Association of Hemodynamic Changes with the Scan Parameters of a Dipyridamole-induced Stress Myocardial Perfusion Scintigraphy with Technetium-99m Sestamibi in Patients with Suspected Coronary Artery Disease

Noel Christi C. Macapagal, MD, Jerry M. Obaldo, MD, MHA

Division of Nuclear Medicine , Philippine Heart Center
E-mail address: noel.macapagal@gmail.com, jerryobaldo@yahoo.com

ABSTRACT

Introduction:

A dipyridamole induced stress myocardial perfusion scintigraphy with Tc-99m Sestamibi is utilized for diagnosing coronary artery diseases. The use of dipyridamole as form of pharmacologic stressor has expected hemodynamic changes.

Objective:

The objective of this study was to determine the association of these changes with the scan parameters in patients with suspected coronary artery disease (CAD).

Methodology:

A total of 101 patients, with suspected CAD, who underwent a dipyridamole-induced stress myocardial perfusion scintigraphy using Tc-99m Sestamibi from January 2019 to March 2020 were included in this study. The patient databases, monitoring sheets, and scan results were reviewed .

Results:

The blood pressure responses had no significant association with the scan parameters and results. The normal (> 1.2) and abnormal (<1.2) heart rate ratios (HRR), which is the peak HR/baseline HR, likewise had no significant association with the scan results. However, in terms of the median HRR, the higher ratio of 1.29 (normal scan results) against the ratio of 1.25 (abnormal scan results) was determined to be significant (p-value of 0.032). The HRR also had a direct and indirect weak correlation with stress and rest Left Ventricular Ejection Fraction (LVEF) values (p-values of 0.09 and 0.011) and Summed Rest Score (p-value of 0.007), respectively. For the 12-L ECG, only the baseline normal (P-value of 0.018) and infarct findings (p-value of 0.017) were similarly associated with normal and abnormal scan results, respectively.

Conclusion:

For patients with suspected CAD, the higher HRRs and baseline 12-L ECG of normal and infarct findings relates to the expected scan result. For scan parameters, the higher HRRs were also correlated with higher stress and rest LVEF values, and normal SRS, albeit a weak correlation. Notably, the blood pressure and post-infusion 12-L ECG changes had no significant association. In summary, the higher HRRs indicates normal scan results, normal SRS, and better LVEF values which increases the diagnostic confidence in the interpretation and management, especially in some equivocal cases.

Keywords: *dipyridamole, hemodynamic changes, myocardial perfusion scintigraphy*

INTRODUCTION

Coronary artery disease is chronic condition that affects the morbidity and quality of life and is the third leading cause of cardiovascular disease in the Philippines [1]. Therefore, a myocardial perfusion scintigraphy is used in determining the adequacy of blood flow to the myocardium. To increase its sensitivity, a form of stress is used which may be through exercise, or a pharmacologic stress agent. A vasodilator stress agent such as Dipyridamole produces indirect coronary dilation with a concomitant systemic vasodilatory effect wherein there is a decrease in blood pressure and reflex tachycardia [2]. These hemodynamic changes may provide useful information in imaging abnormalities in coronary artery disease.

It has been well documented that the intravenous use of dipyridamole produces mild hemodynamic changes with a near peak effect at 3 minutes from its infusion with side effects of hypotension, headache, dizziness, and dyspnea [3]. These side effects have demonstrated a correlation with hemodynamic variables but did not affect the imaging or ECG findings [4]. A blunted heart rate response to Dipyridamole infusion was associated with an LVEF of less than 45% and was also an independent predictor of an elevated summed stress scores (SSS), higher resting heart rate, and lower HDL levels [2, 5].

However, several studies have noted that the clinical significance of these hemodynamic responses is currently debatable [6]. An abnormal HRR and systolic blood pressure response may suggest an inadequate patient response to dipyridamole infusion. The aim of this study was to determine the association of hemodynamic changes with the scan parameters of a dipyridamole-induced stress myocardial perfusion scintigraphy with Technetium-99m Sestamibi in patients with suspected CAD.

