

TECHNETIUM-99M MIBI GATED MYOCARDIAL PERFUSION SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY IMAGING - VALIDATION OF STRESS ONLY PROTOCOL

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ABSTRACT

Objective: To validate 'stress only' protocol against 'rest stress protocol in normal and essentially normal cases undergoing Tc-99m MIBI gated myocardial perfusion Single Photon Emission Computed Tomography imaging.

Study Design: A retrospective observational study.

Place and Duration of Study: Department of Nuclear Cardiology, Armed Forces Institute of Cardiology/National Institute of Heart Disease, Rawalpindi, Pakistan, from Jul to Sep 2019.

Methodology: 136 cases were included. Patients underwent Tc-99m gated Single Photon Emission Computed Tomography MPI using a single day, rest/stress protocol. The rest study was performed first with 8-10 mCi Tc-99m MIBI followed by stress study, 3 hours later with 3 times the rest dose. The most common stress technique was pharmacological stress and bicycle ergometer exercise with 0.14 mg/kg/min adenosine infusion. Few patients underwent physical stress using Bruce protocol, achieving a minimum of 85% of the target heart rate. Mages-stress followed by rest-were evaluated by two experienced nuclear cardiologists (blinded to the MPI reports) and interpreted as 'normal' or 'essentially normal'.

Results: Evaluation of stress-only and rest-stress Single Photon Emission Computed Tomography myocardial images yielded a concordance rate of 84.56% with Cohen's kappa coefficient of 0.69.

Conclusion: Substantial agreement and good concordance were found in normal and essentially normal 'stress only' and 'rest stress protocols.

Keywords: Myocardial perfusion imaging, Rest/stress imaging, 99mTc-MIBI.

How to Cite This Article: Dar ZS, Raza M, Atif M, Bukhari AR. Technetium-99m MIBI Gated Myocardial Perfusion Single Photon Emission Computed Tomography Imaging - Validation of Stress Only Protocol. Pak Armed Forces Med J 2021; 71(5): 1741-1745. doi: <https://doi.org/10.51253/pafmj.v71i5.5391>

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INTRODUCTION

Myocardial perfusion SPECT imaging (SPECT MPI) is a commonly used imaging modality for diagnosis, evaluation and risk stratification of ischaemic heart disease (IHD). Worldwide, 15-20 million MPI procedures are done annually.¹ International guideline recommends several imaging protocols for MPI studies using Tc-99m or Tl-201 radioisotopes, most common being rest stress dual-phase imaging with Tc-99m radiopharmaceutical.^{2,3}

However, SPECT MPI with an average effective dose of 26mSV with Tl-201 and 12mSv with rest/stress Tc-99m imaging poses certain radiation-related risks.⁴ Since the radiation-related adverse effects are stochastic in nature, there is no set safe lower limit of exposure below which the risk becomes zero. Hence, the field of nuclear medicine is governed by the principle of ALARA.⁵

In this regard, the American Society of Nuclear

Cardiology in 2010 had set a target of achieving <9mSv effective dose in at least 50% of the studies by 2014.⁶ However, INCAPS worldwide survey (2013) showed an effective dose ranging from <5 to >18 mSv with only 30% laboratories achieving the goal of <9mSv. In Pakistan, the figure stood at >11 mSv.⁷

Although with judicious clinical application, the benefits of MPI outweigh the risks involved, recommendations have been made to minimise the radiation burden. These include low dose radiopharmaceuticals and stress-only imaging, where applicable. Omitting the rest scan not only saves time and cost,⁵ but also reduces radiation exposure by 80%.⁷ The usefulness of stress-only MPI has been confirmed by many large study groups, in whom stress-only protocol showed a good prognosis in patients with normal stress perfusion.⁸

The rationale of this study was to validate the 'stress only' protocol for MPI studies in our centre against the 'rest stress protocol in normal and essentially normal cases and consider omitting rest phase imaging in these patients; thus saving costs and time and decreasing radiation exposure.

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Received: 24 Sep 2020; revision received: 10 Nov 2020; accepted: 11 Nov 2020

METHODOLOGY

This retrospective study was carried out in the Department of Nuclear Cardiology, Armed Forces Institute of Cardiology and National Institute of Heart Diseases, Rawalpindi, Pakistan, after approval from institutional ethics review committee (Ref no. 3/08/R&D/2020/71). All MPI scans done between July to September 2019, were evaluated. Stress phase was evaluated first, followed by the rest/stress images.

Inclusion Criteria: The patients with no evidence of perfusion abnormality on stress phase of MPI were included in this study through non probability consecutive sampling.

