Chapter 5

DISCUSSION

In this study we demonstrated the usefulness of SPECT Tc-99m Sestamibi imaging in the detection of restenosis after PTCA

The restenosis rate of patients was 58%, whereas the restenosis rate of lesions was 51%. It is quite a higher than the previous study in which the average of restenosis is rate approximately 30-40%. The true incidence of restenosis in our study is probably lower because:

1) Most of the patients who refused to undergo repeated angiography were asymptomatic. The patients population is thus biased in favor of those with recurrent stenosis.

2) We enrolled only the patients who could reimburse or had pension because of the high cost of the MIBI scan. So we can not study in all cases.

3) The major PTCA lesions in our study is type C which is a complex lesion and difficult to perform PTCA. The probability of restenosis is higher regarding to the nature of lesion characterstics.

4) We also included only the patients who had history of known previous restenosis before being enrolled in the study.

For detection of restenosis after PTCA the clinical and noninvasive tests, including anginal chest pain, exercise stress test and MIBI scan were compared with coronary angiography; the results are:

Chest pain : The recurrent of anginal chest pain after PTCA in our study occurred only 37 %. Sensitivity and specificity of anginal chest pain for detection restenosis were only 39.4% and 66.7%, respectively. It is similar to the previous report and, thus, anginal chest pain is confirmed to be an insensitive marker for restenosis. The positive and negative predictive value of recurrent chest pain for detection restenosis was 65.0 % and 41.2 % respectively. The positive predictive value is similar to the previously reported studies, (44-92 %); however in our study the negative predictive value was quite lower than the other studies(70-95%). The reasons of low incidence of recurrent anginal pain may be due to unaware symptom of patients, limited activity after post PTCA and the high

percentage of patients continuing antianginal medications. Thus recurrence of anginal chest pain is an insensitive, nonspecific marker for detection of restenosis after PTCA.

The occurrence of angina during the treadmill test in our study is only 10% which is less than the previous study (34-40%). So it is also not a useful indicator for detection of restenosis in our study.

Exercise stress test: Positive exercise stress test during the follow up after PTCA was 45% in our study, and the incidence of chest pain on the treadmill evaluation was 10 %. Sensitivity and specificity for detection of restenosis was 63.6% and 66.7% respectively. This study also confirm the insensitivity of EST in the detection of restenosis. Although our sensitivity is higher than that in the previous reports (24-52%),it is far from acceptable as a diagnostic tool. The positive and negative predictive value of exercise stress test were 75.0% and 53.8% which are similar to what stated in the previous reported studies.

It should be emphasized that all patients achieve maximal predicted HR during exercise testing. In our study, most the patients (83%) achieved > 85 % of the predicted maximal heart rate. So it dose not explain the reason of insensitive marker of EST due to submaximal exercise.

The other problems which may interfere the interpretation of the exercise stress test and contribute to insensitive and nonspecific results are multi-vessel disease groups. Because the other area which had disease may cause the EST positive, even though there was no restenosis in the dilated vessels. So the patients with multivessel disease, angina and/or an abnormal stress test may reflecte the status of the untreated coronary artery and not the dilated vessels. Additionally, individuals who are receiving medications which prolong exercise capacity may have restenosis despite the lack of angina or a positive stress test. However, it may be neither safe nor realistic to discontinue in an attempt to improve sensitivity.

The false negative may occur in case of nonsufficient stenosis (50-75%) which does not result in exercise-related changes in electrocardiogram but that has led to sufficient abnormality in coronary flow reserve to result in abnormalies on the perfusion scan. Conversely, the false positive may result from procedure-related changes in coronary flow reserve, or may be related to small vessel disease or dynamic vasoreactivity,

abnormality such as coronary artery spasm which induce abnormal ECG changes although the patients have not angiographic restenosis(<50%).

Therefore, when comparing with MIBI scan, especially when detecting moderate coronary artery narrowing, the exercise stress test was less sensitive because the lack of early indicator of the presence of a non-critical stenosis and still it was insufficient to induce ST-segment depressing during exercise.

However, the usefulness of an exercise treadmill test for managing a patient after PTCA can be maximized by considering each of the components of the test, rather than simply examining the overall test interpretation. In this study, we hypothesized that the test interpretation, duration of exercise, maximum ST- segment deviation from baseline and presence of angina during the test would be most strongly related to the presence of restenosis.

