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Myocardial Perfusion Gated SPECT in Prognostic Stratification of Egyptian Population with Suspected Ischemic Heart Disease

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ABSTRACT

Background: Evaluation of the left ventricular perfusion and function is important in clinical cardiology. Quantifying the degree and extent of functional abnormalities of the left ventricle permits a systematic assessment of the disease state. Gating provides additional information that cannot be obtained by perfusion imaging alone. The diagnostic role of myocardial perfusion gated SPECT in patients with coronary artery diseases is well recognized, however its role in risk stratification, and prognostication is still growing.

Objective: To assess the feasibility of ^{99m}Tc-MIBI myocardial perfusion gated SPECT (GSPECT) in prognostic risk stratification of an Egyptian population with known or suspected coronary artery disease.

Methods: Clinical data and SPECT results were analyzed in 165 consecutive patients that were monitored for mean follow up period of 13.8 ± 5.3 months. Semi quantitative visual scoring of perfusion and function was performed while post-stress EF, EDV and ESV were automatically generated. Multivariate Cox proportional hazards regression models were used to identify independent predictors of cardiac events while survival analysis was performed using Kaplan-Meier method.

Results: Perfusion findings were abnormal in 98 patients. During follow-up, death occurred in 5 patients; nonfatal myocardial infarction in 14; coronary revascularization in 48 and unstable angina in 4 patients. In multivariable Cox proportional hazards model, DM (p=0.002), previous MI (p=0.029), and reduced EF (p<0.001) were independent predictors for major events (death and MI), while independent predictors for total events include the same parameters in addition to high cholesterol level (p=0.015) and number of both normal and ischemic segments (p=0.001). Patients with history of DM, previous MI and EF<50% had reduced event free survival. Patients with low EF<35% and those with multivessel disease were at higher risk and had shorter event free survival.

Conclusion: Myocardial perfusion gated SPECT parameters are considered not only a powerful independent predictors for cardiac events but also have an incremental prognostic value over the pre scan clinical variables for risk stratification in Egyptian patients with known or suspected CAD.

Key Words: Coronary artery disease; Gated SPECT; prognosis

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INTRODUCTION:

Evaluation of the left ventricular (LV) perfusion and function is important in clinical cardiology. Quantifying the degree and extent of the LV function abnormalities permits a systematic assessment of the disease process on the myocardial performance, provides an objective basis for the risk stratification and therapeutic strategy and allows for the sequential follow-up of the therapeutic response[(1)]. Left ventricular dysfunction is the most important predictor of mortality following myocardial infarction. The diagnostic role of myocardial perfusion SPECT in patients with coronary artery diseases (CAD) is well recognized. Gating Provides additional information that cannot be obtained by perfusion imaging alone[(2).] A number of studies have demonstrated the clinical usefulness of GSPECT. The value of GSPECT in assessment of ischemic severity is well documented. The role in risk stratification, prognostication, viability assessment, and follow-up is still growing[(3)].

MEHODS:

Study population

We identified 165 consecutive patients who underwent TC-99m MIBI myocardial perfusion gated SPECT imaging between January 2008 and October 2010. Patients with known valvular heart disease or non-ischemic cardiomyopathy were excluded. Patients were followed up for 13.8 ± 5.3 months for cardiac events. Events were defined as Major events (death & nonfatal MI), coronary revascularization (> 60 days post imaging) and unstable angina[(4, 5)]**.** At the time of the radionuclide study, all patients were subjected to evaluation by clinical history taking, risk factors assessment, resting and exercise ECG and ^{99m}Tc-Sestamibi myocardial perfusion GSPECT imaging. Events were noted and confirmed whenever possible by review of hospital medical records, charts or medical reports, through direct interviews or telephone contact.

Myocardial Perfusion Protocol

Patients were fasting for at least 4 hours before the study. In all patients, ß-blockers and calcium channel antagonists were discontinued 48 hours before testing, nitrate compounds were discontinued at least 12 hours before testing and coffee and tea avoided in the day of the study. Patients underwent myocardial perfusion GSPECT imaging using either one or two day's protocol. More than 95% of patients underwent exercise stress testing using standard Bruce's protocol with 12-lead ECG. Few patients (less than 5%) were subjected to pharmacological stress using dipyridamol at a rate of 0.14 mg/kg/min for 4 minutes.

SPECT Acquisition Protocol:

Patients underwent myocardial perfusion gated SPECT imaging using either one or two days protocol. For one day protocol, I.V. injection of 300-370 MBq of ^{99m}Tc-MIBI was done at the first phase and the second phase was done after I.V injection of 925-1100 MBq of ^{99m}Tc-MIBI. In two days protocol ^{99m}Tc-MIBI was injected in a dose of 740-925 mCi for each phase. Imaging was acquired 45-60 min after isotope injection at rest or post stress.

