ACE Inhibition Reduces Cardiac Iodine-123-MIBG Release in Heart Failure

Yasuchika Takeishi, Hiroyuki Atsumi, Satomi Fujiwara, Kazuei Takahashi and Hitonobu Tomoike
First Department of Internal Medicine and Division of Radiology, Yamagata University School of Medicine, Yamagata, Japan

Radioiodinated metaiodobenzylguanidine (^{123}I-MIBG), an analog of norepinephrine, has been used to assess cardiac sympathetic nerve activity. Decreased myocardial accumulation and enhanced washout of ^{123}I-MIBG have been reported in patients with congestive heart failure (CHF). The purpose of this study was to determine whether angiotensin converting enzyme (ACE) inhibition reduced ^{123}I-MIBG release and improved cardiac ^{123}I-MIBG accumulation in patients with CHF. **Methods:** Twenty-nine patients receiving conventional treatment for CHF, New York Heart Association (NYHA) functional class 2–3, were studied. Nineteen patients received additional treatment with enalapril, an ACE inhibitor, and 10 patients who were treated with conventional therapy alone were defined as a control group. Iodine-123-MIBG imaging and echocardiography were performed on all patients before treatment and repeated after 9.1 ± 3.0 mo of treatment. Images were obtained 30 min and 4 hr after injection of ^{123}I-MIBG, and a heart to mediastinum (H/M) ratio was defined to quantify cardiac ^{123}I-MIBG uptake as a fraction of the mean counts per pixel in the heart divided by those in the mediastinum. The washout rate of ^{123}I-MIBG from the heart was calculated as follows: (early counts − delayed counts)/early counts × 100 (%). **Results:** In patients with enalapril group, the H/M ratio of ^{123}I-MIBG was increased after treatment (early image: 1.60 ± 0.22 vs. 1.73 ± 0.28, $p < 0.05$, delayed image: 1.63 ± 0.28 vs. 1.82 ± 0.33, $p < 0.01$). The washout rate of ^{123}I-MIBG was reduced from 38% ± 11% to 30% ± 12% after treatment ($p < 0.01$). However in the conventional therapy group, the H/M ratios in the early and delayed images (early image: 1.58 ± 0.31 vs. 1.52 ± 0.23, delayed image: 1.49 ± 0.27 vs. 1.49 ± 0.25) and the washout rate (34% ± 8% vs. 33% ± 7%) remained unchanged after treatment. In patients with an increased H/M ratio of enalapril group (n = 13), a left ventricular ejection fraction increased from 48% ± 12% to 55% ± 9% ($p < 0.01$) after treatment. **Conclusion:** ACE inhibition reduces cardiac ^{123}I-MIBG release and thus lowers cardiac sympathetic nerve activity. Iodine-123-MIBG may be helpful in evaluating the therapeutic effects of ACE inhibition on the cardiac sympathetic nervous system in patients with CHF.

Key Words: iodine-123-MIBG; heart failure; angiotensin-converting enzyme inhibitor

J Nucl Med 1997; 38:1085–1089

Radioiodinated metaiodobenzylguanidine (^{123}I-MIBG), an analog of norepinephrine, has been used to evaluate cardiac sympathetic nerve activity (*1–3*). Reduced myocardial accumulation and enhanced washout of ^{123}I-MIBG have been reported in patients with congestive heart failure (CHF) of various causes (*4–7*). These abnormal findings have been considered to reflect a decreased uptake and accelerated release of norepinephrine from adrenergic nerve endings. It has been also known that a reduced heart-to-mediastinum ratio of ^{123}I-MIBG is the best noninvasive predictor of survival of patients with CHF (*8*). CHF is a major and growing public health problem, and the prognosis of CHF still remains poor (*9*). The prevention trials, such as the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS (*10*)) and the Studies of Left Ventricular Dysfunction (SOLVD (*11*)), have clearly shown that therapy with an angiotensin converting enzyme (ACE) inhibitor improves left ventricular ejection fraction and exercise tolerance and reduces mortality, the incidence of heart failure and the rate of related hospitalizations in patients with CHF. On the basis of these findings, ACE inhibitors have been used increasingly for treatment of CHF. Since the activated renin-angiotensin system in CHF facilitates cardiac norepinephrine release, treatment with an ACE inhibitor may affect cardiac sympathetic activity (*12,13*). However, the effect of ACE inhibition to cardiac ^{123}I-MIBG kinetics has not been examined rigorously in in vivo studies.