Methodology

This is a retrospective cross-sectional study that included 101 adult patients referred to the Division of Nuclear Medicine, Philippine Heart Center for a dipyridamole-induced stress myocardial perfusion scintigraphy with Tc-99m Sestamibi for the assessment of suspected coronary artery disease between January 2019 and March 2020. Patients with an incomplete information sheet, database, or images were excluded.

The patients included must have strictly followed the Standard Operating Procedure (SOP-M-AMS-NMD-023) for a dipyridamole-induced stress myocardial perfusion scintigraphy with Tc-99m Sestamibi of this institution. The data compiled was then checked for any inconsistencies/errors to the procedure.

The patients' data were obtained from their information sheet, databases, monitoring sheets, and official scan results. These included the following: demographic data, clinical history, blood pressure and heart rate readings, electrocardiographs, and scan results. The pertinent data were entered into the prepared collection forms/ spreadsheets for statistical analysis.

The patients were then categorized based on their recorded blood pressures and heart rates as normal or abnormal. A normal systolic blood pressure (SBP) response was defined as a reduction of more than or equal to 10 mmHg from the baseline and a normal heart rate response was based on the heart rate ratio (peak HR/baseline HR) of more than 1.2. An abnormal hemodynamic response was less than 10 mmHg from the baseline for SBP and less than or equal to 1.2 for the heart rate ratio (HRR) [7]. Other variables considered were the ECG findings before and after dipyridamole infusion, time when the hemodynamic change was noted, and side effects.

Dependent variables are the scan findings of perfusion defects interpreted as reversible (ischemia) or fixed (infarct/fibrosis) – which were noted in the official reports. The widely adopted American College of Cardiology/American Heart Association (ACC/AHA) 17 segment polar map of the left ventricle with a five-point score scale was used for the summed stress score (SSS), summed rest score (SRS), and the summed difference score (SDS). The left ventricle ejection fraction values (LVEF) at stress and rest were also included. The scan results were likewise determined as either having normal or abnormal as indicated in the official reports. Normal scans were defined by the absence of any defect as seen in the final interpretation of the scan report and any finding that indicates otherwise were noted as abnormal.

Sample Size Calculation

With the G*Power 3.1.9.2, a minimum of 89 patients were needed for this study based on the average heart rate before (82) and after (92) the Dipyridamole test, common standard deviation of 10, 5% level of significance and 90% power.

Statistical Analysis

Descriptive statistics were used to summarize the demographic and clinical data of the patients. Frequency and proportion were then used for the categorical variables, median and inter quartile range for non-normally distributed continuous variables and mean and SD for normally distributed continuous variables. Independent Sample T-test, Mann-Whitney U, and Fisher's Exact/Chi-square test were used to determine the difference of mean, rank and frequency, respectively, between patients with normal versus abnormal result. Paired sample T-test was used to compare blood pressure and heart rate at baseline and after dipyridamole infusion. Spearman correlation analysis was used to determine the correlation of difference from baseline SBP and HRR to both the myocardial perfusion scores and LVEF values. Chi-square test for association was undertaken to establish the association of Myocardial Perfusion Score category and LVEF to Baseline ECG findings. Shapiro-Wilk was then used to test the normality of the other continuous variables. Missing variables were neither replaced nor approximated. Null hypotheses were rejected at 0.05 α- level of significance. STATA 13.1 was used for the entire data analysis.

RESULTS

In all, a total of 101 patients were included in this study with their demographic profile and test as seen in Table 1. There was a significant difference for the older age (p-value of 0.018) and female sex (p-value of 0.006) with the normal scan results.

A significant difference for patients with abnormal results was noted for those with chronic kidney disease (3.96%). Most of the patients were hypertensive (83.17%). Other demographic and procedural data such as the anthropometrics, administered activities (mCi), dipyridamole infused (0.56 mg/Kg), other comorbidities, and symptoms before infusion showed no significant difference.

