Original Article

Correlation Between Dipyridamole-Induced Electrocardiogram Arrhythmia and Risk Stratification in Myocardial Perfusion SPECT Imaging

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ABSTRACT

Background: Dipyridamole is administered as a substitute for physical activity during myocardial perfusion imaging (MPI). The purpose of this work was to evaluate the correlation between any kind of electrocardiogram (ECG) arrhythmia induced by dipyridamole and MPI findings in single-photon emission computed tomography (SPECT) imaging.

Methods: This study included 759 patients referred to the Nuclear Medicine Department of Hazrat Rasoul Akram Hospital. The study population underwent the dipyridamole MPI SPECT protocol. ECG for all the patients before and during dipyridamole infusion was obtained and assessed by cardiologists. All the patients underwent stress-rest technetium (^{99m}Tc) sestamibi-gated SPECT imaging using a 2D protocol.

Results: ST depression and ST elevation were observed in 69 (9.1%) and 23 (3%) patients, respectively, which had significant relationships with the moderate/high-risk stratification outcomes of MPI. Atrioventricular block, premature ventricular contractions, paroxysmal supraventricular tachycardia, bradyarrhythmia, and tachycardia showed no significant associations with moderate or high levels of risk stratification in MPI, and they were seen in 34 (4.5%), 34 (4.5%), 24 (3.2%), 16 (2.1%), and 39 (5.1%) patients, respectively.

Conclusions: High-risk MPI scan patterns had a significant correlation with ST depression and a relatively appraisable correlation with ST elevation in dipyridamole-induced ECG arrhythmia. ***(Iranian Heart Journal 2022; 23(3): 108-113)***

KEYWORDS: Arrhythmia, SPECT, Risk stratification, Dipyridamole, MPI

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Using myocardial perfusion imaging (MPI) to make decisions has prognostic efficacy in cardiology. A normal single-photon emission computed tomography (SPECT) MPI affirms the low risk of further adverse clinical events.[1] Imaging variables, particularly stress SPECT, provide additional prognostic information to clinical diagnosis. Nonetheless, findings in patients who undergo pharmacologic stress

MPI differ from findings in patients who undergo the exercise stress test.[2,3] Pharmacologic-induced stress regularly enhances the blood flow to the myocardium during the MPI process. Dipyridamole is one of the most frequently used vasodilators and enforces its effect by increasing the endogenous levels of adenosine.[4,5] Electrocardiographic (ECG) changes during dipyridamole stress tests considerably affect the prognosis of cardiac death in patients.[6,7]

In the present study, we sought to evaluate the frequency of dipyridamole-related ECG alterations experienced by patients undergoing the technetium (^{99m}Tc) sestamibi MPI stress test. We also aimed to investigate the correlation between any pharmacologic-induced ECG changes and the risk stratification of patients by assessing MPI findings.

METHODS

The present study enrolled 759 patients (58.81±15.20 y/o) referred to the Nuclear Medicine Department of Hazrat Rasoul Akram Hospital from the beginning of March to the end of September 2020 for dipyridamole stress MPI SPECT imaging according to the standard protocol.[8]

All the patients were guided to suspend taking xanthine-containing compounds and dipyridamole from 24 hours before the test and fast for 8 hours. They were also instructed to interrupt β-blockers for 48 hours and calcium channel blockers and long-acting nitrates for 24 hours, if possible. Dipyridamole (0.56 mg/kg) was infused intravenously for 4 minutes. Blood pressure and heart rate were measured in the supine position at rest and at 1-minute intervals after dipyridamole infusion commencement for 10 minutes. Three to 5 minutes after the end of dipyridamole infusion, ^{99m}Tc sestamibi was injected.

Patients who already had any kind of arrhythmia were excluded from the study. ECG changes were evaluated to compare any observed induced arrhythmias such as ST depression, ST elevation, atrioventricular (AV) block, premature ventricular contractions (PVCs), paroxysmal supraventricular tachycardia (PSVT), bradyarrhythmia, and tachycardia.

Written informed consent was obtained from the entire study population, and the study protocol was approved by the local ethics committee.