The purpose of this study was to determine the effect of ACE inhibition on cardiac accumulation and washout of ^{123}I-MIBG in patients with CHF. Iodine-123-MIBG imaging and echocardiography were performed before and after treatment with enalapril, an ACE inhibitor, in patients with CHF, and these findings were compared with those treated with conventional therapy alone.

MATERIALS AND METHODS

Subjects and Study Protocol

We examined 29 patients with CHF. The subjects consisted of 23 men and 6 women with a mean age of 59 yr. The symptoms of heart failure graded 2–3 in the functional classification of the New York Heart Association (NYHA) had persisted for more than 6 mo in all patients. The causes of heart failure were idiopathic dilated cardiomyopathy (n = 13), previous myocardial infarction (n = 8), valvular disease (n = 7) and hypertension (n = 1). All patients were taking drugs other than an ACE inhibitor as part of conventional therapy for CHF such as digitalis, diuretics and vasodilators. Treatment with enalapril was started in 19 patients with a dose of 5 mg a day and increased to 10 mg a day. Ten patients who were treated with conventional therapy alone were defined as a control group. There were no differences in patients' characteristics between the two groups (Table 1). Iodine-123-MIBG imaging and echocardiography were performed in all patients before treatment and repeated after 9.1 ± 3.0 mo treatment. The study protocol was approved by the Committee of Human Research of Yamagata University Hospital. Written informed consent was obtained from all patients.

Iodine-123-MIBG Imaging

After an overnight fast, a dose of 148 MBq ^{123}I-MIBG was injected in the resting supine position. A 5-min static acquisition was performed 30 min and 4 hr after the ^{123}I-MIBG administration in the anterior view, as previously described (*14*). All images were obtained on a rotating gamma camera equipped with a parallel-hole, high-resolution collimator. Energy discrimination was provided by a 15% window centered at 159 keV. Data processing was performed on a nuclear medicine computer system. A square ROI (7 × 7 pixels in size) was defined for areas of the left ventricle with the peak count density as previously described (*8,14*). Another ROI

Received Jul. 25, 1996; revision accepted Nov. 7, 1996.
For correspondence or reprints contact: Yasuchika Takeishi, MD, First Department of Internal Medicine, Yamagata University School of Medicine, 2-2-2 Iida-Nishi, Yamagata, 990-23 Japan.

TABLE 1
Baseline Characteristics of Patients in the Two Treatment Groups

	Conventional therapy (n = 100)	Angiotensine-converting enzyme inhibition (n = 19)
Age, mean	59 yr	58 yr
Sex (male)	8 (80%)	15 (79%)
Blood pressure		
Systolic, mean	123 mm Hg	119 mm Hg
Diastolic, mean	78 mm Hg	76 mm Hg
Heart rate, mean	78 bpm	80 bpm
NYHA* functional class		
II	4 (40%)	10 (53%)
III	6 (60%)	9 (47%)
Atrial fibrillation	3 (30%)	7 (37%)
Disease history		
Cardiomyopathy	4 (40%)	9 (48%)
Myocardial infarction	3 (30%)	5 (26%)
Valvular	3 (30%)	4 (21%)
Hypertensive	0 (0%)	1 (5%)
Ejection fraction (%)	46 ± 15	44 ± 14
Drug therapy		
Digitalis	8 (80%)	14 (74%)
Diuretics	10 (100%)	18 (95%)
Vasodilators		
Any	4 (40%)	7 (37%)
Nitrate	3 (30%)	7 (37%)
Beta blocker	1 (10%)	2 (11%)
Antiplatelet agents	5 (50%)	12 (63%)
Anti-arrhythmic agents	2 (20%)	5 (26%)

*NYHA = New York Heart Association.

was placed over the upper mediastinum area. The heart-to-mediastinum ratio (H/M ratio) was calculated to quantify cardiac ^{123}I-MIBG uptake as a fraction of the mean counts per pixel in the heart divided by those in the mediastinum.

The washout rate of ^{123}I-MIBG from the myocardium was calculated from the absolute counts in early (Ce) and delayed (Cd) images as follows:

$$\text{Washout rate (\%)} = (Ce - Cd \times Cf) \times 100/Ce.$$

$$Cf = 1/(1/2)^x,\ x = (Td - Te)/13.2$$

where Td is the time for the delayed image and Te is the time for the early image.