Gated SPECT was performed using large field of view dual-head (Philips) Gamma camera equipped with a low energy high-resolution collimator. A protocol consisting of a 64 x 64 matrix, 32 projections per head for 35 seconds per projection was applied. Gated acquisition using 8 frames per cycle was applied during both phases of the study to assess LVEF, EDV, ESV, wall motion and thickening. All studies were reconstructed from row data using filtered back-projection and Butterworth reconstruction smoothening filter (cut-off frequency 0.5). The trans-axial slices were then oriented along cardiac planes into the standard short axis, horizontal long axis and vertical long axis.

Analysis of Perfusion and Function

Stress and rest perfusion images were scored semiquantitatively using a 20-segment model of the left ventricle and a 5-point scale (0, normal uptake; 1, mildly reduced uptake; 2, moderately reduced uptake; 3, severely reduced uptake; 4, no uptake)[4, 5]. After automatic reorientation, gated short-axis images were processed using quantitative gated SPECT software. The EDV, ESV and EF were automatically calculated.

Statistical Analysis

Perfusion scores, Wall motion, wall thickening, and global function were presented as mean and SD. Comparisons were performed using a two sided independent samples *t*-test for continuous variables and X^2 test for categorical variables. A probability value of <0.05 was considered significant. Receiver-operator characteristics (ROC) analysis was used to detect thresholds for EF, SDS, EDV, ESV, SWMS and SWTS that best predict cardiac events. The independent predictors of event free survival were identified using multivariate Cox regression analysis that only included the statistically significant variables from the univariate analysis. Forward stepwise method for selection of variables was used with entry significance level set to $p<0.05$ and removal significance level set to $p>0.10$. All such analysis were performed separately for each study end point (Major events or Total events). Kaplan-Meier curves were presented to display total events free survival curves stratified by the most powerful independent predictors of cardiac events with *p*-values calculated according to the log-rank test (Mantel-Cox test). Statistical analysis was performed using SPSS13.0 software.

RESULTS:

The demographic data of the study population and their characteristics are shown in Table (1). The mean age was 54.0 ± 8.0 years. Males represented 134 (81.7%) with M:F ratio of 4.3:1. The prevalence of CAD risk factors including diabetes mellitus, systemic hypertension, hypercholesterolemia, smoking and presence of family history were 42%, 71%, 55%, 55% and 12% respectively. Patients were further classified according to myocardial perfusion imaging (MPI) into negative and positive groups for better demonstration of these subgroups characteristics. The mean follow up time for the entire population was 13.8 ± 5.3 month.

Table (1): Demographic data of the study group

	Study Population n=165	Negative study n=67 (41%)		Positive study n=98 (59%)
Mean Age (years)	54.0 ± 8.0		54.0 ± 6.0	56.0 ± 8.0
M/F ratio	4.3: 1	2.5: 1		7.2: 1
Diabetes mellitus	69 (42.3%)	23 (34%)		46 (47%)
Systemic HTN	116(70.7%)	43 (64%)		73 (74.5%)
High cholesterol	90 (54.5%)	30 (45%)		60 (61%)
Smoking	90 (54.5%)	30 (45%)		60 (61%)
Family history	19 (11.5%)	11 (16.4%)		8 (8%)
Previous MI	32 (19%)	0		32 (32.6%)
Previous PCI	15 (9%)	0		15 (15%)
Previous CABG	6 (3.6%)	0		6 (6%)

Outcome events

The relationship between scan results and cardiac events for all patients is shown in Table 2. Among the study population, total cardiac events represent 71 (43%), Major cardiac events (death or MI) occurred in 19 (11.5%) of the patients (Death in 6 and non-fatal MI in 13 cases). Late revascularization (>60 days post imaging) represented 48/98 (49%). Unstable angina was noted in 4 (2.4%) patients.

Table (2): Outcome events for patients with negative and positive MPI study

Cardiac event	Study Population n=165	Negative study n=67 (41%)	Positive study n=98 (59%)
Total Cardiac Events	71 (43%)	11 (16.4%)	60 (61%)
Major Events (death or MI)	19 (11.5%)	4 (5.9%)	15 (15.3%)
Death	6 (3.6%)	2 (2.98%)	4 (4.1%)
MI	13 (7.9%)	2 (2.98%)	11 (11.2%)
Late Coronary Revascularization	48 (29%)	7 (10%)	41 (42%)
Unstable Angina	4 (2.4%)	None	4 (4%)

Univariate predictors of major and total cardiac events

As shown in Table 3, univariate clinical predictors of major events included DM and previous MI. In addition to these variables, Age, and high cholesterol level were predictive for total cardiac events. All these parameters showed significant statistical difference as (p<0.05*)*. As regards the major cardiac events all the imaging functional parameters exhibit statically significant difference (p<0.05).

