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ORIGINAL RESEARCH ARTICLE

Prognostic value of left ventricular sphericity indexes using gated SPECT and echocardiography in heart failure: A prospective study

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ABSTRACT

Introduction: Morphological remodeling of the heart during Heart failure (HF) can be detected by gated myocardial perfusion single-photon emission computed tomography (Gated SPECT) using left ventricular shape index (LVSI). This study aimed to investigate the prognostic value of LVSI measured by Gated SPECT and echocardiography in HF patients.
Methods: This prospective study involved 96 patients referred for myocardial perfusion scans, divided into two groups: those with heart failure (HF) and those without. The study analyzed cardiac sphericity indexes, including end-diastolic and end-systolic LVSI and the Eccentricity index (EI). The LVSI index was also measured by echocardiography at the end of diastole. The patients were followed for one year to evaluate the occurrence of cardiac events and underwent echocardiography at the end of this period.
Results: End-diastolic and end-systolic LVSI in the resting phase were 0.70±0.10 and 0.60±0.11 in the group of patients with HF, and 0.66±0.06 and 0.45±0.06 in the group of patients without heart failure, respectively. These values had a significant correlation with the similar index in echocardiography (p-value=0.001). In the group of HF patients, 20 people experienced cardiac events during one year of follow-up. However, there was no significant relationship between the values of LVSI measured by Gated SPECT and echocardiography and the incidence of cardiac events.
Conclusion: Although the values of LVSI in patients with HF were higher compared to those without HF, the indexes of heart shape change did not significantly predict the one-year prognosis of HF patients.

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INTRODUCTION

Heart failure (HF) is a clinical condition characterized by considerable morbidity and mortality [1]. Mortality prediction enables developing personalized prevention and treatment strategies in patients with HF [2]. Several studies assessed the clinical consequences of left ventricular deformation by focusing on ventricular volumes and ejection fraction (EF) [3]. However, few studies have investigated left ventricular shape index (LVSI) as a measurement parameter of heart remodeling [4].

Left ventricular (LV) remodeling is an essential precursor of clinical heart failure [5]. End-systolic and end-diastolic ventricular volume indexes and diameters are markers of HF severity and remodeling [6, 7]. Additionally, assessment of the shape of the ventricle is known as a marker of pathological remodeling in patients [8]. Previous studies based on echocardiography have shown the prognostic and clinical importance of left ventricular geometry [9, 10]. Almost all echocardiography studies have described this parameter in two dimensions [11].

LV remodeling can also be assessed through Myocardial Perfusion Imaging [12], particularly Gated myocardial perfusion SPECT (Gated SPECT). Gated SPECT enables measuring quantitative parameters in an operator-independent modality[13] which also provides three-dimensional measurement, together with perfusion evaluation [14]. LV adverse remodeling has been commonly evaluated through LVEF and LV volumes via Gated SPECT or positron emission tomography (PET) modality; however, the behavior of LVSI and eccentricity index (EI) has not been widely investigated by these imaging modalities [4]. Furthermore, it has not yet been established whether the LVSI has prognostic value in patients with heart failure. In this study, we aim to investigate whether LVSI and EI derived from gated SPECT and echocardiography can predict short-term cardiac events in patients with heart failure.

METHODS

Ethical approval and consent to participate

This study fully complies with the Declaration of Helsinki and was approved by the Ethics Committee of Mashhad University of Medical Sciences under the code of IR.MUMS.fm.REC.1395.520. All participants were informed of the study protocol and signed an informed written consent to participate in this study.

Study design and population

In this prospective cohort study, we recruited 96 patients referred for myocardial perfusion scan. Participants were divided into two groups: patients with HF and patients without HF. HF was detected based on the Framingham criteria, which include major criteria (paroxysmal nocturnal dyspnea or orthopnea, jugular venous distension, pulmonary rales, cardiomegaly, acute pulmonary edema, third heart sound, elevated venous pressure >16 cm H_2O, and hepatojugular reflux) and minor criteria (ankle edema, nocturnal cough, dyspnea on exertion, hepatomegaly, pleural effusion, and tachycardia >120 beats per minute). A weight loss of more than 4.5 kg within 5 days of treatment can be considered a major or minor criterion. Diagnosis of HF required either two major criteria or one major plus two minor criteria. Moreover, patients with an ejection fraction (EF) ≤ 40% on echocardiography were classified in the group of HF [15]. The non-HF group included patients with normal systolic function (EF ≥ 50%), absence of clinical HF symptoms, and no prior history of heart failure. Sampling was performed consecutively among all eligible patients meeting these inclusion criteria.

Patients with severe comorbid conditions, including advanced malignancies and end-stage renal disease, were excluded from the study.

Data collection and baseline assessments

After obtaining written informed consent, patient data, including patient symptoms, previous medical history, drug history, risk factors for coronary artery disease, New York Heart Association (NYHA) Functional Classification, and information on echocardiography, exercise test, angiography, and revascularization (if performed), were recorded prior to gated SPECT. Patients underwent echocardiography within a week after the Gated SPECT to evaluate the diastolic and systolic function of the left ventricle according to the guidelines of the American Society of Echocardiography and the European Society of Cardiovascular Imaging [16].

Echocardiography procedure

Echocardiography data were derived from the Echocardiography Registry of Mashhad University of Medical Sciences. Echocardiography was performed using Philips Affiniti 50 (model 795208; Philips Healthcare/Philips Ultrasound, Bothell, WA, USA) and Philips IE33 xMATRIX echocardiography system (Philips Medical Systems, Andover, MA, USA) devices with a 2-4 MHz probe according to the American Society of Echocardiography guideline [16] and by implementing standard parasternal short- and long-axis views and apical two- and four-chamber views.

Patients were positioned in the Left Lateral Decubitus. An experienced echocardiographer performed all echocardiographic examinations (blinded to the patient's records and scan results) to avoid inter-observer variation for each patient. At the same time, the images were digitally recorded for later analysis. A Comprehensive investigation, including M-Mode, two-dimensional Doppler (pulsed-wave and continuous-wave), and tissue Doppler imaging (TDI) was performed. Myocardial wall velocities were measured using TDI, with the sample volume (1–2 mm) placed at the lateral and distal mitral annulus, and the average value was reported. Systolic annular velocity (S'), early diastolic annular velocity (e'), along with the E/e' ratio for estimating left ventricular filling pressure, were measured.

