Impairment of Cardiac Neuronal Function in Acute Myocarditis: Iodine-123-MIBG Scintigraphy Study

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Abnormalities of norepinephrine uptake have been found to reflect impairment in adrenergic nerve function that has influenced the cardiac outcome of patients with heart failure. The aim of this study was to explore the cardiac neuronal function by using ^{123}I-metaiodobenzylguanidine (MIBG) scintigraphy in patients with acute myocarditis. **Methods:** We studied 15 patients (age range 42 ± 10 yr) with clinical, biological, electrocardiographic and radionuclide left ventricular ejection fraction (LVEF) (41% ± 7%) data indicating myocarditis and 10 normal subjects (age range 36 ± 7 yr, mean radionuclide LVEF 69% ± 8%, $p < 0.05$). Fourteen patients had positive histologic findings of myocarditis and 1 had nonspecific histological data. All patients underwent planar cardiac imaging after intravenous injection of 185 MBq ^{123}I-MIBG and right ventricular biopsy within 7 days. A chest anterior view was acquired 4 hr later. Heart-to-mediastinum ratio activity was measured, as previously described in our laboratory. **Results:** Significant impairment of cardiac neuronal uptake of MIBG was observed and based on a reduction of heart-to-mediastinum ratio (148% ± 16% versus 234% ± 36%, $p < 0.05$). A significant correlation was observed between LVEF and MIBG uptake in patients ($y = 1.58x + 83.7$, $r = 0.72$, $p < 0.01$). **Conclusion:** Acute myocarditis is associated with an injury of the cardiac adrenergic neuronal function. In addition to the inflammatory injury of the myocytes, the impairment of adrenergic function may be involved in the cardiac pump failure induced by myocarditis.

Key Words: myocarditis; cardiac neuronal function; metaiodobenzylguanidine; scintigraphy

J Nucl Med 1998; 39:1841–1844

Although a presumptive diagnosis of myocarditis can be made on the basis of clinical findings, the histologic demonstration of a cell infiltrate associated with necrotic or degenerative myocytes is necessary for a definitive diagnosis (*1*). Acute myocarditis is characterized histopathologically by the presence of both inflammation and necrosis (*1,2*). Right ventricular endomyocardial biopsy, although specific, is an insentive technique due to the focal nature of the condition (*2*). However, we used radionuclide imaging [metaiodobenzyguanidine (MIBG) scintigraphy] to determine cardiac neuronal function, which is an index of catecholamine uptake and storage in humans (*3–5*).

MIBG is an analog of guanethidine that is taken up by the adrenergic nerve endings and appears to share common uptake and storage mechanisms with norepinephrine (*3,4*). When labeled with ^{123}I, MIBG allows evaluation of myocardial adrenergic uptake in humans (*5*).

By using cardiac ^{123}I-MIBG imaging, cardiac adrenergic innervation in heart diseases (idiopathic dilated and ischemic cardiomyopathy) (*6–9*) and pheochromocytoma (*10*) can be assessed. To determine if acute myocarditis is associated with cardiac neuronal dysfunction, a series of patients with proven histologically acute myocarditis were evaluated prospectively with ^{123} I-MIBG scintigraphy.

Received Oct. 1, 1997; revision accepted Jan. 30, 1998.
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MATERIALS AND METHODS

Patients

Between November 1991 and June 1997, 15 patients (11 men, 4 women; age range 42 ± 10 yr) were selected because of the absence of antecedents of heart failure, clinical symptoms, electrocardiographic, biological creatine phosphokinase, echocardiographic and histologic results on biopsy (Table 1). All patients underwent right and left heart catheterization, coronary arteriography, right ventricular endomyocardial biopsy, radionuclide left ventricular ejection fraction (LVEF) and ^{123}I-MIBG scintigraphy. Normal coronary anatomy was demonstrated in all patients by selective coronary angiography. No patients had diabetes mellitus or chronic renal failure disease, which could affect ^{123}I-MIBG uptake or metabolism (*11,12*).