Patients with major events had lower EF (36±15, p<0.001), higher EDV (244 ± 114, p=0.002) and ESV (149 ± 95, p=0.002) values, impaired SWMS (23.9 ± 13.9, p=0.001), SWTS (13.0 ± 10.5, p=0.004) and more frequent TID (p=0.001). The most important variable for univariate prediction of major events is EF (p<0.001*)*. Other perfusion variables showed statistically significant difference including number of normal (p= 0.012) and infracted segments (p=0.011). All the perfusion and function parameters showed statistically significant differences as regards total cardiac events.

Table (3): Clinical and imaging variables in patients with and without major and total events

	Variable	Major events (Death or MI) Yes n=19 (11.5%)	Major events (Death or MI) No n=146 (88.5%)	*p* Value	Total events Yes n=52 (32%)	Total events No n=113 (68%)	*p* Value
Clinical Variables	Age (years)	54.95± 7.0	52.68± 9.3	0.309	55.0 ± 7.0	50.0 ± 9.0	0.027*
	Men	18 (95%)	116 (79.4%)	0.118	44 (85%)	90 (79.6%)	0.512
	Female	1 0 (5%)	30 (20.5%)	0.118	8 (15 %)	23 (20.4%)	0.512
	DM	13 (68%)	56 (38.4%)	0.014*	30 (57.7%)	39 (34.5%)	0.007*
	HTN	17 (89.5%)	99 (68%)	0.560	41 (78.8%)	75 (66.4%)	0.120
	High cholesterol	14 (74%)	73 (50%)	0.550	36 (69%)	51 (45%)	0.005*
	Smoking	13 (68%)	77 (52.8%)	0.207	30 (57.7%)	60 (53.1%)	0.622
	Family history	1 (5%)	18 (12.3%)	0.360	5 (9.6%)	14 (12.4%)	0.591
	Previous MI	9 (47%)	23 (15.8%)	0.001*	18 (34.6%)	14 (12.4%)	<0.00*
	Previous PCI	3 (16%)	12 (8.2%)	0.291	7 (13.5%)	8 (7.0%)	0.198
	Previous CABG	2 (10.5%)	4 (2.7%)	0.090	2 (3.8%)	4 (3.5%)	0.931
Imaging Variables	Normal seg.	13± 5.6	16.7±3.8	0.012*	13.5± 4.6	17.6 ±3.0	<0.001*
	Ischemic seg.	3.0±2.7	2.0±2.6	0.392	3.6±2.9	1.3±2.0	<0.001*
	Infracted seg.	4.4± 4.7	1.3±2.5	0.011*	3.0± 3.8	1.0±2.0	<0.001*
	SSS	20.00± 12.9	15.70±7.6	0.172	20.00± 10.7	14.0±65	<0.001*
	SRS	17 ± 12.	13.6 ± 6.7	0.198	16.6 ± 9.6	13.0 ± 6.0	0.002*
	SDS	2.63± 2.7	2.10± 2.3	0.362	3.0± 3.0	2. 0± 1.7	<0.001*
	EF	36±15	54±10	<0.001*	33 (63%)	29 (25.6 %)	<0.001*
	EDV (ml)	244 ± 114	148 ± 56	0.002*	190 ± 88.0	145 ± 59	<0.001*
	ESV (ml)	149 ± 95	68 ± 41	0.002*	100 ± 72	68 ± 44	0.003*
	SWMS	23.9 ± 13.9	10.7 ± 8.4	0.001*	18 ± 11	10.0 ± 8..5	<0.001*
	SWTS	13.0 ± 10.5	5.5 ± 4.0	0.004*	9.6 ± 7.6	5.0± 4.0	<0.001*
	TID	13 (68%)	42 (28.8%)	<0.001*	30 (58%)	25 (22%)	<0.001*

*p value <0.05

Multivariate Cox Proportional Regression Analyses

Table 4 summarizes the independent variables for major events that were accepted in the final multivariate model. Variables of previous MI, DM, and EF were significant predictors in the ascending order of strength based on chi square (χ^2) score values with global model χ^2 score of 39.380 (p<0.0001). The model for prediction of total events is shown in (Table 5). In addition to the above mentioned clinical variables this model included, high cholesterol level (overall score = 24.492, p<0.001). Significant improvement in the global model χ^2 score (overall score = 46.615 Vs 24.492: p<0.001) was noted after addition of the mean number of both normal and ischemic segments. Further addition of EF>50% to clinical and perfusion parameters revealed significant improvement in the global score (49.96 Vs 46.62; p<0.001).

