^{111}In-Labeled Antimyosin Scintigraphy for Detection of Cardiac and Skeletal Muscular Involvement in Hereditary Muscular Dystrophy

TO THE EDITOR: Antimyosin monoclonal antibodies or fragments labeled with ^{111}In are successfully used for the detection of myocardial disease such as infarction, myocarditis, cardiac transplant rejection and anthracycline toxicity (*1*). Because the primary abnormality in muscular dystrophy is either a shortage or an abnormal structure of dystrophin (*2*), these antibodies may provide a specific tool for the scintigraphic detection of muscular dystrophy, assuming that there is damage to the myocyte membrane permitting the antibody to pass through and bind to intracellular myosin or for the myosin to be exposed. Skeletal muscular involvement in muscular dystrophy has been successfully demonstrated by imaging with antimyosin monoclonal antibodies (*3–4*).

To observe the myocardial and skeletal muscular involvement in hereditary muscular dystrophy (HMD), a radioimmunoscintigraphic study was performed in 10 patients with a confirmed diagnosis of HMD (9 males, 1 female; mean age 8.5 y), among whom 8 were Duchenne type, 1 was Becker type and 1 was autosomal recessive HMD. Commercially available Fab fragments of the monoclonal antibody R11D10, directed against the heavy chain of cardiac myosin, were used. Patients were administered a 0.25-mg dose of murine antimyosin Fab fragments labeled with 37 MBq ^{111}InCl3 by slow intravenous injection, and whole-body scintigraphy was performed 24–48 h later. Heart-to-lung (H/L) ratios were calculated using a region-of-interest technique based on measurements of counts per pixel in cardiac muscle and lung regions. No adverse effects were observed. In 2 patients with HMD who had extensive muscle wasting, we also performed whole-body ^{201}Tl scintigraphy. Normal tracer accumulation was seen in the kidneys, liver and, to a lesser extent, bone marrow. In addition, intense antimyosin uptake into the myocardium and skeletal proximal/distal muscle groups was observed. ^{111}In-antimyosin uptake correctly detected myocardial involvement in 10 of 10 cases of muscular dystrophy in which H/L ratios were >2. These values seem to be significantly high compared with the previously reported normal H/L ratios for ^{111}In-antimyosin uptake (normal < 1.55) (*5*). The measurement of left ventricular function using cardiac echocardiography revealed normal to mildly abnormal wall motion in 7 patients and moderate to severe wall-motion abnormality in 3 patients.

To our knowledge, this is the first report on cardiac muscle damage in muscular dystrophy investigated using ^{111}In-antimyosin, a novel tracer for the evaluation of the integrity of myocardium. Considering the clinical role of ^{111}In-antimyosin imaging, it is concluded that this technique is useful for confirming cardiomyopathy in muscular dystrophy and for monitoring patient outcome. ^{111}In-antimyosin scintigraphy, in early to intermediate stages of muscular dystrophy, may be a useful method for evaluating subclinical cardiomyopathy, and the noninvasiveness of the procedure makes it an easily applicable parameter to be used in follow-up.

REFERENCES

1. Morguet AJ, Munz DL, Kreuzer H, Emrich D. Immunoscintigraphy with ^{111}In antimyosin Fab [review]. *Nucl Med Commun.* 1990;11:727–735.
2. Hoffman EP, Fischbeck KH, Brown RH, et al. Characterization of dystrophin in muscle-biopsy specimens from patients with Duchenne's or Becker's muscular dystrophy. *N Engl J Med.* 1988;318:1363–1368.
3. Lofberg M, Liewendahl K, Savolainen S, et al. Antimyosin scintigraphy in patients with acquired and hereditary muscular disorders. *Eur J Nucl Med.* 1994;21:1098–1105.
4. Ilgin N, Gokcora N, Gucuyener K, Kose G, Unlu M. In-111 antimyosin scintigraphy in hereditary muscular dystrophy [abstract]. *Eur J Nucl Med.* 1995;22:763.
5. Ballester M, Obrador D, Carrio I, et al. Indium-111 monoclonal antimyosin antibody studies after the first year of heart transplantation: identification of risk groups for developing rejection during long-term follow-up and clinical implications. *Circulation.* 1990;82:2100–2108.