Twelve patients had dilated cardiomyopathy at the time of presentation with a global LVEF < 0.50 by equilibrium-gated, blood-pool imaging; the remaining 3 patients had nondilated cardiomyopathy and LVEF > 0.50. Eight patients presented with heart failure, 4 had chest pain, 1 had chest pain and ischemia on the electrocardiogram (ECG), 1 had chest pain and atrial fibrillation and 1 had chest pain and syncopa.

All patients with heart failure received diuretic and angiotensin-converting-enzyme inhibitor drugs. One patient with human immunodeficiency virus was treated with immunosuppresive therapy [prednisone at doses ranging from 20–60 mg/day and azathioprine at doses of 2 mg/kg per day and the dose was decreased with leukopenia (white blood count < 5000^3 mm)]. Prednisone was given at 1.25–1.5 mg/kg per day in divided doses. One patient with Lyme disease was treated with an appropriate antibiotic (amoxicillin).

Ten normal subjects (10 men, age range 36 ± 7 yr) were selected without antecedents of cardiac disease, no cardiac symptoms and normal ECG. They underwent radionuclide LVEF imaging and ^{123}I-MIBG scintigraphy.

Transvenous Right Ventricular Endomyocardial Biopsy and Pathologic Examination

Patients underwent right ventricular biopsy by means of the right internal jugular vein as previously described. Multiple biopsy specimens (usually five to seven, each measuring 2–5 mm in diameter) were obtained from the right ventricular septum using biotome and were fixed immediately by immersion in buffered 10% formalin (*2*). Paraffin sections were stained with hematoxylin-eosin, Masson's trichome and Congo red. Specimens were divided into three categories on the basis of light microscopic study: (a) specimens defined as showing myocarditis contained an inflammatory infiltrate adjacent to interstitial fibrosis; (b) specimens showing myocyte hypertrophy, interstitial or replacement fibrosis, or both, but no evidence of myocarditis, were classified as showing nonspecific changes (*3*); and normal specimens showed no diagnostic abnormalities. All biopsy samples were analyzed without prior knowledge of the MIBG scan results.

TABLE 1
Features of Patients with Acute Myocarditis

Age (yr)	Sex	Biopsy results	LVEF (%)	ECG	H/M Ratio (%)	CPK	Comments
45	F	+	30	SR	115	680	CP
23	M	+	52	SR	167	542	S+CP
45	M	+	41	LBBB	154	690	CHF
32	M	Toxoplasmosis	32	SR	142	1200	CHF, HIV +
30	M	Lyme disease	43	AF	138	665	CP
36	F	+	28	SR	144	988	CP
41	M	+	39	SR	136	1100	CHF
38	F	ns	43	SR	156	770	CHF
49	M	+	39	SR	139	550	CHF
52	M	+	47	AF	147	800	CHF
45	M	+	51	SR	187	740	CP
56	M	+	36	SR	151	580	CHF
32	M	+	36	SR	138	995	CHF
39	M	+	50	IS	158	1500	CP
62	F	+	42	SR	147	1470	CP
42 ± 10*			41 ± 7*		148 ± 16*	885 ± 314*	

*Mean ± s.d.

H/M = heart-to-mediastinum ratio activity; ECG = electrocardiogram; SR = sinusal rhythm; LBBB = left bundle branch block; AF = atrial fibrillation; IS = ischemia; LVEF = left ventricular ejection fraction; S = syncopa; CP = chest pain; CHF = congestive heart failure; HIV = human immunodeficiency virus; CPK = creatine phosphokinase; ns = nonspecific.

Planar Metaiodobenzylguanidine Imaging

The pharmacological precursor, meta-iodobenzyl guanidium sulfate, was obtained commercially (CIS Biointernational, Gif-sur-Yvette, France). The radiochemical purity of the radioisotope was guaranteed to exceed 99.8% by the manufacturer at the time of delivery. Thin-layer chromatography demonstrated that the radiopharmaceutical purity of each dose exceeded 90%.