Tc-99m Sestamibi SPECT imaging: At week 3 and 4, we found complete revascularizaion only 32 % and improvement or partial revascularization 68 %. In the previous study, the average of complete revascularization was 79-86 % after PTCA. However the optimal timing after angioplasty is controversial. In our study the false positive transient myocardial perfusion abnormality early after angioplasty was demonstrated, because all exercise-related perfusion scan subsequently normalized at 2 to 4 months. It is presumably caused by delayed return of coronary artery. From our study the optimal timing for evaluation revascularization may be after 4 weeks. If the study had been performed earlier after dilatation, it would have demonstrated a false positive in prediction of restenosis. We suggested that diagnostic evaluation with exercise Tc-99m Sestamibi SPECT imaging probably should not be done before week 4 and 6 after PTCA.

There is no previous report about detection of restenosis by SPECT Tc-99m Sestamibi imaging. In our study, sensitivity, specificity and accuracy of MIBI scan are 84.8%, 71.4% and 79.7% respectively which are higher than anginal chest pain and exercise stress test with statistical significance ($p<0.05$). And, our results are similar to the previous study by using Thallum-201 imaging (table 1).

There are many variables that affect sensitivity and specificity of Tc-99m Sestamibi SPECT imaging as shown in table 20 and 21. The possible variables that may cause the decrease in sensitivity of Tc-99m MIBI scan for detection of restenoses in our study are lesser degrees of coronary narrowing(> 50-75%), low exercise work load without

symptoms, antianginal drug therapy during testing, coronary collaterals which are protective in maintaining normal perfusion during exercise testing, and high proportion single-vessel disease in our study.

The important problem of decreasing specificity in our study is no knowledgeable regarding attenuation artifacts or variants of normal, especially using visual interpretation. Tc-99m MIBI is diminished at the apex of the left ventricle and base of the heart in areas of the outflow and inflow tracts. Breast, high left hemidiaphragm, bone and soft tisssue may also cause an attenuation artifact. It should be aware and well considered in the next study.

Table 20 Possible variables affecting sensitivity of Tc-99m Sestamibi SPECT imaging for detection of restenosis

Enhancing Sensitivity
Severe degree of myocardial ischemia
Achieving high exercise heart rate or work rate
Presence of multiple coronary stenoses
Coronary stenoses of >> 50%
Proximal location of stenoses
Associated abnormal ST segment response
Quantitative analysis of scintigrams
Diminishing Sensitivity
Circumflex coronary stenoses
Branch (e.g. circumflex marginal) or distal stenoses
Single-vessel CAD
Coronary collaterals
Lesser degrees of coronary narrowing
Low exercise work load without symptoms
Antianginal drug therapy during testing

Table 21 possible variables affecting specificity of Tc-99m Sestamibi SPECT imaging for detection of restenosis

No skill or knowledge of attenuation artifacts or variants of normal
Diminished uptake at thinner part (apex, base of heart at outflow and inflow tract)
Overlying bone and soft tissue
Breast tissue, high left hemidiaphram

Although the sensitivity and specificity of Tc-99m MIBI scan for detection of restenosis are quite lower than the standard value, when we sub-classified to detect restenosis of individual vessel, the improvement of sensitivity of MIBI scan was demonstrated (95.2%) in LAD but the specificity (60.6%) also decreased. Conversely, LCX and RCA showed the improvement of specificity (90.8%, 96.1%, respectively), but there was insensitivity (55.6%, 60.0%, respectively). We found that most of LAD lesion had presence of multiple vessel disease and it supplied a large area of myocardium, so it was not surprising to have higher sensitivity than LCX and RCA. We recognized one of the cause of decreased specificity of LAD distribution in our study which occurs from obliteration of side branch after stent placement of LAD in some cases. This event causes false positive during interpretation by using Tc-99m MIBI scan of myocardial ischemia that produced from occlusion of side branch, although there is no restenosis of dilated lesions. Moreover, from the previous report by using thallium-201 imaging, RCA and LCX usually had lower specificity (table 22) that they contrast with our result. A Higher specificity of Tc-99m MIBI scan for detection of restenosis of RCA or LCX in our study may be due to our awareness of attenuation artifact (e.g. high left hemidiaphragm, breast tissue) during interpretation. However, the result still cannot be explained overall. Thus, a further study is needed due to few numbers of patients included in our study.