Echocardiography

The heart was imaged by an experienced cardiologist. Echocardiograms of the left ventricle from the parasternal long- and short-axis views and apical 4- and 2-chamber views were recorded in the standard manner. A left ventricular ejection fraction was calculated according to the American Society of Echocardiography criteria with the area length method or Simpson's rule (*15*).

Statistical Analysis

Data were reported in mean ± 1 s.d. Continuous variables were compared by a Wilcoxon matched-pairs ranks test, and the differences in proportion (categorical variables) were examined by a Fisher's exact probability test. A p value < 0.05 was considered significant.

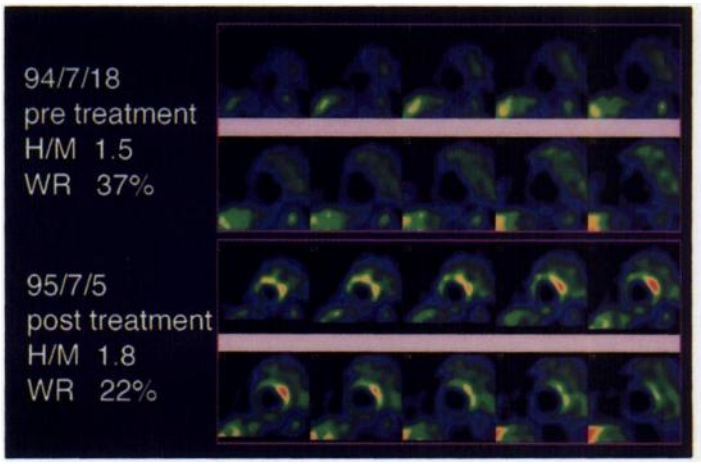

FIGURE 1. Iodine-123-MIBG images of a patient with dilated cardiomyopathy. Before treatment, cardiac ^{123}I-MIBG uptake was markedly reduced (H/M ratio 1.5). After treatment with an ACE inhibitor for about 12 mo, ^{123}I-MIBG accumulation increased (H/M ratio 1.8). Iodine-123-MIBG washout decreased from 37% to 22% after treatment.

RESULTS

Case Presentation

Figure 1 shows resting ^{123}I-MIBG images of a patient with dilated cardiomyopathy. Left ventricular ejection fraction was 43% and cardiac ^{123}I-MIBG uptake was markedly decreased. A H/M ratio was 1.5, and the washout rate was 37%. After treatment with enalapril for 12 mo, a H/M ratio was increased to 1.8, and the washout rate was reduced to 22%.

Changes in Iodine-123-MIBG Uptake and Washout Rate after Treatment

Changes in the H/M ratio and washout rate after treatment are shown in Figure 2. In patients with enalapril group (Fig. 2A), the H/M ratio of ^{123}I-MIBG was increased after treatment (early image: 1.60 ± 0.22 versus 1.73 ± 0.28, $p < 0.05$; delayed image: 1.63 ± 0.28 versus 1.82 ± 0.33, $p < 0.01$). The washout rate of ^{123}I-MIBG was reduced from 38% ± 11% to 30% ± 12% after treatment ($p < 0.01$, Fig. 3). However, in the conventional therapy group, the H/M ratios in the early and delayed images (early image: 1.58 ± 0.31 versus 1.52 ± 0.23; delayed image: 1.49 ± 0.27 versus 1.49 ± 0.25) and the washout rate (34% ± 8% versus 33% ± 7%) remained unchanged after treatment (Figs. 2B and 3).

Changes in Left Ventricular Ejection Fraction After ACE I

A left ventricular ejection fraction was compared before and after treatment in the enalapril group. In 19 patients with the enalapril group, a left ventricular ejection fraction increased after treatment, but this change was not statistically significant (44% ± 14% versus 49% ± 16%, $p = 0.061$). However, in patients with the increased H/M ratio ($n = 13$), the left ventricular ejection fraction increased from 48% ± 12% to 55% ± 9% ($p < 0.01$) after treatment. Left ventricular end-diastolic volume was slightly decreased after treatment (146 ± 54 ml vs. 140 ± 47 ml, $p = 0.08$). In patients with the increased H/M ratio ($n = 13$), left ventricular volume decreased from 144 ± 49 ml to 134 ± 45 ml ($p < 0.05$).

