

Assessment of Viable Myocardium by Nitrate Augmented ^{99m}Tc MIBI Myocardial perfusion Imaging

Kashif Niyaz, Khalid Niaz, Maseeh uz Zaman, Shahid Kamal, Sharjeel Usmani, Salman Habib, Hina Hashmi, S. Waqar Hussain

Karachi Institute of Radiotherapy and Nuclear Medicine (KIRAN), Karachi.

Abstract

Objective: To determine the efficacy of ^{99m}Tc MIBI with nitrate administration for the detection of viable myocardium in patients with MI.

Methods: Thirty-five patients (31 men, 4 women; mean age 51.91 ± 8.86 years, median = 50) with previous history of myocardial infarction (with mean duration of 11.50 ± 11.4 , median = 4 months after MI) were included in the study. All patients underwent baseline rest and Nitroglycerine ^{99m}Tc MIBI myocardial perfusion imaging (2 day protocol). Fifteen out of 34 patients were also submitted for rest and redistribution TI-201 imaging (3 day protocol). The data were reconstructed in transaxial slices and then reoriented into short, vertical long and horizontal long axis slices. The images were divided into seven different segments for qualitative as well as semi quantitative analysis. The images were interpreted by two independent observers. The segments with tracer activity of more than 55% as compared to maximum, were considered as viable.

Results: In the baseline study with ^{99m}Tc MIBI, 168/245 (68.57%) were viable segments and these were increased to 197 (80.40%) in the Nitrate MIBI study ($p=0.001$ vs. baseline). Total 21 (60%) out of 35 patients demonstrated viable myocardium. The concordance for viable segments detection between Nitroglycerine MIBI and redistribution TI-201 imaging was found in 100 out of 105 segments (95.24%) for 15 patients, with significant kappa = 0.746 ± 0.079 SE.

Conclusion: The data suggest that use of nitrate augmented ^{99m}Tc MIBI protocol in Cardiac SPECT imaging results in improved detection of viable but hypoperfused segments and achieves results similar to those from standard TI-201 rest and redistribution protocol (JPMA 57:83;2007).

Introduction

The extent of myocardial viability in patients with chronic coronary artery disease, previous myocardial infarction (MI), and reduced left ventricular systolic function has both prognostic and therapeutic significance.¹ Its assessment is therefore important in the clinical treatment of such patients, especially when a revascularization procedure is being considered.² The concept of myocardial viability was proposed to explain the improvement of LVEF and heart failure symptoms after revascularization. Dysfunctional but viable myocardium (Hibernating) is likely to regain contractile function after coronary revascularization. On the other hand, dysfunctional non-viable myocardium (scar tissue) clearly will not improve.³ Myocardial Perfusion Imaging (MPI) is a common application for the diagnosis of CAD, but it is increasingly being used for diagnosis of acute MI, risk stratification after infarction and assessment of viable myocardium versus scar in patients with chronic coronary disease. Thallium-201 is considered a reliable agent for the recognition of viable myocardium if appropriate imaging protocols are used. The reliability of ^{99m}Tc MIBI in evaluating myocardial viability has been established.⁴ After initial concerns myocardial perfusion imaging

with ^{99m}Tc MIBI, particularly in combination with nitrate administration, has been demonstrated to give reliable results in the detection of viable hibernating myocardium. However scanty data is available in this regard. The aim of our study was to determine the role of ^{99m}Tc MIBI with nitrate administration for the detection of viable myocardium.

Patients and Methods

Patients referred by cardiologists to the Karachi Institute of Radiotherapy and Nuclear Medicine (KIRAN) were evaluated in the study. The inclusion criteria were, a history of previous myocardial infarction with a median duration of 4 months. A detailed history of each patient was noted and informed consent taken.

Study protocols

All patients were studied at least 48 hours after nitrate withdrawal. The patients were advised other anti-anginal medications and short acting nitrates to control the symptoms when long-acting nitrates were stopped 48 hours prior to the study. The Radiopharmaceutical used for the ^{99m}Tc Technetium (^{99m}Tc) study was the copper complex of 2-

2-methoxy-isobutyl isonitrile [Cu (MIBI) 4] supplied by IPD, PINSTECH under the name of PINSCAN MIBI. All the patients had two intravenous injections (740 MBq) of $^{99m}\text{TcMIBI}$ on two separate days, 2 days apart: one under baseline resting conditions (Baseline MIBI study) and other 15-20 minutes after sublingual nitrate administration (Nitrate MIBI study). Heart rate (HR) and blood pressure (BP) were monitored at baseline and 5 min intervals for 1 hour. All patients were ambulatory but remained in a resting state for 30 min before each study. A light fatty meal was given 15-20 min after the injection and SPECT imaging was acquired 1 hour following the injection of the radionuclide. Fifteen out of 35 patients were also called randomly for rest redistribution TI-201 SPECT. 3 mCi (111MBq) of TI-201 was injected at rest and scans were acquired 10- 15 minutes after injection. The redistribution images were collected after 3-4 hours delay of the resting injection.