ECG evaluations were performed using the standard 12-lead ECG in the supine position at rest simultaneously with a Nihon Kohden Recorder (Tokyo, Japan), which was set at a paper speed of 25 mm/s and 1 mV/cm standardization. For the reduction of measurement errors, the ECGs were assessed by 2 cardiologists, who determined QRS and all interval duration measurements and deviations. ST deviations more than 1 mm (in height or depth from the baseline) and less than 1 mm were identified as significant and insignificant changes, respectively. T-wave inversion, pathologic Q wave, poor R progression, bundle branch block, and any kind of arrhythmia (premature atrial contractions [PACs], PVCs, salvos, and ventricular tachycardia [VT]) were recorded before and after dipyridamole administration.[9,10]

Dipyridamole-induced stress-gated SPECT MPI was used for clinical risk assessment. Prognostic nuclear perfusion imaging was conducted according to summary recommendations from the International Nuclear Cardiology Retreat[11] and the American College of Cardiology/American Heart Association (ACC/AHA) 2012 guidelines.[12,13] The patients were categorized as either low risk or intermediate/high risk. Stress-induced or fixed perfusion defects of small size with normal left ventricular ejection fraction (LVEF) were considered low risk. Patients with the following characterizations were identified as intermediate risk:

- Stress-induced or fixed perfusion defects of moderate size without LV dilation or increased thallium-201 lung uptake
- Mildly-to-moderately depressed resting LVEF of between 35% and 49%

The following MPI findings were identified as high-risk stratifications:

- Large stress-induced perfusion defects (particularly if anterior)
- Multiple stress-induced perfusion defects of moderate size
- Large, fixed perfusion defects with LV dilation or increased thallium-201 lung uptake
- Moderate stress-induced perfusion defects with LV dilation, increased thallium-201 lung uptake, diabetes mellitus, or severely depressed LVEF (<35%) [12]

The acquired data were evaluated for any type of arrhythmia in both groups based on MPI results.

Statistical Analysis

Continuous variables were expressed as the mean ± the standard deviation (SD). Comparisons between the groups were performed using the Student *t* test. Categorical (nonparametric) variables were expressed as Yes or No and evaluated using the χ^2 test. A *P* value of less than 0.05 was considered statistically significant. The statistical analyses were performed using the PASW software, version 18 (SPSS Inc, Chicago, Illinois, USA).

RESULTS

All 759 patients underwent dipyridamole vasodilator MPI. The patients' demographic data and frequencies of the different types of arrhythmias are reported in Table 1. The average age of the patients was 58.81±15.20 years, with approximately an equal percentage of both sexes. After dipyridamole administration, 69 patients (9.1%) had ST depression and 23 (3%) had ST elevation on their ECGs. AV block, PVCs, and PSVT were observed in 34 (4.5%), 34 (4.5%) and 24 (3.2%) patients, respectively. Tachycardia was reported in 39 patients (5.1%) and bradyarrhythmia in 16 (2.1%). The clinical risk assessment identified 511 patients (67.4%) as low risk and 247 (32.6%) as intermediate/high risk. All data on the different types of dipyridamole-induced ECG arrhythmias in both risk levels are presented in Table 2. The χ^2 test indicated significant differences ($P<0.0001$) in the risk level between the patients with ST depression or ST elevation and those without these arrhythmias on their ECGs. Cramér's V of ST depression (0.41) demonstrated a high impact on the risk level of MPI in comparison with Cramér's V of ST elevation (0.25). The other types of arrhythmias, namely AV block, PVCs, PSVT, bradyarrhythmia, and tachycardia, did not show significant differences ($P>0.05$) in both risk levels.

Table 1: Frequencies of the demographic and clinical variables

Demographics (n=759)	No. (%)	Type of Arrhythmia	No. (%)
Age	58.81 ± 15.20 Years	ST depression(+)	69(9.1%)
Female sex	349(52%)	ST elevation(+)	23(3%)
Smoking (+)	118(15.6%)	AV block(+)	34(4.5%)
Hypertension (+)	262(34.6%)	PVC (+)	34(4.5%)
Hyperlipidemia (+)	263(34.7%)	PSVT (+)	24(3.2%)
Diabetes (+)	203(26.8%)	Bradyarrhythmia (+)	16(2.1%)
CABG (+)	113(14.9%)	Tachycardia (+)	39(5.1%)
Chest pain (+)	279(36.8%)	*Risk stratification*	Num.(%)
Palpitations (+)	203(26.8%)	Low	511(67.4%)
TID (+)	38(5%)	Intermediate/High	247(32.6%)