TABLE 1. Demographic profile and procedural data of the patients

	Scan result			**P-value**
	Total (n = 101)	**Abnormal (n = 33)**	**Normal (n = 68)**	
	Frequency (%); Mean ± SD; Median (IQR)			
Age (years)	61.02 ± 14.4	56.18 ± 16.03	63.37 ± 13.02	**0.018**
Sex				**0.006**
Male	50 (49.5)	23 (69.7)	27 (39.71)	
Female	51 (50.5)	10 (30.3)	41 (60.29)	
Weight (kg)	67.15 ± 15.89	68.35 ± 16.79	66.57 ± 15.53	0.600
Height (cm)	159.40 ± 9.26	161.24 ± 8.68	158.5 ± 9.46	0.164
Administered Activity				
Rest (mCi)	327 (310 to 355)	326 (303 to 350)	328 (313 to 359)	0.304
Stress (mCi)	834 (815 to 870)	825 (808 to 857)	841 (818 to 873)	0.182
Dipyridamole (mg)	36.4 (31.8 to 44.3)	36.4 (32.4 to 43.7)	36.95 (31 to 44.5)	0.688
Comorbidities				
Hypertension	84 (83.17)	29 (87.88)	55 (80.88)	0.572
Dyslipidemia	44 (43.56)	13 (39.39)	31 (45.59)	0.670
Diabetes Mellitus	33 (32.67)	12 (36.36)	21 (30.88)	0.653
Smoker	7 (6.93)	3 (9.09)	4 (5.88)	0.680
ESRD	4 (3.96)	3 (9.09)	1 (1.47)	0.101
CKD	4 (3.96)	4 (12.12)	0	**0.010**
Symptoms before infusion				
Easy fatigability	24 (23.76)	8 (24.24)	16 (23.53)	1.000
Exertional dyspnea/DOB	23 (22.77)	11 (33.33)	12 (17.65)	0.127
Asymptomatic	17 (16.83)	4 (12.12)	13 (19.12)	0.572

TABLE 2. Blood pressure and heart rate before and after dipyridamole infusion

	Before	After	P-value
	Mean ± SD		
All patients			
SBP	137.62 ± 19.19	119.80 ± 21.4	**<0.001**
DBP	83.26 ± 10.4	70.3 ± 12.37	**<0.001**
Heart rate	69.89 ± 12.64	89.92 ± 13.47	**<0.001**
Patients with Abnormal scan results			
SBP	136.91 ± 19.1	120.15 ± 19.2	**<0.001**
DBP	81.31 ± 9.43	69.56 ± 11.12	**<0.001**
Heart rate	71.06 ± 13.82	87.42 ± 13	**<0.001**
Patients with Normal scan results			
SBP	139.09 ± 19.58	119.09 ± 25.66	**<0.001**
DBP	87.27 ± 11.26	71.81 ± 14.67	**<0.001**
Heart rate	69.32 ± 12.09	91.13 ± 13.62	**<0.001**

TABLE 3. Hemodynamic changes in dipyridamole-induced stress

	Scan result			P-value
	Total (n = 101)	Abnormal (n = 33)	Normal (n = 68)	
	Frequency (%); Median (IQR)			
SBP decrease	20 (30 to 10)	20 (30 to 10)	20 (30 to 10)	0.366
Normal SBP decrease (≥10 mm Hg)	79 (78.22)	27 (81.82)	52 (76.47)	0.615
Abnormal SBP decrease (< 10 mm Hg)	22 (21.78)	6 (18.18)	16 (23.53)	
HR Ratio (HRR)	1.28 (1.2 to 1.42)	1.25 (1.1 to 1.33)	1.29 (1.2 to 1.4)	**0.032**
Normal (> 1.2)	66 (65.35)	18 (54.55)	58 (70.59)	0.124
Abnormal (≤1.2)	35 (34.65)	15 (45.45)	20 (29.41)	

The blood pressure and heart rate before and after dipyridamole infusion (Table 2) were statistically significant. This was also seen for both the normal and abnormal scan results (p value of < 0.001).