All sympathomimetic medicines that could potentially interfere with the uptake of MIBG were discontinued for at least five half-lives before the procedure. Patients were pretreated with 30 drops of Lugol's solution in a cup of water 2 days before and 4 days after the administration of the radiopharmaceutical. Approximatively 185 MBq ^{123}I-MIBG were administered intravenously. Scans were performed 4 hr later for cardiac evaluation. An Elscint Apex-415 camera (Elscint, Haifa, Israel) was used, and images were acquired via a dedicated nuclear medicine computer. Energy discrimination was provided by a 20% window centered on the 159 keV photopeak of ^{123}I. The thorax was imaged in anterior view with a gamma camera equipped with low-energy, all-purpose, large-field-of-view, parallel-hole collimators.

The uptake of MIBG to the heart was semiquantified with a region of interest (ROI) manually drawn to a suitable size in each subject. The ROI was placed in the cardiac area and the same size ROI was placed in the upper mediastinum area to standardize cardiac uptake, as previously described (*8–10,13*). Cardiac uptake was measured by two independent observers unaware of the clinical status. To determine the control data, we performed MIBG myocardial scintigraphy in normal subjects with the same protocol. To evaluate whether abnormalities in MIBG uptake were confined mainly to the heart or were also present in others organs, MIBG uptake was also measured in the lungs, and the lung ratio mediastinum activity (LRM) was calculated for both patients and control subjects.

Radionuclide Left Ventricular Ejection Fraction Imaging

After in vivo red blood cell labeling with 925 MBq ^{99m}Tc, with the subjects supine, gated blood-pool scans were acquired with the same gamma camera in the left anterior oblique 30–50° projection and 50–10° caudal tilt to provide the best separation between both ventricles and the atria. The cardiac cycle was separated into 16, 64 × 64 frames, with a minimum of 300,000 counts collected in each frame. Data were stored on a magnetic disk for subsequent analysis. LVEF was measured with a semiautomatic edge detection and counts technique with a varying ROI. Fourier phase and amplitude images were generated to help trace ROIs.

The determination of LVEF was performed after optimization of medical therapy for all patients with heart failure at presentation (from 2–4 days after the acute event). Then, MIBG imaging was performed 48 hr after the LVEF imaging.

Statistical Analysis

The unpaired Student's t-test was used to evaluate differences between variables in the control group and the patients. Paired Wilcoxon and Spearman's rank correlation coefficient analysis were applied to evaluate the reproducibility of MIBG results. Statistical significance was set at a p value of 0.05. Results are expressed as the mean values ± 1 s.d.

RESULTS

Iodine-123-MIBG was administrated with no untoward reaction in any subjects. Hemodynamic parameters showed heart rate (95 ± 12 bpm), systolic blood pressure (150 ± 11 mmHg) and diastolic blood pressure (82 ± 6 mmHg), all within the normal range. The clinical comments and histologic, LVEF and cardiac ^{123} I-MIBG uptake results are listed in Table 1.

Endomyocardial Biopsy Findings

Right ventricular biopsies showed myocarditis in 12 patients. The 3 other patient's biopsies showed the presence of toxoplasma gondii, Lyme disease with interstitial congestion associated with inflammatory infiltrates and eosinophilic polymorphonuclears, and the latter showed nonspecific changes with myocyte hypertrophy and interstitial or replacement fibrosis.

Metaiodobenzylguanidine and Left Ventricular Ejection Fraction Imaging

Myocardial ^{123} I-MIBG uptake was observed in all patients, with a mean heart-to-mediastinum (H/M) ratio activity of 148% ± 16%, 4 hr after injection.

The H/M ratio of patients was decreased significantly when compared with the H/M ratio of normal subjects (234% ± 36%,