DISCUSSION

The sympathetic nervous system plays an important role in the development and progression of heart failure (*16*). Myocardial norepinephrine content decreases with progression of heart failure (*17, 18*). A close relation between myocardial norepinephrine content determined from transvenous myocardial biopsy and left ventricular function is found in dilated cardiomy-

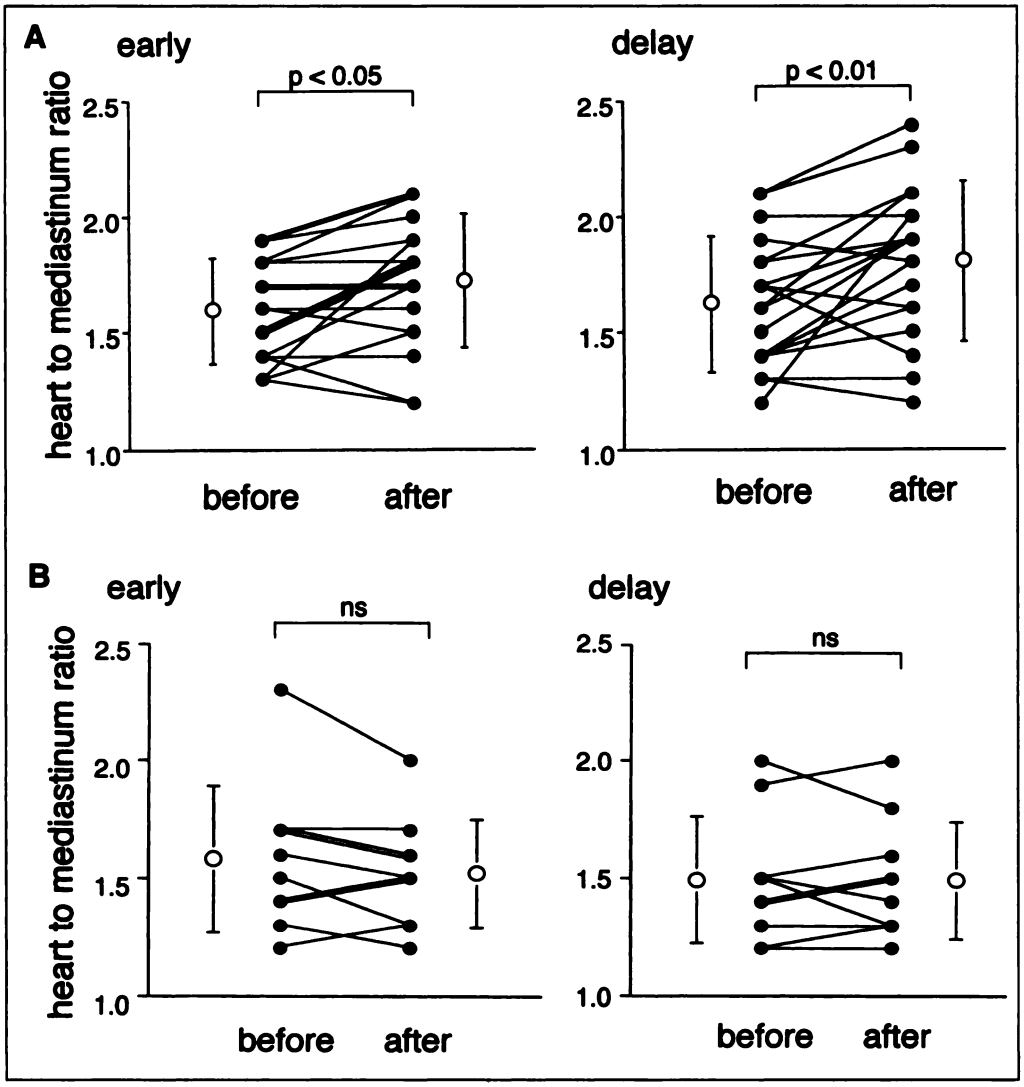

FIGURE 2. (A) Changes in heart-to-mediastinum ratios after treatment with an ACE inhibitor and (B) conventional therapy.

opathy (*19*). It has also been reported that plasma norepinephrine concentration is increased in patients with heart failure (*20, 21*). As an aorto-coronary sinus plasma catecholamine gradient and the rate of norepinephrine spillover to plasma from the heart increase, an activation of cardiac adrenergic nervous system has been suggested in congestive heart failure (*22, 23*). Schofer et al. (*24*) have reported that the heart to mediastinum ratio of ^{123}I-MIBG activity significantly related to myocardial norepinephrine concentration and left ventricular ejection fraction. An inverse correlation between plasma catecholamine concentration and cardiac MIBG activity also has been demonstrated (*25*). Since MIBG shares many transport