For the hemodynamic changes in a dipyridamole-induced stress (Tables 3 & 4), twenty-two patients (21.78%) had an abnormal SBP decrease (< 10 mmHg) while 35 patients (34.65 %) had an abnormal HRR. Overall, 50 patients (49.5%) had abnormal SBP decrease and/or HRR.

The median SBP decrease was at 20 mmHg from the baseline. A normal SBP decrease (> 10 mmHg) was noted in majority of the patients (78.22%) with 52 patients (76.47%) corresponding with a normal scan result. An abnormal SBP decrease was also noted with the normal scan results of 16 patients (23.53%). However, these findings were not statistically significant.

For the HRR, the median ratio was 1.28 with a significantly lower ratio of 1.25 for the abnormal scan results compared to a ratio of 1.29 for a normal scan result (p-value of 0.032). Although, there was no statistically significant difference between the normal (> 1.2) or abnormal (<1.2) HRR and the scan results.

Other hemodynamic changes (Table 4), such as the DBP decrease and patients with abnormal SBP decrease and/or HRR were not statistically significant. In terms of the double product or rate pressure product, which is the product of the HR and SBP, only the post-infusion double product was determined to have a statistically significant difference with the scan results (p-value of 0.044). The post-infusion double product was noted to be higher for normal scans [10.68 (9.2 to 12.84)] than those with abnormal scan results [10.22 (8.46 to 11.18)]. There was also a statistically significant difference from the baseline to post-infusion change of the double product for entire study population and for the those with normal scans (p-value of < 0.001).

TABLE 4. Other hemodynamic changes in dipyridamole-induced stress

	Scan result			p-value
	Total (n = 101)	Abnormal (n = 33)	Normal (n = 68)	
	Frequency (%); Median (IQR)			
DBP decrease	10 (20 to 10)	20 (20 to 10)	10 (20 to 0)	0.113
Abnormal SBP decrease and/or HRR	50 (49.5)	17 (51.52)	33 (48.53)	0.834
Double Product[i]				
Baseline	9.1 (7.93 to 10.64)	8.58 (7.93 to 10.4)	9.33 (7.92 to 11.05)	0.233
Post-Infusion	10.56 (9.02 to 12.18)	10.22 (8.46 to 11.18)	10.68 (9.2 to 12.84)	**0.044**
Difference	0.99 (-0.15 to 2.46)	0.78 (-0.49 to 1.84)	1.10 (0.03 to 2.75)	0.158
p-value (Baseline vs post-infusion)	**<0.001**	0.061	**<0.001**	

[i]Double Product = HR x SBP

TABLE 5. 12-L ECG findings before and after dipyridamole infusion

	Scan result			p-value
	Total (n = 101)	Abnormal (n = 33)	Normal (n = 68)	
	Frequency (%); Mean ± SD			
Baseline ECG				
Normal	42 (42.58)	8 (24.24)	34 (50)	**0.018**
Conduction findings	39 (38.61)	14 (42.42)	25 (36.76)	0.665
Infarct findings	12 (11.88)	8 (24.24)	4 (5.88)	**0.017**
Ischemic findings	14 (13.86)	4 (12.12)	10 (14.71)	1.000
Hypertrophy findings	11 (10.89)	6 (18.18)	5 (7.35)	0.170
After Dipyridamole infusion ECG				
No change	88 (87.13)	26 (78.79)	62 (91.18)	0.113
With change	13 (12.87)	7 (21.21)	6 (8.82)	
ST segment depression	6 (46.15)	2 (33.33)	4 (57.14)	0.592
Other changes	7 (53.85)	4 (66.67)	3 (42.86)	

Most of the baseline ECG findings were normal (42.58%) and with no apparent change after dipyridamole infusion (87.13%). There was a statistically significant difference for the normal baseline (p-value of 0.018) and infarct ECG findings (p-value of 0.017); and normal/abnormal scan results, respectively. The changes in the ECG after dipyridamole infusion were only noted in 13 patients (12.87%), wherein 6 patients were noted with an ST segment depression and that only 2 patients had the presence of ischemia in their scan results. This, however, was not statistically significant.

