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ORIGINAL ARTICLE

Early left ventricular dyssynchrony in acute ST elevation myocardial infarction: A gated single photon emission computed tomography study

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KEYWORDS

Myocardial perfusion imaging;
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Abstract *Introduction:* The resulting left ventricular (LV) dysfunction in acute STEMI is definitely secondary to loss of myocardial muscle mass (Krumholz et al., 2009; Guerchicoff et al., 2014) but may have an additional component of LV dyssynchrony.

Aim: Detection of LV dyssynchrony in acute STEMI patients and its relation to LV dysfunction in these patients.

Patients and methods: 60 patients presenting with acute STEMI were injected with 25 mCi of Tc^{99m} SestaMIBI prior to primary PCI. Acquisition was deferred after the procedure within 6 h of injection. Images were analyzed using QGS Cedars Sinai software to measure the histogram bandwidth, standard deviation and entropy using GSPECT phase analysis. The results were compared to 60 patients with negative perfusion scans upon maximal exercise imaged using the same protocol during rest.

Results: Our study included a total number of 60 acute STEMI patients, 54 males, mean age 54.8 ± 10.38 years, Compared to 60 controls mean age 50.7 + 20.3 years. Risk factors for CAD were smoking in 41 patients, hypertension in 17, dyslipidemia in 7, diabetes in 15, and positive family history of CAD in 21. 30 patients had acute anterior STEMI and 30 had inferior. LVEDV and LVESV were larger compared to controls; 133.0 ± 88.7 vs. 62.0 ± 19.2 ml and 89.7 ± 82.1 vs.

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19.9 ± 12.3 ml respectively, $p < 0.001$, and lower LVEF 39.0 ± 16.8 vs. 71.1 ± 10.4%, $p < 0.001$. Histogram bandwidth (BW), standard deviation (SD) and entropy (E) values were significantly higher in patients when compared to controls; 76.2 ± 54.7 vs. 17.8 ± 5.3, 20.7 ± 15.2 vs. 4.1 ± 2.0 and 51.1 ± 18.6 vs. 21.8 ± 7.1 degrees respectively, $p < 0.001$. BW, SD and E significantly negatively correlated with LVEF in acute STEMI cases; $r = -.733$, $p < 0.001$, $r = -.75$, $p < 0.001$, and $r = -.858$, $p < 0.001$ respectively.

Conclusion: LV dyssynchrony may be acquired acutely very early in STEMI and may have a negative impact on LV ejection fraction.

1. Introduction

Acute myocardial infarction is a devastating condition carrying high incidence of morbidity and mortality despite considerable advances in lines of therapy over years [1]. The resulting left ventricular (LV) dysfunction is definitely secondary to loss of myocardial muscle mass [1,2] but may have an additional component of LV dyssynchrony. All the efforts in the last decade focused mainly on decreasing infarction size through early reperfusion and adjunctive medical therapy [1–3]. Several studies could find some relation between LV dyssynchrony and acute myocardial infarction, however in these studies modest duration of time elapsed between the incidence of STEMI and imaging used [4–6]. In addition to date there is no evidence that early LV dyssynchrony can affect acutely the LV function. With the advances, ease and popularity in resynchronization therapy positive modification of dyssynchrony toward synchrony may be of value in the acute phase of STEMI. Gated SPECT was studied as a valuable tool to evaluate dyssyn-

Table 1 Risk factors for coronary artery disease.

Risk factors	Frequency	Percentage (%)
Smoking	41	68
F.H of CAD	21	35
Hypertension	17	28
Diabetes	15	25
Dyslipidemia	7	12

Table 2 The demographic data for controls.

	Control (N. 60)
Age	50.9 ± 10.4
Gender (Male)	28 (46.7%)
Diabetes	17 (28.3%)
Hypertension	33 (55.0%)
FH of CAD	13 (21.7%)
Smoking	15 (25.0%)
Dyslipidemia	15 (25.0%)

Table 3 Comparison between the case and controls.

	Control (N. 60)	Case (N. 60)	*p* value
Age	50.9 ± 10.4	54.0 ± 10.4	.104
Gender (Male)	28 (46.7%)	54 (90.0%)	.001
Diabetes	17 (28.3%)	15 (25.0%)	.541
Hypertension	33 (55.0%)	17 (28.3%)	.003
FH of CAD	13 (21.7%)	21 (35.0%)	.156
Smoking	15 (25.0%)	41 (68.3%)	.001
Dyslipidemia	15 (25.0%)	7 (11.7%)	.097

Table 4 Comparison between both groups as regards Left Ventricle gated SPECT and phase analysis results for left ventricle end systolic volume (LVESV), left ventricle end diastolic volume (LVEDV), left ventricle ejection fraction (LVEF), Histogram Bandwidth (BW), Standard Deviation (SD),and Entropy (E) in (degree, millisecond).