Table (4): Cox proportional hazards regression model for prediction of major events (Death or MI)

Parameter		Wald	*p* value	Overall (χ^2scor)	*p* value	HR
Clinical Variables	Previous MI	0.964	0.326	11.585	0.001*	1.644
	Diabetes	2.743	0.098	16.813	<0.001*	2.297
Imaging Variables	EF*	17.281	<0.001	39.380	<0.0001*	0.928

***p<0.05*; Significant; **HR, Hazard ratio [Hazard rate per 1 unit change]

Table (5): Cox proportional hazards regression model for prediction of total-events (Death, MI & Late Revascularization)

Parameter		Wald	*p* value	Overall (χ^2score)	*p* value	HR
Clinical variables	Diabetes	7.630	0.006	11.577	<0.001*	2.178
	↑↑ Cholesterol	5.908	0.015	18.887	<0.001*	2.083
	Previous MI	8.997	0.003	24.492	<0.001*	2.409
Imaging Variables	Normal segments (mean)	31.529	<0.001	44.312	<0.001*	0.855
	Ischemic segments (mean)	14.142	<0.001	46.615	<0.001*	1.200
	EF>50	5.188	0.023	49.956	<0.001*	0.491

***p<0.05*; Significant

Kaplan Meier survival Analysis

The Kaplan-Meier survival curves in Figures 1 and 2 illustrate the different survival rates according to DM and previous MI. In patients without history of DM, the prognosis was most favorable compared to diabetic patients (p= 0.015). The event free survival rate was higher in patients who are free from prior MI compared to those with previous MI (p=0.005). Figure 3 demonstrates that Patients with high cholesterol level had significantly lower event free survival (p=0.01). Patients with EF<50% had significantly lower event free survival for total events (Figure 4). Patients with ischemia (expressed as >1 ischemic segment) and EF<50% were at the highest risk for total events with significantly lower event free survival compared to those with no ischemia and normal EF (P<0.0001) and those with either ischemia alone or EF<50% alone (Figure 5). Similar results of Kaplan-Meier analysis were noted for major events as regarding DM, previous MI and EF.

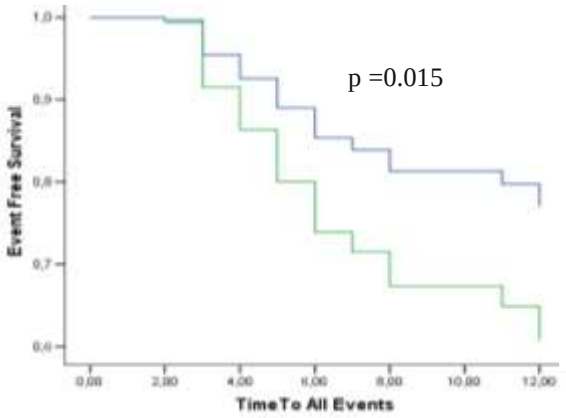

Figure 1 Freedom from total events stratified by DM

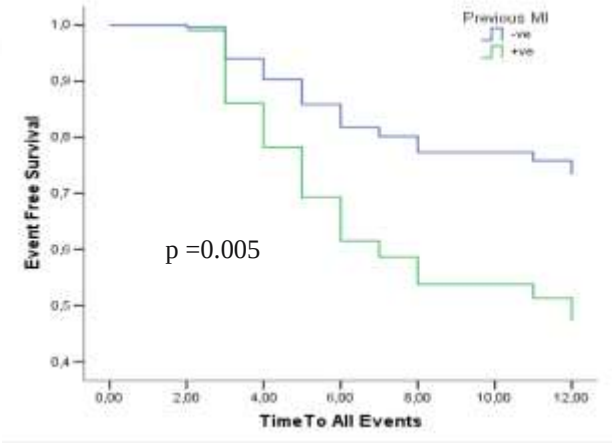

Figure 2 Freedom from total events stratified by presence of previous MI

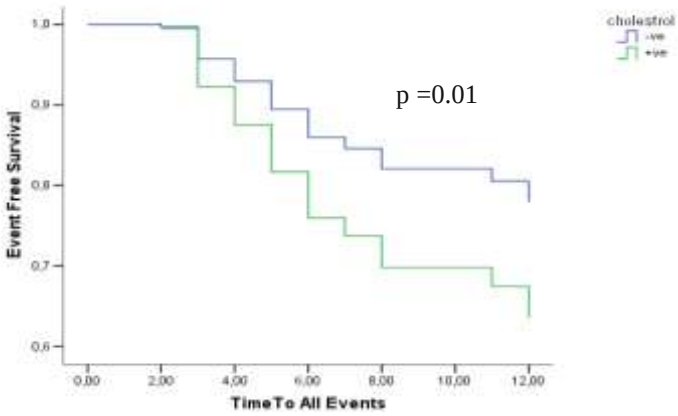

Figure 3 Freedom from total events stratified by presence or absence of hypercholesterolemia

