The accuracy of technetium-99m tetrofosmin myocardial perfusion scintigraphy in patients with coronary stents: a comparison to coronary angiography

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Introduction

Recently, stent implantation and percutaneous transluminal coronary angioplasty (PTCA) are the popular treatment methods for coronary artery disease (CAD). Restenosis after stent implantation and PTCA has become a significant clinical problem in parallel to increase application of these methods. The reported incidence of restenosis after PTCA and stent implantation varies between 30%-45% and 5%-37%, respectively (1-5).

Clinical trials have been shown that Technetium-99m (Tc-99m) tetrofosmin myocardial perfusion SPECT (MPSPECT) has a high sensitivity and specificity for the detection of CAD when compared with coronary angiography (6-9). Tc-99m tetrofosmin is characterized by a rapid heart uptake and stable retention, without evidence of redistribution for up to 3 hours (9,10). Rapid washout from blood, liver and lungs and good physiological properties of Technetium -99m for gamma cameras are the advantages of Tc-99m tetrofosmin (11, 12).

The role of perfusion scintigraphy in the management of patients after revascularization procedures have been reported by several studies (13-17); but there are limited data regarding the diagnostic role of Tc-99m tetrofosmin perfusion scintigraphy in patients...
between MPSPECT and PTCA/Stent implantation was 6 month. In all patients stress testing and control coronary angiography was performed within one week before and after MPSPECT, respectively.

**Stress testing**
Stress testing was performed after treadmill exercise using a standard Bruce protocol to a symptom-limited endpoint or to > 85% age-predicted maximal heart rate of the patients.

Clinical symptoms, for example the appearance of dyspnea or angina, were documented during the stress tests. A horizontal or downsloping ST-depression ≥ 1 mm in standard leads and ≥ 2 mm in precordial leads was considered a significant change indicating the presence of myocardial ischemia.

**Scintigraphic procedures**
Beta blockers and calcium-channel blockers were stopped 48 hour before and during the MPSPECT study. Patients were also overnight fast.

Technetium-99m tetrofosmin was prepared from a freeze-dry kit (Myoview, Amersham International, England) by reconstitution with approximately 5 ml of a sterile sodium pertechnetate solution. Radiochemical purity was determined by thin layer chromatography and only preparations with 90% and greater were used.

Myocardial perfusion scintigraphy was performed using same-day protocol. Following administration 222-296 MBq (6-8 mCi) of Tc-99m tetrofosmin at rest and fasting state, a light meal or a glass of milk was given. Imaging was started 30 minutes after injection. Tomographic imaging was performed using a single-
head gamma camera (GE, XCT) collecting 32 frame with 40 sec duration over 180° from 45° right antero- or oblique to 135° left posterior oblique positions and stored in 64x64 matrix. Stress tetrofosmin study was performed 4 hours later. For stress study all patients were stressed with treadmill by using standard Bruce protocol. At peak exercise, 740-925 MBq (20-25 mCi) of Tc-99m tetrofosmin was injected and exercise was continued for an additional minute. After 10-15 min of recovery each patient was asked to have a light meal or a glass of milk to accelerate hepatobiliary clearance. Stress imaging was started approximately 30-40 minutes later. Stress tomographic imaging was performed in a similar fashion.

**Image analysis**

After tomographic acquisition, projection data were smoothed using Hanning filter with a cutoff frequency of 0.5 cycles per pixel, and series of 6-mm thick transverse slices were reconstructed using a filtered backprojection with a Ramp filter. Data were reoriented to obtain oblique slices to the long-axis and short-axis of the left ventricle. No attenuation or scatter correction was performed.

Paired images of stress and rest short axis and vertical and horizontal long-axis slices were generated for visual analysis. Tc-99m tetrofosmin uptake in vascular territory of stented or PTCA arteries were classified in individual cases as: (a) normal; (b) stress-induced perfusion defect with complete normalization at rest; (c) stress-induced perfusion defect with incomplete normalization at rest; (d) perfusion defect at stress without significant improvement at rest (persistent defect) by the consensus of two experienced readers. The observers had no knowledge about neither the results of coronary angiography at the time of stent implantation and PTCA nor the results of control coronary angiography. The assignment of myocardial segments to individual vessels was guided by the coronary anatomy obtained from angiograms recorded at the time of stent implantation or PTCA. Either a reversible defect or a partially reversible defect was considered a sign of stent/PTCA restenosis.

