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Relationship of Electrocardiographic Dynamicity to Ischemic Burden Using Myocardial Perfusion Imaging in Patients without Previous Myocardial Infarction

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Abstract

Objectives: To examine Relationship of Electrocardiographic Dynamicity to Ischemic Burden Using Myocardial Perfusion Imaging in Patients without Previous Myocardial Infarction**.**

Background: Myocardial perfusion Imaging (MPI) provides powerful diagnostic and prognostic information in the management of patients with known or suspected coronary artery disease (CAD). The purpose of this study was to study the relationship of electrocardiographic dynamicity to ischemic burden using MPI in patients without previous myocardial infarction.

Method: our study was a prospective observational which was carried out on 175 patients referred for diagnosis or risk stratification for coronary artery disease, patients were subjected to a history checkup and full clinical examination, a standard 12-lead electrocardiograms at rest & subjects underwent technetium(Tc)-99m sestamibi rest-stress gated SPECT MPI.

Results: There was a fair agreement between exercise treadmill induced electrocardiogram (ECG) ischemic changes in anterior leads and myocardial perfusion defects in MPI at stress of the studied patients, and there was a moderate agreement between, exercise treadmill induced ECG ischemic changes in inferior leads and negative stress ECG, and myocardial perfusion defects in MPI at stress of the studied patients. In Age <50y with one or no risk factors, there was a fair agreement between MPI and stress ECG. In Age >50y with one or more risk

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

factors, there was a moderate agreement between MPI and stress ECG. Stress ECG can diagnose CAD and ischemic heart disease as MPI at stress with82.9% sensitivity, 69.0% specificity.

Conclusions: Exercise treadmill induced ECG ischemic changes can diagnose the ischemic burden with less accuracy than the MPI at stress regarding the evidence of ischemia while it was irrelevant with myocardial perfusion defects in MPI at stress regarding the distribution of ischemic changes.

Keywords: Electrocardiograph, Dynamicity, Ischemic Burden, Myocardial Perfusion Imaging, Myocardial Infarction

Background:

Nuclear cardiology involves the imaging of cardiac radio-pharmaceutical distribution to characterize physiologic and patho-physiologic processes in the heart. The ability to image myocardial perfusion, function, and metabolism non-invasively with nuclear techniques has led to the development of a field that has been validated extensively and provides powerful diagnostic and prognostic information in the management of patients with known or suspected coronary artery disease (CAD)[1, 2].

Extensive literature evaluating the sensitivity and specificity of Single-photon emission computed tomography (SPECT) MPI for detecting obstructive CAD has been published over the years. SPECT MPI provides incremental diagnostic value over exercise ECG testing in various patient cohorts[3].

Exercise stress testing without adjunct noninvasive imaging is frequently used as the initial screening test in patients without known CAD who have chest pain syndromes or symptoms suggestive of ischemia[4]. The diagnostic performance of this test varies greatly depending on the pretest likelihood of the population being studied[5].

Ischemic heart disease (IHD) is the most common, serious, chronic, life-threatening illness in the United States, where 13 million persons have IHD >6 million have angina pectoris, and >7 million have sustained a myocardial infarction. Genetic factors, a high-fat and energy-rich diet, smoking, and a sedentary lifestyle are associated with the emergence of IHD[4, 6].

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

This study's objectives were to study the relationship of electrocardiographic dynamicity to ischemic burden using myocardial perfusion imaging (MPI)in patients without previous myocardial infarction.

Methods:

The current study is a prospective observational study conducted at Menoufia University Hospitals, Menoufia, Egypt in the period from first of January 2022 to the end of April 2023.

The study adhered to the guidelines of Menoufia University's Ethics Committee. All enrolled participants, or their care givers, provided an informed signed consent.

Excluded criteria: Prior myocardial infarction, pathological Q wave, left bundle branch block, Right bundle branch block, heart block, previous percutaneous coronary intervention, Coronary artery bypass grafting (CABG), pericardial diseases, lung disease, patients with implantable intra-cardiac devices (pacemaker, cardiac resynchronization therapy (CRT), implantable cardioverter-defibrillator (ICD)) and atrial fibrillation and those who refused to participate in the current study.

Studied participants were subjected to a detailed history taking, clinical Examination, Standard 12-leads electrocardiogram (ECG) at rest, in supine position that was calibrated at 10 mm/mv and was recorded at paper speed of 25 mm/s [7] and 12 leads ECG.