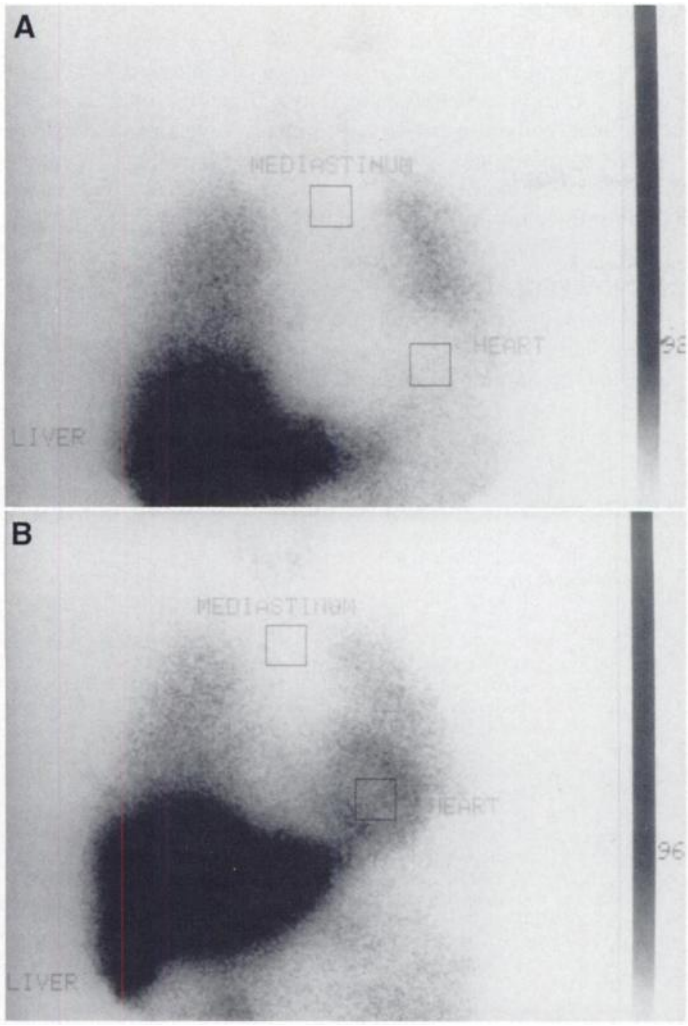

FIGURE 1. Scintigraphic image obtained in the anterior view of the chest 4 hr after ^{123}I-MIBG injection (A) in a 32-yr-old patient and (B) a 38-yr-old normal control subject. Heart and mediastinum were selected as shown on (A) and (B) to measure H/M ratio activity. Significant decrease in cardiac MIBG uptake is observed (H/M ratio: 142%) (A) in patient with acute myocarditis when compared with (B) uptake of normal control subject (H/M ratio: 223%).

$p < 0.05$). All patients, except one with biopsy-proven myocarditis, had reduction of MIBG uptake.

The LRM of MIBG uptake was similar in two groups (142% ± 12% versus 130% ± 15%, p = ns) suggesting that abnormal cardiac MIBG findings in myocarditis were predominantly confined to the heart.

LVEF in patients with acute myocarditis was reduced significantly when compared with normal subjects (41% ± 7% versus 69% ± 8%, $p < 0.05$).

Figure 1A shows a scintigraphic image of cardiac MIBG uptake in a patient with acute myocarditis (H/M ratio = 142%). Figure 1B shows a scintigraphic image of cardiac MIBG uptake in a control subject matched in age and sex (H/M ratio = 223%).

Figure 2 shows a significant correlation between MIBG uptake and LVEF in patients with acute myocarditis ($y = 1.58x + 83.7$, $r = 0.72$, $p < 0.001$).

Reproducibility of Metaiodobenzylguanidine Results

In the 10 patients with myocarditis who underwent a follow-up MIBG study, H/M ratio was 152% ± 19% on the first and 144% ± 16% on the second test (p = ns).

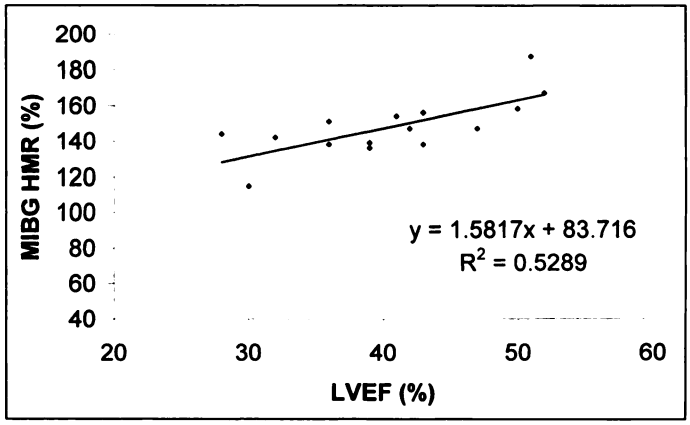

FIGURE 2. Correlation between cardiac MIBG uptake as expressed as H/M ratio and left ventricular ejection fraction in patients with acute myocarditis.