Left ventricular end-diastolic and end-systolic diameters (LVEDD, LVESD) and volumes (LVEDV, LVESV) were measured in the parasternal long-axis view using M-mode and biplane Simpson's method, respectively. Left ventricular ejection fraction (LVEF) was calculated using the biplane Simpson's method. Interpapillary distance was analyzed as the distance between the tips of the papillary muscles measured at end-diastole in the parasternal short-axis view. Right ventricular end-diastolic diameter (RVEDD) was also evaluated along the short-axis in the apical four-chamber view, at a level that was nearly one-third from the base of the ventricle. Tricuspid annular plane systolic excursion (TAPSE) was assessed in the apical four-chamber view using M-mode. Pulmonary Arterial Pressure (PAP) was estimated using Doppler by adding the estimated right atrial pressure to the peak pressure gradient between the right ventricle and the right atrium. LVSI was defined as the ratio of the short-axis length to the long-axis length, measured at end-diastole in the apical four-chamber view using manual calipers.

Gated SPECT imaging procedure

Myocardial perfusion scan was conducted using the Gated SPECT method. This technique was implemented one hour after intravenous injection of 740-925 mega becquerels of Tc99m-Sestamibi, and it was performed by Siemens dual head variable angle gamma camera (e.cam, Siemens Medical Solutions USA), utilizing syngo® MI Applications platform (e.soft, Siemens Medical Solutions USA, Inc.). Along with a low-energy, high-resolution collimator. The scans were accomplished in supine position through two stages of pharmacological stress with Dipyridamole (0.56 mg/kg infusion over 4 minutes) and rest.

Imaging was performed using 32 projections (20 seconds per projection) from the Right Anterior Oblique to the Left Posterior Oblique with a Matrix of 64*64. Photopic energy at 140 keV was utilized, with 15% energy window. Gated images were captured with eight frames per cardiac cycle and 20% window. Reconstruction of images was done with Filtered Back Projection along with a Butterworth filter (cut-off frequency: 0.55 and order: 5). Two nuclear medicine specialists reviewed the scans and the results of the scan, and the extent and severity of the disorder were reported based on the 17-segment 5-scoring method.

Quantitative function parameters including PER (Peak Ejection Rate), PFR (Peak Filling Rate), MFR/3 (Mean filling rate at first of 1/3 diastole), Time to Peak Filling Rate (TTPF), EDV (End diastolic Volume), ESV(end systolic volume), LV EF (Ejection Fraction), Eccentricity Index (EI), and LVSI (in two systolic and diastolic phases of the cardiac cycle) in two stages of stress and rest gated images was calculated via QGS software (Cedars-Sinai Medical Center, Los Angeles, CA).

Perfusion parameters such as Summed Stress Score (SSS), Summed Rest Score (SRS), Summed Difference Score (SDS), and Total Perfusion Deficit (TPD) using Quantitative Perfusion SPECT software (QPS). Since the QPS software used in our study did not provide an option for calculating the transient ischemic dilation (TID) ratio, we employed the ECT software for this purpose, as we have extensive experience using it for TID ratio analysis. LVSI was also calculated manually as the ratio of the largest short-axis diameter of the heart cavity to the largest vertical long-axis diameter (the distance from the endocardial surface from the apex to the base) at rest and during stress. The base (basal limit) corresponds to the most basal slice where LV cavity activity is still clearly visualized, before tracer counts drop.

Follow-Up assessments

At two milestones, six months and one year after the start of the study, all patients were re-examined in terms of clinical symptoms (NYHA Functional Classification). Participants also underwent echocardiography by the same cardiologist (without knowledge of prior results or patient records) at the end of the first year.

Statistical analysis

Data were analyzed using SPSS for Windows TM, version 21.0 software packages. Different variables were described by descriptive statistics. Mean of quantitative variables, as Mean ±SD, was calculated. An independent-samples T-test analysis was performed in order to compare these values between the group of patients with heart failure and patients without heart failure. Pearson's correlation test was used to check the correlation between the quantitative variables obtained from echocardiography and the values obtained from the myocardial perfusion scan. Qualitative variables based on the chi-square test were checked. Then, based on Cox-regression survival analysis, the effect of the LVSI variable, as well as other risk factors, on the occurrence of cardiac events was analyzed.

RESULTS

Population characteristics

This study population consisted of 96 patients (66 men and 30 women) referred for myocardial perfusion scan. The characteristics of the patients in each group at the beginning of the study are shown in Table 1.

In the heart failure group, 3 participants were not taking any medication. Nine people were treated only with beta-blocker, one person was treated only with Angiotensin Converting Enzyme Inhibitor (ACEI), and 10 people were treated simultaneously with ACEI and beta-blocker drugs. Twenty-four patients utilized beta-blockers, ACEI, and diuretics, and in 3 patients, digoxin was also added to beta-blockers, ACEI, and diuretics. (Figure 1)

Table 1. Characteristics of subjects in two groups of patients with HF and without HF at the beginning of the study

Characteristic	All patients N=96	Patients with heart failure n= 50	Patients without heart failure n= 46	p-value
Age (years)	59.4±10.6	60.4±11.5	58.3±9.6	0.338
Gender (male) (%)	68.8	70	67.4	0.783
Smoking (%)	24	26	21.7	0.625
Family history of coronary disease (%)	18.8	18	19.6	0.844
Hypertension (%)	44.8	48	41.3	0.510
Diabetes (%)	25	26	23.9	0.814
Hyperlipidemia (%)	41.7	34	50	0.112
History of heart attack (%)	50	88	8.7	<0.001
The presence of angina (%)	63.5	84	41.3	0.112
Presence of known coronary disease (%)	68.8	86	50	<0.001
History of hospitalization due to coronary disease (%)	71.9	94	47.8	<0.001
History of hospitalization due to HF (%)	12.5	24	0	<0.001
NYHA class 1, 2, 3, 4 (number)	-	6, 34, 7, 3	-	-