**Coronary arteriography**

Selective right and left coronary angiography were performed according to the Judkins method. To determine the luminal diameter at the location of stent and the adjacent reference regions, the projection was chosen that showed the highest grade of stenosis. All implanted stents were bare stents, there was no drug eluting stent. The percent diameter of the stenosis was graded as wall surface irregularity, ≥25%, ≥50%, ≥75%, ≥90%, ≥99% stenosis or total occlusion. Restenosis was defined as a diameter of stenosis ≥50%.

**Statistical Analysis**

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated using standard formulae.

**Results**

Coronary arteriography revealed restenosis in 8 arteries of 7 patients. Restenosis was found in 5 LAD and 3 RCA that were stented. In twenty-three arteries, there was no evidence for restenosis.

Restenosis was found in four of 13 patients who had angina. In three patients there was no angina while their stented arteries were restenotic. Basal ECG showed ischemic findings in 7 patients. Coronary angiography demonstrated stenosis in two of these 7 patients’ stented arteries.

Stress electrocardiography testing revealed the presence of ischemia in 14 patients. Angiographically there was evidence for restenosis in 6 of these 14 patients. In two patient, restenosis was demonstrated but stress testing was normal. The sensitivity, specificity, PPV, NPV and accuracy of stress testing in demonstrating restenosis were 75%, 63%, 44%, 87% and 61% respectively.

With MPSPECT, 6/8 vascular territories with restenosed stents showed stress induced ischemia (sensitivity: 75), 21/23 territories without restenosis did not (specificity: 91%). PPV, NPV and accuracy of Tc-99m tetrofosmin MPSPECT were: 75%, 91%, 87%, respectively.

Table 2 shows the results of prerevascularization coronary angiography, control angiography and Tc-99m tetrofosmin MPSPECT findings in patients who have true positive, false positive and false negative Tc-99m tetrofosmin MPSPECT.

The sensitivity, specificity, PPV, NPV and accuracy of stress testing and Tc-99m tetrofosmin MSPECT were demonstrated in a Table 3.

**Discussion**

Myocardial perfusion SPECT is a reliable method to investigate myocardial ischemia and infarction in patients with coronary artery diseases. Tc-99m tetrofosmin is an alternative radiopharmaceutical beyond the other radionuclide or radiopharmaceuticals such as Tl-201 and Tc99m-isonitriles. Tc-99m tetrofosmin has some advantages such as easy and fast preparation with fine physical properties of Tc-99m. The diagnostic value of Tc-99m tetrofosmin in demonstrating stress induced ischemia is well documented in series of studies. The reported sensitivities and specificities of Tc-99m tetrofosmin imaging for detection of individual coronary artery stenosis were 53%-91% and 58%-88%, respectively (6-8).
Restenosis in stent and PTCA is the major limitation of intracoronary stent implantation and PTCA. Since stent implantation has been shown to significantly reduce restenosis as compared to PTCA in selected lesions (4-5), there is a growing interest of its use in the treatment of patients with coronary artery disease. As a result of dramatic increase in stent implantation numbers worldwide, in-stent stenosis has been closed as a new entity with significant clinical and socioeconomic implications. With more than 1000000 stent implantations per year and a estimated overall clinical restenosis rate of 15-25%, between 150000 and 250000 patients will present with in-stent restenosis in a year and require treatment (20-21). The mechanism of in-stent-stenosis has been shown to be neointimal tissue proliferation (22). Patient related variables (e.g. diabetes) and lesion-related variables (e.g. vessel size) have a major impact on restenosis (3).

The diagnosis of restenosis in stent and PTCA depends on coronary angiographic findings. Before coronary angiography, patient symptoms, exercise electrocardiography were assessed for the possibility of restenosis in the patient. A series of studies has been shown that chest pain is not a reliable criterion for the restenosis. (17, 23). In our study, only 55% of patients with stenotic coronary arteries had angina pectoris. The sensitivity and specificity of exercise electrocardiography in restenosis detection have been reported as 24-52% and 60-64%, respectively (17, 24-25). We found that similar specificity (63%) but higher sensitivity (75%) values compared to the previous literature findings.

