ORIGINAL CONTRIBUTION

Evaluation of Tc-99m Tetrofosmin Scan for Coronary Artery Disease Diagnosis

Elie Chammas, MD, Ahmad Yatim, MD[1], Chadi Hage, MD, Kozhaya Sokhn, MD, Walid Tarcha, MD, Georges Ghanem, MD

Department of Cardiology
[1]Department of Nuclear Medicine
Rizk Hospital
Beirut, Lebanon

ABSTRACT

Detection of myocardial perfusion abnormalities using Tc-99m tetrofosmin was evaluated for sensitivity and specificity compared to coronary angiography. Between January 1996 and January 1998, exercise stress tests and myocardial scintigraphy were performed in 58 patients, followed by coronary angiography within 2 months. There were 48 males and 10 females, aged 33 to 72 years (mean, 57 years). The sensitivity and specificity of exercise stress tests were 64% and 68%, respectively, while the sensitivity and specificity of Tc-99m tetrofosmin scans were 88% and 75%, respectively, compared to angiography. For Tc-99m tetrofosmin scans, the sensitivity was 78% for the left anterior descending artery, 66% for the left circumflex artery, and 76% for the right coronary artery; specificity was 74% for the left anterior descending artery, 90% for the left circumflex artery, and 75% for the right coronary artery. It was concluded that Tc-99m tetrofosmin allowed high-quality myocardial perfusion imaging with results comparable to those obtained using thallium-201 chloride.

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INTRODUCTION

The use of nuclear techniques for noninvasive studies of cardiovascular disease is well established. Nuclear cardiology provides unique pathophysiological insights unavailable by other procedures.[1,2] Thallium-201 is still the most widely used agent in myocardial perfusion imaging for diagnosis of exercise-induced myocardial ischemia, and evaluation of the site and extent of post-infarction scarring and myocardial viability.[3,4] However, technetium-99m has certain advantages over thallium-201, and the use of Tc-99m-labeled pharmaceuticals in cardiology is increasing.[1,2] The newest Tc-99m-labeled agent used in nuclear medicine is tetrofosmin.[5]

PATIENTS AND METHODS

A prospective study was conducted in this hospital between January 1996 and January 1998, to assess the diagnostic efficacy of Tc-99m tetrofosmin in cases of known or suspected coronary artery disease. There were 58 consecutive patients (48 males and 10 females), aged 33 to 72 years (mean, 57 years). Patients were considered eligible for this study if they had clinical symptoms suggestive of coronary artery disease, a past history of myocardial infarction, a baseline electrocardiogram (ECG) with premature ventricular contractions, or such ECG findings after a revascularization procedure. Exclusion criteria were recent myocardial infarction (within 2

For reprint information contact:
Elie Chammas, MD Tel: 961 1 20 0800 Fax: 961 1 32 1521 email: echammas@inco.com.lb
Department of Cardiology, Rizk Hospital, P.O. Box 11-3288, Achrafieh, Beirut, Lebanon.

months), unstable angina, significant congestive heart failure, valvular disease, left bundle branch block, congenital heart disease, and significant concomitant noncardiac disease. Each patient had Tc-99m tetrofosmin stress and resting imaging studies of 4 hours' duration, and coronary arteriography 1 to 47 days later (mean, 14 days). All patients underwent a symptom-limited upright bicycle exercise test using stepwise increments of 30 watts every 3 minutes. The ECG and arterial blood pressure were monitored continuously and recorded before and at 2-minute intervals during exercise and recovery. Exercise stress testing was conducted on a Marquette case 15 stress test system (GE Medical Systems, Inc., Milwaukee, WI, USA). A test was considered submaximal if the attained maximum heart rate was below 85% of the predicted maximum heart rate (220 minus the patient's age in years). An ischemic response was defined as typical chest pain and/or ST depression > 1 mm with a horizontal or downward sloping segment, or ST elevation without evidence of myocardial infarction.