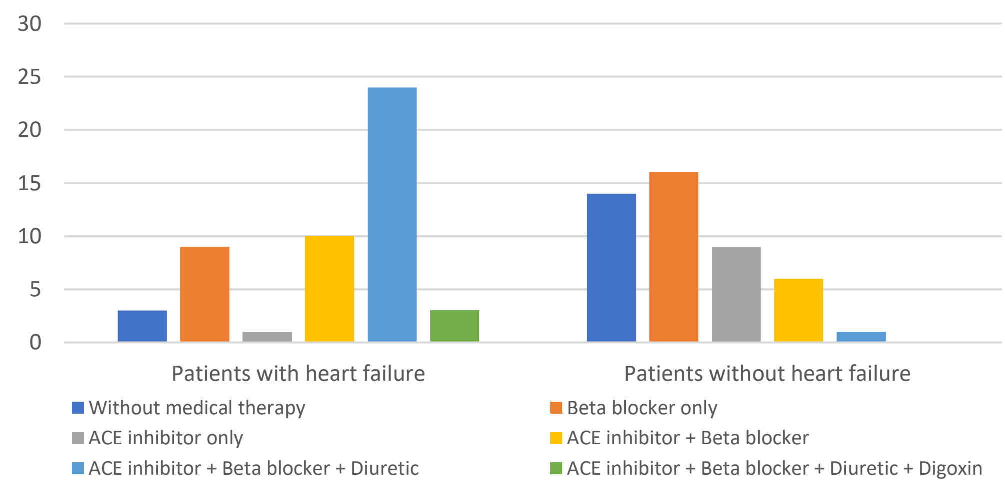

Figure 1. Medication distribution among patients with and without heart failure

Quantitative imaging in gated SPECT analysis

Patients with heart failure had significantly greater left ventricular end-diastolic volume (144.49 ± 66.71 mL vs. 59.60 ± 18.18 mL, p < 0.001) and end-systolic volume (101.33 ± 59.83 mL vs. 18.02 ± 12.08 mL, p < 0.001), along with markedly reduced ejection fraction (33.22 ± 10.79% vs. 72.39 ± 12.17%, p < 0.001), compared to patients without heart failure (Table 2).

There was no significant difference for TID (p = 0.119), SDS (p = 0.947), and TTPF during stress (p = 0.138) and rest (p = 0.557) between HF and non-HF groups. All other perfusion and functional indices differed significantly ($p < 0.05$).

The geometric indexes of the heart were analyzed separately in the scan. As shown in Table 3, the values of LVSI indexes in the stress and rest phase, as well as at the end of systole and diastole, were significantly higher in the group of patients with HF in comparison with patients without heart failure. Only the mean values of LVSI at the end of diastole and in the stress phase were not significantly different between the two groups (p-value: 0.206). Additionally, the values of EI in patients with HF were lower than those without HF, and this value was not significantly different in the stress phase between the two groups (p-value: 0.06) (Figure 2).

Table 2. Mean ± SD values of quantitative parameters of myocardial perfusion scan in two groups of patients with HF and without heart failure

Variable	HF Patients (Mean ± SD)	Patients Without HF (Mean ± SD)	p-value
QPS-SSS	19.65 ± 12.69	4.47 ± 3.91	< 0.001
QPS-SDS	3.50 ± 2.51	3.55 ± 3.55	0.947
QPS-SRS	18.34 ± 13.35	1.07 ± 1.81	< 0.001
Stress TPD	26.93 ± 17.96	5.26 ± 4.58	< 0.001
Rest TPD	26.66 ± 18.23	3.25 ± 3.46	< 0.001
TID	1.04 ± 0.17	0.98 ± 0.17	0.119
Visual SSS	19.30 ± 10.86	3.52 ± 3.69	< 0.001
Visual SRS	16.66 ± 11.21	1.64 ± 2.11	< 0.001
Visual SDS	4.65 ± 5.04	2.06 ± 2.51	0.005
Stress EDV	128.51 ± 50.16	55.68 ± 17.14	< 0.001
Stress ESV	86.82 ± 39.84	15.89 ± 10.09	< 0.001
Stress EF	33.56 ± 7.94	74.05 ± 12.36	< 0.001
Rest EDV	144.49 ± 66.71	59.60 ± 18.18	< 0.001
Rest ESV	101.33 ± 59.83	18.02 ± 12.08	< 0.001
Rest EF	33.22 ± 10.79	72.39 ± 12.17	< 0.001
Stress PER	-1.72 ± 0.88	-3.83 ± 1.73	< 0.001
Stress PFR	1.49 ± 0.79	2.79 ± 1.11	< 0.001
Stress MFR/3	0.72 ± 0.40	1.42 ± 0.49	< 0.001
Stress TTPF	148.46 ± 60.24	168.91 ± 63.35	0.138
Rest PER	-1.50 ± 0.78	-3.56 ± 2.24	< 0.001
Rest PFR	1.31 ± 0.62	2.77 ± 0.93	< 0.001
Rest MFR/3	0.65 ± 0.31	1.59 ± 43.90	< 0.001
Rest TTPF	146.88 ± 61.34	153.37 ± 43.90	0.557

Table 3. Geometric parameters of gated SPECT in two groups of patients with HF and without heart failure

Variable	HF Patients (Mean ± SD)	Patients Without HF (Mean ± SD)	p-value
Stress EI	0.80 ± 0.06	0.82 ± 0.07	0.06
Rest EI	0.80 ± 0.06	0.83 ± 0.05	0.008
Stress-diastolic-LVSI	0.71 ± 0.11	0.68 ± 0.08	0.206
Stress-systolic-LVSI	0.59 ± 0.12	0.44 ± 0.08	< 0.001
Rest-diastolic-LVSI	0.70 ± 0.10	0.66 ± 0.06	0.048
Rest-systolic-LVSI	0.60 ± 0.11	0.45 ± 0.06	< 0.001
Stress-manual-LVSI	0.41 ± 0.08	0.32 ± 0.04	< 0.001
Rest-manual-LVSI	0.45 ± 0.12	0.32 ± 0.04	< 0.001