For the frequency of myocardial perfusion scores (Table 6), majority of the patients had a normal SSS (81.19%), SRS (87.13%), and SDS (84.16%). Ischemia (51.61%) was the most common defect noted followed by fibrosis and infarct findings.

As seen in Table 7, there was no statistically significant correlation between the SBP decrease and myocardial perfusion scores. The HRR showed a statistically significant direct/indirect weak correlation for the rest and stress LVEF values (p-values of 0.09 and 0.011) and SRS (p-value of 0.007). This implies that higher HRRs, the better LVEF values. This is also the case for SRS wherein a score of less than 4 is normal. However, the level of association was weak for these findings.

Table 8 shows the other findings monitored during the dipyridamole infusion period. For the time in which the peak HR (p-value of 0.003) was attained, patients with

TABLE 6. Myocardial Perfusion Scores

	Frequency (%); Median (IQR)
Description of Defect (n=31)	
Ischemia	16 (51.61)
Infarct	4 (12.9)
Fibrosis	5 (16.13)
SSS	8 (4 to 19)
Normal (< 4)	82 (81.19)
Mild (4-8)	8 (7.92)
Moderate (9-12)	1 (0.99)
Severe (>12)	10 (9.90)
SRS	9 (4 to 16)
Normal (< 4)	88 (87.13)
Mild (4-8)	6 (5.94)
Moderate (9-12)	1 (0.99)
Severe (>12)	6 (5.94)
SDS	7 (3 to 15)
Normal (<2)	85 (84.16)
Mild (2-3)	5 (4.95)
Moderate (4-7)	3 (2.97)
Severe (>8)	8 (7.92)

TABLE 7. Correlation of SBP decrease and HRR to Myocardial Perfusion Scores and Left Ventricle Ejection Fractions

	Correlation coefficient	Level of association	p-value
SBP decrease			
SSS	-0.1426	Indirect weak correlation	0.155
SRS	-0.0988	Indirect weak correlation	0.325
SDS	-0.0605	Indirect weak correlation	0.548
Rest LVEF	0.0624	Direct weak correlation	0.536
Stress LVEF	0.0378	Direct weak correlation	0.707
HRR			
SSS	-0.0906	Indirect weak correlation	0.368
SRS	-0.2650	Indirect weak correlation	**0.007**
SDS	0.0013	Direct weak correlation	0.990
Rest LVEF	0.2591	Direct weak correlation	**0.009**
Stress LVEF	0.2516	Direct weak correlation	**0.011**

normal scan results had an average of 8.15 (+ 2.94) minutes compared to 6.56 (+ 2.21) minutes for those with abnormal results. The time attained for the lowest SBP decrease and symptom/s during infusion were not statistically significant. Chest heaviness (35.64%) was the most frequent symptom noted.

For the association of the baseline ECG findings with the myocardial perfusion scores (Tables 9, 10, and 11), the infarct findings showed statistically significant association with the SSS (p-value of < 0.001), SRS (p-value of < 0.001), and SDS (p- value of 0.005); and the normal baseline ECG with SRS (p-value of 0.028).

DISCUSSION

Dipyridamole is a phosphodiesterase enzyme inhibitor that indirectly increases myocardial perfusion by inhibiting the reuptake of endogenous adenosine [8]. Through this mechanism, it provides an alternative form of stress with expected hemodynamic changes which may have a clinical significance.

TABLE 8. Dipyridamole induced stress monitoring

	Scan result			p-value
	Total (n = 101)	Abnormal (n = 33)	Normal (n = 68)	
	Frequency (%); Mean ± SD; Median (IQR)			
Time attained (minutes)				
Lowest SBP decrease	7.07 ± 3.13	7.45 ± 2.84	6.88 ± 3.27	0.392
Peak HR	7.08 ± 2.57	6.56 ± 2.21	8.15 ± 2.94	**0.003**
Symptom during infusion	5.86 ± 2.64	5.66 ± 2.53	6.37 ± 2.91	0.328
Symptom/s during infusion				
Chest heaviness/discomfort	36 (35.64)	10 (30.30)	26 (38.24)	0.510
Light headedness	24 (23.76)	9 (27.27)	15 (22.06)	0.621
Abdominal pain	23 (22.77)	7 (21.21)	16 (23.53)	1.000
Headache	21 (20.79)	6 (18.18)	15 (22.06)	0.796
Dizziness	9 (8.91)	1 (3.03)	8 (11.76)	0.265
SOB	6 (5.94)	1 (3.03)	5 (7.35)	0.661
Others	11 (10.89)	5 (15.15)	6 (8.82)	0.333

