in humans. More studies are needed to address the impact of carvedilol on the presynaptic cardiac neuronal function.

It might be anticipated that myocardial MIBG uptake in fibrotic areas is lower than in normal myocardium because of sympathetic denervation. However, the current method does not assess segmental cardiac MIBG uptake and instead assesses global neuronal uptake.

These data suggest that cardiac planar MIBG scintigraphy can be used as a noninvasive method to assess changes in cardiac sympathetic neuronal function caused by carvedilol treatment in chronic heart failure, even in instances in which the variation of MIBG uptake was moderate.

Carvedilol and Hemodynamic and Systolic Functions

Metra et al. (*6*) randomly assigned 40 patients with NYHA class II or III heart failure and LVEF $< 35\%$ to carvedilol or placebo. Compared with placebo, 3 mo of carvedilol produced improvement in pulmonary artery and pulmonary capillary wedge pressures, stroke volume, and stroke volume indices; submaximal exercise capacity; quality-of-life score; and NYHA functional class. Carvedilol also improved resting LVEF from 20% to 30%. In addition,

Olsen et al. (*7*) evaluated carvedilol in a randomized, placebo-controlled trial in 60 patients whose NYHA assessments ranged from class II to intravenous heart failure. The carvedilol group improved in symptom score, pulmonary artery and pulmonary capillary wedge pressures, stroke volume, and LV stroke work. LVEF increased with carvedilol from 21% to 32%. Thus, results of these trials have shown consistent improvement in hemodynamics but inconsistent results in exercise tolerance. In our study, we also observed an improvement in NYHA functional class, a reduction in resting heart rate, and an improvement in LVEF from 22% to 30%.

The improved LV function resulting from carvedilol therapy might also improve cardiac sympathetic activity. However, it is unclear whether LVEF changed as much compared with the small but significant change in MIBG uptake.

Carvedilol might indirectly confer benefits on cardiac sympathetic activity. However, the absence of significant correlation between cardiac MIBG uptake and LVEF can be explained by the fact that neuronal adrenergic uptake is not a major parameter accounting for the determination of LV systolic function. The MIBG ratio may reflect 1 of the mechanisms of cardiac neuronal function. In our study, there is no evidence of improvement of MIBG uptake in patients with the lowest LVEF or the poorest clinical state. It is difficult to recommend that such patients be receiving carvedilol. However, it is of paramount importance to determine in additional randomized studies who will and will not respond to carvedilol.

Comparison with Other Therapeutic Approaches in DCM

ACE Inhibitors. In patients with congestive heart failure, the cardiac MIBG uptake score is a useful index for evaluating the stage of the disease and the responses to medications such as ACE inhibitors (*39,40*). ACE inhibitors (in this study, enalapril) seemed to improve cardiac sympathetic neuronal uptake function but did not significantly affect plasma noradrenaline concentrations in patients with moderate heart failure.

Cardiac Rehabilitation. Exercise rehabilitation (*22*) can improve cardiac neuronal function in patients with ischemic and dilated cardiomyopathy within a 6-mo period of training. The relative change of cardiac MIBG uptake was +17% (−20, +47) without change of LVEF after 6 mo of rehabilitation. In this study, no patient underwent exercise rehabilitation.

Limitations of Study

A possible limitation of the study is the small number of patients included. Because each patient served as his or her own reference, a placebo-treated control population was not studied. This was considered appropriate, because no subjective endpoints were used. All variables were assessed automatically (except for NYHA functional class) and underwent a masked analysis. Having the ROIs in different locations on the separate studies may contribute error in determining heart-to-mediastinum ratios. It should be interesting in acquiring dynamic images during the first few minutes after the MIBG injection which should have provided better localization of the heart.

It was of great importance that no myocardial ischemic events that could increase adrenergic stimulation and interfere with MIBG uptake occurred during the period of treatment. No patients with serious ventricular arrhythmias were recruited; hence, it may be argued that these patients were not truly representative of a general DCM population.

Assessment of changes of plasma catecholamine levels after carvedilol would permit more precise interpretation of cardiac MIBG uptake in patients with DCM. However, Merlet et al. (*18*) showed that the competition between plasma catecholamines and MIBG uptake is not the major mechanism underlying abnormalities of cardiac neuronal function.

No data are available on myocardial perfusion before and after carvedilol treatment. Some heterogeneous perfusions have been described in DCM and may result in changed delivery of MIBG to hypoperfused areas and, thus, modified cardiac MIBG uptake.

Because amiodarone has blocking properties, we looked at the 6 patients who were receiving amiodarone and did not see any difference in terms of cardiac MIBG uptake and LVEF between these patients and the larger study group.

CONCLUSION

These data suggest that cardiac MIBG scintigraphy can be used as a noninvasive method to assess changes in cardiac sympathetic neuronal function caused by pharmacologic intervention. Long-term treatment with carvedilol primarily improves cardiac neuronal and systolic functions in patients with DCM. Future studies must determine the relation between cardiac MIBG uptake and the beneficial effects of carvedilol on mortality and morbidity.

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