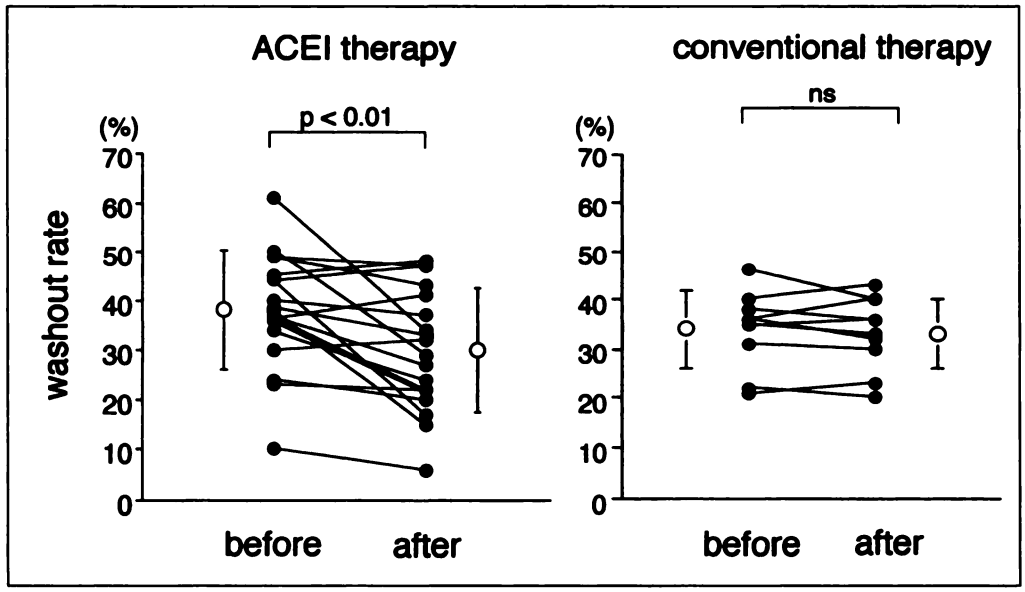

FIGURE 3. Changes in washout rate of ^{123}I-MIBG after treatment.

properties with norepinephrine, ^{123}I-MIBG can be used to assess cardiac adrenergic nervous system disintegrity in human heart failure (*1–3*). Imamura et al. (*6*) have recently 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. They have demonstrated that myocardial washout of ^{123}I-MIBG reflects cardiac adrenergic nervous activity in patients with heart failure, independent of the underlying cause. Merlet et al. (*8*) have reported that a heart-to-mediastinum ratio of ^{123}I-MIBG is the best noninvasive predictor of survival of patients with CHF. Cardiac ^{123}I-MIBG is most potent to predict survival among x-ray cardiothoracic ratio, echocardiographic end-diastolic diameter and radionuclide left ventricular ejection fraction.

We used echocardiography to measure left ventricular ejection fraction and end-diastolic volume in this study. Echocardiography is not adequate when it is used in such a heterogeneous population, because the potential error is likely to be different in ischemic, valvular or idiopathic cardiomyopathy. However, echocardiography is a practical method for evaluating cardiac function. It is useful especially to monitor the changes in left ventricular function in patients with CHF, because repeated examination can be performed easily at the bedside.

After treatment with an ACE inhibitor, there were six patients with unchanged or decreased H/M ratios, and three of six patients were hospitalized because of worsening CHF. The incidence of degraded NYHA functional class and the rate of related hospitalizations were higher in patients with unchanged or decreased H/M ratios than in those with increased H/M ratios.

CHF is a serious condition with a high death rate (*9*). The prevention trials have demonstrated a significant reduction in mortality and hospitalizations for CHF in patients with treated with an ACE inhibitor, enalapril, in addition to conventional therapy for heart failure (*10, 11*). The plasma and left ventricular tissue angiotensin II levels are markedly high in patients with heart failure. An ACE inhibition lowers peripheral vascular resistance by reducing vasoconstriction induced by angiotensin II (*26*). The other proposed mechanism of beneficial effects of ACE inhibition is its effect on resting sympathetic tone. The CONSENSUS trial (*27*) showed that there was a positive correlation between mortality and baseline levels of angiotensin II and norepinephrine. Since angiotensin II facilitates presynaptic norepinephrine release (*12, 13*), ACE inhibition reduces norepinephrine release in the heart and lowers plasma norepinephrine level (*28*). Thus, treatment with an ACE inhibitor may modulate ^{123}I-MIBG kinetics in the heart (*29*). However, the effects of ACE inhibition to ^{123}I-MIBG kinetics have not been rigorously examined in human heart failure.