TABLE 9. Association of Baseline ECG findings and SSS

Baseline ECG	Normal (n = 82)	Mild (n =8)	Moderate (n = 1)	Severe (n = 10)	p-value
	Frequency (%)				
Normal	39 (47.56)	1 (12.5)	0	2 (20)	0.066
Infarct findings	5 (7.58)	1 (12.5)	1 (100)	5 (50)	**<0.001**
Ischemic findings	12 (14.63)	1 (12.5)	0	1 (10)	1.000
Hypertrophy findings	8 (9.76)	0	1 (100)	2 (20)	0.073
Conduction findings	30 (36.59)	6 (75)	0	3 (30)	0.124

TABLE 10. Association of Baseline ECG findings and SRS

Baseline ECG	Normal (n = 88)	Mild (n = 6)	Moderate (n = 1)	Severe (n = 6)	p-value
	Frequency (%)				
Normal	41 (46.59)	0	0	1 (16.67)	**0.028**
Infarct findings	6 (6.82)	1 (16.67)	1 (100)	4 (66.67)	**<0.001**
Ischemic findings	12 (13.64)	1 (16.67)	0	1 (16.67)	1.000
Hypertrophy findings	9 (10.23)	0	0	2 (33.33)	0.328
Conduction findings	33 (37.5)	5 (83.33)	0	1 (16.67)	0.054

TABLE 11. Association of Baseline ECG findings and SDS

Baseline ECG	Normal (n = 85)	Mild (n = 5)	Moderate (n = 3)	Severe (n = 8)	p-value
	Frequency (%)				
Normal	37 (43.53)	2 (40)	1 (33.33)	2 (25)	0.856
Infarct findings	6 (7.06)	1 (20)	1 (33.33)	4 (50)	**0.005**
Ischemic findings	14 (16.47)	0	0	0	0.782
Hypertrophy findings	8 (9.41)	1 (20)	1 (33.33)	1 (12.5)	0.231
Conduction findings	34 (40)	1 (20)	1 (33.33)	3 (37.5)	0.918

The hemodynamic changes in the SBP showed no significant difference between the myocardial perfusion scores (SSS, SRS & SDS), stress/rest LVEF, and the eventual scan result. The diastolic blood pressure changes likewise showed no significant difference. These findings were congruent with the study by Ghoobli, et al. in 2017 wherein abnormal SBP changes are not associated abnormal scan findings and myocardial perfusion scores [2]. It was also noted that the absence of SBP response correlation may be affected by the

presence of LV dysfunction in the study population.

The normal (> 1.2)/abnormal (< 1.2) heart rate ratios (HRR) also had no significant difference with the scan results while the median HRR was determined to have had a significant difference. The median HRR for this study was noted to be at 1.28 which is a normal response with a higher ratio of 1.29 for normal results compared to 1.25 for the abnormal results. This implies that a higher HRR or greater increase from the baseline HR is associated with normal scan results, but the cut-off value of 1.2, as previously defined, is uncertain for this study [9]. Though, it has likewise been suggested that further investigations are needed to determine the ideal limits for HR response to vasodilators as previous studies have reported a high number of abnormal HRRs [5, 9]. It has also been stated that reduced HRR to vasodilators is associated with increased risk and as well as an independent predictor of cardiac death [2, 5, 10]. For the myocardial perfusion scores, only the SRS had an indirect correlation with HRR albeit the level of association was weak. The stress and rest LVEF values also showed a direct weak correlation. Overall, the higher HRRs may indicate normal SRS (< 4) and higher stress/rest LVEF values which relates to normal scan results. This provides diagnostic confidence in understanding the effects of the Dipyridamole, particularly its effect on heart rate, wherein a substantial increase from baseline implies a normal myocardial perfusion.