Exclusion Criteria: Patients with past history of myocardial infarction (MI) or any revascularization procedure (PTCA/CABG) were excluded from the study.

Finally, 136 cases were evaluated. As per imaging protocol, patients had abstained from all caffeine containing drinks for at least 24 hours. Beta-blockers, long-acting nitrates and calcium channel blockers were suspended for 24 hours as well. On the day of scan, patients had observed NPO for at least 6 hours.

All the patients underwent gated SPECT MPI using single day rest/stress protocol. The rest study was performed first with 8-10 mCi Tc-99m MIBI given intravenously followed by stress study, 3 hours later, with 3 times the rest dose. The most frequently employed stress technique was pharmacological stress with 0.14 mg/kg/min adenosine infusion over 6 minutes, augmented by bicycle ergometer exercise and radiopharmaceutical injection at 3rd minute. Few patients underwent physical stress on treadmill using Bruce protocol, achieving minimum of 85% THR, with radiopharmaceutical injection given at peak exercise and exercise continued for at least 1 more minute.

Image acquisition was done 45-60 minutes after administration of the radiopharmaceutical. Images were acquired using dual-head, Cardio MD® (Phillips) or Pulse CDC Positron® (IS2 Medical Systems) gamma camera system, equipped with low energy - high resolution collimators. Gated SPECT acquisition consisted of 8 time intervals per cardiac cycle, 64 projections, and time of 30 seconds per projection in rest phase and 25 seconds per projection in stress phase, in a 64 x 64 matrix. Studies were processed through Filtered Back Projection (FBP) with Butterworth filter applied at cut-off of 0.5 and order of 5. No post-filtering or attenuation correction was employed.

Stress images followed by rest images were evaluated by two experienced nuclear cardiologists (blinded to the MPI reports). Raw images were specifically evaluated in case of suspected attenuation artefacts. No attenuation correction was applied. Myocardial perfusion was assessed as 'normal' or 'essentially normal'. Essentially normal scans included those with suspected attenuation artifacts.

Data was analyzed using Microsoft Excel® 2010 software. For comparison of perfusion status in stress and rest phase images of each study, concordance rates of scan assessment (percentages of patients with similar assessment) and Cohen's kappa coefficient were calculated. In addition, range, mean and standard deviation of variables like age; and frequency of gender and co-morbid diseases like Diabetes Mellitus (DM) and hypertension (HTN) were also calculated.

RESULTS

A total of 136 patients were included in the study, with ages ranging from 22-81 years (mean age of 52.27 ± 12.18 years). Eighty subjects (58.8%) were males and 56 (41.2%) were females. Sixty (44.1%) had no co-morbid condition while 6 (4.4%) patients had diabetes, 38 (27.9%) were had hypertension and 32 (23.5%) had both diabetes and hypertension. About 117 (86%) patients were administered pharmacological stress whereas only 19 (14%) underwent physical stress over a treadmill with Bruce protocol.

On the evaluation of stress images, 67 (49.3%) patients were assessed as 'normal' and 69 (50.7%) were assessed as 'essentially normal'. However, after additional evaluation including both rest and stress images, 52 patients (38.2%) were assessed as 'normal' and 84 (61.8%) were assessed as 'essentially normal'. Essentially normal scans included 21 (15.4% of total) patients with suspected artefacts as shown in Figure-1 & 2. Of these, 11 (52.4%), all males, had diaphragmatic attenuation artefact; while 10 (47.6%), all females, had breast attenuation artefact.

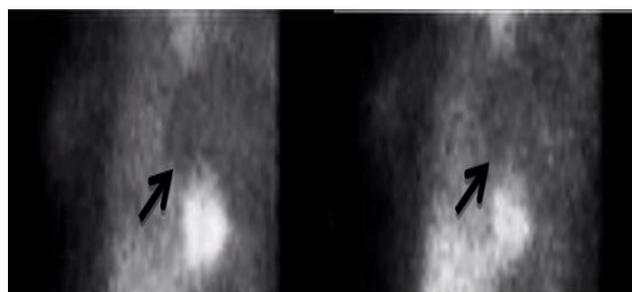


Figure-1: Raw images for stress and rest phase showing Breast attenuation artefact.