Nese Ilgin
Nahide Gokcora
Kivilcim Gucuyener
Gulin Vural
Gulsen Kose
Mustafa Unlu
Gazi University Medical School
Ankara, Turkey

Chest Pain in Women: Dobutamine Stress Echocardiography or Myocardial Perfusion Scintigraphy?

TO THE EDITOR: We read with interest the recent article by Santana-Boado et al. (*1*) and the accompanying editorial by Cacciabaudo and Hachamovitch (*2*). Application of the Diamond correction to Bayes' theorem (*3*) to a series of ^{99m}Tc-methoxyisobutyl isonitrile myocardial SPECT studies performed on a population of women suggests that test accuracy is, in fact, very similar to studies on their male counterparts. The high test diagnostic accuracy reported provides supportive evidence for using myocardial SPECT as the cornerstone of the noninvasive evaluation of chest pain in women.

We propose a similar role for dobutamine stress echocardiography. The technique requires a high level of operator skill but has a sensitivity and specificity similar to SPECT (*4,5*). We have analyzed the results of more than 400 studies in our institution, including 211 in women, of whom a select minority of 85 have had coronary angiography. Application of the Diamond correction to our series' results revealed a sensitivity of 95%, a specificity of 74% and an overall diagnostic accuracy of 84% for the detection of significant coronary artery disease in women. These figures are comparable with previously published series and similar to those using SPECT (*5*).

Dobutamine stress echocardiography is not universally available, but in expert hands it offers a quick, inexpensive and safe alternative to perfusion scanning without exposing patients to ionizing radiation. It is an "office-based" technique that has the important additional advantage of allowing patients with valvular heart disease or cardiomyopathies to be fully assessed. Current developments in the field of stress echocardiography, especially

involving the use of myocardial contrast agents, may allow this method to form the new cornerstone of noninvasive assessment of chest pain in women.

We propose that, when accessible, dobutamine stress echocardiography be considered as the initial diagnostic test in preference to exercise electrocardiography in women with uninterpretable ST segments and as a second-line screen in all those with intermediate to high postexercise test risk of coronary artery disease. Myocardial perfusion scintigraphy should be reserved for women with poor echocardiographic windows or those who are unable to tolerate the dobutamine.

David J. Brull
John G. Coghlan
John Buscombe
Royal Free Hospital
London, England

REFERENCES

1. Santana-Boado C, Candell-Riera J, Castell-Conesa J, et al. Diagnostic accuracy of technetium-99m-MIBI myocardial SPECT in women and men. *J Nucl Med.* 1998;39:751–755.
2. Cacciabaudo JM, Hachamovitch R. Stress myocardial perfusion SPECT in women: is it the cornerstone of the noninvasive evaluation? *J Nucl Med.* 1998;39:756–759.
3. Diamond GA. Reverend Bayes silent majority: an alternative factor affecting sensitivity and specificity of exercise electrocardiography. *Am J Cardiol.* 1986;57: 1175–1180.
4. Dionisopoulos PN, Collins JD, Smart SC, Knickelbine TA, Sagar KB. The value of dobutamine stress echocardiography for the detection of coronary artery disease in women. *J Am Soc Echocardiogr.* 1997;10:811–817.
5. Takeuchi M, Sonoda S, Miura Y, Kuroiwa A. Comparative diagnostic value of dobutamine stress echocardiography and stress thallium-201 single-photon-emission computed tomography for detecting coronary artery disease in women. *Coronary Artery Dis.* 1996;7:831–835.

REPLY: Recent data indicate that there is no gender-based difference in diagnostic accuracy of dobutamine echocardiography (*1*) and stress perfusion scintigraphy (*2*) in detecting coronary artery disease, mainly if the silent majority is considered (*3*). Therefore, both tests are an adequate alternative to a nondiagnostic exercise electrocardiography test.

It is generally accepted that stress echocardiography may be more specific than stress perfusion scintigraphy and that this test is more sensitive than stress echocardiography (*4*). Thus, stress perfusion scintigraphy would be indicated in patients with high prevalence of coronary artery disease, and stress echocardiography in patients with low prevalence. However, specificity values of dobutamine echocardiography in the silent majority, reported by Brull et al. and by Dionisopoulos et al. (*1*) in the select minority (74% and 79%, respectively), are clearly lower than our own (91%) in the silent majority of women (*3*). Our results should prompt us to consider stress myocardial scintigraphy also in women with low prevalence of coronary artery disease.