For the double product or rate pressure product, the post-infusion value for the normal and abnormal scan results [10.68 (9.2 to 12.84) vs 10.22 (8.46 to 11.18)] was determined to have had a significant difference. The median post-infusion double product was 10.56 (9.02 to 12.18) for this study. The double product is used as a measure of myocardial oxygen demand and that dipyridamole causes a decrease in in BP and increase in HR which supports the values obtained for this study [11]. A preliminary study likewise had similar findings for post-infusion double product and observed a significant difference for Δ double product [11]. It was noted that the double product is related to sympathetic nervous system activity and decreased parasympathetic nervous system activity for which dipyridamole is not affected.

Baseline normal and infarct ECG findings showed a significant difference with normal and abnormal scan results, respectively. Myocardial perfusion scores (SSS, SRS, and SDS) correlated with the baseline infarct findings while only the SRS for the baseline normal ECG findings. Although, it should be noted that SDS is used as an index for ischemic burden and the most frequent defect noted for this study population was also ischemia. After dipyridamole infusion, most ECG findings remained unchanged with no significant difference for those 13 patients (12.87%) with only 6 developing the presence of ST segment depression. This is expected since dipyridamole does not induce absolute ischemia in most patients.

In terms of the demographic profile, patients that were younger (56.18 + 16.03) had abnormal scan results. This suggests that these patients may have developed comorbidities earlier, hence the abnormal scan results. It should also be noted that these patients were preferably requested to undergo a dipyridamole induced stress rather than exercise; and are being considered for suspected CAD, which suggests a higher risk profile. Males were also noted to have an abnormal scan result, likely due to the greater influence of common factors (age, hypertension, etc.) than women thus the greater risk of cardiovascular disease [12, 13].

Another finding noted to be significant was the time (minutes) to reach the maximal HR upon dipyridamole infusion which was longer for those with normal scan results (8.15 + 2.94 vs. 6.56 + 2.21). This implies that a longer and possibly sustained increase in the HR may indicate a better HRR which would be congruent with a normal scan result as previously noted.

This retrospective study is limited as a single-center study referred to our institution for patients with suspected CAD. Cardiac autonomic dysfunction was also not confirmed which may help in understanding abnormal hemodynamic response.

CONCLUSION

In patients with suspected CAD who undergo a dipyridamole-induced stress myocardial perfusion scintigraphy –Tc-99m Sestamibi, the higher HRRs and baseline 12-L ECG (normal and infarct) findings, relates with the expected scan results. This implies that higher HRRs and normal baseline ECG finding are associated with normal scan results, and baseline infarct findings relate with abnormal scan results. The higher HRRs were also associated with the higher stress/rest LVEF and normal SRS, which supports a normal scan result.

However, there was no significant association for the blood pressure responses and post-infusion 12-L ECGs with any of the scan findings/results. Overall, the results may guide the clinician and reader in the study interpretation, thereby increasing diagnostic confidence and having a clearer understanding of the hemodynamic effects of Dipyridamole, especially in equivocal findings