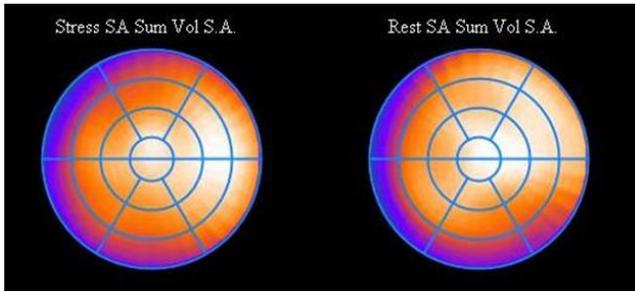


Figure-2: Polar maps of same patient in 4DM SPECT software.

Comparison of assessment of stress only images with rest-stress images from the same patients yielded a concordance rate of 84.56% as shown in Table-I and Cohen’s kappa coefficient of 0.69 as shown in Table-II.

Table-I: Comparison of assessment of stress only images with rest-stress images; concordance rate.

	Rest - Stress Imaging			Total
	Normal	Essentially Normal		
Stress Only Imaging	Normal	49 (36%)	18 (13.2%)	67 (49.2%)
	Essentially Normal	3 (2.2%)	66 (48.6%)	69 (50.6%)
		52 (38.2%)	84 (61.8%)	136 (100%)
Concordance Rate				84.56%

Table-II: Computation of Cohen’s Kappa coefficient.

Parameters	Normal	Essentially Normal	Total
Actual observed agreement	49 (36%)	66 (48.6%)	115 (84.6%)
Agreement by chance (%)	18.84%	31.34%	50.17%
Agreement by chance (no. of cases)	25.62	42.62	68.24
Cohen’s Kappa Coefficient			69.01%

DISCUSSION

PET and SPECT MPI are safe, accurate, data-supported and cost-effective tools for cardiac imaging, which have played a major role in early diagnosis as well as risk stratification of IHD.⁹ Individuals with a normal MPI have an estimated annual rate of 0.7% (exercise stress) and 1.2% (pharmacological stress) for any hard cardiac event or cardiac death, not significantly different from those with no CAD.¹⁰ Moreover, those with an abnormal MPI have up to a 12 fold increased risk of such cardiac events.¹¹

The last 20 years have seen a significant decline in the proportion of abnormal MPI scans, raising concerns about the overutilization of this entity. The decline in the frequency of abnormal MPI scans from 41% in 1991 to just 9% in 2009 has been reported. Other large studies have also shown a rate of normal MPI

scans between 60-70%, obviating the need of omitting rest MPI.¹²

Despite the fact that a long time has passed since the first application of the stress-only protocol,¹³ and 10 years from the time when EANM and ESC included the possibility of omitting rest MPI in its recommendation,¹⁴ the protocol is not being used widely. Mercuri *et al*, observed that a 21% reduction in radiation exposure could be achieved in the US by adopting a stress-only imaging protocol.¹⁵

In our study, patients were divided into 2 categories, normal and essentially normal. Essentially normal scans included those with suspected artefacts. In 115/136 (84.6%) the diagnosis made on the stress images was not altered after evaluating stress/rest dual images. However, in 21/136 (15.4%) patients the stress images were somewhat different from the rest images, although the initial diagnosis was not changed. About 18 out of these 21 patients had a normal stress scan, hence labelled a normal study, but the rest images were essentially normal, most likely due to lower dose resulting in some attenuation and poorer image quality. Three patients had essentially normal stress but normal rest images.

About 21/136 (15.4%) had an otherwise normal stress image but with a perfusion defect attributable to an artefact, as observed on raw images. The artefacts were present in the rest images as well. Of 10/21 patients, all females, had breast attenuation while 11/21, all males, had diaphragmatic attenuation artefacts.

Statistical analysis showed a concordance rate of 84.56% between ‘stress only’ and ‘rest/stress’ protocols with Cohen’s kappa coefficient of 0.69 which shows substantial agreement between the two modalities. This implies that a normal or near-normal set of stress images is enough to declare the scan as normal and omit the need of doing the rest images.

Włodarczyk *et al* suggested that neither a history of PCI nor the type of stress affected the concordance rate of stress-only imaging with rest/stress MPI. Attenuation Correction, however, improved the concordance rate significantly, from 60-68% ($p=0.018$). BMI also affected the concordance rates, from 72% in non-obese to 59% in obese patients ($p=0.05$). Rest study was felt necessary in about 20% of non-obese and about 50% of obese patients. However, a lower concordance rate in obese patients did improve when used with attenuation correction.⁸

Milan *et al*, calculated the concordance between stress-only and rest/stress MPI in non-Attenuation corrected studies in 200 patients. Out of 112 patients who had normal stress-only study, only 5% had an abnormal rest/stress study.¹⁶