Gated SPECT	Controls	Cases	*p* value
LVEDv (ml)	62.0 ± 19.2	133.0 ± 88.7	< .001
LVESv (ml)	19.9 ± 12.3	89.7 ± 82.1	< .001
LV EF%	71.1 ± 10.4	39.0 ± 16.8	< .001
Histogram bandwidth (millisecond)	37.3 ± 11.9	152.4 ± 110.9	< .001
Histogram SD (millisecond)	9.2 ± 4.2	40.4 ± 36.3	< .001
Histogram bandwidth (degree)	17.8 ± 5.3	76.2 ± 54.7°	< .001
Histogram SD (degree)	4.1 ± 2.0	20.7 ± 15.2°	< .001
Histogram entropy (%)	21.8 ± 7.1	51.1 ± 18.6%	< .001

Table 5 Range of Histogram band width and standard deviation and entropy values in STEMI cases.

Case	Range	Mean	Std. deviation
Histogram BW	12–234	76.2	54.7
Histogram SD	1.6–60.8	20.7	15.2
Histogram entropy	6–85	51.1	18.6

Table 6 Range of Histogram band width and standard deviation and entropy values in normal (control) subject.

Control	Range	Mean	Std. deviation
Histogram BW	6–30	17.8	5.3
Histogram SD	0.6–13.5	4.1	2.0
Histogram entropy	1–39	21.8	7.1

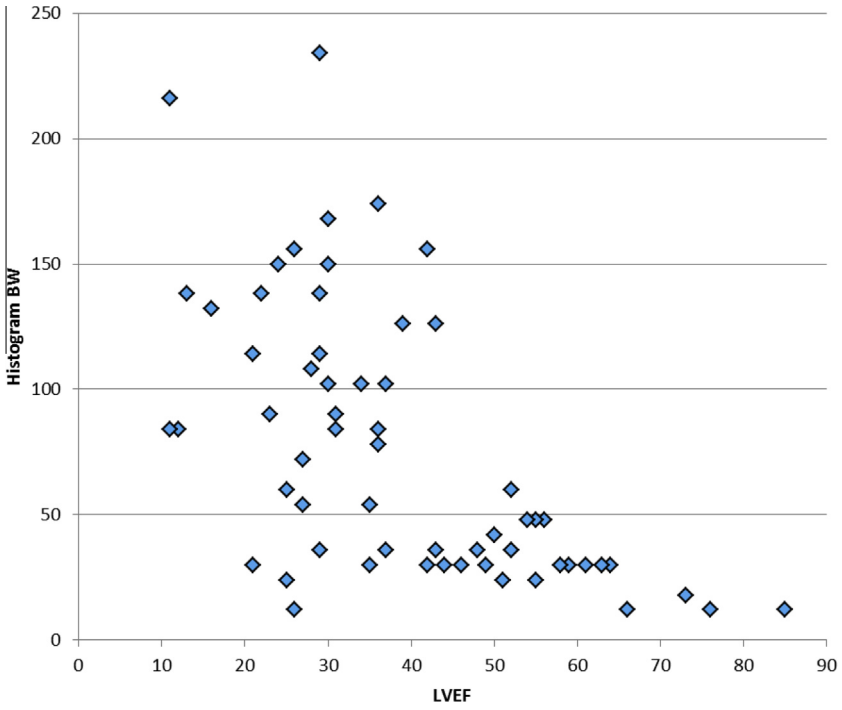

Fig. 1 Correlation between histogram BW and LVEF in acute myocardial infarction cases.

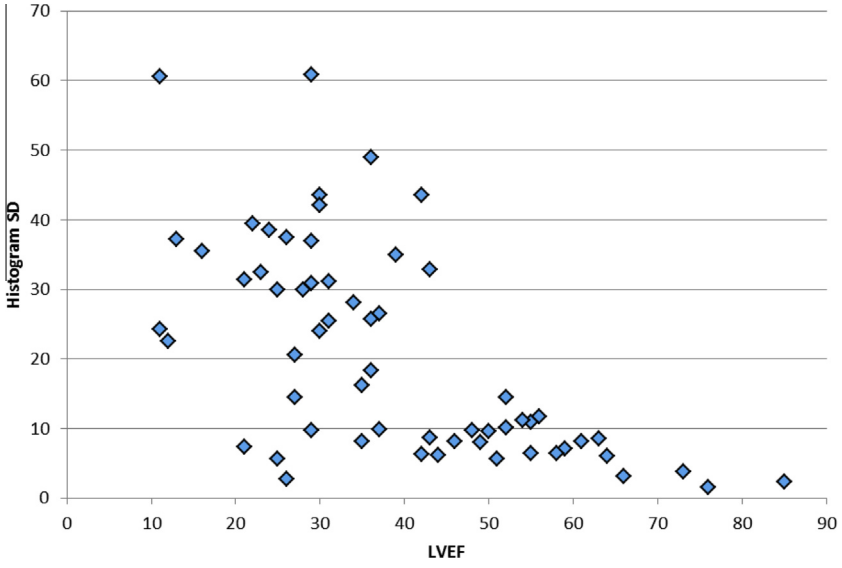

Fig. 2 Correlation between histogram SD and LVEF in acute myocardial infarction cases.

Table 7 Correlation between histogram Band width, standard deviation and entropy and Left ventricular ejection fraction in STEMI cases.