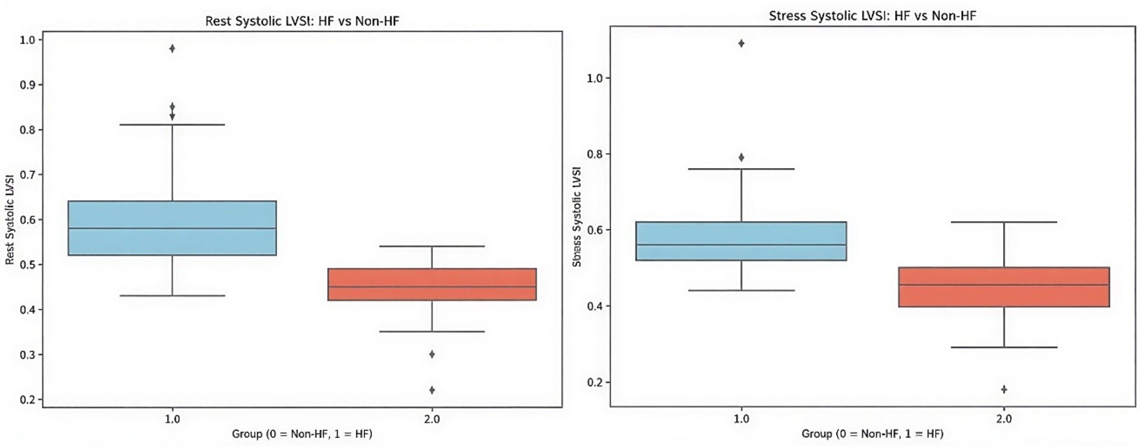

Figure 2. Box plot for LVSI values at the end of systole in the stress phase (left side) and rest phase (right side) in patients with and without heart failure

Quantitative imaging in echocardiography

After performing the myocardial perfusion scan, echocardiography was performed for the patients (Table 4). The volumes and diameters of the left ventricle at the end of diastole and end of systole, as well as LVSI, were greater in the HF group than in the other group, and this difference was significant in all cases (p-value: < 0.001). Only E and RVEDD showed no significant difference between the two groups.

Correlation of perfusion and geometric indexes with echocardiographic LVSI

There was a significant correlation between all the values of the remodeling indexes obtained from the myocardial perfusion scan and the indexes of the echocardiography in all patients (Table 5 and Figure 3). EI in the resting phase had the highest negative correlation (correlation coefficient: -0.624), and diastolic LVSI in the stress phase had the highest positive correlation (correlation coefficient: 0.611) with the echocardiography data. This analysis was also performed for patients with HF, which showed similar results; however, there was no significant correlation between LVSI measured by a non-automatic method and in the stress phase, with the LVSI parameter obtained from echocardiography (p-value: 0.062)

Table 4. Mean ± SD values of quantitative parameters of echocardiography in two groups of patients with HF and without heart failure

Variable	HF Patients (Mean ± SD)	Patients Without HF (Mean ± SD)	p-value
Echocardiography			
EF	27.82 ± 7.52	58.98 ± 6.11	< 0.001
E	62.94 ± 24.18	63.82 ± 16.46	0.82
e'	5.09 ± 1.61	7.29 ± 2.22	< 0.001
E / e'	13.14 ± 6.52	9.21 ± 2.65	< 0.001
PAP	33.65 ± 11.58	27.42 ± 6.43	0.002
LVESV	103.50 ± 49.62	38.19 ± 11.46	< 0.001
LVEDV	151.28 ± 56.08	87.69 ± 20.61	< 0.001
LVEDD	6.01 ± 0.92	4.66 ± 0.52	< 0.001
LVESD	4.78 ± 0.93	2.81 ± 0.50	< 0.001
RVEDD	2.99 ± 0.42	2.98 ± 0.39	0.845
Interpapillary Distance	2.71 ± 0.48	2.12 ± 0.35	< 0.001
S'	9.50 ± 2.36	12.00 ± 2.38	< 0.001
LVSI	0.57 ± 0.10	0.53 ± 0.06	0.016

Table 5. Correlation of geometric parameters of gated SPECT and LVSI in echocardiography

Variable	Pearson Correlation Coefficient (All Patients)	p-value	Pearson Correlation Coefficient (HF Patients)	p-value
Stress-EI	-0.575	<0.001	-0.693	<0.001
Rest-EI	-0.624	<0.001	-0.647	<0.001
Stress-diastolic-LVSI	0.611	<0.001	0.653	<0.001
Stress-systolic-LVSI	0.397	<0.001	0.597	<0.001
Rest-diastolic-LVSI	0.528	<0.001	0.502	<0.001
Rest-systolic-LVSI	0.418	<0.001	0.446	0.001
Stress manual LVSI	0.317	0.003	0.302	0.062
Rest manual LVSI	0.419	<0.001	0.367	0.009

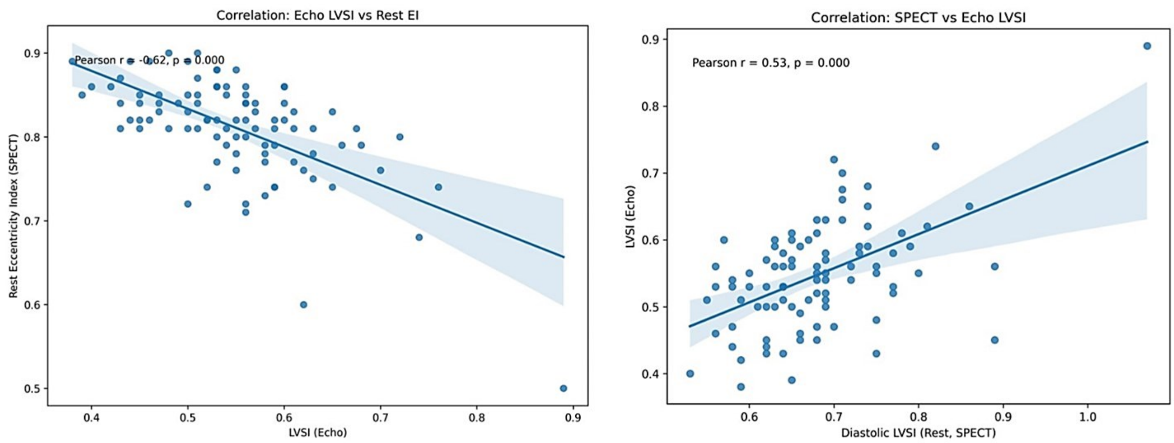

Figure 3. Assessing the correlation of LVSI measured by echocardiography and EI (right) and end-diastolic LVSI (Left) in resting phase of myocardial perfusion scan