REFERENCES

1. Sison J, Divinagracia R, Nailes J. Asian management of hypertension: Current status, home blood pressure, and specific concerns in Philippines (a country report). J Clin Hypertens (Greenwich). 2020 Mar;22(3):504-507. doi: 10.1111/jch.13802. Epub 2020 Feb 28. PMID: 32108413; PMCID: PMC8030094.
2. Gholoobi A, Ayati N, Baghyari A, Mouhebati M, Atar B, Dabbagh Kakhki VR. Relationship between gated myocardial perfusion SPECT findings and hemodynamic, electrocardiographic, and heart rate changes after Dipyridamole infusion. Int J Cardiovasc Imaging. 2017 Jun;33(6):951-956. doi: 10.1007/s10554-017-1074-6. Epub 2017 Feb 1. PMID: 28150082.
3. Ogilby JD, Kegel JG, Heo J, Iskandrian AE. Correlation between hemodynamic changes and tomographic sestamibi imaging during dipyridamole-induced coronary hyperemia. J Am Coll Cardiol. 1998 Jan;31(1):75-82. doi: 10.1016/s0735-1097(97)00448-8. PMID: 9426021.
4. Javadi H, Shariati M, Mogharrabi M, Asli IN, Jallalat S, Hooman A, Seyedabadi M, Assadi M. The association of dipyridamole side effects with hemodynamic parameters, ECG findings, and scintigraphy outcomes. J Nucl Med Technol. 2010 Sep;38(3):149-52. doi: 10.2967/jnmt.109.072629. Epub 2010 Aug 19. PMID: 20724532.
5. Gorur GD, Ciftci EA, Kozdag G, Isgoren S, Oc MA, Haksal C, Gur M, Demir H. Reduced heart rate response to dipyridamole in patients undergoing myocardial perfusion SPECT. Ann Nucl Med. 2012 Oct;26(8):609-15. doi: 10.1007/s12149-012-0618-z. Epub 2012 Jun 20. PMID: 22714113.
6. Mishra RK, Dorbala S, Logsetty G, Hassan A, Heinonen T, Schelbert HR, Di Carli MF; RAMPART investigators. Quantitative relation between hemodynamic changes during intravenous adenosine infusion and the magnitude of coronary hyperemia: implications for myocardial perfusion imaging. J Am Coll Cardiol. 2005 Feb 15;45 (4):553-8. doi: 10.1016/j.jacc.2004.10.064. PMID: 15708703.
7. Hatutale A, Vorster M, Ankrah AO, Rheeder P, Sathekge MM. Association of hemodynamic response during dipyridamole stress testing with 99mTc-MIBI SPET myocardial perfusion image findings. Hell J Nucl Med. 2013 Sep-Dec;16(3):181-5. doi: 10.1967/s002449910096. Epub 2013 Oct 2. PMID: 24137582.
8. Gupta A, Samarany S. Dipyridamole Nuclear Stress Test. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-.[cited 2022 Oct] Available from: https://www.ncbi.nlm.nih.gov/books/NBK544321/
9. Mathur S, Shah AR, Ahlberg AW, Katten DM, Heller GV. Blunted heart rate response as a predictor of cardiac death in patients undergoing vasodilator stress technetium-99m sestamibi gated SPECT myocardial perfusion imaging. J Nucl Cardiol. 2010 Aug;17(4):617-24. doi: 10.1007/s12350-010-9242-2. Epub 2010 May 19. PMID: 20490960.
10. Bhatheja R, Francis GS, Pothier CE, Lauer MS. Heart rate response during dipyridamole stress as a predictor of mortality in patients with normal myocardial perfusion and normal electrocardiograms. Am J Cardiol. 2005 May 15;95(10):1159-64. doi: 10.1016/j.amjcard.2005.01.042. PMID: 15877986.
11. Ansari M, Javadi H, Pourbehi M, Mogharrabi M, Rayzan M, Semnani S, Jallalat S, Amini A, Abbaszadeh M, Barekat M, Nabipour I, Assadi M. The association of rate pressure product (RPP) and myocardial perfusion imaging (MPI) findings: a preliminary study. Perfusion. 2012 May;27 (3):207-13. doi: 10.1177/0267659112436631. Epub 2012 Feb 2. PMID: 22301391.
12. Galiuto L, Locorotondo G. Gender differences in cardiovascular disease. J. Integr. Cardiol. 2015;1(1):20-2. doi: 10.15761/JIC.1000107.
13. Gao Z, Chen Z, Sun A, Deng X. Gender differences in cardiovascular disease. Medicine in Novel Technology and Devices. 2019 Dec 1;4:100025. doi.org/10.1016/j.medntd.2019.100025.

Acknowledgement

I would like to express gratitude to the consultants, co-residents, and staff of the Division of Nuclear Medicine, Philippine Heart Center for their unwavering support of this endeavor