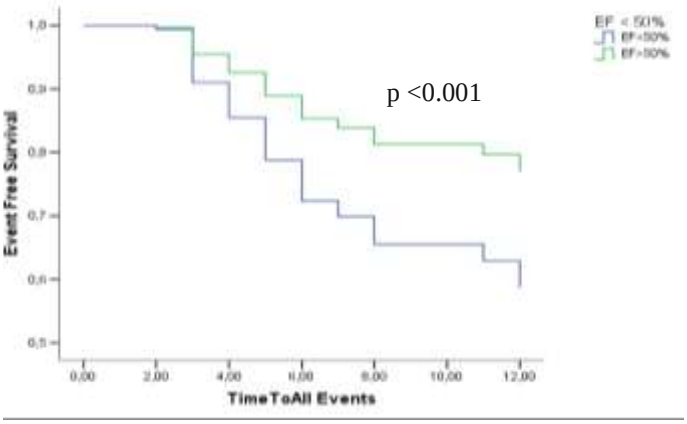

Figure 4 Freedom from total events stratified by EF< or >50%

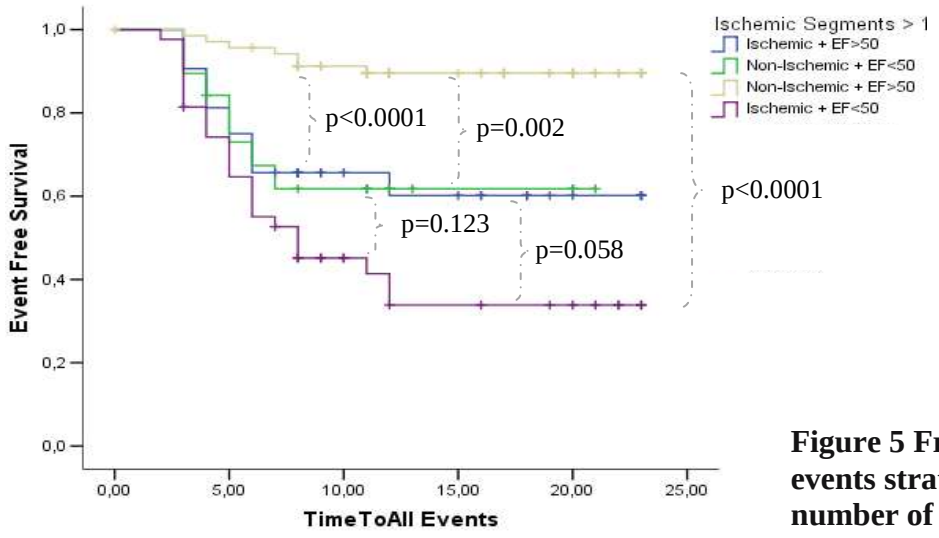

Figure 5 Freedom from total events stratified by EF and number of ischemic segments

DISCUSSION:

Myocardial perfusion imaging with gated SPECT is generally accepted as a valuable tool for estimating patient risk and planning further clinical management with stable coronary artery disease (CAD) [6]. In our study using Egyptian population, DM, hypertension, dyslipidemia and smoking were present in 69 (42.3%), 116 (70.7%), 90 (54.5%) and 90 (54.5%) of study population respectively. Traditional risk factors as defined by the Framingham for CAD are cigarette smoking of any amount, elevated blood pressure, elevated serum total cholesterol and low-density lipoprotein cholesterol, low serum high-density lipoprotein cholesterol, DM, and advancing age[7]. In our data the univariate analysis of clinical parameters for major and total cardiac events showed that DM and history of prior MI were important predictors for events. It was found that DM is a predictor of both MI and cardiac death. Asymptomatic patients with DM frequently have abnormalities on perfusion imaging and are likely to be at increased risk of an adverse outcome from their silent ischemia[8]. Also, it was found that DM is one of the most important predictors for cardiac events in all Western and Japanese-Asian studies[9]. Diabetes mellitus similarly increased total cardiac event rate, and it has been considered as a common risk factor in all nations[10]. Our results revealed that age and high cholesterol level were identified as additional predictors of univariate analysis for total cardiac events Hayes et al., in 2003, reported that univariate predictors for total events include age, gender, hypertension, DM, history of MI and revascularization, adenosine stress and high SSS[11]. Matsuo et al., in 2008 showed that age, DM, hypertension and hypercholesterolemia were independent predictors of all cardiac events[12]. Several studies have shown that not only does scan data provide incremental prognostic information over prescan information, but prescan data (e.g., age, prior CAD, DM, hypertension, hypercholesterolemia, smoking, atrial fibrillation and pharmacologic stress) also yield incremental prognostic information over MPS results[12,14]. In the current study the univariate analysis of the imaging parameters for the major and total cardiac events revealed that all the perfusion and function imaging parameters included in this study had significant statistical difference in prediction of events ($p<0.05$). Multiple previous studies revealed that nuclear perfusion and function parameters including SSS, SRS, SDS, LVEF, EDV, ESV, SWMS, SWTS and TID were significant predictors in univariate analysis for both hard and total cardiac events[15, 16, 17]. McLaughlin and Danias in 2002 revealed that the transient ischemic cavity dilation (TID) from stress-to-rest images, extent of regional wall thickening or wall motion abnormalities, EF, ESV, and EDV are powerful independent predictors for cardiac events[18]. Diabetes mellitus and number of coronary lesions, myocardial defect scores (SSS, SDS), EDV, ESV and EF were significant variables in univariate analysis for stratifying patients based on the risk for hard events[19]. Elhendy et al., demonstrated that abnormal perfusion was predictive of hard events in patients with CAD[20]. Gimelli et al, in 2004 showed that gated SPECT data including LVEF, EDV, ESV, SWMS, SWTS, SSS and SDS for prediction of cardiac events in patients with stable ischemic heart disease were significant predictors of cardiac event free survival[15]. It was demonstrated that a gated SPECT post-stress EF of <45% was an independent predictor of hard cardiac events[5].

