PROGNOSTIC VALUE OF STRESS-ONLY GATED SPECT MYOCARDIAL PERFUSION IMAGING: TIME FOR PARADIGM SHIFT

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ABSTRACT

Prognostic value of a normal rest-stress gated SPECT myocardial perfusion imaging (MPI) is well documented. A normal stress-only MPI study saves time, cost and avoids significant radiation exposure but its safety is questioned. **AIM:** Compare the prognostic value of normal stress-only and rest-stress MPIs. **PATIENTS AND METHODS:** This is a prospective study conducted at Nuclear Cardiology Department of Karachi Institute of Heart Diseases (KIHD) from December 2008 till May 2009. A rest-stress (same day) protocol was used in all patients but patients with lower pre-test probability for CAD in which stress (stress-only if MPI is normal) followed by a resting study (same day) if stress study is positive or equivocal. The protocol was decided by a board certified nuclear cardiologist. A dual head dedicated (Cardio MD, Philips) camera was used to acquire data. These patients / families were questioned on telephone regarding fatal or non-fatal myocardial infarction at 12-18 month. **RESULTS:** Study included 265 patients (104 males and 161 females, mean age of 52 – 10 years) having a normal GSPECT studies (normal LV perfusion and function parameters). The stress-only cohort included 47 patients (13 males and 34 females, mean age of 51 – 08 years) while rest-stress cohort had 218 patients (91 males and 127 females, mean age of 50 – 10 years). On follow up (12-18 months, mean 15 –3.4) only one death was reported among 265 patients (in rest-stress group due to fatal myocardial infarction). Negative predictive value (NPV) for stress-only cohort was 100% while it was 99.5% for stress-rest cohort (p =0.382). **CONCLUSION:** We conclude that a normal stress-only GSPECT MPI has an excellent and comparable short term prognosis with a normal rest-stress study. We recommend using this protocol as routine in low risk patients to save time, reduce cost and avoid significant radiation exposure.

Key Words: GSPECT, Stress-Only, MPI, rest-stress, ^{99m}Tc MIBI

Introduction

Stress single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) has enjoyed great success over 25 years as the most robust non-invasive test for diagnosing and risk stratifying patients with suspected or known coronary artery disease (CAD).[1] In USA about 18 million MPI were conducted in 2006 which is about 50% of procedures around the globe. In recent years stress MPI has been challenged by stress echocardiography and coronary CT angiogram (CCTA) due to its weaknesses like unacceptably long time (3-5 hours, or even 2 days) and significant radiation exposures like 11 18 mSv (for ^{99m}Tc tracers) and 27 30 mSv (for dual isotope rest Tl-201/stress ^{99m}Tc procedures).[2] Positive efforts have been made to address these issues in recent years by introducing new camera system (like semiconductor cameras), new image reconstruction methods and adjusting imaging protocols.

Rest-stress same day (8-15 mCi at rest and 25-35 mCi at stress) protocol continues to dominate American Society of Nuclear Cardiology (ASNC) guidelines.[3] This allows acquisition of both sets of images over a

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relatively short time period and requires little physician involvement until the time interpretation of study is rendered. An alternative approach is a same day stress-rest imaging protocol where a relatively low dose of radiotracer is injected at peak stress (i.e., 8 15 mCi) with avoidance of the higher 25 35 mCi rest dose if the stress acquisition is normal. This ensures a significant reduction in radiation exposure to patients (61% reduction),[4] save time and cost of second dose of ^{99m}Tc which has become very important in the current global Molybdenum-99 shortage. Basic reasons for reluctance to more uniformly adopt stress-only imaging as the preferred protocol are the requirement to assess each patient at the time of their arrival to the laboratory, presence of physicians to interpret with confidence that a stress image is normal, lack of sufficient clinical data to demonstrate the safety of stress-only imaging over the integrated interpretation of two sets of images (stress and rest).

The excellent 1 year prognosis of a normal rest-stress study is well recognized[5,6] however, apprehension remains about the reliability, diagnostic and prognostic accuracy of a normal stress-only study.

The objective of this prospective study was to determine prognosis of a normal stress-only MPI compared to a normal rest-stress MPI.

Patients and Methods

Study Design: This is a prospective study conducted at Nuclear Cardiology Department of Karachi Institute of Heart Diseases (KIHD) from December 2008 till May 2009. Our department follows rest-stress (same day) protocol as per ASNC/ American Heart Association (AHA) guidelines in all patients but patients with lower pre-test probability for CAD in which stress (stress-only if MPI is normal) followed by a resting study (same day) if stress study is positive or equivocal. The protocol was decided by a board certified nuclear cardiologist. Patients with a normal MPI, defined as absence of perfusion defects on stress images, normal left ventricular ejection fraction (EF ≥ 50%) and normal wall motion were included in the study while patients with known CAD or previous history of revascularization or positive MPI were excluded. Prognosis of normal stress-only study was compared to a normal rest-stress MPI by interviewing patients/family on telephone (12-18 months follow up) regarding major cardiac events (MACE) like fatal or non-fatal myocardial infarction (MI).