A dedicated computerized high-resolution large-field rotating Siemens E-Cam Gamma camera with low energy all-purpose (LEAP) collimator was used to acquire SPECT images. Total 32 frames each of 30 seconds were acquired in continuous acquisition mode over 180 degree, anteriorly circular arc, with a starting angle of 315 degree right anterior oblique (RAO) position to the 135 degree left posterior oblique position. A 15% symmetric energy window centered at 140 KeV was used. A zoom of 1.6 was applied during acquisition. All projection images were stored on magnetic disc by means of 64 X 64 word matrix. Total study duration was 20 minutes.

Data processing was done on the ICON 8.5 Macintosh system interfaced with the Gamma camera. The raw data were corrected for decay factor and then filtered back-projection was performed. Reconstruction was performed manually and a Hann filter was applied. Transaxial tomographic scans of 6-mm thickness were obtained encompassing the whole heart. Sagittal and oblique long and short axis tomograms were reconstructed from the data obtained for the transaxial scans. The best slices were chosen from all three projections for diagnostic work-up.

Data analysis

For the semi quantitative as well as qualitative evaluation of the SPECT images, the short axis, vertical long axis and horizontal long axis slices were divided into seven different segments representing different vascular territories. Out of seven, 4 segments were assigned for left anterior descending artery, 2 for the left circumflex artery and 1 for the right coronary artery.

Total 245 segments were analyzed for the 35 patients. For visual analysis the segments with tracer uptake

equal to normal adjacent wall were considered as viable while those having uptake less than normal on visual analysis were defined as defective.

For semi quantitative analysis, images were split into 10 different color segments using 10 steps model on software, each colour showing percentage uptake. The segments with tracer activity of more than 55% as compared to maximum were considered as viable while those less than 55% were defined as defect. All images were interpreted by 2 independent observers, blinded with respect to the patient's name, diagnosis and other investigations. The inter-observer variability was present but was insignificant.

Statistical Analysis

The data was analyzed by comparing two percentages of viable myocardium before and after Nitrate MIBI scan and statistical significance (p-value) was drawn by comparison of proportion method. P-value for the change in haemodynamic parameter was determined using t-test method.

Results

Thirty five patients (31 males and 4 females) were studied. The age range was between 38 and 78 years (mean age 51.91 ± 8.8 years, median age 50 years). The past history had revealed that 16 patients had an anterior wall MI, 4 had anteraoseptal, 3 had lateral and 11 had interior wall MI. One patient had history of non-ST elevation MI. On Echocardiography the average ejection fraction of 35 patients was found to be 41.12 ± 14.99 . Total 63 segments were found to have wall motion abnormalities of which 34 were akinetic, 23 hypokinetic and 6 dyskinetic. Septum and anterior wall were the most commonly affected segments on echocardiography. Majority (50%) of the patients were asymptomatic, with episodes of post MI angina requiring antianginal treatment.

Haemodynamic Parameters of Nitrate MIBI study

There was a significant increase in heart rate ($p=0.01$) and drop in both systolic ($p=0.009$) as well as diastolic BP ($P<0.0003$) when baseline parameters were compared to post nitrate ones.

In the Base line MIBI study (which was carried out in resting condition without any pharmacological interventions); a total of 245 segments were analyzed of which, 168 (68.57%) were viable and 77 (31.42%) segment had perfusion defects. The LAD territory had the most, 45 defects, which was in concordance with Echocardiography findings.

Baseline vs. Nitrate MIBI study

The Nitrate MIBI study was performed after giving sublingual nitrate to the patients. It was observed that the detection efficacy of viable segments was enhanced as compared to baseline MIBI study (Table). Out of 77 perfusion defects in the baseline study a total of 29 (37%) segments improved, 48 (63%) remained unchanged while no segment

Table. Baseline MIBI Vs. Nitrate MIBI study.