According to the variability of all these data, which may indicate different characteristics of patients, methods, level of operator skill and interpretation criteria, we do not think it advisable to propose, as Brull et al. do, dobutamine echocardiography as the initial diagnostic test when results of exercise electrocardiography are uninterpretable, with perfusion scintigraphy being reserved for women with poor echocardiographic windows or who are unable to tolerate dobutamine. From our point of view, both tests have similar indications, and each hospital, depending on different factors such as feasibility and experience, should decide which test is preferable for each patient, either woman or man.

Jaume Candell-Riera
César Santana-Boado
Joan Castell-Conesa
Santiago Aguadé-Bruix
Hospital General Universitari Vall d'Hebron
Barcelona, Spain

REFERENCES

1. Dionisopoulos PN, Collins JD, Smart SC, Knickelbine TA, Sagar KB. The value of dobutamine stress echocardiography for the detection of coronary artery disease in women. *J Am Soc Echocardiogr.* 1997;10:811–817.
2. Takeuchi M, Sonoda S, Miura Y, Kuroiwa A. Comparative diagnostic value of dobutamine stress echocardiography and stress thallium-201 single photon-emission computed tomography for detecting coronary artery disease in women. *Coronary Artery Dis.* 1996;7:831–835.
3. Santana-Boado C, Candell-Riera J, Castell-Conesa J, et al. Diagnostic accuracy of technetium-99m-MIBI myocardial SPECT in women and men. *J Nucl Med.* 1998;39:751–755.
4. O'Keefe JH, Barnhart CS, Bateman TM. Comparison of stress echocardiography and stress myocardial perfusion scintigraphy for diagnosing coronary artery disease and assessing its severity. *Am J Cardiol.* 1995;75:25D–34D.

Inverse Correlation Between ^{99m}Tc-Tetrofosmin Uptake and P-Glycoprotein in Non–Small Cell Lung Cancer

TO THE EDITOR: We read with interest the article by Kostakoglu et al. (*1*) in which they report an inverse correlation between the tumor-to-normal tissue uptake ratio and the expression of P-glycoprotein (Pgp) determined by immunohistochemistry in 46 patients with lung cancer (26 squamous cell carcinomas and 20 small cell carcinomas). We would like to describe our experience with ^{99m}Tc-tetrofosmin (TF), another Pgp substrate (*2*), in patients with non–small cell lung cancer (NSCLC) and its correlation with Pgp expression determined by immunohistochemistry.

A total of 18 patients (17 men, 1 woman; age range 52–83 y) with NSCLC (2 with undifferentiated large cell carcinoma, 5 with adenocarcinoma and 11 with squamous cell carcinoma) were studied by ^{99m}Tc-TF and thoracic SPECT. The ^{99m}Tc-TF study was performed during the week before surgery. It involved the intravenous administration of 740 MBq (20 mCi) ^{99m}Tc-TF for the acquisition, 10 and 60 min later, of anterior and posterior planar images. SPECT acquisition was performed at 70 min. Image processing included semiquantitative analysis of the uptake in certain areas of interest outlined in transverse, coronal and sagittal SPECT sections to compare the counts in tumor tissue with those registered in healthy tissue, which provided the ^{99m}Tc-TF uptake index. Paraffin-embedded samples were taken for immunohistochemical staining using JSB-1, a monoclonal antibody that binds to an internal epitope of Pgp, at a dilution of 1:20. The results were considered to be positive when >10% of the visible cells were stained.

The immunohistochemical study of the 18 tumors identified 12 Pgp-positive lesions (2 adenocarcinomas, 2 undifferentiated large cell carcinomas and 8 squamous cell carcinomas) and 6 Pgp-negative lesions (3 adenocarcinomas and 3 squamous cell carcinomas).

For the Pgp-positive tumors, size ranged between 2.0 and 6.5 cm in largest diameter (mean 3 ± 1.2 cm), between 15% and >60% of