In our study the multivariate analysis of the clinical and imaging variable for major events, revealed that independent prognostic variables included in the final model were in ascending order of strength DM, history of previous MI and the post stress EF. The post-stress EF was the most powerful predictor among all variables studied. Major events rate were higher in

patients with DM (68.4%), previous MI (47.4%) and Post stress EF<50% (78.9%). The contribution of perfusion and function data in predicting non-fatal MI and death as separate endpoints were not assessed in our study because of the relatively small number of such events during the follow-up period. The presence of DM in patients with ischemic heart disease indicates a poorer prognosis for any degree of image abnormality in prediction of hard events[8]. It is known that the presence of DM increases cardiac event rate and is comparable to prior myocardial infarction[10]. Our univariate analysis findings were consistent with previous data by Hachamovitch et al. that showed that the amount of perfusion abnormality at stress is a predictor of both non-fatal MI and death[21]. In a previous study, post-stress EF and end-systolic LV volumes were shown to have incremental prognostic values over prescan and perfusion information and post stress EF was the strongest predictor of MI and mortality. Patients at highest risk for hard cardiac events (cardiac death or infarction) are those with a low resting left ventricular ejection fraction with associated moderate or severe stress-induced reversible perfusion abnormalities[5]. In our study multivariate analysis revealed that DM, high cholesterol level and previous history of MI were independent clinical predictors of total events, while the imaging variables included mean number of the normal and ischemic segments as well as the EF>50%. Hachamovitch et al., in 2004 found that SDS, type of stress, DM, hypercholesterolemia, and ischemic ECG response to stress were independent predictors for cardiac events[22]. All-cause mortality and cardiac mortality were increased in patients with advanced age, male gender, smoking, and hyperlipidemia [23]. Also, the extent of the perfusion abnormality was one of the most important prognostic predictors of cardiac events in patients with CAD[19].A study by Shaw et al. in 2008 including 7849 patients revealed for every 1% increase in ischemic myocardium and for every 1% increase in resting myocardial defect, there was a 7% and 3% respectively increase in risk of cardiac events (cardiac death, MI and heart failure)[24]. This was consistent with the results of our much smaller population with 20% increase in risk of total events for every 1/20 ischemic myocardial segment and 15% reduced risk for every 1/20 normal segment.

We found that the post stress EF is a powerful predictor of total cardiac events with efficient stratification of patients using EF≥50% versus EF<50. Travin et al., in 2004 demonstrated that EF is an independent predictor in patients with CAD. Studies demonstrated that higher risk occurred significantly among patients with reduced post stress EF (30%-50%) compared to those with normal function (EF >50%)[16]. In our study Kaplan-meier analysis for both major and total cardiac events revealed that in the presence of DM or previous MI, there is significantly reduced event free survival. Moreover, Patients with high cholesterol level had lower rate of event free survival as regarding total cardiac events compared to patients with normal cholesterol level. In a study done by Giri et al., in 2002 for assessment of the impact of DM on risk stratification of patients with symptoms suggestive of CAD, revealed that DM worsens the prognosis for any given finding on radionuclide perfusion imaging even in patients with lower-risk studies[25]. Nishimura, et al., in 2008 found that in patients with ischemic heart disease the prognosis was most favorable among non-diabetic patients without prior MI compared to diabetic patients with prior MI with an event rate of 2.15% versus 11.68% per 3 years respectively. The event rates were similar among non-diabetic patients with previous MI and diabetic patients without prior MI: 5.06% and 5.73% per 3 years, respectively[17].

In our study population patients with ischemia (expressed as >1 ischemic segment) and EF<50% were at higher risk for total events with significantly lower event free survival compared to those with no ischemia and normal EF and those with either ischemia alone or EF<50% alone.