Case		BW^0	SD^0	Entropy
LVEF%	*R* value	−0.594	−0.628	−0.731
	p value	< 0.0001	< 0.0001	< 0.0001

chrony in heart failure patients [7]. Using technetium Sesta-MIBI offers the advantage of injecting the isotope on admission and acquiring the study after the revascularization without delay in the treatment offered for the patient [8–11].

2. Aim of work

Detection of LV dyssynchrony in Acute STEMI patients and its relation to LV dysfunction in these patients.

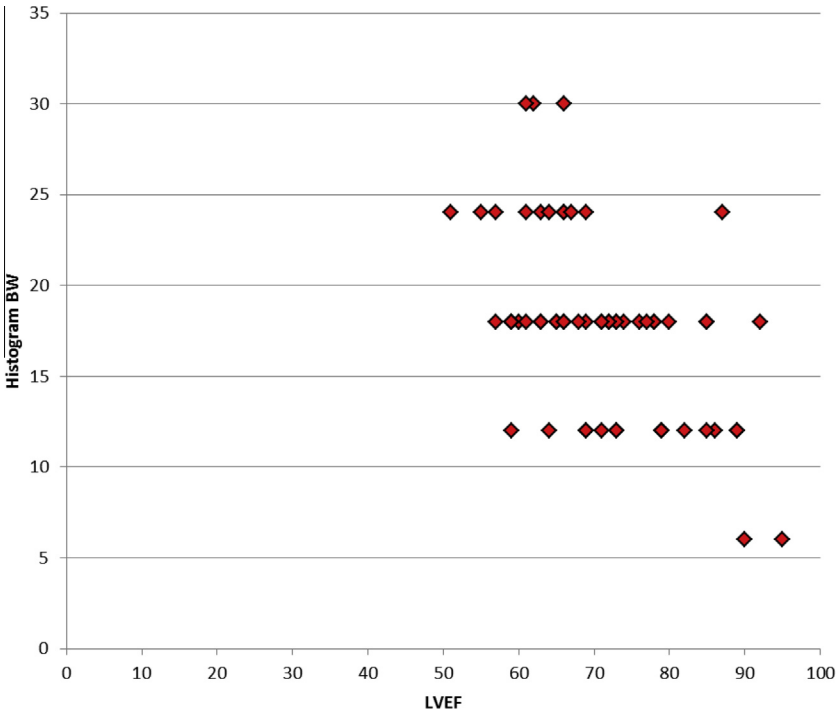

Fig. 3 Correlation between histogram BW and LVEF in controls.

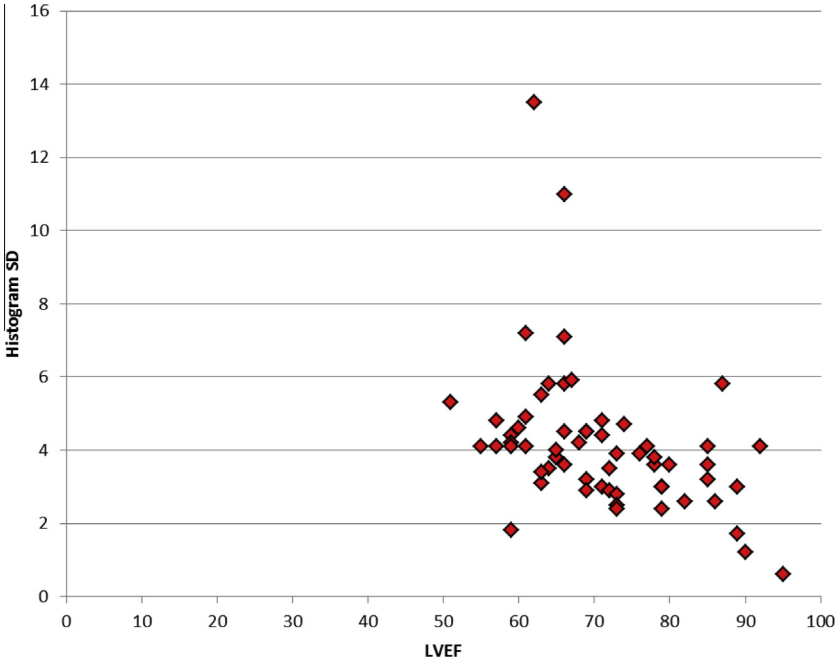

Fig. 4 Correlation between histogram SD and LVEF in controls.

3. Patients and methods

Case control non randomized observational study. All patients signed written consent. The study was approved by the research council in Cairo University.

3.1. Inclusion criteria

Cases: Sixty acute STEMI patients admitted to the critical care department Cairo University were included in our study.