Thallium-201 (Tl-201) and Tc-99m sestamibi are the reported radionuclide and radiopharmaceutical for detection of restenosis after PTCA and stent implantation (13-16). Hecht et al (13) reported the role of Tl-201 exercise and redistribution imaging in the detection of restenosis after PTCA. They compared exercise electrocardiogram versus Tl-201 SPECT and reported the sensitivity increased from 52% to 93%, specificity from 64% to 77% and accuracy from 57% to 86%. In the study of Milan et al (15), the sensitivity, specificity, accuracy, PPV and NPV in the detection restenosis after PTCA have been reported as 87.5%-50%-75%, 78%-65%-74%, 83%-57%-74%, 81%-60%-76%, 86%-56%-74% for qualitative, semiquantitative and quantitative analysis of Tc-99m sestamibi myocardial perfusion SPECT, respectively. Significant differences in sensitivity and in negative predictive value were also found between qualitative and semiquantitative analysis. Qualitative analysis showed higher values than semiquantitative analysis. Tc-99m sestamibi SPECT has also been reported to detect stent-restenosis with sensitivity of 79% and specificity of 78%.

There are few published studies investigating the
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Table 3. The sensitivity, specificity, PPV, NPV and accuracy of stress testing and Tc-99m tetrofosmin myocardial perfusion SPECT (MPSPECT) in detecting restenosis in patients after revascularization.

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diagnostic value of Tc-99m tetrofosmin SPECT in detecting restenosis post PTCA and stent implantation (17-19). Georgoulas et al.(17) studied with 41 consecutive patients who had only PTCA using Tc-99m tetrofosmin myocardial perfusion SPECT. They found that Tc-99m tetrofosmin SPECT was 81.3% sensitive and 88% specific for the detection of stenosis in the group of patients with PPV of 81% and NPV of 88%. In the other study of Galassi et al. (18), the study group consisted of 97 patients who had successful stenting procedures in native coronary arteries, prospectively underwent Tc-99m-tetrofosmin tomographic myocardial scintigraphy and coronary angiography. In this study using exercise tomographic myocardial scintigraphy with Tc-99m-tetrofosmin, detection of stent restenosis was obtained with a sensitivity of 82%, a specificity of 84%, and a predictive accuracy of 83%. When the authors divided their results into subgroups, the results were as follows: in patients who achieved 85% maximal heart rate, stent restenosis was detected in 74 vascular regions with a sensitivity of 86%, specificity of 83% and predictive accuracy of 84% whereas in those who achieved <85% maximal heart stent restenosis was detected in 33 vascular regions, with a sensitivity of 68%, specificity of 81, and predictive accuracy of 76%. In patients without myocardial infarction, sensitivity was 76%, specificity 95%, and predictive accuracy 89%. In patients with myocardial infarction, sensitivity was 88%, specificity was 71%, and predictive accuracy was 76%.

In patients with complete revascularization the sensitivity of perfusion scintigraphic studies was significantly higher than that of the presence of angina or significant electrocardiographic changes during exercise testing. In our study group, there was no patient with prior myocardial infarction and all patients achieved 85% maximal heart rate in stress testing. All lesions in the presented study were de-nova lesions and there was no side-branch stenosis during stent implantation. We found the sensitivity and specificity of Tc-99m tetrofosmin MPSPECT study were 75% and 91%, respectively. The accuracy of Tc-99m tetrofosmin MPSPECT in our study was 87%. Our results seem well correlated with the other published data. The major limitation of the study is the small number of patients with restenosis after stent implantation. The further studies with larger number of patients with restenosis after stent implantation are needed.

Conclusion
The sensitivity, specificity, PPV, NPV and accuracy values of Tc-99m tetrofosmin MPSPECT were compatible with each other and acceptable for diagnosing restenosis after successful stent implantation and PTCA. We concluded that Tc-99m tetrofosmin MPSPECT may be noninvasive test in detecting restenosis after stent implantation and successful PTCA, even in the absence of pre-PTCA MPSPECT study.

References


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