Studies had reported that patients with no ischemia were at very low risk of CD (<1%/y), and patients with a large amount of ischemia (SDS>7) had a death rate of >1%/y regardless of their cardiac function. However, patients with a mild or moderate amount of ischemia (SDS=2–7) could be stratified further to very low risk if they had normal ventricular function (EF>50%) and intermediate risk if they had mild to moderate ventricular dysfunction (EF = 30%–50%)[5, 26]. Left ventricular ejection fraction is a powerful prognostic predictor among patients with ischemic heart disease as determined by radionuclide angiography. The prognosis of patients with no angiographic abnormalities as well as normal perfusion and function has been considered good, but poor cardiac function (EF < 45%) in fact induced a higher cardiac event rate among patients with 3VD. The cardiac event rate in the patients with EF <45% was higher than those with EF ≥ 45%[19]. In the current study 79% of patients with low EF(<35%) developed total events versus 45% in those with intermediate EF (35-49%) while major cardiac events in these two groups were 27% versus 10% respectively. Patients with a normal exercise MPI have a combined rate of CD/MI of less than 1% per year, even in the presence of an abnormal stress electrocardiogram or coronary angiography that shows significant CAD[27]. Many studies show a risk of CD/MI that is lowest in patients with normal MPI, moderate in those with mildly abnormal MPI, and highest in those with a large area of abnormal perfusion. The annual death or non-fatal infarction rate is 0.7% in patients with normal MPI, versus 5.6% in patients with an abnormal scan[28].

Also, Elhendy et al., in 2005 found that in patients with typical angina complaints, a normal MPI is indicative of lower annual event rate of 1.5%, but MPI with perfusion abnormalities is indicative of higher annual event rate of 4.5%[29]. The outcome events in the current study displayed that patients with normal MPI study had lower events rate compared to those with abnormal MPI. They represented 4 (5.9%) versus 15 (15.3%) in major events and 11 (16.4%) versus 60 (61%) in total events over the entire study follow up period. The risk for total event rates were higher in those with more ischemia and/or reduced EF, indicating that perfusion and function findings can stratify cardiac risk in such patients. Studies had showed that patients with more extensive perfusion abnormalities had a relatively higher cardiac event rate[30]. Travin et al., reported that patients with an LVEF lower than 30% and defects in multiple territories had a particularly poor prognosis[16].

In a large recent multicentre study with long term follow up, it had been demonstrated that patients with significant ischemia without extensive scar were likely to gain a survival benefit from early revascularization while survival of those with minimal ischemia was superior with medical therapy[31]. The data from the current study revealed that myocardial perfusion gated SPECT is a powerful predictive tool for cardiac events with incremental prognostic value over prescan clinical variables and could be used to guide the decision process either by referring to intervention or conservative management. Further studies are required to establish therapeutic strategies for patients who are at a greater risk of cardiac event.

REFRENCES:

1. **Cullom SJ, Case JA, Bateman MD.** Electrocardiographically gated myocardial perfusion SPECT: technical principles and quality control considerations. J Nucl Cardiol; 5:418-425, 1998

2. **Lipke CSA, Kühl HP, Nowak B, et al.** Validation of 4DMSPECT and QGS for quantification of left ventricular volumes and ejection fraction from gated 99mTc-MIBI SPET: comparison with cardiac

magnetic resonance imaging. Eur J Nucl Med Mol Imaging; 31: 482-490, 2004.

3. **Hida S, Chikamori T, Usui Y, et al.** Effect of percutaneous coronary angioplasty on myocardial perfusion, function, and wall thickness as assessed by quantitative gated single-photon emission computed tomography. Am J Cardiol; 91:591-594, 2003.
4. **Matsumoto N, Sato Y, Suzuki Y, et al.** Incremental Prognostic Value of Cardiac Function Assessed by ECG-Gated Myocardial Perfusion SPECT for the Prediction of Future Acute Coronary Syndrome. Circ J; 72: 2035-2039, 2008.
5. **Sharir T, Germano G, Kang X, et al.** Prediction of myocardial infarction versus cardiac death by gated myocardial perfusion SPECT: risk stratification by the amount of stress-induced ischemia and the poststress ejection fraction. J Nucl Med; 42:831-837, 2001.
6. **Hendel RC, Berman DS, Di Carli MF, et al.** ACCF/ASNC/ACR/ AHA/ ASE/ SCCT/ SCMR/ SNM 2009 Appropriate use criteria for cardiac radionuclide imaging. J Am Coll Cardiol; 9;53:2201-29, 2009.
7. **Agarwal R, Nissenson AR, Batlle D, et al.** Prevalence, treatment, and control of hypertension in chronic hemodialysis patients in the United States. Am J Med; 115:291-297, 2003.
8. **Wackers FJ, Young LH, Inzucchi SE, et al.** Detection of Ischemia in Asymptomatic Diabetics Investigators. Detection of silent myocardial ischemia in asymptomatic diabetic subjects: the DIAD study. Diabetes Care; 27:1954-1961, 2004.
9. **Kawano H, Soejima H, Kojima S, et al.** Sex differences of risk factors for acute myocardial infarction in Japanese patients. Circ J; 70:513–7, 2006.
10. **Nakajima K, Matsuo S, Okuyama C, et al.** Cardiac Event Risk in Japanese Subjects Estimated Using Gated Myocardial Perfusion Imaging, in Conjunction With Diabetes Mellitus and Chronic Kidney Disease. Circ J; 76: 168-175, 2012.
11. **Hayes SW, De Lorenzo A, Hachamovitch R, et al.** Prognostic implications of combined prone and supine acquisitions in patients with equivocal or abnormal supine myocardial perfusion SPECT. J Nucl Med; 44:1633-40, 2003.
12. **Matsuo S, Nakajima K, Horie M, et al.** Prognostic value of normal stress myocardial perfusion imaging in Japanese population. Circ J; 72:611-713, 2008.
13. **Hachamovitch R, Hayes SW, Friedman JD, et al.** Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation; 107:2900-2907, 2003.
14. **Abidov A, Hachamovitch R, Rozanski A,et al.** Prognostic implications of atrial fibrillation in patients undergoing myocardial perfusion single-photon emission computed tomography. J Am Coll Cardiol; 44:1062-1070, 2004.
15. **Gimelli1A, Rossi G, Landi1P, et al.** Stress/Rest Myocardial Perfusion Abnormalities by Gated SPECT: Still the Best Predictor of Cardiac Events in Stable Ischemic Heart Disease. J Nucl Med; 50:546-553, 2009.
16. **Travin MI, Heller GV, Johnson LL, et al.** The prognostic value of ECG-gated SPECT imaging in patients undergoing stress Tc-99m sestamibi myocardial perfusion imaging. J Nucl Cardiol; 11:253-62, 2004.