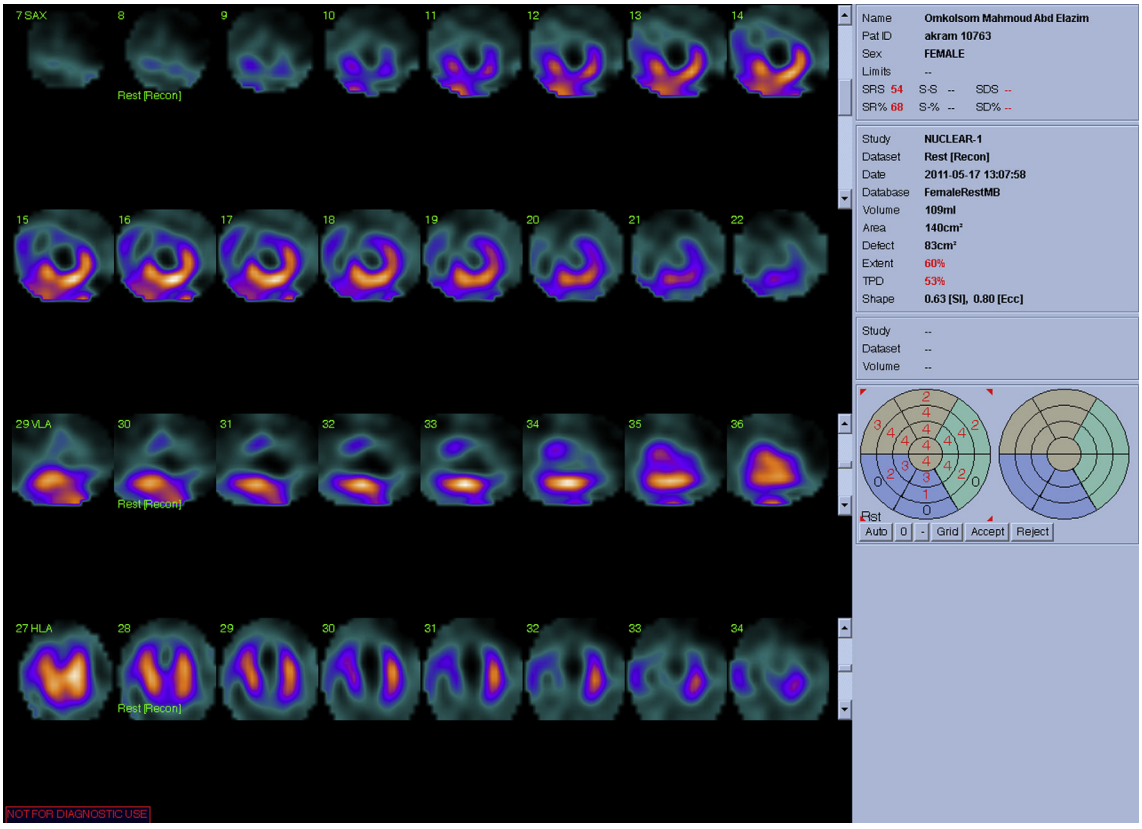

Fig. 5a A case of acute anterior ST elevation myocardial infarction showing large defect involving the left ventricular apex, anteroapical, inferoapical, anteroseptal, anterior and anterobasal segments. The semi quantitative analysis showed the defect size to be 54% of the myocardium and the automated total perfusion defect to be 53% of the myocardium. The gated data are presented in Fig. 5b.

Control group: Sixty control subjects were chosen from the patients referred for diagnostic stress SestaMIBI MPI on elective bases. All controls had normal basic ECG, no history of coronary angiography or CABG, normal LV function and normal stress perfusion scans.

3.2. Exclusion criteria

Controls with abnormal ECG stress test and who developed significant symptoms or apparent structural abnormalities on perfusion scans (e.g. LV hypertrophy or dilatation) were excluded. STEMI Patients with a history or ECG evidence of old myocardial infarction, cardiomyopathy, left bundle branch block, patients who are not eligible for revascularization and refusal of myocardial perfusion imaging were excluded from the study.

STEMI diagnosis was based upon the European Society of Cardiology/ACCF/AHA/World Heart Federation Task Force for the Universal Definition of Myocardial Infarction which includes characteristic symptoms of myocardial ischemia associated with ST segment elevation and subsequent rise in serum biomarkers. New ST elevation at the J point in at least 2 contiguous leads of $\geqslant$2 mm (0.2 mV) in men or $\geqslant$1.5 mm (0.15 mV) in women in leads V2–V3 and/or of $\geqslant$1 mm (0.1 mV) in other contiguous chest leads or the limb leads [12].

All patients were subjected to:

History taking and physical examination, Twelve lead ECG, Cardiac biomarkers including CPK, CK MB and Troponin T. Rest gated Technitium^{99m} SestaMIBI Myocardial perfusion study was performed as follows; Patients were injected intravenously with 25 mCi Technetium SestaMIBI on admission. After being subjected to primary PCI within 90 min from admission, patients were transferred to the nuclear cardiology laboratory integrated in the critical care department and a rest ECG gated single photon emission computed tomography (SPECT) study was acquired. Acquisition of images done in the nuclear cardiology lab which is integrated in the critical care department Cairo University. Images were acquired in our dual head gamma camera (Symbia E, Siemens Medical Solutions USA, Inc., IL,USA) utilizing Cedars Sinai software, USA, 2009 (8 frames per cycle). Images were gated to the R wave of the ECG, and image acquisition was interrupted for one beat if the R–R interval varied by 15% of the preceding R–R interval.