Chang *et al* followed more than 16000 patients for over 4 and a half years, half of whom had stress only imaging. The mortality rate in patients with normal stress-only imaging was similar to those who underwent traditional rest/stress images.¹⁷

Duvall *et al* investigated 3,658 patients who underwent stress MPI. About 1,215 patients had Tl-201 MPI out of whom 716 (67%) had a normal stress-only study. Out of 2,443 patients who underwent Tc-99m MPI, 1,098 had normal stress-only studies while 493 had normal rest-stress studies. They were followed for an average time of 23.3 ± 5.3 months. Unadjusted all-cause mortality at the end of follow-up was 7.1% in the Tl-201 stress-only group, 6.3% for Tc-99m stress-only patients, and 4.3% in the Tc-99m rest/stress cohort. The risk-adjusted 1-year survival was between 98.5% and 98.8% in the three groups.¹⁸

Nappi *et al* did a single centre; single-arm prospective trial on 2106 suspected CAD patients, who had normal half dose stress-only MPI with conventional camera and wide beam reconstruction. Patients were followed for over 6.6 years. The incidence rate of cardiac death or nonfatal MI in patients with normal stress only images was 1.2%, which was not different from those undergoing standard dose stress-only and standard-dose rest/stress imaging.¹⁹

Songy *et al* recruited 1901 consecutive patients, without known CAD, who were injected with 1.8 MBq/kg (0.05 mCi) of Tc-99m radiopharmaceutical (Sestamibi or Tetrofosmin) and a CZT camera was used for imaging. 1400 patients with normal stress-only scans were followed for 39 months. In 1288 patients (92%) who achieved full follow-up, 22 cardiac and 16 non-cardiac deaths were reported yielding annualized rates of 0.55% and 0.37% respectively. Normal ultra-low-dose stress MPI with a CZT camera had a high negative predictive value and the effective dose was less than 1 mSv²⁰.

Gutstein *et al* followed up a group of 2465 patients. Out of 1114 (45.2%) patients had stress-only supine MPI, 388 (15.7%) had stress-only supine and prone imaging and the remaining 963 (39.1%) patients underwent a stress/rest SPECT protocol. The statistically similar annual mortality rate was observed between the stress-only supine/prone group (1.3%), the stress-

only supine (1.5%), and the stress/rest (1.5%) group ($p=0.47$).²¹

A local study by Zaman *et al* included 265 patients having a normal Gated SPECT study (normal LV perfusion and function parameters). The stress-only subgroup had 47 patients while the rest/stress sub-group included 218 patients. On 12-18 months follow up, only one death was reported, that too in rest/stress group, due to MI. Hence, the negative predictive value (NPV) for the stress-only cohort was 100% while it was 99.5% for the stress-rest cohort ($p=0.382$).²²

Some prior studies have also validated the image quality of half-dose stress-only imaging, which was found to be comparable to full dose rest/stress imaging but could not validate the prognostic significance.^{23,24}

Stress-only MPI studies in low to intermediate risk CAD patients also makes it at par with cardiac CT studies in terms of time to diagnosis, length of hospital stay and cost, with obviously improved prognostic accuracy and radiation burden.²⁵

LIMITATIONS OF THIS STUDY

a. As the data were retrospective, exact details of pre-test likelihood of disease in the patients studied were not available. However, the study included patients belonging to low and intermediate disease probability groups, with high disease probability patients excluded earlier on.

b. As our department follows single day, 'rest stress protocol for Tc-99m SPECT MPI, all patients underwent low dose rest imaging first, followed by stress imaging with three times higher radiopharmaceutical dose. When employing 'stress only' protocol, the possibility of inferior image quality and interpretation problems with the use of lower radiopharmaceutical dose can therefore not be excluded.

CONCLUSION

Substantial agreement and good concordance were found in normal and essentially normal Tc-99m MIBI myocardial perfusion SPECT scans done through 'stress only' or 'rest stress protocols. Rest phase imaging may be omitted if 'stress only' Tc-99m SPECT MPI reveals a normal or essentially normal outcome; thus saving cost, time and radiation exposure.

Conflict of Interest: None.

Authors' Contribution

ZSD: Conception and design of study, acquisition of data, interpretation of data, statistical analysis of data, drafting of manuscript, final approval, MR:

Conception and design of study, interpretation of data, statistical analysis of data, revision of manuscript, final approval, MA: Statistical analysis of data, literature review, revision of manuscript, final approval, ARB: Statistical analysis of data, literature review, revision of manuscript, final approval.

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