12 leads ECG for all patients as follow: Heart rate and rhythm, chambers enlargement, any possible ischemia induced arrhythmias, ST changes whether ST elevation in STEMI, or ST depression in NSTEMI/Unstable Angina, QRS complex composition and duration and Newly presumed Bundle Branch Blocks and T waves dynamic changes.

The 12-lead surface ECG was analyzed as follows:

ST-segment depression was measured 80 milliseconds after the J point while ST-segment elevation was measured 20 milliseconds after the J-point. The preceding TP segment was used as baseline (iso-electric line), ST-segment shift of ≥0.05 mV and T-wave inversion of >0.1 mV was considered as significant. T-wave was measured 120 milliseconds after the J point. It was considered positive if it was 1 mm or more above the iso-electric line and considered negative if it was 1 mm or more below the iso-electric line (including the normalization of a known

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

negative T-wave), ECG was considered abnormal if isolated T-wave inversion of >0.1 mv (including normalization of a known negative T-wave), isolated ST-segment depression of >0.05 mv, ST-segment depression with concomitant T-wave inversion in same leads, or ST-segment depression and T-wave inversion in different leads [7].

Stress myocardial perfusion imaging:

Subjects underwent technetium (Tc)-99m Sestamibi rest-stress gated SPECT MPI with either a 1- or 2-day protocol. All patients performed a symptom-limited treadmill exercise test using standard Bruce protocols. During exercise, 12-lead ECG recording was performed at each minute of stress with continuous monitoring. At near maximal exercise, a weight-adjusted dose of Tc-99m Sestamibi was injected and exercise continued for 1 min after injection. Tc-99m Sestamibi SPECT imaging began 30 min after isotope injection. SPECT MPI was performed using an elliptical 180◦acquisition for 64projections at 20 s per projection. No attenuation or scatter correction was used. After filtered back-projection, short-axis, vertical, and horizontal long-axis tomograms were generated [7].

MPI scans were assessed semi-quantitatively by segmental visual interpretation, using short-axis and vertical long-axis tomograms divided into 20 segments. Each segment was scored by consensus of two experienced observers [7] [SPECT-MPI was performed on a dual-head camera SPECT/CT system (GE-NM 830) in the spine position with a low-dose CT scan acquisition for attenuation correction and stress-gated images were acquired using a 15% window centered over the 140KeV photo-peak of ^{99m}Tc with parallel hole, low energy, and high-resolution collimators. The matrix size that was used is 64 × 64 with a maximum zoom of 1.46. Thirsty-two projections of 20 each were taken per head, for a total of 64 images in step and shoot method for 180° orbit starting from 45° right anterior to 135° left posterior].

ECG changes were analyzed and were considered positive if fulfilling the following criteria: [Horizontal or down-sloping ST segment depression ≥ 1mm compared to that in resting ecg if lasted at least 0.08 seconds in three consecutive beats [7], T wave inversion of >0.1 mV was considered significant and up Sloping ST segment depression ≥ 3mm with chest pain].

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

Patients who achieved 85% of the maximum predicted Heart rate without developing either “a” or “b” or “c” changes were considered to have a negative exercise ECG. Other ECG changes were analyzed as Arrhythmia developed during exercise. The degree of changes and the number of ECG leads affected were compared to SPECT MPI findings (areas of perfusion defects) to distinguish the relationship between both [7].

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD). Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. The Kappa test was used to show the agreement. A two-tailed P value < 0.05 was considered statistically significant.

Results

The mean age was 58.56±7.82 years. 83 (47.43%) patients were males while 92 (52.57%) patients were females. In our study population we found that 53(30.29%) patients were diabetic, 152 (86.86%) patients were hypertensive, 101 (57.71%) patients had Dyslipidemia, 21 (12%) patients were smokers and 16 (9.14%) patients had peripheral arterial disease. **Table 1**

Table 1: Demographic data and Co morbidities distribution among the studied patients.

		N=175
Age (years)		58.6 ± 7.82
Sex	**Male**	83 (47.43%)
	Female	92 (52.57%)
Diabetes		53 (30.29%)
HTN		152 (86.86%)
Dyslipidemia		101 (57.71%)
Current Smoking		21 (12%)
Peripheral arterial disease		16 (9.14%)

Data are presented as mean± SD or frequency (%). HTN: Hypertension.

