Original Article

Correlation Between Ventricular Perfusion Ischemia and Left Ventricular Dyssynchrony in Phase Analysis by Gated SPECT MPI

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ABSTRACT

Background: The gated single-photon emission computed tomography (Gated SPECT), myocardial perfusion imaging (MPI) is one of the most accurate methods to evaluate the extent of myocardial ischemia. The present study aimed to assess the correlation between the severity of ischemia and left ventricular dyssynchrony in phase analysis with GATED SPECT MPI by comparing the indices of perfusion, function, and phase analysis in stress and rest phases.

Methods: This cross-sectional study was performed on patients referred for Gated SPECT MPI. Fifty-six patients with ischemic heart disease based on Gated SPECT MPI and invasive coronary angiography were included. Parameters regarding myocardial perfusion and function in stress and rest conditions and coronary vessel parameters were assessed. Phase analysis indices, including phase standard deviation (PSD), phase histogram bandwidth (PHB), and entropy, based on Gated SPECT MPI (with the QGS software) were also evaluated

Results: Phase parameters, including PSD, PHB, and entropy, showed a good correlation with the severity of ischemia in stress conditions ($P<0.05$).

Conclusions: Scintigraphic indices of ischemia severity were highly correlated with phase analysis indices by Gated SPECT MPI. Therefore, an evaluation of these indices may accurately estimate systolic ventricular dyssynchrony, predict relative poor outcomes of cardiac ischemic events, and determine priorities for interventional cardiologists. ***(Iranian Heart Journal 2022; 23(1): 184-191)***

KEYWORDS: Dyssynchrony, Phase analysis, Ischemia, Gated SPECT, MPI

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Coronary heart disease is one of the major causes of mortality and morbidity, and patients with this disease are at high risk for progression to coronary heart failure and left ventricular dysfunction. [1,2] Therefore, identifying the underlying cause of heart failure and immediate treatment will prevent the progressive damage of the myocardium and may even result in the reversibility of left ventricular function. In patients with left ventricular dysfunction, the persistence of the viable tissues accelerates recovery. [3] Recently, it has been shown that not only myocardium viability but also severe left ventricular dyssynchrony is an independent factor in predicting the outcome of these patients. [4] Further, left ventricular mechanical dyssynchrony in patients with cardiomyopathy is responsible for mortality and morbidity in these patients. [5] Different methods such as tissue Doppler imaging (TDI), cardiac magnetic resonance imaging (MRI), cardiac computed tomography (CT), and electrocardiography-gated single-photon emission computed tomography-myocardial perfusion imaging (Gated SPECT MPI) are used to evaluate dyssynchrony. [6,7] The Gated SPECT MPI technique is widely used to explore ischemia, treatment response evaluation, risk assessment, infarct size determination, prognosis, and viability. [8] The existence of automated methods for measuring left ventricular function is one of the advantages of this assessment method. The GATED SPECT MPI technique allows the simultaneous evaluation of left ventricular mechanical synchrony, along with ventricular function and perfusion. [9] The GATED SPECT MPI method has other important advantages such as easy availability, repeatability, and the possibility of using retrospective data. [10] Indices such as phase-derived standard deviation (PSD) and phase histogram bandwidth (PHB) have a good relationship with left ventricular dyssynchrony assessed via the TDI technique are, thus, very useful in patients with heart failure. [11,12]

The aim of the present study was to assess the correlation between ischemia and left ventricular dyssynchrony in phase analysis with GATED SPECT MPI by comparing the parameters of perfusion, function, and phase analysis in stress and rest phases.

METHODS

Patients

In a 6-month period, this cross-sectional study was performed on patients with evidence of cardiac ischemia referred to the Nuclear Medicine Department of Rajaie Cardiovascular Medical and Research center, a tertiary care center for patients with cardiovascular disease in Tehran, Iran. Patients with evidence of cardiomyopathy, idiopathic cardiac dilatation, poor quality of images due to gastrointestinal activity, motion artifacts, and conduction system disorders (except for PAC and PVC) were all excluded.