A Sopha single-head DSX tomograph (GE Medical Systems, Inc., Milwaukee, WI, USA) was used for all patients. A solution of Tc-99m tetrofosmin was prepared from a freeze-dried kit (Myoview; Amersham Health, Little Chalfont, Buckinghamshire, England, UK) conserved in a 10-mL glass vial stored at 2°C to 8°C. The vial was reconstituted with 5 mL of sodium pertechnetate solution by diluting the eluate from a technetium-99m generator with 0.9% saline. The vial was shaken gently to insure complete dissolution of the lyophilized powder, and left at room temperature (15°C to 25°C) for 15 minutes, according to the manufacturer's instructions. The injection was used within 6 hours of reconstitution. A dose of 7 mCi of Tc-99m tetrofosmin was injected at peak exercise, and 20 mCi 4 hours thereafter; the images began to appear 30 minutes after each injection. The perfusion pattern was assessed by single photon emission computed tomography in 5 segments: anterior, inferior, lateral, septal, and apical; which were described as either normal, reversible, or fixed abnormality (scar). Perfusion abnormalities (ischemia) in the anteroseptal area reflected disease of the left anterior descending artery (LAD), those in the inferior wall were due to right coronary artery (RCA) disease, and those in the posterolateral wall represented disease in the left circumflex artery (LCx). Apical abnormalities were not specific for any of these 3 vascular territories. Selective coronary angiography was performed in multiple views by the Judkins technique, using a Philips angiographic system (Philips Medical Systems, Vienna, Austria). Coronary arteriography results were considered positive if significant stenosis (> 60%), diffuse, or multiple lesions were visualized in at least one major vessel.

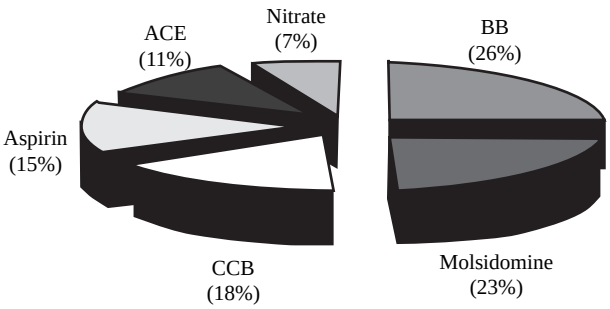

Figure 1. Cardiac medications in 34 patients. ACE = angiotensin-converting enzyme inhibitor, BB = beta blocker, CCB = calcium channel blocker.

RESULTS

Of the 58 patients with suspected coronary artery disease, 34 were taking cardiac medications (Figure 1), 17 (29%) were hypertensive, 9 of whom (53%) were receiving appropriate treatment and 8 (47%) were untreated. Coronary arteriography was positive in 45 patients: 12 (27%) had single-vessel disease, 20 (44%) had double-vessel disease, and 13 (29%) had triple-vessel disease. There were 35 LAD lesions, 31 RCA lesions, and 25 LCx lesions.

In stress tests, the attained maximum heart rates were between 67% and 104% of the predicted maximum heart rates. The mean load was 143 watts, and the normal interval was 70 to 210 watts. No patient developed stress-test complications. The test was negative in 30 patients (52%) and positive in 28 (48%), of whom 28% attained submaximal effort. Based on coronary angiography, the sensitivity was calculated as 64% and the specificity was 68%.

Perfusion scans were negative in 12 patients (21%). A perfusion defect was observed in 46 patients (79%), of whom 8 had irreversible defects; 7 of them had positive angiograms that correlated with the ischemic segments, but one appeared to have normal coronary arteries on angiography. Of the 24 patients showing reversible perfusion defects, 20 had corresponding significantly diseased coronary arteries, and the others (2 septal, 1 anterior, 1 inferior) had completely normal angiograms. The remaining patients showed fixed lesions with corresponding abnormal coronaries. Among the 22 hypertensives, 2 of the 17 patients with normal angiograms had a positive scan, indicating a 12% false-positive rate. These anomalous perfusion defects appeared in the septum, correlating with well-known septal false-positive Tc-99m tetrofosmin results in the hypertensive population.[6] The overall sensitivity and specificity of Tc-99m tetrofosmin was calculated as 88% and 75%, respectively, compared to coronary angiography. The sensitivity was 78% for the LAD, 66% for the LCx, and 76% for the RCA. Specificity was 74% for the LAD, 90% for the LCx, and 75% for the RCA.