DISCUSSION

This study showed an impairment of cardiac neuronal uptake in acute myocarditis. MIBG is a guanethidine analog compound that shares uptake/retention mechanisms as norepinehrine at sympathetic nerve terminals (*5*), and myocardial scintigraphy can be used to assess the adrenergic innervation of the heart (*6,8,9*). Many studies have demonstrated the affinity of MIBG for the adrenal medulla and adrenergic nerves (*4*) resulting in pathologic cardiac MIBG uptake in humans. Images of the heart obtained 4 hr after administration of MIBG reflect cardiac neuronal activity because, at that point, a plateau value of 50% is reached in intravesicular MIBG concentration (*14*).

Metaiodobenzylguanidine Uptake in Chronic Heart Failure

Decreased myocardial MIBG accumulation has also been described in conditions in which norepinephrine content or uptake is reduced (i.e., myocardial infarction (*7*); congestive heart failure (*8–11*), either idiopathic or of other origin; cardiac denervation (*15*); and neuropathies such as diabetic autonomic neuropathy (*11*). However, when the circulating norepinephrine level is increased (i.e., pheochromocytoma), cardiac MIBG uptake is also decreased (*10*).

In the chronic stage of dilated cardiomyopathies, decreased MIBG uptake may reflect neuronal injury or adrenergic dysfunction (*8,9*). Glowniak et al. (*16*) demonstrated decreased MIBG uptake and faster MIBG washout in idiopathic dilated cardiomyopathy. Decreased MIBG uptake in these patients suggests sympathetic dysfunction, whereas rapid washout could reflect increased sympathetic neuron activity.

Metaiodobenzylguanidine Uptake in Acute Myocarditis

The abnormalities of adrenergic activity in our patients seemed to be localized in the heart, rather than being systemic, as suggested by the absence of difference between patients and control subjects in the LRM of MIBG uptake. However, urinary or plasma catecholamines concentration levels were not measured during the acute event. However, a decreased cardiac MIBG uptake associated with normal circulating norepinephrine concentration has been observed in patients with moderate heart failure (*8,9*). This finding suggested that the elevation of circulating norepinephrine concentrations was not the only factor involved in the decrease in MIBG uptake in congestive heart failure. MIBG results were highly reproducible in 10 patients who underwent a follow-up study 6 mo after the first MIBG assessment. These findings indicated the presence of an abnormal function of efferent cardiac sympathetic nerve endings during a short period after the acute myocarditis.

There are several possible mechanisms to explain the MIBG abnormalities detected in this study. Experimental work (*17,18*)

has demonstrated that cardiac MIBG defects may reflect sympathetic denervation, and clinical studies in patients with myocardial necrosis (*19,20*) or heart transplantation (*21*) have suggested that this condition can also occur in humans. However, it seems that reduction of cardiac MIBG uptake can be caused by denervation in patients with acute myocarditis.

Reduction of MIBG uptake can most likely be accounted for by functional mechanisms, such as, in particular, an increased cardiac spillover of norepinephrine (*22*), resulting in antagonistic competition with MIBG for uptake at nerve terminals.

Therefore, a reduced number of sympathetic neuron with increased amounts of interstitial fibrotic tissue together with increased MIBG turnover in the dilated myocardium could account for these phenomena.

Kinoshita et al. (*23*) showed denervation, but viable myocardium, by using ^{201}Tl and MIBG SPECT imaging after an episode of acute myocarditis in 1 patient.

Myocardial MIBG uptake may be interfered with by a variety of drugs such as adrenergic receptor antagonists, calcium antagonists and labetalol (*24,25*). However, in our series, no patients received such drugs at the time of radionuclide imaging.

In our patients with acute myocarditis, it was impossible to determine if the decreased myocardial MIBG uptake preceded deterioration of LVEF.