Correlation of cardiac geometric indexes with other indexes of perfusion and cardiac function in the resting phase

In the resting phase, there was no significant correlation between EI and other indexes. There was a significant correlation between LVSI in the systolic phase, as well as manually measured LVSI, and all indexes (p-value < 0.001). A negative correlation was calculated for LVEF and diastolic indexes. Furthermore, in the case of diastolic LVSI, correlation with only ventricular volumes was observed (Table 6).

Follow-up

All patients completed a one-year follow-up to assess new symptoms and heart events. Eleven patients did not consent to one-year echocardiography. During the follow-up period, no deaths due to heart disease were found. Moreover, 20 patients in the HF group experienced cardiac events (Figure 4). One patient was in NYHA functional class 1, ten patients were in functional class 2, six patients were in functional class 3, and three patients were in functional class 4. Patients with a higher functional class had a lower event-free survival, which was statistically significant (p-value: 0.001) (Figure 5).

Investigating the predictive value of remodeling indexes in myocardial perfusion scan and echocardiography

Mean ± SD values of myocardial perfusion scan and echocardiography remodeling parameters were extracted in the group with cardiac events and the group without cardiac events. The effect of these indexes on the occurrence of cardiovascular events over time was investigated. No statistically significant impact on causing cardiovascular events in the HF patients was observed (Table 7).

Effects of quantitative indexes of myocardial perfusion scanning in the development of cardiovascular events over time

The effect of quantitative indexes of myocardial perfusion scan and echocardiography on cardiovascular events over time was assessed, and there was no significant difference (Table 8).

Finally, the mean values of cardiac remodeling indexes in myocardial perfusion scan in two groups of patients with and without exacerbation of heart failure according to clinical or echocardiographic findings were compared, and there was no significant difference between them (Table 9).

Table 6. Investigating the correlation of geometric parameters of perfusion scan with other parameters of perfusion and function in resting phase

Variable		Q-SRS	V-SRS	TPD	EDV	ESV	EF	PFR	MFR/3
EI	PCC	-0.080	0.092	-0.056	-0.117	-0.159	-0.154	0.098	0.122
	p-value	0.442	0.383	0.589	0.267	0.129	0.143	0.356	0.247
Diastolic-LVSI	PCC	0.056	0.092	0.06	0.209	0.228	-0.188	-0.195	-0.144
	p-value	0.598	0.383	0.567	0.046	0.029	0.072	0.066	0.170
Systolic-LVSI	PCC	0.376	0.445	0.403	0.621	0.652	-0.724	-0.634	-0.610
	p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Manual LVSI	PCC	0.681	0.722	0.672	0.798	0.814	-0.635	-0.494	-0.499
	p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

PCC: Pearson Correlation Coefficient

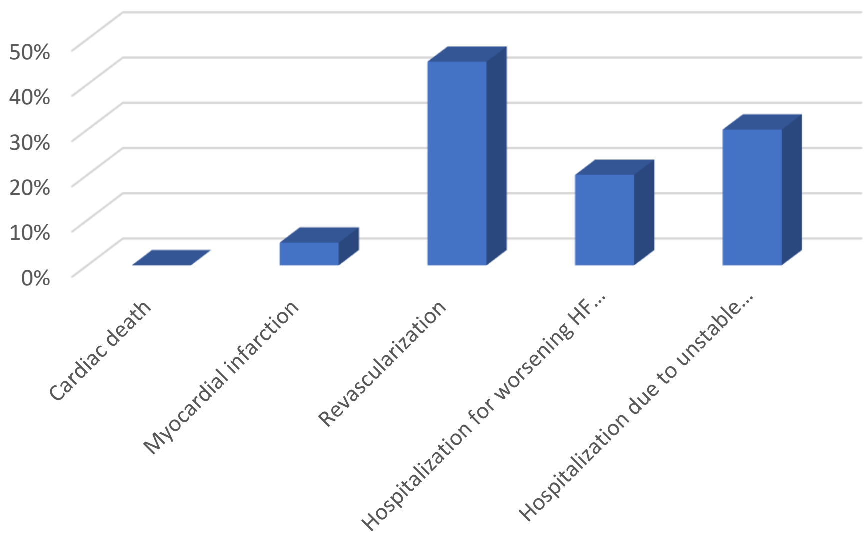

Figure 4. Relative frequency of cardiac event types in patients with heart failure (HF: heart failure)

DISCUSSION

In this study, we investigated the association of remodeling indexes, myocardial perfusion parameters, and functional indexes in Gated SPECT and echocardiography with the occurrence of cardiac events over time. LVSI parameters were calculated at the end of systole and diastole. Additionally, EI was also used as an index of heart remodeling. Both parameters were evaluated by the automated software program. This method minimizes operator-dependent error and offers high reproducibility [17]. These parameters assess the shape of the heart in three dimensions [18]. In addition to the calculated indexes by the software, these geometric indexes were calculated manually in the rest and the stress phases.

Our findings indicate that the mean EI values were lower in the HF group, whereas the average LVSI values in both systole and diastole were higher in patients with HF than in those without HF. Regarding LVSI in the systolic phase, there was little overlap between the HF and the non-HF groups, suggesting this parameter can be used to differentiate between normal and pathological ventricles. Our results corroborate with Hamalainen et al. study, which reported that end-systolic and end-diastolic shape indexes are higher in patients with LV mechanical desynchrony or lower EF [19].