First, Myocardial Perfusion images to calculate the myocardium at risk using the 20 segment scoring system. *Second*, LV functional parameters to derive the LVEDV, LVESV and LVEF. *Third*, Phase images where the expected LV dyssynchrony parameters were used, the latter included the histogram bandwidth, histogram standard deviation and entropy [7].

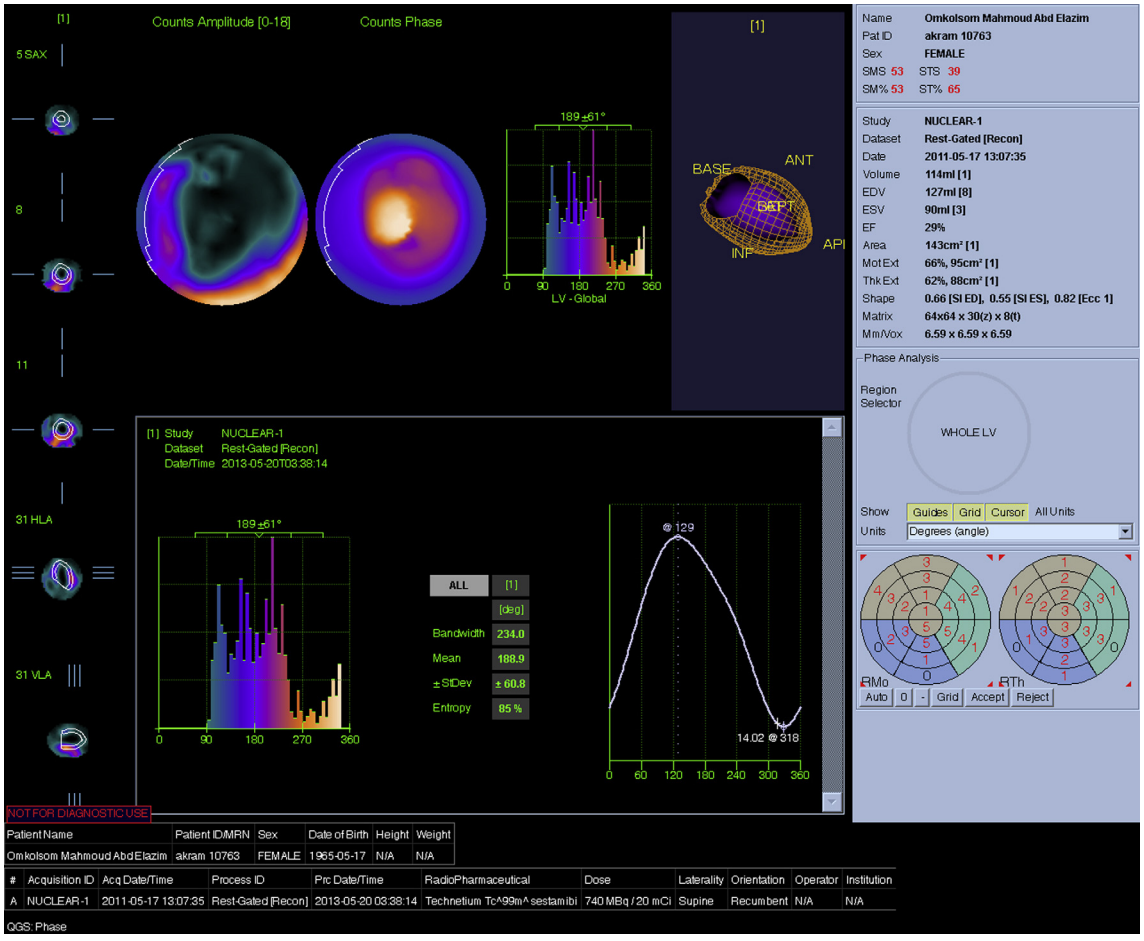

Fig. 5b The gated SPECT study of the patient with anterior ST elevation myocardial infarction presented in Fig. 5a. The left ventricle ejection fraction is significantly affected with left ventricle ejection fraction (LVEF) of 29% and there is evident dispersion in the LV histogram with a bandwidth of 234°, standard deviation of ± 60° and entropy 85%. These values represent significant left ventricular dyssynchrony.

Gated SPECT MPI was obtained at rest with Tc^{99m} Sesta-MIBI according to ESC guidelines [13]. The step and shoot protocol was used, 180_ elliptical orbit with 32 projections. The patient was transferred after the primary percutaneous coronary intervention (PCI) procedure and stabilization within 6 h of trace injection to the nuclear cardiology lab integrated into the critical care department, Cairo University. A dual-head detector Symbia E gamma camera (Siemens) with high resolution, low energy collimator was used. A window of 15% was centered on the 140 keV gamma peak, and the ECG gating was done with 8 frames per R–R cycle.

Butterworth filtering followed by filtered back projection reconstruction performed on a 64×64 matrix. The images were reviewed and interpreted by 2 senior operators blinded to the ECG and PCI data and on separate occasion.