Stress and Imaging Protocols: Gated SPECT (GSPECT) was performed using dedicated dual head cardiac (Cardio MD, Philips) gamma camera with LEAP collimator, 32 projections around a 180 degree arc, a 64 x 64 matrix and 16 frames per cardiac cycle. Image reconstruction and LV functional parameters (LVEF, end diastolic volume [EDV], end systolic volumes [ESV] and wall motion [WM]) were measured by using commercially available Astonishfi and Autoquanfi software packages respectively. A LVEF ≥ 50%, ESV ≤ 70 ml and WM score of zero (in 17 segment model) were considered normal.

^{99m}Tc Methoxy IsoButyl Isonitrile (MIBI) was injected in dose of 10-15 mCi for stress (in stress-only or stress-rest protocols) or resting study (in rest-stress protocol). 25-30 mCi of ^{99m}Tc MIBI was injected for stress (in rest-stress protocol) or resting study (in stress-rest protocol). Image acquisition began 30-45 min after tracer injection. No attenuation correction technique was used and instead systolic wall thickening (SWT) and wall motion were used to rule out breast or diaphragmatic attenuation. However, in equivocal stress study, resting study was performed.

Standard exercise (Bruce or Modified Bruce Protocols) or pharmacological (using dipyridamole at 0.56 mg/kg in 4 minute) protocols were employed in each individual. Radiotracer was injected 1 minute before terminating exercise or 3-4 minute after dipyridamole infusion.

Statistical Analysis: Demographic and stress test variables were prospectively collected for all patients at the time of stress testing in the Nuclear Cardiology Database. Characteristics of the study population were described based on the type of stress protocol employed. A two-tailed student t-test was used to compare continuous variables and a chi-squared test was used to compare categorical variables. A 2 x 2 contingency table was used to estimate negative predictive value.

Results

During the study period (December 2008 till May 2009) 265 patients (104 males and 161 females, mean age of 52 – 10 years) were reported to have a normal GSPECT studies (normal LV perfusion and function parameters). The average weight of studied cohort was 71 – 12 Kg and risk factor assessment revealed hypertension in 191 (72%), diabetes in 85 (32%), dyslipidemia in 84 (32%), history of smoking in 35 (13%) and positive family history for CAD in 96 (36%) patients. Dynamic exercise was performed in 198 (75%) patients (Bruce 184 and Modified Bruce Protocol in 14) while dipyridamole intervention was used in 67 (25%) individuals (Tab.1).

Table 1. Patients Demographic Details

	Total population (265)	Stress only (47)	Rest Stress (218)
Age (mean–SD) years	52 – 10	51 – 8	50 – 10
Gender			
Male	104 (39)%	13 (28%)	91 (42%)
Female	161 (61%)	34 (72%)	127 (58%)
Risk Factor			
HTN	191 (72%)	37 (79%)	154 (71%)
DM	85 (32%)	12 (26%)	73 (33%)
DYSLIP	84 (32%)	13 (28%)	71 (33%)
F/H	96 (36%)	15 (32%)	81 (37%)
SMOKER	35 (13%)	3 (6%)	32 (15%)
Stress protocol			
Bruce	184 (69%)	36 (77%)	148 (68%)
Modified Bruce	14 (6%)	1 (2%)	13 (6%)
Persantin	67 (25%)	10 (21%)	57 (26%)

SD= Standard Deviation, HTN=Hypertension, DM=Diabetes Mellitus, DYSLIP=Dyslipidemia F/H=Family History

The stress-only cohort included 47 patients (13 males and 34 females, mean age of 51 – 08 years). The average weight of this cohort was 70 – 12 Kg and risk factor assessment revealed hypertension in 37 (79%), diabetes in 12 (26%), dyslipidemia in 13 (28%), history of smoking in 3 (6%) and positive family history for CAD in 15 (32%) patients. Dynamic exercise was performed in 37 (79%) patients (Bruce 36 and Modified Bruce Protocol in 01) while dipyridamole intervention was used in 10 (21%) individuals (Fig. 1).