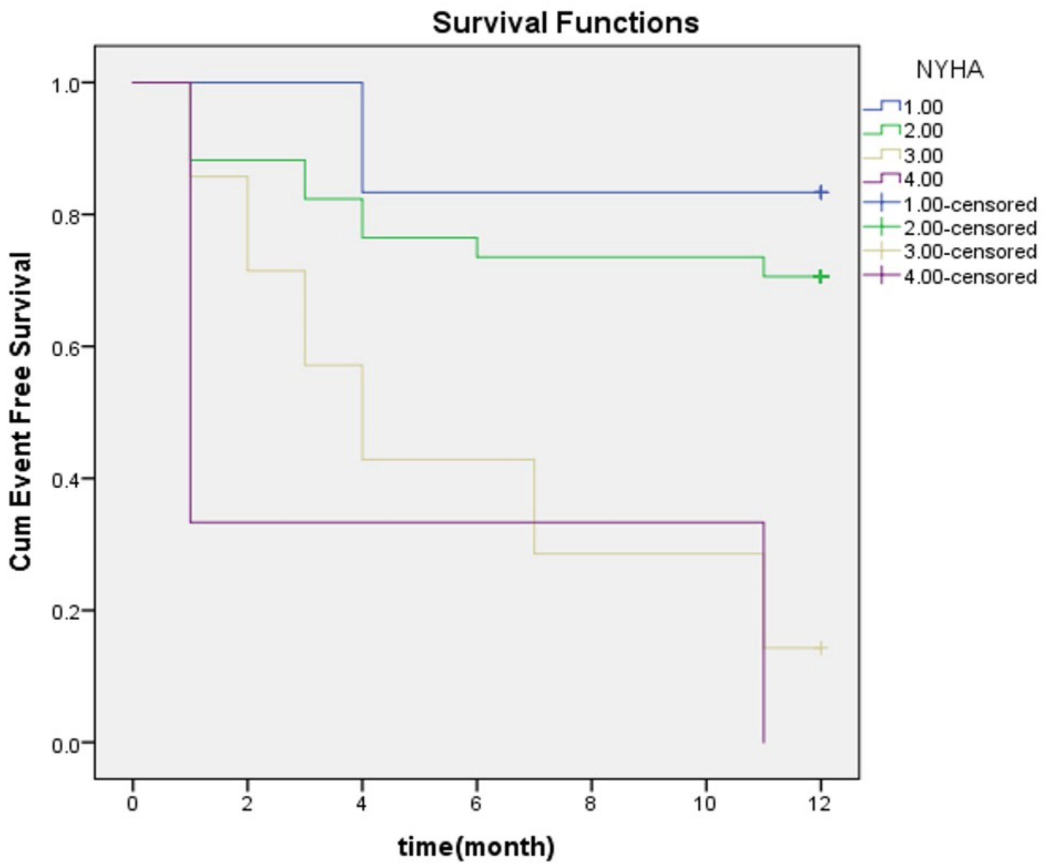

Figure 5. Examination of cardiovascular events in different NYHA functional class groups using Kaplan-Meier

Table 7. Investigating the effects of remodeling indexes in myocardial perfusion scan and echocardiography in the development of cardiovascular events over time

Factor	Imaging Modality	Incident	Mean±SD	Hazard Ratio (95% CI)	p-value
Stress EI	Gated SPECT	Cardiac Event	0.80 ± 0.05	1.293 (0.001 - 1397.712)	0.957
		No Cardiac Event	0.80 ± 0.06		
Rest EI	Gated SPECT	Cardiac Event	0.80 ± 0.05	3.715 (0.002 - 7035.071)	0.733
		No Cardiac Event	0.80 ± 0.07		
S-diastolic-LVSI	Gated SPECT	Cardiac Event	0.70 ± 0.09	0.331 (0.002 - 67.449)	0.684
		No Cardiac Event	0.71 ± 0.12		
S-systolic-LVSI	Gated SPECT	Cardiac Event	0.58 ± 0.07	0.442 (0.003 - 60.252)	0.745
		No Cardiac Event	0.59 ± 0.13		
R-diastolic-LVSI	Gated SPECT	Cardiac Event	0.67 ± 0.07	0.023 (0.001 - 4.975)	0.169
		No Cardiac Event	0.71 ± 0.11		
R-systolic-LVSI	Gated SPECT	Cardiac Event	0.59 ± 0.10	0.338 (0.004 - 25.898)	0.623
		No Cardiac Event	0.60 ± 0.12		
Stress manual LVSI	Gated SPECT	Cardiac Event	0.40 ± 0.09	0.025 (0.001 - 35.203)	0.318
		No Cardiac Event	0.42 ± 0.08		
Rest manual LVSI	Gated SPECT	Cardiac Event	0.46 ± 0.14	2.334 (0.062 - 87.073)	0.646
		No Cardiac Event	0.44 ± 0.10		
ECHO LVSI	Echocardiography	Cardiac Event	0.60 ± 0.09	24.369 (0.467 - 1271.026)	0.113
		No Cardiac Event	0.55 ± 0.10		

Table 8. Investigating the effects of quantitative indices in myocardial perfusion scanning and echocardiography in the development of cardiovascular events over time