Study Limitations

Quantitation of myocardial MIBG activity on scintigraphic images has technical limitations. Tomographic imaging provides an opportunity to study the myocardial distribution of MIBG uptake in myocardial infarction (*7*). In this study, the decrease in MIBG uptake in patients induced difficulties in reconstructing the images, which hindered the use of tomographic imaging. Consequently, planar imaging was used to quantify the cardiac MIBG uptake.

It is impossible to make any type of quantitative statement about sympathetic nerve activity based on measurements at a single time point. Decreased activity at a single point could be due to rapid washout of MIBG and a normal initial uptake or decreased initial uptake with normal washout. This does not mean that useful data cannot be obtained from single measurements. It has been shown, for example, that decreased cardiac MIBG activity 4 hr after injection was a better predictor of survival in patients with heart failure than LVEF, cardiothoracic ratio or left ventricular end-diastolic diameter (*8,9*). Therefore, we used the single measurement point.

Decreased cardiac output of any etiology, from acute blood loss to chronic myocardial disease, will cause activation of the sympathetic nervous system. However, our patients did not have antecedents of cardiac and/or hematological diseases.

The differentiation of patients with left ventricular dysfunction due to active myocarditis from the much larger group of patients with idiopathic dilated cardiomyopathy remains difficult and currently requires endomyocardial biopsy. Therefore, we selected patients with proven histological myocarditis.

It would have been useful to have performed a greater number of repeat MIBG scans. Repeat studies can provide information of possible reversibility of cardiac neuronal function in myocarditis. It was evident that spontaneous resolution of myocarditis can occur and that resolution of myocardial necrosis, as judged by endomyocardial biopsy, could be associated with reversibility of MIBG uptake. The explanation for observed differences between MIBG and LVEF imagings and biopsy findings would require a larger study group and possible serial scans and biopsies. However, no reversibility of MIBG uptake was obtained 6 mo later in our 10 patients with myocarditis.

CONCLUSION

Our series showed that cardiac ^{123}I-MIBG scintigraphy can detect an impairment of sympathetic function and, consequently, reflects an actual change in cardiac neuronal catecholamine metabolism in patients with acute myocarditis. In addition to the inflammatory injury of the myocytes, the impairment of adrenergic function may be involved in the cardiac pump failure induced by myocarditis.

ACKNOWLEDGMENTS

We thank the technical staff from the department of cardiology and nuclear medicine for valuable assistance. This article was presented as an oral communication at the European Nuclear Medicine Congress in Copenhagen, September 1996. The session was entitled: Cardiac Innervation.