17. **Nishimura T, Nakajima K, Kusuoka H, et al.** Prognostic study of risk stratification among Japanese patients with ischemic heart disease using gated myocardial perfusion SPECT: J-ACCESS study. Eur J Nucl Med Mol Imaging; 35:319-328, 2008.
18. **McLaughlin MG and Danias PG.** Transient ischemic dilation: a powerful diagnostic and prognostic finding of stress myocardial perfusion imaging. J Nucl Cardiol; 9:663-667, 2002.
19. **Nakajima K, Momose M & Nishimura Tsunehiko.** Prognostic significance of stress myocardial gated SPECT among Japanese patients referred for coronary angiography: A study of data from the J-ACCESS database. Eur J Nucl Med Mol Imaging; 36:1329-1337, 2009.
20. **Elhendy A, Schinkel AF, van Domburg RT, et al.** Risk stratification of patients after myocardial revascularization by stress Tc-99m tetrofosmin myocardial perfusion tomography. J Nucl Cardiol; 10:615-22, 2003.
21. **Hachamovitch R, Berman DS, Shaw LJ, et al**. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. Circulation; 97:535-543, 1998.
22. **Hachamovitch R, Abidov A, Rozanski A, et al**. Prognostic implications of atrial fibrillation in patients undergoing myocardial perfusion single-photon emission computed tomography. J Am Coll Cardiol; 44: 1062-1070, 2004.
23. **Duvall WL, Wijetunga MN, Klein TM, et al.** Prognosis of a normal stress-only Tc-99m myocardial perfusion imaging study. J Nucl Cardiol; 17, 370-7, 2010.
24. **Shaw LJ, Hendel RC, Heller GV, et al.** Prognostic estimation of coronary artery disease risk with resting perfusion abnormalities and stress ischemia on myocardial perfusion SPECT. J Nucl Cardiol; 15:762-73, 2008.
25. **Giri S, Shaw LJ, Murthy DR, Travin MI, Miller DD, Hachamovitch R, et al.** Impact of diabetes on coronary artery disease. Circulation; 105:32-40, 2002.
26. **Soman P, Parson A, Lahiri N, et al.** The prognostic value of a normal Tc-99m sestamibi SPECT study in suspected coronary artery disease. J Nucl Cardiol; 6:252-256, 1999.
27. **Brown KA and Rown M.** Prognostic value of a normal exercise myocardial perfusion imaging study in patients with angiographically significant coronary artery disease. Am J Cardiol; 71: 865-7, 1993.
28. **Zafrir N, Dahlberg ST, Villegas BJ, et al.** Prognostic utility of increased pulmonary thallium uptake in patients without ischemia. J Nucl Cardiol; 3:301-7, 1996.
29. **Elhendy A, Schinkel AF, Van Domburg RT, et al.** Risk stratification of patients with angina pectoris by stress 99mTc-tetrofosmin myocardial perfusion imaging. J Nucl Med; 46:2003-8. 11, 2005.
30. **Momose M, Nakajima K & Nishimura K.** Prognostic significance of stress myocardial gated SPECT among Japanese patients referred for coronary angiography: A study of data from the J-ACCESS database. Eur J Nucl Med Mol Imaging; 36:1329-1337, 2009.
31. **Hachamovitch R, Rozanski A, Shaw LJ, et al.** Impact of ischaemia and scar on the therapeutic benefit derived from myocardial revascularization vs. medical therapy among patients undergoing stress-rest myocardial perfusion scintigraphy. Eur Heart; 32:1012-102.