Factor	Imaging Modality	Incident	Mean ± SD	Hazard Ratio (95% CI)	p-value
QPS SSS	Gated SPECT	Cardiac Event No Cardiac Event	20.79 ± 12.61 19.04 ± 12.94	1.009 (0.967 - 1.053)	0.679
QPS SDS	Gated SPECT	Cardiac Event No Cardiac Event	3.64 ± 2.59 3.42 ± 2.51	1.016 (0.827 - 1.248)	0.880
QPS SRS	Gated SPECT	Cardiac Event No Cardiac Event	18.65 ± 14.20 18.13 ± 12.99	1.001 (0.968 - 1.034)	0.974
Stress TPD	Gated SPECT	Cardiac Event No Cardiac Event	28.43 ± 18.13 26.12 ± 17.17	1.006 (0.976 - 1.037)	0.685
Rest TPD	Gated SPECT	Cardiac Event No Cardiac Event	25.75 ± 20.31 27.04 ± 17.51	0.996 (0.972 - 1.021)	0.739
TID	Gated SPECT	Cardiac Event No Cardiac Event	1.01 ± 0.16 1.06 ± 0.17	0.288 (0.010 - 8.496)	0.471
Visual SSS	Gated SPECT	Cardiac Event No Cardiac Event	20.50 ± 12.30 18.65 ± 10.19	1.016 (0.965 - 1.069)	0.556
Visual SRS	Gated SPECT	Cardiac Event No Cardiac Event	17.15 ± 12.68 16.33 ± 10.32	1.004 (0.964 - 1.046)	0.838
Visual SDS	Gated SPECT	Cardiac Event No Cardiac Event	6.86 ± 6.06 3.46 ± 4.03	1.094 (1.000 - 1.197)	0.050
Stress EDV	Gated SPECT	Cardiac Event No Cardiac Event	137.14 ± 57.50 123.68 ± 46.09	1.005 (0.994 - 1.016)	0.372
Stress ESV	Gated SPECT	Cardiac Event No Cardiac Event	92.57 ± 45.18 83.60 ± 37.11	1.005 (0.992 - 1.019)	0.435
Stress EF	Gated SPECT	Cardiac Event No Cardiac Event	34.64 ± 9.40 32.96 ± 7.13	1.017 (0.950 - 1.090)	0.624
Rest EDV	Gated SPECT	Cardiac Event No Cardiac Event	165.00 ± 83.32 131.50 ± 51.07	1.004 (0.999 - 1.010)	0.116
Rest ESV	Gated SPECT	Cardiac Event No Cardiac Event	120.37 ± 76.61 89.26 ± 43.52	1.005 (0.999 - 1.011)	0.116
Rest EF	Gated SPECT	Cardiac Event No Cardiac Event	31.05 ± 12.98 34.60 ± 9.12	0.975 (0.931 - 1.022)	0.291
Stress PER	Gated SPECT	Cardiac Event No Cardiac Event	-1.85 ± 0.59 -1.65 ± 1.00	0.794 (0.391 - 1.610)	0.522
Stress PFR	Gated SPECT	Cardiac Event No Cardiac Event	1.54 ± 0.64 1.46 ± 0.87	1.108 (0.587 - 2.090)	0.753
Stress MFR/3	Gated SPECT	Cardiac Event No Cardiac Event	0.78 ± 0.37 0.69 ± 0.42	1.442 (0.426 - 4.884)	0.556
Stress TTPF	Gated SPECT	Cardiac Event No Cardiac Event	144.93 ± 50.82 150.44 ± 65.84	0.999 (0.990 - 1.008)	0.816
Rest PER	Gated SPECT	Cardiac Event No Cardiac Event	-1.36 ± 0.81 -1.59 ± 0.75	1.177 (0.737 - 1.880)	0.496
Rest PFR	Gated SPECT	Cardiac Event No Cardiac Event	1.38 ± 0.60 1.28 ± 0.64	1.333 (0.626 - 2.836)	0.456
Rest MFR/3	Gated SPECT	Cardiac Event No Cardiac Event	0.62 ± 0.36 0.66 ± 0.28	0.726 (0.163 - 3.238)	0.675
Rest TTPF	Gated SPECT	Cardiac Event No Cardiac Event	152.05 ± 58.41 143.63 ± 63.89	1.002 (0.994 - 1.009)	0.642
EF	Echocardiography	Cardiac Event No Cardiac Event	25.50 ± 7.76 29.37 ± 7.07	0.953 (0.898 - 1.011)	0.109
E	Echocardiography	Cardiac Event No Cardiac Event	66.84 ± 26.69 60.43 ± 22.56	1.009 (0.990 - 1.027)	0.360
e'	Echocardiography	Cardiac Event No Cardiac Event	4.63 ± 1.50 5.40 ± 1.63	0.757 (0.534 – 1.072)	0.116
E/e'	Echocardiography	Cardiac Event No Cardiac Event	15.27 ± 7.83 11.80 ± 5.23	1.052 (0.995 - 1.114)	0.076
PAP	Echocardiography	Cardiac Event No Cardiac Event	35.50 ± 14.63 32.32 ± 8.86	1.017 (0.982 - 1.054)	0.340
LVESV	Echocardiography	Cardiac Event No Cardiac Event	114.60 ± 53.45 96.10 ± 46.33	1.006 (0.998 - 1.014)	0.172
LVEDV	Echocardiography	Cardiac Event No Cardiac Event	162.45 ± 62.32 143.83 ± 51.24	1.005 (0.997 - 1.012)	0.196
LVEDD	Echocardiography	Cardiac Event No Cardiac Event	6.06 ± 1.17 5.98 ± 0.72	1.099 (0.646 - 1.872)	0.727
LVESD	Echocardiography	Cardiac Event No Cardiac Event	5.04 ±1.06 4.60 ± 0.81	1.488 (0.935 - 2.368)	0.094
RVEDD	Echocardiography	Cardiac Event No Cardiac Event	3.09 ± 0.49 2.92 ± 036	2.480 (0.776 - 7.923)	0.125
S'	Echocardiography	Cardiac Event No Cardiac Event	9.05 ± 2.33 9.80 ± 2.38	0.925 (0.935 2.368)	0.396
Interpapillary Distance	Echocardiography	Cardiac Event No Cardiac Event	2.73 ± 0.50 2.70 ± 0.47	1.070 (0.427 - 2.681)	0.886

Table 9. Mean±SD values of heart geometry parameters in myocardial perfusion scan in two groups of patients with and without exacerbation of heart failure in clinical or echocardiographic findings

Variable	Patients with Exacerbation (N=15)	Patients without Exacerbation (N=35)	p-value
Stress-EI	0.79 ± 0.06	0.80 ± 0.06	0.842
Rest-EI	0.79 ± 0.05	0.80 ± 0.07	0.735
Stress-diastolic-LVSI	0.069 ± 0.10	0.71 ±0.11	0.670
Stress-systolic-LVSI	0.56 ± 0.09	0.60 ± 0.12	0.381
Rest-diastolic-LVSI	0.67 ± 0.06	0.71 ± 0.11	0.275
Rest-systolic-LVSI	0.58 ± 0.10	0.60 ± 0.12	0.579
Stress manual LVSI	0.44 ± 0.09	0.40 ± 0.08	0.297
Rest manual LVSI	0.49 ± 0.10	0.43 ± 0.12	0.095

Likewise, we observed that patients with lower EF (HF in our case) showed higher LVSI in comparison to those without HF.