ECG, resting trans-thoracic echocardiogram, stress-induced ECG changes, arrhythmia in recovery, MPI at stress, results of the stress ECG, and MPI at stress were enumerated in this table. **Table 2**

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

Table 2:Resting ECG, resting trans-thoracic echocardiogram, stress induced ECG changes, arrhythmia in recovery, MPI at stress, results of the stress ECG, MPI at stress of the studied patients

		N=175
Resting ECG	**T wave inversion**	65 (37.14%)
	Subtle ST depression	69 (39.43%)
	Horizontal ST depression	1 (0.57%)
	Sinus Bradycardia	1 (0.57%)
	Sinus Tachycardia	3 (1.71%)
	LVH	1 (0.57%)
	Non-significant abnormalities	35 (20%)
LVEF (%)		56.7 ± 9.08
IVS diameter (cm)		1.2 ± 0.26
Posterior wall diameter (cm)		1.2 ± 0.23
Left ventricular wall hypertrophy		88 (50.29%)
Left atrial size (cm)		3.4 ± 0.73
Left atrial enlargement		35 (20%)
Wall motion abnormalities	**Normal**	134 (76.57%)
	Segmental Hypokinesia	34 (19.43%)
	Global Hypokinesia	7(4%)
Diastolic dysfunction		132(75.43%)
Mitral inflow velocities	**Reversed E/A wave**	110(62.86%)
	Pseudo normal E/A pattern	22(12.57%)
Aortic root diameter (cm)	**Mean ± SD**	3.1±0.45
ECG leads	**Anterior (v3, v4)**	34 (19.43%)
	Lateral (LI, Avl, v5, v6)	11 (6.29%)
	Inferior (LII, III, Avf)	39 (22.29%)
	Antero-lateral	47 (26.86%)
	Infero-lateral	2 (1.14%)
	Non-significant abnormalities	42 (24%)
Arrhythmia in recovery	**No**	125 (71.43%)
	PVCs	50 (28.57%)
Left ventricular size	**Normal**	130 (74.29%)
	Borderline	30 (17.14%)
	Dilated	15 (8.57%)
Myocardial Perfusion defects	**Anterior**	42 (24%)
	Inferior	62 (35.43%)
	Antero-lateral	23 (13.14%)
	Apical	19 (10.86%)
	Negative	29 (16.57%)
Stress ECG	**Positive**	130 (74.28%)
	Negative	45 (25.71%)
MPI at stress	**Positive**	146 (83.43%)
	Negative	29 (16.57%)

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

Data are presented as mean± SD or frequency (%). ECG: Electrocardiogram, LVH: left ventricular hypertrophy, LVEF: left ventricular ejection fraction, IVS: Inter-ventricular septum, ECG: Electrocardiogram, PVCs: Premature ventricular contractions, MPI: myocardial perfusion imaging.

Exercise treadmill-induced ECG ischemic changes can diagnose ischemic burden with less accuracy than the MPI at stress, while it was irrelevant with myocardial perfusion defects in MPI at stress regarding the distribution of ischemic changes. **Table 3**

Table 3: Distribution of stress induced ECG changes and Myocardial Perfusion defects of the studied patients

	Stress ECG leads	Myocardial Perfusion defects
Anterior	34 (19.43%)	42 (24%)
Lateral	11 (6.29%)	0(0%)
Inferior	39 (22.29%)	62 (35.43%)
Antero-lateral	47 (26.86%)	23 (13.14%)
Infero-lateral	2 (1.14%)	0(0%)
Apical	0(0%)	19 (10.86%)
Non-significant abnormalities (negative)	42 (24%)	29 (16.57%)

Data are presented as frequency (%). ECG: Electrocardiogram, MPI: myocardial perfusion imaging.

There was a fair agreement between exercise treadmill induced ECG ischemic changes in anterior leads and myocardial perfusion defects in MPI at stress of the studied patients, and there was a moderate agreement between, exercise treadmill induced ECG ischemic changes in inferior leads and negative stress ECG, and myocardial perfusion defects in MPI at stress of the studied patients. There was a slight agreement between exercise treadmill induced ECG ischemic changes in (lateral, antero-lateral and infero-lateral leads) and myocardial perfusion defects in MPI at stress of the studied patients. **Table 4**