The LV volumes and EF were measured from the rest gated images based on the method described by Germano et al. [14] perfusion defects were interpreted and quantified using the 20 segment scoring system available in the Cedars Sinai QPS package 2009, to get the myocardium at risk for the acquired set of images.

Phase analysis of gated SPECT was done by the following 3 quantitative indexes obtained from the phase analysis of all patients:

1) Histogram bandwidth: includes 95% of the elements of the phase distribution [7].
2) Phase SD: is the SD of the phase distribution [7].
3) Phase Entropy: is considered by some authors as a more appropriate dispersion measure than SD, which is expressed from 0% to 100%. In this modality perfect synchrony would be 0% of entropy being significant from 60% and corresponding to 100%, the theoretical maximum possible dyssynchrony [15].

The gated SPECT acquisition followed the method described by Germano et al. [16]. The criteria for dyssynchrony has been described by Chen et al. [5] and we used the methodology described by Boogers et al. [14] for phase analysis and distribution using the Cedars Sinai QGS software. In brief, three-dimensional count distributions were extracted from each of the LV short-axis data set, submitted to Fourier phase

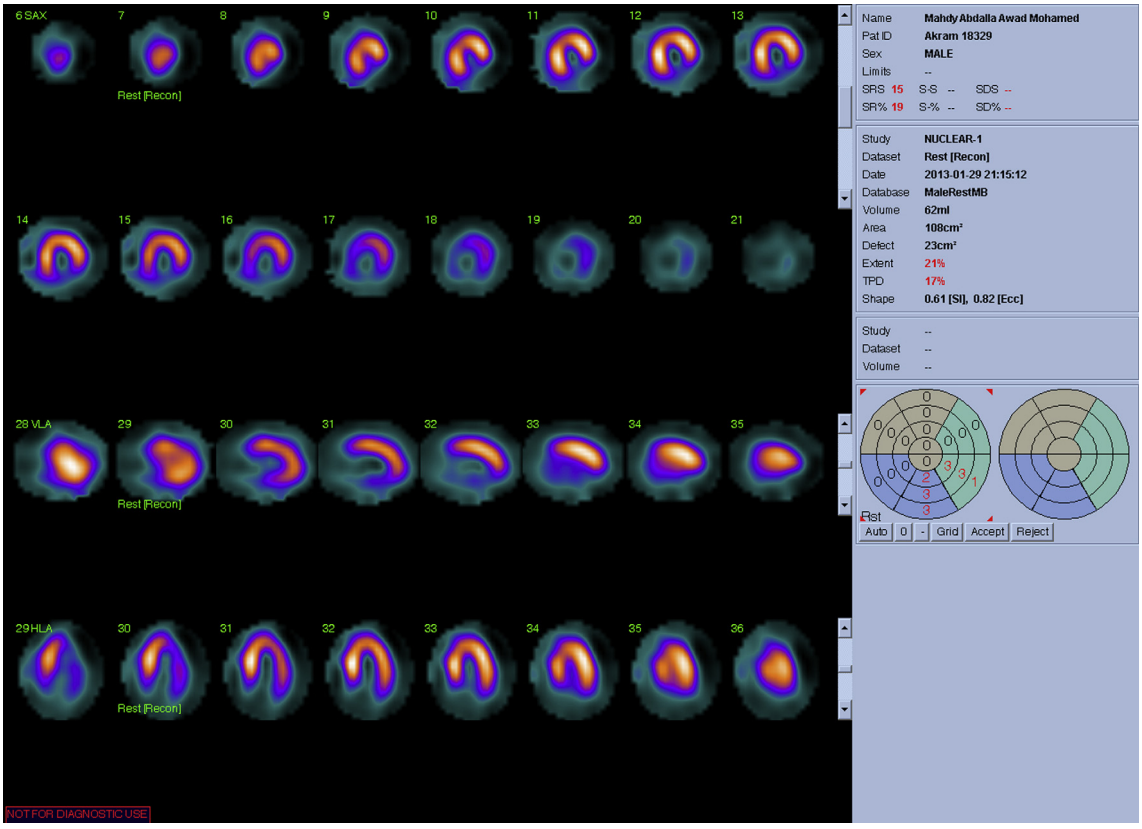

Fig. 6a A patient with acute inferior ST elevation myocardial infarction showing a large defect at the inferior, inferolateral and posterior segments. Semi quantitative analysis showed the defect size to be 15% and automated total perfusion defect to be 17% of the left ventricle mass.

analysis, and that generated a three-dimensional phase distribution (0–360°) over the whole R–R interval and represented on a histogram.

All controls were subjected to:

Two days stress and rest imaging according to imaging guidelines [17,13] using the same acquisition technique and tools described earlier. Patients were exercised according to Bruce protocol to reach age predicted target heart rate. Only patients who reached 100% of the target heart rate were included in the study. All exercised patients were injected intravenously at the peak of exercise with Tc^{99m} SestaMIBI (hexakis-isobutyl-isonitrile) (monrol weight based dose and imaged 30–45 min later. Rest gated SPECT studies were acquired on separate day. Data from rest studies were used in comparisons for the control against the studied group. Only patients with essentially normal perfusion and functional scans were included.