	Segments	Viable Segments on Rest MIBI	Viable Segments on Nitrate MIBI	Percentage improvement of viability after nitrate	p-value
Total	245	168 (68.57%)	197 (80.40%)	(+) 17.26	0.001
LAD	140	95 (67.85%)	110 (78.527%)	(+) 15.78	0.03
LCX	70	51 (72.85%)	56 (80%)	(+) 9.8	0.15
RCA	35	22 (62.85)	31 (88.57%)	(+) 40.9	0.0004

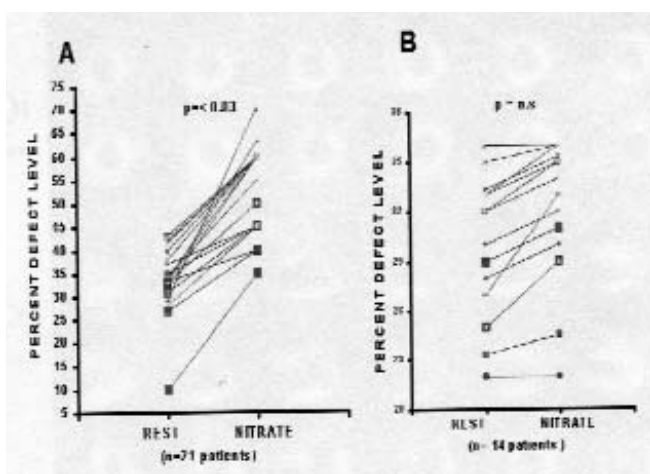


Figure 1. Average percent defect levels of individual patients at Rest and after Nitrate MIBI scan of both (A) with significant change ($p=0.03$) and (B) without significant change ($p=n.s.$).

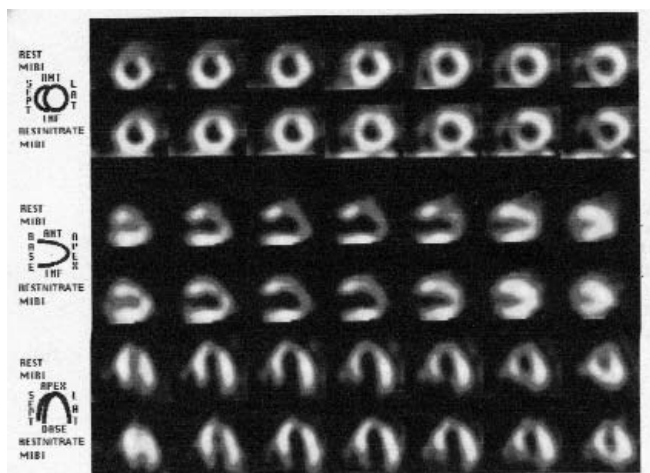


Figure 2. Myocardial perfusion scan showing improvement of defects of apico-anterior wall, apex and apical portion of septum after Nitrate MIBI study.

demonstrated worsening of tracer uptake after Nitrate MIBI

scan. The viable segments increased from 168 (68.57%) in the resting study to 197 (80.4%) in the nitrate study ($p=0.001$). The improvement in the territory of RCA ($p<0.001$) and LAD ($p<0.03$) was significant (Table 1).

The same number of viability and defect segments were observed on both visual as well as semi-quantitative analysis. Twenty one (60%) out of 35 patients (Figure 1A) showed improvement in average percent defect level from $33.5\% \pm 7.33$ in rest MIBI study to $53.25\% \pm 9.56$ in the nitrate augmented MIBI study ($p<0.03$). However in remaining 14 (40%) patients (Figure 1B) change of percent defect level (29.9 ± 4.34 to 32.06 ± 4.40) was not found to be significant.

Rest vs. Redistribution TI-201 study

In 15 patients the rest and 4 hours delayed redistribution TI-201 study was also done to compare the viable segments. A total 105 segments of 15 patients were analyzed to detect the viable tissues. It was observed that in rest TI-201 study, the number of viable segments had increased to 85 (80.95%) ($p<0.005$). Perfusion defects were 37 and 17 (45.94%) defects had improved in the 4 hours delayed redistribution TI-201 study, whereas 20 (54%) remained unchanged.

The 100 out of 105 (concordance=95.23%) segments showed the same segments of viability and defects in both TI-201 and Nitrate MIBI study, detected 5 viable segments (discordance=4.76%) more than the MIBI Nitrate study. The two data were significantly correlated with kappa = 0.740.079SE. It is concluded that both protocols are equally effective in the detection of viable myocardium (Figure 2).