The norepinephrine spillover is a leak from the norepinephrine pool present in the synapse that is a result of a complex interaction between norepinephrine release, reuptake, synthesis and concentration in the coronary bed. Increased neuronal release of norepinephrine and decreased efficiency of norepinephrine reuptake both contribute to increased norepinephrine spillover in CHF (*30*). Decreased norepinephrine store size in the failing heart appears to result from chronically increased norepinephrine turnover and reduced efficiency of norepinephrine reuptake and storage (*30*). Iodine-123-MIBG washout from the myocardium in this study may be related to the norepinephrine spillover. We showed that enhanced ^{123}I-MIBG washout from the heart in patients with heart failure was reduced after treatment with an ACE inhibitor. In addition, cardiac ^{123}I-MIBG uptake was improved after treatment. Whether ACE inhibition decreases ^{123}I-MIBG release or improves efficiency of reuptake is unknown. An experimental report has showed that ACE inhibition markedly reduces norepinephrine release in the perfused heart with an activated renin-angiotensin system (*28*). Thus, the inhibition of neurotransmitter release by an ACE inhibitor is considered to be one of the possible mechanisms for the reduction of washout rate of ^{123}I-MIBG (*29*). This report confirms the beneficial effects of ACE inhibition on cardiac sympathetic nervous activity in human heart failure.

CONCLUSION

ACE inhibition reduces cardiac ^{123}I-MIBG release and thus lowers cardiac sympathetic nerve activity. Iodine-123-MIBG may be helpful for evaluating the therapeutic effects of ACE inhibition on the cardiac sympathetic nervous system.

ACKNOWLEDGMENT

This research was supported in part by a grant-in-aid for scientific research, number 08770488, from the Ministry of Education, Science and Culture of Japan.

REFERENCES

1. Kline RC, Swanson DP, Wieland DM, et al. Myocardial imaging in man with I-123 meta-iodobenzylguanidine. *J Nucl Med* 1981;22:129–132.
2. Sisson JC, Shapiro B, Meyers L, et al. Metaiodobenzylguanidine to map scintigraphically the adrenergic nervous system in man. *J Nucl Med* 1987;28:1625–1636.
3. Dae MW, O'Connell W, Botvinicke EH, et al. Scintigraphic assessment of regional cardiac adrenergic innervation. *Circulation* 1989;79:634–644.
4. Henderson EB, Kahn JK, Corbett JR, et al. Abnormal I-123-metaiodobenzylguanidine myocardial washout and distribution may reflect myocardial adrenergic derangement in patients with congestive cardiomyopathy. *Circulation* 1988;78:1192–1199.
5. Glowniak JV, Turner FE, Gray LL, Palac RT, Lagunas-Solar MC, Woodward WR. Iodine-123-metaiodobenzylguanidine imaging of the heart in idiopathic congestive cardiomyopathy and cardiac transplants. *J Nucl Med* 1989;30:1182–1191.
6. Imamura Y, Ando H, Mitsuoka W, et al. Iodine-123-metaiodobenzylguanidine images reflect intense myocardial adrenergic nervous activity in congestive heart failure independent of underlying cause. *J Am Coll Cardiol* 1995;26:1594–1599.
7. Wakasugi S, Wada A, Hasegawa Y, Nakano S, Shibata N. Detection of abnormal cardiac adrenergic neuron activity in adriamycin-induced cardiomyopathy with I-125-metaiodobenzylguanidine. *J Nucl Med* 1992;33:208–214.
8. Merlet P, Valette H, Dubois-Rande J, et al. Prognostic value of cardiac metaiodobenzylguanidine imaging in patients with heart failure. *J Nucl Med* 1992;33:471–477.
9. McFate SW. Epidemiology of congestive heart failure. *Am J Cardiol* 1985;55(suppl):3A–8A.
10. The CONSENSUS trial study group: effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS) *N Engl J Med* 1987;316:1429–1435.
11. The SOLVD investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med* 1991;325:293–302.
12. Hughes J, Roth RH. Evidence that angiotensin enhances transmitter release during sympathetic nerve stimulation. *Br J Pharmacol* 1971;41:239–255.
13. Antonaccio MJ, Kervin L. Evidence for prejunctional inhibition of norepinephrine release by captopril in spontaneously hypertensive rats. *Eur J Pharmacol* 1980;68:209–212.
14. Takeishi Y, Sukekawa H, Sakurai T, et al. Noninvasive identification of anthracycline cardiotoxicity: comparison of ^{123}I-MIBG and ^{123}I-BMIPP imaging. *Ann Nucl Med* 1994;8:177–182.
15. Schiller NB, Shah PM, Crawford M. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr* 1989;2:358–367.
16. Meredith IT, Eisenhofer G, Lambert GW, Dewar EM, Jennings GL, Esler MD. Cardiac sympathetic nervous activity in congestive heart failure: evidence for increased neuronal norepinephrine release and preserved neuronal uptake. *Circulation* 1993;88:136–145.
17. Dequattro V, Nagatsu T, Mendez A. Determinants of cardiac noradrenaline depletion in human congestive failure. *Cardiovascular Research* 1973;7:344–350.
18. Rose CP, Burgess JH, Cousineau D. Tracer norepinephrine kinetics in coronary circulation of patients with heart failure secondary to chronic pressure and volume overload. *J Clin Invest* 1985;76:1740–1747.
19. Schofer J, Tews A, Langes K, Bleifeld W, Reimitz PE, Mathey DG. Relationship between myocardial norepinephrine content and left ventricular function: an endomyocardial biopsy study. *Eur Heart J* 1987;8:748–753.
20. Thomas JA, Marks BH. Plasma norepinephrine in congestive heart failure. *Am J Cardiol* 1978;41:233–243.
21. Viquerat CE, Daly P, Swedberg K, et al. Endogeneous catecholamine levels in chronic heart failure: relation to the severity of hemodynamic abnormalities. *Am J Med* 1985;78:455–460.
22. Rose CP, Burgess JH, Cousineau D. Reduced aortocoronary sinus extraction of