DISCUSSION

Myocardial scintigraphy and coronary angiography are two complementary investigations, one giving a

physiologic assessment of myocardial perfusion, the other providing an anatomic description of coronary lesions. When this study began, the use of Tc-99m tetrofosmin was just starting in the United States, but its role in nuclear cardiology, especially in the diagnosis and management of coronary artery disease, has become well defined.[7] Tetrofosmin offers many advantages over other products because of its biophysical and biokinetic properties.[8,9] In this study, stress test specificity (64%) was the same as the internationally established specificity (mean, 66%; range, 17% to 100%); however, stress test sensitivity (68%) was lower (mean, 82%; range, 40% to 100%).[10] The fact that 59% of patients were receiving medication is a possible explanation for the small differences in the results. It was difficult to obtain a statistical comparison between patients under treatment and those without medication, because of the limited numbers. Hypertensive patients accounted for 25% in this study; it has been demonstrated that hypertension increases the incidence of false-positive results, thus decreasing the specificity of the Tc-99m tetrofosmin scan. The effect of longstanding hypertension on myocardial perfusion imaging is still controversial.[6] It is well established that hypertension increases the positivity of stress tests. A positive coronary angiography threshold of stenosis of 60% instead of 70% to 75% increases the sensitivity of the test, but decreases its specificity. The predictive value of Tc-99m tetrofosmin scans was highest in the mixed-lesion group, and the presence of associated reversible and irreversible perfusion defects at the same site was indicative of a corresponding coronary lesion.

This series consisted of only 58 patients, and such a small number might influence the reproducibility of the results. A substantially larger number is obtainable only in a multicenter study. There were 34 patients under various medical treatments that appeared to affect the results of both stress testing and Tc-99m tetrofosmin scanning, which was due to the fact that the majority were referred by cardiologists using different modes of therapy. Cardiac medications could blunt positive stress test results and prevent the patient from reaching the maximum predicted effort. Because of the heterogeneity of the population, dipyridamole stress testing was not undertaken.

Coronary angiography has been considered the gold standard for assessing the severity and extent of coronary artery disease. However, several limitations have been recognized: the planar perspective of angiography may significantly misrepresent the severity of complex luminal narrowing because it provides only a silhouette of the lumen.[10] Two orthogonal angiograms should adequately portray most lesions, but orthogonal views may be difficult to obtain in the clinical setting, especially when the disease involves bifurcation sites and tortuous segments. In fact, some coronary narrowings are so complex, particularly following angioplasty, that no combination of angiographic views may accurately depict their extent. Necropsy studies have demonstrated that coronary disease is frequently diffuse with no truly normal segment from which to calculate the percentage reduction in diameter. Thus, in the presence of diffuse disease, angiography may systematically underestimate disease severity. In addition to important discrepancies between antemortem angiography and necropsy findings, large intra- and interobserver variability has been noted, as well as a poor correlation between the angiographic appearance of coronary obstruction and the physiological consequences of the lesions.[11] Furthermore, coronary angiography is unable to assess the significance of collaterals perfusing chronically ischemic myocardium. These collaterals mainly consist of microvessels that are not accurately visualized by standard imaging techniques. Therefore, a severely stenotic coronary artery might correspond to a well-perfused segment that would not meet the physiological criteria for determining stenosis.

It was concluded from this study that Tc-99m tetrofosmin provided high-quality myocardial perfusion imaging with results comparable to those obtained with the widely used thallium-201 chloride. Because of the advantages of Tc-99m over Tl-201, we recommend that thallium should be reserved for studies concerning myocardial viability, while awaiting the results of studies on the use of Tc-99m agents for evaluation of myocardial viability.

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