Discussion

This study was designed to show whether administration of short acting nitrates could influence the rest uptake of $Tc-^{99m}$ MIBI in hypoperfused segments and hence useful in the detection of viable hibernating myocardium. In this study it was observed that there was significant number of viable segments ($p<0.001$) using nitrate in MIBI scan as compared to the resting study both on visual and semi quantitative analysis. The results of this study suggest that Nitrate administration prior to $Tc-^{99m}$ MIBI imaging enhances the detection of severely hypoperfused but still viable myocardium. The role of $Tc-^{99m}$ MIBI imaging to identify severely ischaemic but viable myocardium in patients with CAD has been established.⁵ However, the clinical experience with MIBI for detecting viable but hypoperfused myocardium has been variable. MIBI is a liposoluble cationic compound that is taken up by the myocardium through the transmembrane potential gradient and is fixed to the mitochondria. Its uptake is proportional to the coronary flow and therefore is a good perfusion tracer. Cell viability has a direct influence on the integrity of sarcolemma

and metabolic activity.⁶ Studies have shown that quantitative analysis of Tc-^{99m} MIBI uptake in resting conditions may similarly differentiate viable from non-viable myocardium and predict reversibility of regional wall motion after coronary revascularization.^{7,8} However, some studies have shown that Tc-^{99m} MIBI may underestimate the presence of viable tissue when used alone.^{9,10}

As Technetium-^{99m} MIBI alone has its limited role as tracer agent for viability so the additional agents have been used with it to enhance its ability to detect the viable myocardium. Nitrate administration improves regional coronary blood flow.¹¹ It is likely that coronary vasodilatation leads to improved delivery of tracer to areas where perfusion is reduced, thereby enhancing the MIBI uptake. Increased perfusion using nitrate is also due to the increase in the collateral flow. As Technetium-^{99m} is flow and perfusion dependent so when we use nitrate in combination, the perfusion of the previously hypoperfused segments are improved and tracer reaches these areas.

In this study focus was given to areas or segments of myocardium, which were hypoperfused or have absent perfusion in the resting condition using rest Tc-^{99m} MIBI perfusion scintigraphy. Viable hibernating myocardial segments remain under-perfused and nonfunctional under resting conditions but have their membrane intact. Administration of nitrate before reinjection Tc-^{99m} study results in increased perfusion of these segments. The viable segments now show increased uptake of the tracer. Hence segments showing reversible ischemia using nitrate augmented MIBI were regarded as viable hibernating myocardium. While the segments showing irreversible defects in both the studies are due to scar or fibrotic tissues having no viable tissues in them.

Similar results of improved Tc-^{99m} MIBI uptake has been found using sub lingual or intravenous nitrates in literature. Maurea et al have shown improvement in 27% of the perfusion defects after using nitroglycerine in technetium-^{99m} MIBI imaging.¹² Galli et al demonstrated a significant decrease in mean perfusion defect in 54% of the patients¹³ after receiving sublingual nitroglycerine. Sciagra et al, demonstrated a significantly higher ($p=0.0002$) Nitrate activity in the viable territories using Tc-^{99m} MIBI as a tracer.¹ According to results of Bisi et al. nitrate in the form of isosorbide dinitrate infusion caused post-revascularization functional recovery in 7 out of 10 patients and caused a significant decrease in extent of global uptake defect.¹⁴ Sciagra et al, in another study have shown a significantly higher number of viable segments ($p<0.002$) when comparing baseline and nitrate.¹⁵ Bisi et al, in one of his studies identified hibernating myocardium in eleven out of twenty eight patients by functional recovery in post-revascularization.¹⁶

So by improving 37% viable segments in 60% of the patients in our study and previous studies described above clearly suggest that nitrate is an important adjunct in Tc-^{99m} MIBI perfusion scan for the detection of viable myocardium.

We studied 105 segments of 15 randomly selected patients for Tl-201 rest-redistribution study. We compared the results of these in 15 patients and found that 100 out of 105 (concordance=95.23%) segments had similar results in the two scans. Previous studies have also shown similar results and proved that there is not much difference in the two tracers for viability segment detection. Sciagra et al, found that percent activity within asynergic territories was significantly influenced by their viability and type of acquisition but not by the tracer used. He further concluded that Baseline nitrate Tc-^{99m} MIBI SPECT appears no less effective than rest-redistribution Tl-201 in predicting post revascularization recovery.¹ As our data are also showing that there are no differences in detecting viable segments in between the two tracers, specially using nitrates with Technetium-^{99m} MIBI, so it can be considered as an equally good protocol

Conclusion

In patients with chronic ischaemic heart disease, use of nitrate augmented Tc-^{99m} MIBI protocol in Cardiac SPECT imaging, results in improved detection of viable but hypoperfused segments ($p < 0.001$). It is a good indicator for differentiating viable tissues from the scar. Nitrate augmented Tc-^{99m} MIBI protocol is equivalent to Rest-redistribution Tl-201 protocol for detection of viable myocardium.

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