CABG, Coronary artery bypass grafting; AV, Atrioventricular; PVC, Premature ventricular contraction; PSVT, Paroxysmal supraventricular tachycardia

Table 2: Comparison of the results of the χ^2 test between 2 risk levels of myocardial perfusion imaging evaluation and 7 types of arrhythmias

		Risk Stratification				
		Low	Intermediate/High	χ^2 value	*P* value	Cramér's V
ST depression	*Yes*	5(7.2%)	64(92.8%)	124.85	0.0001	0.41
	No	505(73.4%)	183(26.6%)			
ST elevation	*Yes*	0(0%)	23(100%)	49.07	0.0001	0.25
	No	511(69.5%)	224(30.5%)			
Atrioventricular block	*Yes*	22(64.7%)	12(35.3%)	0.119	0.730	0.01
	No	489(67.5%)	235(32.5%)			
Premature ventricular contraction	*Yes*	26(76.5%)	8(23.5%)	1.33	0.250	0.04
	No	485(67.0%)	239(33%)			
Paroxysmal supraventricular tachycardia	*Yes*	17(70.8%)	7(29.2%)	0.13	0.716	0.01
	No	494(67.3%)	240(32.7%)			
Bradyarrhythmia	*Yes*	10(62.5%)	6(37.5%)	0.18	0.670	0.02
	No	501(67.5%)	241(32.5%)			
Tachycardia	*Yes*	28(71.8%)	11(28.2%)	0.359	0.549	0.02
	No	483(67.2%)	236(32.8%)			

DISCUSSION

Intravenous dipyridamole administration is an alternative to exercise during perfusion scintigraphy for risk assessment in coronary artery disease in clinical practice. Dipyridamole increases both LVEF and heart rate and slightly reduces diastolic blood pressure in patients with a lower possibility of having coronary artery disease.[14] Furthermore, post-stress LVEF decreases considerably in individuals with ischemia because of end-systolic ventricular dilation and insufficient ventricular contraction.[15,16] In the current investigation, we detected all types of arrhythmias induced by dipyridamole on the study population's ECGs, but ST depression was associated with a higher probability.

These findings are in line with previous reports. Abbott et al[17] reported findings indicating the appearance of ST depression during adenosine infusion as a relatively specific marker for significant coronary artery disease and the prediction of future cardiac events, regardless of MPI results. Klodas et al[6] showed that vasodilator-induced ischemic ECG arrhythmia had additional prognostic value over normal SPECT MPI. Villanueva et al[18] also demonstrated a correlation between ST-segment depression and chest pain or ECG results and redistribution defects. Their major finding was that St-segment depression in reaction to dipyridamole was most significantly correlated with a higher risk outcome of the MPI test. By univariate analysis, patients with ST depression and ST elevation showed intermediate or high-risk MPI test results, suggesting that increased oxygen demand may also contribute to the development of ST depression and ST elevation after dipyridamole.[18] We studied the correlations between the different types of ECG arrhythmias such as ST depression, ST elevation, AV block, PVCs, PSVT, bradyarrhythmia, and tachycardia in 2 groups of patients. The most frequent arrhythmia was ST depression, which had a significant correlation ($P<0.0001$ and Cramér's V=0.41) with the high-risk MPI test outcome. ST elevation, in comparison with ST depression, had a low frequency and correlation strength (Cramér's V=0.25). The other types of arrhythmias, namely AV block, PVCs, PSVT, bradyarrhythmia, and

tachycardia, showed neither a considerable frequency nor a significant correlation with high-risk levels of MPI. This finding may indicate that ECG changes revealed by dipyridamole are important even when there is no distortion in scintigraphy outcomes.

CONCLUSIONS

In light of the results of the present study, we recommend a close consideration of any alteration on ECG after the administration of dipyridamole during MPI, in particular the appearance of ST depression and ST elevation. These 2 arrhythmias can help physicians prognosticate higher levels of risk on MPI assessment and even refer patients for angiography without performing MPI.

Conflict of Interest

There was no conflict of interest in the design and conduct of this study.
This manuscript was read and approved by all the authors, and it represents our honest report of hard work.

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