3.3. Statistical methods

Numerical variables were described as mean ± SD. Categorical variables were described as percentages. Comparisons were done using Student "t" test for numerical variables and Chi square test for categorical variables. Correlations were plotted and *r* values (correlation coefficients) were stated. *p* value was considered significant if $\leqslant 0.05$. Statistics were calculated using SPSS 17 package.

4. Results

4.1. Study group demographic data

A total number of 60 patients with acute STEMI were included in our study, including 54 males (90%) and 6 females (10%) with a mean age (54.8 ± 10.38 years) range from 29 to 74 years. Besides 60 controls the mean age (50.7 + 20.3 years) ranges from 26–69 years.

4.1.1. Risk factors for coronary artery disease

Smoking was the most prevalent risk factor for coronary artery disease among our patients (Table 1).

4.2. Electrocardiographic data

Electrocardiograms were analyzed to locate site of acute myocardial infarction. Thirty patients had acute anterior STEMI and 30 had acute inferior STEMI (see Tables 2 and 3).

4.3. Scintigraphic data

4.3.1. Acute myocardial perfusion imaging

Most of patients showed a large area of myocardium at risk with a mean of 43.1 ± 20.5% of the myocardium on semi quantitative analysis.

4.3.2. Gated SPECT data

Acute STEMI cases showed increased LV volumes and impaired mean LVEF with significantly higher values of phase parameters Table 4.

There ranges of different phase parameters values are listed in Tables 5 and 6.

There was a significant reverse correlation between phase parameters values and the LV ejection fraction in the studied patients. Histogram entropy was the most correlated value (Figs. 1 and 2, Table 7).

The reverse correlations between different phase parameters and the LVEF were valid in control cases as well as demonstrated in Figs. 3 and 4, and Table 8.

Table 8 Correlation between histogram Band width, standard deviation and entropy and Left ventricular ejection fraction in Normal (control) cases.

Control		BW^0	SD^0	Entropy
LVEF	*R* value	−0.538	−0.405	−0.562
	p value	< 0.000	< 0.001	< 0.000

5. Discussion

Several imaging tools have been used to study LV dyssynchrony, of them new nuclear cardiology technique that used ECG gated SPECT study phase image had good repeatability, reproducibility and predictive value [14,18–20].

Increased bandwidth, standard deviation and entropy had been studied by several investigators especially in heart failure patients [7,14,21,20,22–24]. These parameters improved after cardiac resynchronization therapy.

We used Tc^{99m} SestaMIBI gated SPECT phase imaging to study the effect of LV dyssynchrony in acute STEMI, this was achieved through injecting the tracer on patient admission and the performing of the image acquisition after primary PCI within the first 6 h in the acute setting and compared these results to healthy controls referred for stress myocardial perfusion imaging. The minimal distribution of technetium from the cardiomyocytes allows imaging within 6 h of injection. The acquired image represents the defect at the time of injection "frozen image" or the myocardium at risk. In addition there is no delay in revascularization procedure (see Fig. 6b).