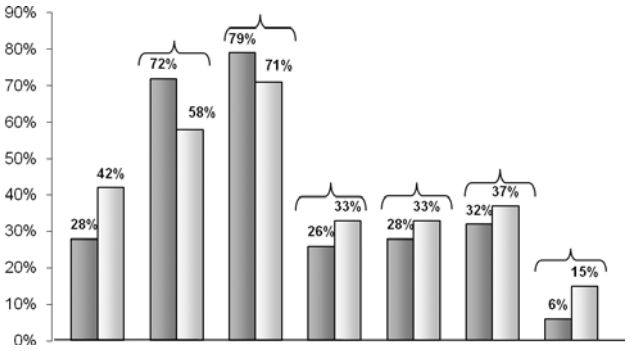

Figure 1: Histogram presentation of patient demographic in both stress only and rest stress protocol population.

The rest-stress cohort having normal LV perfusion and function parameters included 218 patients (91 males and 127 females, mean age of 50 – 10 years). The average weight of this cohort was 71 – 13 Kg and risk factor assessment revealed hypertension in 154 (71%), diabetes in 73 (33%), dyslipidemia in 71 (33%), history of smoking in 32 (15%) and positive family history for CAD in 81 (37%) patients. Dynamic exercise was performed in 161 (74%) patients (Bruce 36 and Modified Bruce Protocol in 01) while dipyridamole intervention was used in 57 (26%) individuals (Fig. 1).

On follow up (12-18 months, mean 15 –3.4) only one death was reported in rest-stress group due to fatal MI (about 9 months after MPI). No non-fatal MI was reported in rest stress cohort. In stress-only cohort, neither death nor non-fatal MI was reported. Negative predictive value (NPV) for stress-only cohort was 100% while it was 99.5% for stress-rest cohort. No significant difference in NPV between stress only and rest-stress cohort is seen (p =0.382) (Fig. 2).

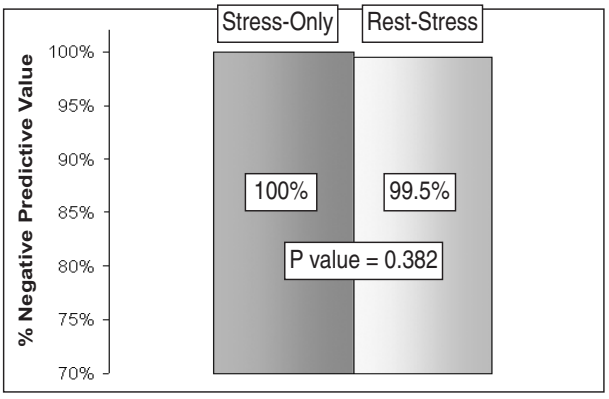

Figure 2: Histogram presentation of prognostic value of stress-only and rest-stress cohort at follow-up.

Discussion

GSPECT myocardial perfusion imaging is well recognized for its robust diagnostic and prognostic strength. Acquisition of two sets of images (either stress-rest or rest-stress sequence) is a routine in patients with known CAD or high risk population. A normal MPI has an excellent 1 year prognosis with annual risk of major cardiac events only 0.6%.[7,5,6] In low risk patients, performing a stress study first and if it is normal, resting study can be avoided as it adds no benefit and saves time and avoid radiation exposure from the second injection. However, the major obstacle in stress-only protocol is the safety as stated in a recent statement from ASNC in 2009 this strategy does not yet have sufficient data to support a widespread utilization.[8]

This study demonstrates that a normal stress-only scan has a benign outcome as compared with normal rest-stress cohort on an average follow up of 15 –3.4 months. Although the stress-only cohort included patients with low risk for CAD, NPV was marginally higher than rest-stress cohort but with non-significant p-value. This clearly supports that stress-only protocol having the ability to provide robust prognostic information with shorter test time (about 60-90 min as compared to 3-5 hr with rest-stress protocol) and 60-70% less radiation exposure. The findings of present study are in concordance with most of published studies like Lavalaye JM et al[9] (without attenuation correction), Duvall et al[10] Chang SM et al[4] (with attenuation correction).

In this study we did not use attenuation correction in either protocol and instead used systolic wall thickening and wall motion on gated analysis. In patients with equivocal findings on gating, a resting study was performed. Attenuation correction of stress MPI using an external source (Gadolinium-153) indeed improves the specificity[11,12] but prolongs the study duration and subtle but appreciable radiation exposure. This is the main reason for low number of patients in stress-only cohort in our study.

In present scenario of global molybdenum-99 (^{99}Mo) shortage and growing concern of radiation exposures caused by medical imaging, a strategy of initial stress imaging with selective rest imaging only among those with equivocal or clearly abnormal stress results should lower cost by eliminating unnecessary imaging time and radiopharmaceutical doses, improve laboratory throughput and significantly lower radiation exposure in a substantial percentage of patients without compromising the patients safety.

Conclusion

We conclude that a normal stress-only GSPECT MPI has an excellent and comparable short term prognosis with a normal rest-stress study. We recommend using this protocol as routine in low risk patients to save time, reduce cost and avoid significant radiation exposure.

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