REFERENCES

1. Woodruff JF. Viral myocarditis:a review. *Am J Pathol* 1980;101:427–484.
2. Fenoglio JJ, Ursell PC, Kellogs CF, Phil M, Drusin RE, Weiss MB. Diagnosis and classification of myocarditis by endomyocardial biopsy. *N Engl J Med* 1983;308:12–18.
3. Wieland DM, Brown LE, Les Rogers W, et al. Myocardial imaging with radioiodonated norepinephrine storage analog. *J Nucl Med* 1981;22:22–31.
4. Kline RC, Swanson DP, Wieland DM, et al. Myocardial imaging in man with iodine-123 metaiodobenzylguanidine. *J Nucl Med* 1981;24:1194–1196.
5. Sisson JC, Wieland DM, Sherman P, et al. Metaiodobenzylguanidine as an index of adrenergic nervous system integrity and function. *J Nucl Med* 1987;28:1620–1624.
6. Schofer J, Spelman R, Schubert A, et al. Iodine-123 metaiobenzylguanidine scintigraphy: a noninvasive method to demonstrate myocardial adrenergic nervous system desintigrity in patients with idiopathic dilated cardiomyopathy. *J Am Coll Cardiol* 1988;12:1252–1258.
7. Henderson EB, Kahn JK, Corbett JR, et al. Abnormal iodine-123 metaiodobenzylguanidine myocardial washout and distribution may reflect myocardial adrenergic derangement in patients with congestive cardiomyopathy. *Circulation* 1988;78:1192–1199.
8. Merlet P, Dubois Randé JL, Adnot S, et al. Myocardial beta adrenergic desensitization and neuronal norepinehrine uptake function in idiopathic cardiomyopathy. *J Cardiovasc Pharmacol* 1991;19:10–16.
9. Merlet P, Valette H, Dubois Randé JL, et al. Prognosis value of cardiac metaiodobenzylguanidine imaging in patients with heart failure. *J Nucl Med* 1992;33:471–477.
10. Agostini D, Scanu P, Babatasi G, et al. Pheochromocytoma and catecholamine induced impairment of cardiac neuronal function. *Am Heart J* 1995;130:1128–1130.
11. Mantysaari M, Kukka J, Mustonen J, et al. Noninvasive detection of cardiac sympathetic nervous dysfunction in diabetes patients using ^{123}I-metaiodobenzylguanidine. *Diabetes* 1992;41:1069–1075.
12. Miyanaga H, Yoneyama S, Kamitani T, et al. Abnormal myocardial uptake and clearance of ^{123}I-labeled metaiodobenzylguanidine in patients with chronic renal failure and autonomic dysfunction. *J Nucl Cardiol* 1996;3:508–515.
13. Agostini D, Babatasi G, Scanu P, et al. Valeur de la Scintigraphie myocardique à la ^{123}I-MIBG et insuffisance cardiaque congestive:mise au point. *Ann Cardiol Angéiol* 1997;46:293–302.
14. Nakajo M, Shimabukuro K, Yoshimura H, et al. Iodine-131 metaiodobenzylguanidine intra and extravesicular accumulation in the rat heart. *J Nucl Med* 1986;27:84–89.
15. Dae MW, De Marco T, Botvinick EH, et al. Scintigraphic assessment of MIBG uptake in globally denervated human and canine hearts:implications for clinical studies. *J Nucl Med* 1992;33:1444–1450.
16. Glowniak JV, Turner FE, Gray LL, et al. Iodine-123 metaiodobenzylguanidine imaging of the heart in idiopathic congestive cardiomyopathy and cardiac transplants. *J Nucl Med* 1989;30:1182–1191.
17. Minardo JD, Tuli MM, Mock BH, et al. Scintigraphic and electrophysiological evidence of canine myocardial sympathetic denervation and reinnervation produced by myocardial infarction or phenol application. *Circulation* 1988;78:1008–1019.
18. Iwasaki T, Suzuki T, Tateno M, Sasaki Y, Oshima S, Imai S. Dual-tracer autoradiography with thallium-201 and iodine-125-metaiodobenzylguanidine in experimental myocardial infarction of rat. *J Nucl Med* 1996;37:680–684.
19. Mc Ghie AI, Corbett JR, Akers MS, et al. Regional cardiac adrenergic function using iodine-123-metaiodobenzylguanidine tomographic imaging after acute myocardial infarction. *J Am Coll Cardiol* 1991;67:236–242.
20. Hartikainen J, Kuikka J, Lansimies E, Pyorala K. Sympathetic reinnervation after acute myocardial infarction. *Am J Cardiol* 1996;77:5–9.
21. De Marco T, Dae M, Yuen-Gree MSF, et al. Iodine-123-metaiodobenzylguanidine scintigraphic assessment of the transplanted human heart: evidence for late reinnervation. *J Am Coll Cardiol* 1995;25:927–931.
22. Imamura Y, Ando H, Mitsuoka W, et al. Iodine-123-metaiodobenzylguanidine images reflect myocardial adrenergic nervous activity in congestive heart failure independent of underlying cause. *J Am Coll Cardiol* 1995;25:1594–1599.
23. Kinoshita T, Itoh H, Takahashi K, Takeda H. Myocardial imaging with iodine-123-MIBG and thallium-201 demonstrates denervated but viable myocardium in a patient with myocarditis. *Clin Nucl Med* 1994;19:649–650.
24. Fagret D, Wolf J, Comet M. Myocardial uptake of meta (^{123}I)-iodobenzylguanidine (^{123}I-MIBG) in patients with myocardial infarct. *Eur J Nucl Med* 1989;15:624–628.
25. Huguet F, Fagret D, Caillet M, et al. Interaction of metaiodobenzylguanidine with cardioactive drugs:an in vitro study comparison. *Eur J Nucl Med* 1996;23:546–549.