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

Stress ECG leads	Myocardial Perfusion defects					P
	Anterior	Inferior	Antero-lateral	Apical	Negative	
Anterior (n=34)	16(47.06%)	4(11.76%)	8(23.53%)	1(2.94%)	5(14.71%)	**<0.001* Kappa** 0. 263
Lateral (n=11)	8(72.73%)	0(0%)	3(27.27%)	0(0%)	0(0%)	1.000 kappa 0. 001
Inferior (n=39)	6(15.38%)	32(82.05 %)	0(0%)	0(0%)	1(2.56%)	**<0.001* Kappa** 0.496
Antero-lateral (n=47)	7(14.89%)	12(25.53 %)	7(14.89%)	17(36.17%)	4(8.51%)	0.678 kappa 0.029
Infero-lateral (n=2)	0 (0%)	2(100%)	0(0%)	0(0%)	0(0%)	1.000 Kappa 0.001
Non-significant abnormalities (negative) (n=42)	5 (11.9%)	12(28.57 %)	5(11.9%)	1(2.38%)	19(45.24%)	**<0.001* Kappa** 0.422

Table 4: Distribution of myocardial perfusion defects according to stress ECG leads of the studied patients
Data are presented as frequency (%). *Significant as P value ≤0.05. ECG: Electrocardiogram.

There was a moderate agreement between stress ECG and MPI at stress (P <0.001, Kappa= 0.425). In Age <50y with one or no risk factors, there was a fair agreement between MPI and stress ECG (P =0.019, Kappa= 0.363). In Age >50y with one or more risk factors, there was a moderate agreement between MPI and stress ECG (P <0.001, Kappa= 0.442). **Table 5**

Table 5: Agreement between stress ECG and MPI at stress and relation between stress ECG and MPI at stress regarding age and risk factors of the studied patients

		MPI at stress		Kappa	P
		Positive	Negative		
Stress ECG	**Positive**	121(82.88%)	9(31.03%)	0.425	**<0.001***
	Negative	25(17.12%)	20(68.97%)		
Age<50y with one or no risk factors					
Stress ECG	**Positive**	20(74.07%)	1(20%)	0.363	**0.019***
	Negative	7(25.93%)	4(80%)		
Age>50y with one or more risk factors					
Stress ECG	**Positive**	101(84.87%)	8(33.33%)	0.442	**<0.001***
	Negative	18(15.13%)	16(66.67%)		

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

Data are presented as frequency (%). *Significant as P value ≤0.05. ECG: Electrocardiogram, MPI: myocardial perfusion imaging.

Stress ECG can diagnose CAD and IHD as MPI at stress with 82.9% sensitivity, 69.0% specificity, 93.1 %PPV, 44.4% NPV, and 80.6% accuracy. **Table 6**

Table 6: Sensitivity, specificity, PPV, NPV and accuracy of stress ECG and MPI at stress

	MPI at stress				
	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
Stress ECG	82.9%	69.0%	93.1%	44.4%	80.6%

PPV: positive predictive value, NPV:negative predictive value, ECG: Electrocardiogram, MPI: myocardial perfusion imaging.

Discussion

Atherosclerosis of the coronary arteries, which is characterized by a narrowing or blockage of the arterial lumen and eventually causes myocardial ischemia, hypoxia, and heart disease (also referred to as ischemic heart disease) is the cause of coronary heart disease[1]

Regarding the statics, LVEF of the studied patients ranged from 39 to 73 % with a mean value (± SD) of 56.69 (±9.08) %. left ventricular hypertrophy was present in 88 (50.29%) patients. Further, left atrial enlargement was present in 35 (20%) patients and ranged from 2.6 to 5 cm with mean value (± SD) of 3.4 (±0.73) cm. Diastolic dysfunction happened in 132 (75.43%) patients. Mitral inflow velocities showed reversed E/A wave 110 (62.86%) patients and Pseudo-Normal E/A pattern in 22 (12.57%) patients.Patel et al.[8] found that a total of 1515 patients of IHD had Mean rest LVEF was 66.0%±12.7%. Median and MBFR were the reasons of the presence of LVH in IHD patients are that CAD and LVH are two common causes of IHD that independently result in myocardial ischemia.

Regarding our statistics, IVS diameter ranged from 0.7 to 1.5 cm with a mean value (± SD) of 1.15 (±0.26) cm. Also, the posterior wall diameter ranged from 0.8 to 1.5 cm with a mean value (± SD) of 1.16 (±0.23) cm. These findings are ascertained by Miftode et al.[9]found that patients with coronary perfusion defect showed IVS diameter 11.78 +/- 1.78 mm and their posterior wall diameter was 11.50 +/- 1.41 mm.