Data Acquisition

The entire study population underwent the stress test by exercise or dipyridamole in a standard 1- or 2-day protocol and after the administration of 15 to 20 mci of a radiotracer (99m Tc-Sestamibi) for MPI with a dual detector SPECT/CT camera (Symbia T2, Siemens Medical Systems) with low-energy high-resolution collimators in the gated mode. Images were interpreted by a nuclear medicine physician. In the presence of perfusion defects in stress images, the patients were also planned for an invasive coronary angiography to confirm ischemic heart disease. Eventually, 50 patients were included in the study. In Gated SPECT MPI, the following parameters were evaluated in 2 conditions of stress and rest: the mean phase, PSD, PHB, and entropy. In patients with ischemic heart disease, perfusion indices were also assessed. The indices consisted of ischemia severity (the percentage of the radiotracer uptake relative to the segment with the most uptake: mild =60–70%, moderate =50–60%, and severe =40–50%/the summed stress score [SSS]: 4-8 [mild], 8-13 [moderate], and >13 [severe]), [17] infarction (the percentage of the radiotracer uptake relative to the segment the with most uptake (<50%), and ventricular function parameters, including left ventricular ejection fraction (LVEF), end-systolic volume (ESV), and end-diastolic volume (EDV). Finally, the correlations between the phase and functional indices and the severity of ischemia were analyzed. An example of the phase analysis is illustrated in Figure 1, which represents a wide histogram bandwidth with evidence of mechanical dyssynchrony in the left ventricle in a patient with a history of myocardial infarction (C & D) compared with narrow bandwidths in normal patients (A & B).

Statistical Analysis

Descriptive analysis was used to describe the data, including the mean ± the standard deviation (SD) for quantitative variables and frequencies (percentages) for categorical variables. The χ^2, independent *t*, and Mann–Whitney *U* tests were used to compare variables. The correlations between quantitative variables were tested using the Pearson correlation test. For the statistical analyses, the statistical software IBM SPSS Statistics for Windows, version 16.0, (IBM Corp, released 2013, Armonk, New York) was employed. A *P* value less than 0.05 was considered statistically significant.

RESULTS

A total of 56 patients were studied. As is presented in Table 1, baseline characteristics of the study population, including age, sex, and cardiovascular risk factors (hypertension, diabetes mellitus, hyperlipidemia, and family history of heart disease) were assessed. Cardiac function parameters (LVEF, EDV, ESV, peak filling rate, and time to peak filling), phase indices (PHB, PSD, and entropy), infarction, and invasive coronary angiography parameters (involved coronary arteries) are also shown.

Our results demonstrated correlations between LV function parameters and phase analysis indices (PHB, PSD, and entropy) in stress and rest phases (Table 2). There was a significant difference in dyssynchrony between mild and severe ischemia. There was also a positive correlation between the severity of ischemia as defined by SSS and phase analysis indices (PHB, PSD, and entropy) in the stress phase ($P<0.05$) (Table 3). However, this correlation could not be found based on the walls separately ($P=0.6$, which is nonsignificant). Invasive coronary angiography parameters (involved coronary arteries) had no correlations with phase analysis indices (PSD, PHB, and the mean peak) in stress and rest phases. Our study did not find any difference concerning Gated SPECT MPI phase indices between patients with infarction and those with infarction.

Table 1. Baseline characteristics of the study population

Male	47 of 56 (84%)		
Age (y)	31-81 (58±11)		
Hypertension	41%		
Diabetes mellitus	23%		
Hyperlipidemia	39%		
Family history	20%		
Infarction	In 29% of the patients (anterior wall: 13.5%, inferior wall: 10.7%, septal wall: 8.9%, lateral wall: 10.7%, and apex: 5.4%)		
Invasive Coronary Angiography	CAD: in 96.4% of the patients (LAD: 64.3%, LCX: 64.4%, and RCA: 32.1%)		
Myocardial ischemia			
Anterior	Mild ischemia (17.9%)	Moderate ischemia (10.7%)	Severe ischemia (12.5%)
Inferior	Mild ischemia (19.6%)	Moderate ischemia (10.7%)	Severe ischemia (7.1%)
Septal	Mild ischemia (14.3%)	Moderate ischemia (12.5%)	Severe ischemia (17.9%)
Lateral	Mild ischemia (14.3%)	Moderate ischemia (14.3%)	Severe ischemia (23.4%)
Apex	Mild ischemia (23.3%)	Moderate ischemia (5.4%)	
All	Mild ischemia (41.1%)	Moderate ischemia (16.1%)	Severe ischemia (37.5%)
LVEF	Stress (66±12%)	Rest (68±10%)	
EDV (mL)	Stress (80±29)	Rest (78±27)	
ESV (mL)	Stress (29±19)	Rest (26±16)	
PFR	Stress (2.2±0.7)	Rest (2.2±0.6)	
TTPF (ms)	Stress (176±33)	Rest (178±29)	
PHB	Stress (37.3±15.3%)	Rest (38.1±16%)	
PSD	Stress (9.4±4.6%)	Rest (9.5±4.4%)	
Entropy	Stress (38.9±9.8%)	Rest (39.5±10.5%)	