Previous studies have investigated the correlation of LV geometry and LV function and volume. Their results have shown that end-systolic LVSI correlates with LV function as measured by PET/CT [4] as well as LV volume and function as measured by ECG-gated SPECT [12]. Our result aligns well with previous studies where there was significant correlation between automatic end-systolic LVSI and manually calculated LVSI indexes with other perfusion and function indexes in myocardial perfusion scan.

Notably, in this study, both the myocardial perfusion scan and echocardiography were performed, and a correlation was observed between the geometric index results from the myocardial perfusion scan and the remodeling index in echocardiography.

After one year of follow-up, Patients with lower activity tolerance experienced shorter event-free survival, and all patients in class IV experienced cardiac events. Although EI was lower in patients who developed cardiac events, this factor was not significantly associated with the occurrence of cardiac events. Similarly, despite higher mean values of LVSI in patients with HF compared to those in the other group, its predictive value was not significant. Our findings contrast with the results of Abidov et al., who described that LVSI can predict the risk of hospitalization due to exacerbation of congestive HF within a 60-day follow-up period [17]. Several factors may justify this discrepancy. First, while their study was retrospective and focused mainly on the exacerbation of congestive heart failure, we considered a broader range of cardiac events, including myocardial infarction, unstable angina, coronary artery revascularization, and exacerbation of HF. Furthermore, differences in study design, population characteristics, and the duration of follow-up may have impacted the prognostic performance of LVSI in our study.

Few other studies have also explored the use of geometric indexes in predicting cardiac events. Gaudieri et al. reported that LVSI obtained from the Myocardial perfusion scan in patients with suspected coronary disease and a normal myocardial perfusion scan can independently predict cardiac events within 4 years of follow-up [20]. However, differences in study population (patients with established HF vs patients with suspected coronary disease) and a shorter follow-up period may partially explain the lack of significant predictive value of LVSI in our cohort. Similarly, studies by Zhao et al. and Wu et al. have shown that shape index and EI are independent predictors of major adverse cardiac events (MACE) in patients with ischemia and preserved ejection fraction (EF) coronary artery disease, respectively [21, 22]. Our study focuses on a more advanced stage of cardiac dysfunction, where underlying ventricular remodeling may already be established, potentially reducing the predictive value of these indexes.

In addition to geometric parameters, we assessed conventional functional indices, including EF and LV volumes, for prognostic value. Despite some studies having shown the prognostic role of functional parameters such as EF and LV volumes [23, 24], our study did not demonstrate a significant correlation between these conventional measures (obtained from gated-SPECT or echocardiography) and event-free survival. Several factors could explain this discrepancy. First, many patients in our cohort already had advanced heart dysfunction and reduced EF, which limited the discriminative power of EF to predict further events. Second, some studies have shown that LVEF alone may not be a great predictor and factors like “LVEF/LV mass” are better predictors for certain HF patients [25]. Third, the relatively small sample size and short follow-up period may have reduced the statistical power to detect modest associations. Finally, differences in imaging modalities and post-processing software may also have affected the strength of prediction.

Several limitations may have influenced the results of this study. Firstly, the relatively small sample size may have compromised our statistical power. Additionally, the short follow-up duration may have limited our ability to detect late-onset cardiac events. Furthermore, most patients in the heart failure group were receiving pharmacological treatment at baseline, and treatment regimens were adjusted or intensified during follow-up, which may have impacted the interpretation of the results.

Another limitation is 8-frame gated SPECT used for evaluation of diastolic functional indices in gated myocardial perfusion SPECT. In routine practice, acquisition of 8 frames per cardiac cycle is considered and it is satisfactory for left ventricular systolic indices [26]. Although 16-frame gated SPECT provides higher temporal resolution, several studies have shown that 8-frame acquisition still yields reliable diastolic indices. Kurisu et al. (2017) reported good correlation between 8- and 16-frame protocols for parameters such as PFR and TTPF, with only mild underestimation using 8 frames [27]. Similarly, Korkmaz et al. (2017) demonstrated that 8-frame gated SPECT effectively detected diastolic dysfunction in diabetic patients [28]. These findings support the clinical usefulness of the 8-frame protocol for routine diastolic assessment.

CONCLUSION

Patients with heart failure (HF) exhibited higher LVSI values and lower Eccentricity Index (EI) values, as assessed by gated SPECT. This 1-year follow-up study found that cardiac geometric parameters, such as LVSI, were not significant predictors of short-term cardiac events in HF patients. Further large-scale, prospective studies are needed to elucidate the prognostic value of LV remodeling indexes.

Abbreviations

EDV: End-Diastolic Volume
EF: Ejection Fraction
EI: Eccentricity Index
ESV: End-Systolic Volume
e′: Early Diastolic Annular Velocity
HF: Heart Failure
LV: Left Ventricular
LVEF: Left Ventricular Ejection Fraction
LVSI: Left Ventricular Shape Index
MFR: Myocardial Flow Reserve
NYHA: New York Heart Association
PAP: Pulmonary Arterial Pressure
PER: Peak Ejection Rate
PET: Positron Emission Tomography
PFR: Peak Filling Rate
RVEDD: Right Ventricular End-Diastolic Diameter
SDS: Summed Difference Score
S′: Systolic Annular Velocity
SPECT: Single Photon Emission Computed Tomography
SRS: Summed Rest Score
SSS: Summed Stress Score
TAPSE: Tricuspid Annular Plane Systolic Excursion
Tc99m: Technetium-99m
TDI: Tissue Doppler Imaging
TID: Transient Ischemic Dilatation
TPD: Total Perfusion Deficit
TTPF: Time to Peak Filling Rate

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