When type classifications-type of CAD was considered, SVD was lower in sensitivity, specificity and accuracy than DVD and TVD. It is similar to the findings of the previous study. The chance of increase sensitivity, specificity and accuracy was more likely in triple vessel disease because of the larger areas and scatter of abnormal myocardial ischemia.

Table 22 Detection of restenosis in individual vessels by SPECT thallium-201 imaging

	No of vessels	Sensitivity (%)	Specificity (%)	Accuracy (%)
Left anterior descending artery	83	89	95	92
Left circumflex artery	62	88	79	82
Right coronary artery	40	76	83	85

When anginal chest pain, EST and MIBI scan are compared, the MIBI scan is a better tool for the detection of restenosis after coronary angioplasty. In addition to identifying the patients with restenosis, SPECT imaging, by virtue of identifying the restenotic vessel and the amount of ischemic myocardium, may be used to assist in determining the need for angiographic reevaluation.

Limitation of clinical and non invasive testings in our study were as follow:

1) Physiologic and anatomic findings are not correlated. The noncritical stenosis (50-75%) may not be sufficient to induce ST segment depression during the exercise although the patients have angiographic restenosis by a criteria >50% stenosis.

2) Patients with multivessel disease, angina and/or an abnormal exercise test may reflect the status of the untreated coronary artery and not the dilated vessel whereas the patients with coronary collteral vessels may have false negative EST and Tc-99m MIBI scan because that collterals are protective in maintaining normal perfusion during exercise testing, as assessed by quantitative Tc-99m MIBI scan.

3) Some patients who are recieving medication which prolong exercise capacity may have restenosis despite the lack of angina or a positive stress test. In our study, most of the patients received antianginal drug, so the clinical symptom was not found, even though the patient had restenosis. Moreover, if the patients could not achieve the target exercise heart rate or work load, the EST and Tc-99 MIBI scan may be false negative. However, it appears that the level of exercise achieved during the exercise stress testing influences the exercise ECG more than the Tc-99m MIBI scan.

4) Visual interpretation of Tc-99m Sestamibi SPECT imaging can be difficult if one is not knowledgeable regarding attenuation artifacts or variants of normal. This should be improved in the next study.

Clinical limitations

Several limitation in our study must be recognized. Patients selection is important, for it affects the properties of the test (i.e. sensitivity, specificity, predictive value) and the implication of the test can be, therefore, derived for clinical practice. It is possible that our patients have high probablity of restenosis by inclusion criteria. A report of true incidence of restenosis rate cannot be achieved. However, this study is a preliminary report of the accuracy. A further study is recommended. The varying definition of restenosis also influences the evaluation of sensitivity, specificity, predictive value of all functional tests such as exercise testing among studies.

The other problem that occurs during our study is unable to blind interventional physicians for the results of Tc-99m MIBI scan because its influence the clinical judgment and management of patients. So our study is a single blind method.

Clinical implications

The clinical implication of Tc-99m MIBI scan for the routine management of patients undergoing PTCA remains to be esablished. Certainly we would like to conclude that an abnormal noninvasive test early after PTCA is an indication for close clinical monitoring in view of the high chance of recurrence of symptoms.

The Tc-99m Sestamibi SPECT imaging should be performed (after 4-6 weeks after PTCA) in case of highly suspected restenosis such as atypical or typical chest pain, abnormal EST to confirm the true presence of restenosis and consideration of management such as repeated PTCA and/or stent. However the exercise ECG alone is still the first most-effective step for screening such asymptomatic patients.

Recommendations

- Fortunately, in our study we did not encounter the problem of disagreement of serial Tc-99m MIBI scan findings. If it occur in the study we suggest that it is necessary to set new diagnostic criteria of interpretation such as definite, possible or no restenosis.

- The next study should be performed with a large number of sample size with randomized method.

- The interpretation of Tc-99m MIBI scan should be done more carefully that of the attenuation artifacts or variants of normal.

- If the patients had not chest pain after PTCA, antianginal drug should be continued.

- Encourage the patients to a maximal target heart rate.

- Use the quantitative coronary analysis for measurement diameter of vessel instead of visual estimation for the improvement of accuracy, because there is intra and interobserver differences in interpretation, especially the difference between 20-80%.

- Compare the accuracy between Tc-99m sestamibi and thallium imaging for detection of restenosis.

- Evaluate risk stratification and follow up the acute cardiac event in long term and prognosis in the group of both symptomatic and asymptomatic patients who have ischemic evidence from MIBI scan for helping adjustment of recatheterization or repeat PTCA.