CAD, Coronary artery disease; LAD, Left anterior descending; LCX, Left circumflex; RCA, Right coronary artery; LVEF, Left ventricular ejection fraction; EDV, End-diastolic volume; ESV, End-systolic volume; PFR, Peak filling rate; TTFP, Time to peak filling; PHB, Phase histogram bandwidth; PSD, Phase standard deviation

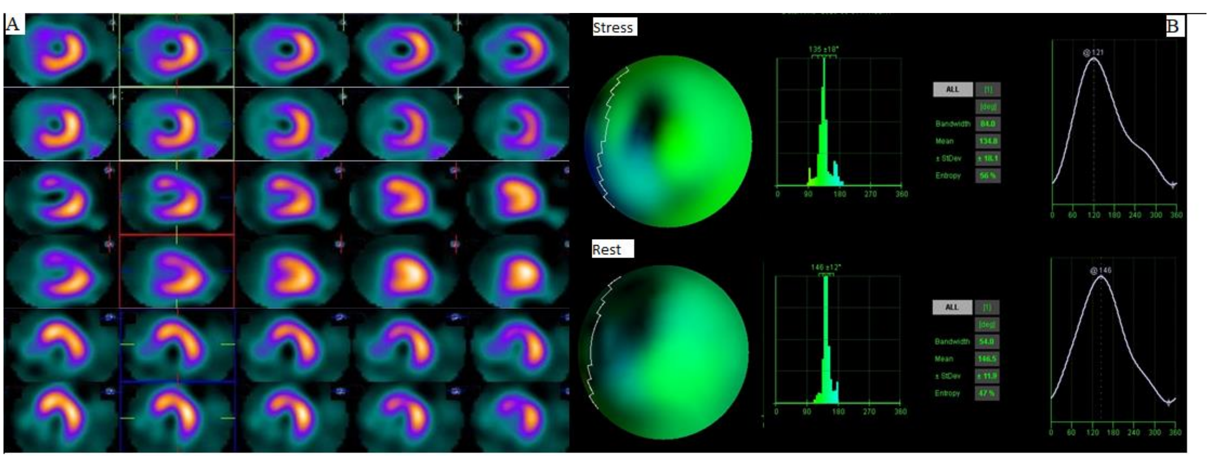

Figure 1. The stress-rest gated myocardial perfusion image shows severe ischemia in the anterior and mid-septal walls. (A) The image shows phase analysis for left ventricular mechanical synchronism assessment by myocardial perfusion single-photon emission computed tomography. In phase analysis, the wide bandwidth can be observed over the histogram with evidence of mechanical dyssynchrony in the left ventricle in a patient with a history of myocardial infarction (B) based on the data obtained in this study.

Table 2. Correlations between GATED SPECT MPI phase indices and function parameters

	Phase Parameter	LVEF (r, *P* value)	EDV (r, *P* value)	ESV (r, *P* value)
Rest	PSD	-0.528 (<0.01)	0.457 (<0.01)	0.435 (<0.01)
	PHB	-0.578 (<0.01)	0.514 (<0.01)	0.480 (<0.01)
	Entropy	-0.649 (<0.01)	0.526 (<0.01)	0.479 (<0.01)
Stress	PSD	-0.656 (<0.01)	0.541 (<0.01)	0.488 (<0.01)
	PHB	-0.640 (<0.01)	0.519 (<0.01)	0.493 (<0.01)
	Entropy	-0.579 (<0.01)	0.467 (<0.01)	0.439 (=0.01)

A *P* value less than 0.05 was considered significant.
SPECT, Single-photon emission computed tomography; PHB, Phase histogram bandwidth; PSD, Phase standard deviation