Our study reports that wall motion abnormalities were normal in134 (76.57%) patients, segmental hypokinesia in 34 (19.43%) patients, and global hypokinesia in 7(4%) patients. Patel et al. [8] supported our findings as they found that a total of 1515 patients of IHD had Mean rest LVEF was 66.0%±12.7%. The reasons for the presence

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

of LVH in IHD patients are that CAD and LVH are two common causes of IHD that independently result in myocardial ischemia. CAD decreases myocardial blood and oxygen supply whereas LVH increases myocardial oxygen demand.

Our statistics reveal that aortic root diameter ranged from 2.4 to 3.9 cm with a mean value (±SD) of 3.1(±0.45) cm. That finding matched with El-Naggar et al. [10]revealed that the aortic root diameter was less than normal and the aortic root showed great stiffness and less distensibility in IHD patients.

Our results reveal that ECG leads changes were evident in anterior in 34 (19.43%) patients, Lateral in 11 (6.29%) patients, inferior in 39 (22.29%) patients, antero-lateral in 47 (26.86%) patients, infero-lateral in 2 (1.14%) patients and non-significant abnormalities in 42 (24%) patients. These findings assure that stress echocardiography is an established technique for the assessment. These observations are in-accordance with Ghuran & Camm et al.[11] observed that arrhythmia mainly PVCs may have occurred in IHD but usually occurred in myocardial infarction which is attributed that myocardial ischemia is characterized by ionic and biochemical alterations, creating an unstable electrical substrate capable of initiating and sustaining arrhythmias, and infarction creates areas of electrical inactivity and blocks conduction, which also promotes arrhythmogenesis.

According to our results, left ventricular size by MPI was normal in 130 (74.29%) patients, borderline in 30 (17.14%) patients and dilated in 15 (8.57%). These results are in agreement with Khalid et al.[6]showed that IHD may associated with left ventricle abnormalities as dilation which is related to lack of adequate blood Supply is not able to meet the myocardial metabolic demands that lead to cell death, fibrosis, left ventricular enlargement and dilation.

Concerning our study, there was moderate agreement between MPI and exercise treadmill ECG. These findings are in-accordance with DesPrez et al.[12]and Koh et al.[12] stated that there was moderate agreement between MPI and exercise treadmill ECG, this study included 6702 patients with suspected CAD and 2008 with known CAD had treadmill exercise MPI and were followed for 2.5 ± 0.9 years for the occurrence of all-cause death.

Our study figures out that exercise treadmill ECG can diagnose CAD and IHD as MPI at stress with 82.9% sensitivity, 69% specificity, 93.1% PPV, 44.4% NPV and 80.6% accuracy. MPI at stress was superior in diagnosis

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

of CAD and IHD than Stress ECG. These observations are on the same line of Ananthasubramaniam et al.[13] demonstrated that the diagnostic value of stress ECG for CAD detection using standard ST-segment depression criteria was sensitivity 81% and specificity 66%.

Our results conclude that in Age <50y with one or no risk factors, there was a fair agreement between MPI and stress ECG but in Age >50y with one or more risk factors, there was a moderate agreement between MPI and stress ECG. Added to that, Takehana et al. [14] found that ischemic ECG changes during exercise stress are well associated with higher incidence of cardiac events in patients demonstrated reversible perfusion defect on MPI.

Limitations of our study included that Single center study that may result in different findings than elsewhere. Lack of studying patients with previous myocardial infarction in our study and significance of MPI and stress ECG findings. Lack of comparing different modalities of stress ECG as medical or exercise or electrical and variable aspects of therapies and changes occurring in MPI and stress ECG.

Conclusions

Finally, we provide the results of our study which revealed that MPI at stress was superior in diagnosis of CAD and IHD than Stress ECG. There was a moderate agreement between MPI and exercise treadmill ECG above age of 50yrs with one or more risk factors, while it was a fair agreement below age of 50yrs with one or no risk factors. Exercise treadmill induced ECG ischemic changes can diagnose the ischemic burden with less accuracy than the MPI at stress regarding the evidence of ischemia while it was irrelevant with myocardial perfusion defects in MPI at stress regarding the distribution of ischemic changes.

List of abbreviations

MPI: Myocardial perfusion imaging

ECG: Electrocardiogram

CAD: Coronary artery disease

IHD: Ischemic heart disease

SPECT: Single-photon emission computed tomography

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 07, 2024

CABG: Coronary artery bypass grafting

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