epinephrine in patients with left ventricular failure secondary to long-term pressure or volume overload. *Circulation* 1983;68:241–244.
23. Hasking G, Esler M, Jennings G, Burton D, Johns J, Korner P. Norepinephrine spillover to plasma in patients with congestive heart failure: evidence of increased overall and cardiorenal sympathetic nervous activity. *Circulation* 1986;73:615–621.
24. Schofer J, Spielmann R, Schuchert A, Weber K, Schluter M. Iodine-123 metaiodobenzylguanidine scintigraphy: a noninvasive method to demonstrate myocardial adrenergic nervous system disintegrity in patients with idiopathic dilated cardiomyopathy. *J Am Coll Cardiol* 1988;12:1252–1258.
25. Nakajo M, Shapiro B, Glowniak J, Sisson JC, Beierwaltes WH. Inverse relationship between cardiac accumulation of meta-131-iodobenzylguanidine (I-131-MIBG) and circulating catecholamine in suspected pheochromocytoma. *J Nucl Med* 1983;24: 1127–1134.
26. Todd PA, Heel RC. Enalapril: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in hypertension and congestive heart failure. *Drugs* 1986;31:198–248.
27. The CONSENSUS trial study group: effects of enalapril and neuroendocrine activation on prognosis in severe congestive heart failure (follow-up of the CONSENSUS trial). *Am J Cardiol* 1990;66:40D–45D.
28. Richardt G, Kranzhofer R, Schomig A. Effect of angiotensin converting enzyme inhibitors on cardiac noradrenaline release. *Eur Heart J* 1991;12(suppl F):121–123.
29. Takatsu H, Uno Y, Fujiwara H. Modulation of left ventricular I-125-MIBG accumulation in cardiomyopathic Syrian hamsters using the renin-angiotensin system. *J Nucl Med* 1995;36:1055–1061.
30. Eisenhofer G, Friberg P, Rundqvist B, Quyyumi A, Lambert D, Esler M. Cardiac sympathetic nerve function in congestive heart failure. *Circulation* 1996;93:1667–1676.