Table 3. Correlations between GATED SPECT MPI p phase indices and the severity of ischemia

	Phase Parameter	Mild ischemia	Severe ischemia	(*P* value)
Stress	PSD	8.2±0.9	11.7±1	0.037 (<0.05)
	PHB	32.8±3.4	44.6±3.1	0.037 (<0.05)
	Entropy	35.6±2.2	43.2±1.7	0.025 (<0.05)

A *P* value less than 0.05 was considered significant.
SPECT, Single-photon emission computed tomography; PHB, Phase histogram bandwidth; PSD, Phase standard deviation

DISCUSSION

Gated SPECT MPI is one of the most accurate methods given its advantages such as high availability, simultaneous evaluation of the severity and extent of ischemic heart disease in various positions associated with cardiac dysfunction, reproducibility, quantitative and analytical evaluations of myocardial parameters, and high accuracy. As we found in the present study, phase analysis parameters evaluated in Gated SPECT MPI had a strong and significant correlation with the severity of myocardial ischemia in stress conditions. In other words, scintigraphic indices of the severity of ischemia had a strong correlation with phase analysis indices based on Gated SPECT MPI (abnormal phase indices in terms of increased PSD, PHB, and entropy in more ischemic severity). Therefore, an evaluation of the phase analysis parameters of Gated SPECT MPI can accurately estimate the severity of ischemia and determine priorities for medical or interventional therapies. Nonetheless, we could not find this correlation based on the walls separately, which is more likely explained by the limited number of our patients.

We found no significant correlation between infarction and phase indices. The absence of correlation between ischemia in each wall and infarction in the entire myocardium and phase indices is probably due to a limited amount of infarction in the wall, which did not affect global LVEF. Reserved LV function in terms of normal LVEF in our patients could probably explain the lack of significant dyssynchrony in the infarcted parts; accordingly, further studies with more extensive infarctions are needed.

Finally, given that Gated SPECT MPI analytical parameters, including phase analysis indices, correlate with the severity of ischemia, these parameters can also be used to predict adverse cardiovascular outcomes following cardiovascular events. A review of similar studies also confirms this claim. In a study by Cho et al, [13] stress PHB, stress PSD, and resting PHB in patients with major adverse cardiac events (MACE) were significantly higher than those in patients without MACE. In a study by Goldberg et al, [14] patients who died had higher PSD and PHB than those who survived. In a study by Uebleis et al, [15] LVEF below 30% and left ventricular dyssynchrony predicted long-term mortality. In an investigation by Trimble et al, [16] patients with heart failure and impaired ventricular reperfusion had higher dyssynchrony based on both PSD and PHB, which is similar to our study. The authors also reported a strong correlation between Gated SPECT MPI parameters and ventricular perfusion indices. Still, given the limited number of patients with infarction (29% of the study population) and the limited extent of infarction (which was not enough to reduce global LVEF), further studies with more patients with infarction and higher extents of infarction are needed to evaluate the exact correlation between infarction and phase analysis indices. Furthermore, our study was not able to predict direct coronary artery involvement in terms of the number of coronary arteries involved, involved territories, electrocardiographic changes, good runoff, or the presence of slow coronary flow.

New Knowledge Gained

Most of the previous studies evaluated dyssynchrony in patients with reduced LVEF and heart failure, whereas we recruited patients with normal LVEF. Moreover, regarding the significant correlation between the severity of ischemia and phase analysis indices in patients with normal LV function, mechanical dyssynchrony might be the first functional parameter to appear in ischemic heart disease and determine the priority of interventional therapies.

CONCLUSIONS

As a general conclusion, the perfusion indices of ischemic severity have a strong correlation with phase analysis indices (PSD, PHB, the mean peak, and entropy). Therefore, an assessment of the various parameters of Gated SPECT MPI (including phase analysis indices) can accurately estimate ischemic heart disease and, thus, predict poorer outcomes of cardiac ischemic events, which could be helpful to determine the priorities of medical or interventional therapies. Consequently, the prediction of MACE will be possible even in the long run by an evaluation of Gated SPECT MPI parameters.

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Availability of Data

The data sets utilized in this study will be available from the corresponding author on reasonable request.

Disclosure

There is no financial or personal relationship between the authors of this paper and other people or organizations that could improperly influence or bias the content of the paper.

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