Adenosine Coronary Vasodilation in Coronary Artery Disease: Technetium-99m Tetrofosmin Myocardial Tomography Versus Echocardiography

Alberto Cuocolo, Pasquale Sullo, Leonardo Pace, Antonio Nappi, Pietro Gisonni, Emanuele Nicolai, Bruno Trimarco and Marco Salvatore

Center for Nuclear Medicine of the CNR, Institute of Radiological Science Internal Medicine, University Federico II, Napoli; IRCCS-Neuromed, Pozzilli, Italy

This study compared the results of adenosine ^{99m}Tc-tetrofosmin cardiac tomography with those of adenosine echocardiography in identifying patients with coronary artery disease (CAD) and in localizing individual stenosed coronary vessels. **Methods:** Twenty-six consecutive patients with suspected or known CAD had simultaneous adenosine (140 μg/Kg/min intravenously) ^{99m}Tc-tetrofosmin tomography and two-dimensional echocardiography. All patients had coronary angiography within 4 wk from imaging studies. Regional ^{99m}Tc-tetrofosmin activity was quantitatively measured in 78 coronary vascular territories and echocardiographic left ventricular function was assessed in corresponding regions. **Results:** At coronary angiography one patient had normal coronary vessels, 12 patients one-vessel and 13 had multivessel disease (≥50% luminal stenosis). Among the 25 patients with CAD, 22 showed perfusion defects at adenosine ^{99m}Tc-tetrofosmin tomography (sensitivity 88%) and 17 had abnormal echocardiographic study (sensitivity 68%, $p < 0.05$ versus ^{99m}Tc-tetrofosmin). Agreement for the identification of patients with CAD between adenosine ^{99m}Tc-tetrofosmin tomography and echocardiography was observed in 21 (81%) of the total 26 patients, with a kappa value of 0.45. Overall sensitivity, specificity and diagnostic accuracy for detection of individual stenosed vessels were 79%, 88% and 83% for ^{99m}Tc tetrofosmin and 57%, 68% and 61% (all $p < 0.05$ versus ^{99m}Tc-tetrofosmin) for echocardiography. Concordance between adenosine ^{99m}Tc-tetrofosmin tomography and echocardiography in the detection of individual stenosed coronary vessels was observed in 57 (73%) of the 78 vascular territories, with a kappa value of 0.36. **Conclusion:** Adenosine-induced coronary vasodilation associated with quantitative ^{99m}Tc-tetrofosmin tomography is more accurate than adenosine echocardiography in identifying patients with CAD and in detecting individual stenosed coronary vessels.

Key Words: myocardial perfusion; left ventricular function; pharmacologic stress test

J Nucl Med 1997; 38:1089–1094

Received Jul. 29, 1996; revision accepted Nov. 7, 1996.
For correspondence or reprints contact: Alberto Cuocolo, MD, Centro per la Medicina Nucleare del CNR, Università Federico II, Via Pansini, 5, 80131 Napoli, Italia.

Although myocardial perfusion imaging and two-dimensional echocardiography associated with dynamic exercise test have been widely used in the noninvasive evaluation of patients with coronary artery disease (CAD) (*1–5*), these procedures may be not accurate in patients unable to perform an adequate maximal test (*3,6*). It also has been demonstrated that approximately 30% of echocardiographic studies are technically suboptimal because of the difficulties due to the rapid and deep respiratory movements during dynamic physical exercise (*6*). Therefore, pharmacological stress testing has been proposed as an alternative to exercise test in evaluating patients with CAD.

Previous studies demonstrated that maximal pharmacological coronary vasodilation induced by adenosine administration combined with ^{201}Tl imaging is a useful noninvasive approach for the diagnosis of CAD showing good agreement with exercise myocardial scintigraphy (*7–10*). However, ^{201}Tl presents some physical and biological limitations as myocardial perfusion agent and, therefore, it is not ideal for cardiac imaging (*11*). Technetium-99m-labeled compounds have been introduced for myocardial perfusion imaging to overcome some of these limitations. In particular, ^{99m}Tc-sestamibi has been used for clinical purposes showing good agreement with ^{201}Tl in detecting CAD (*12–14*). Recent studies suggest that the adenosine test associated with ^{99m}Tc-sestamibi imaging or echocardiography has good diagnostic accuracy for detecting CAD (*15–19*). Technetium-99m-tetrofosmin has been introduced recently for myocardial perfusion imaging (*20–23*) and a good correlation between adenosine and dynamic exercise ^{99m}Tc-tetrofosmin cardiac imaging also has been demonstrated (*24*). However, no data are available comparing adenosine ^{99m}Tc-tetrofosmin tomography with adenosine echocardiography in the same patients. This study was designed to compare the results of adenosine ^{99m}Tc-tetrofosmin cardiac tomography with those of adenosine echocardiography in identifying patients with CAD and in localizing individual stenosed coronary vessels.