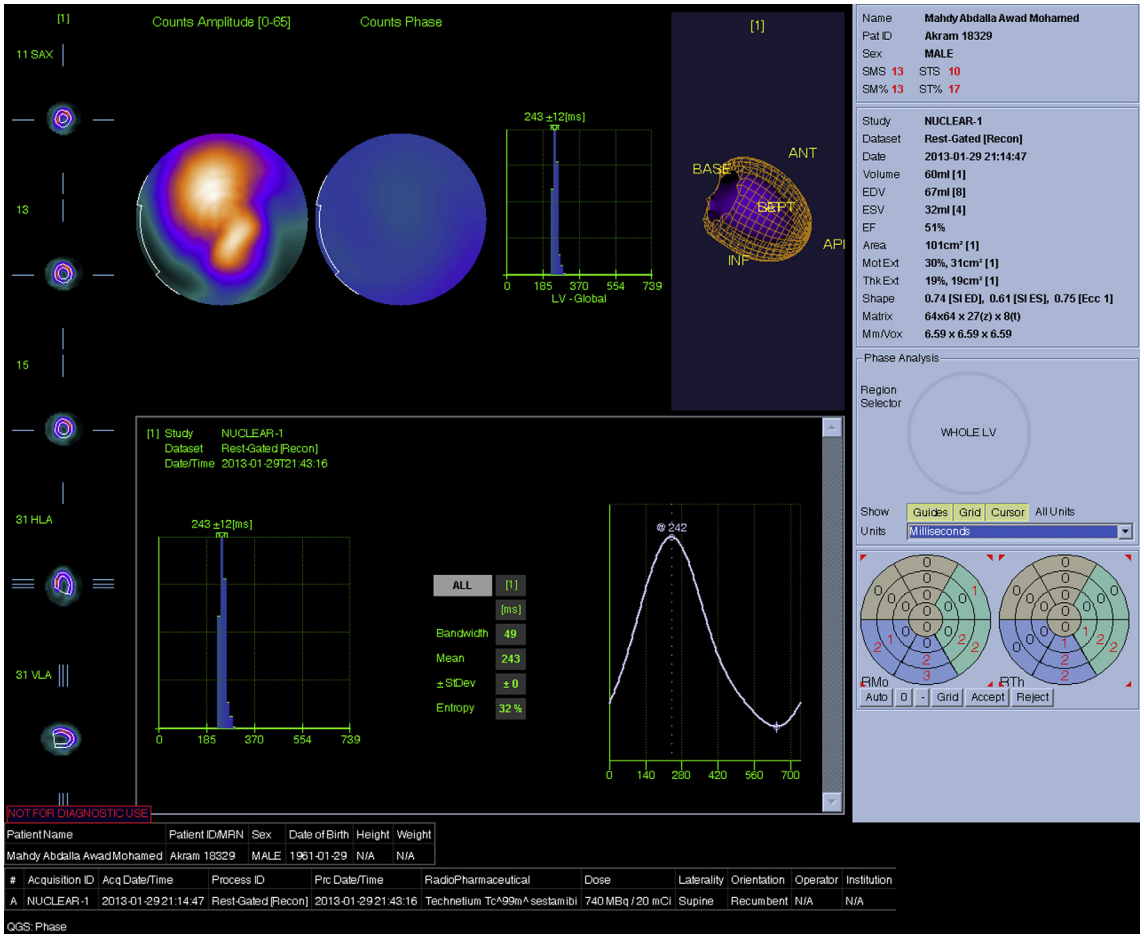

Fig. 6b The gated SPECT study of the patient with inferior ST elevation myocardial infarction presented in Fig. 6a. The left ventricle ejection fraction is preserved with left ventricle ejection fraction (LVEF) of 51% and there is uniformity in the LV histogram distribution with bandwidth of 49°, standard deviation of ±0° and Entropy 32%.These values represent synchronous left ventricular contraction.

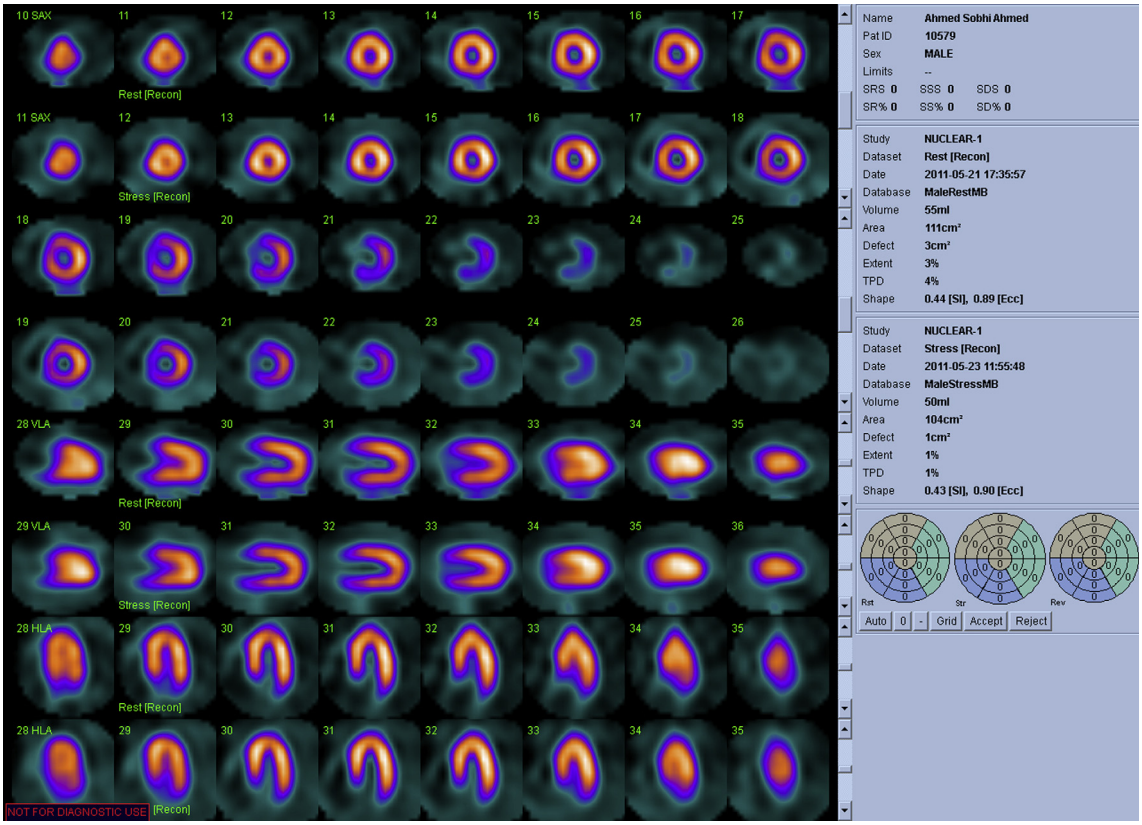

Fig. 7a A stress-rest study from the control group with normal myocardial perfusion.

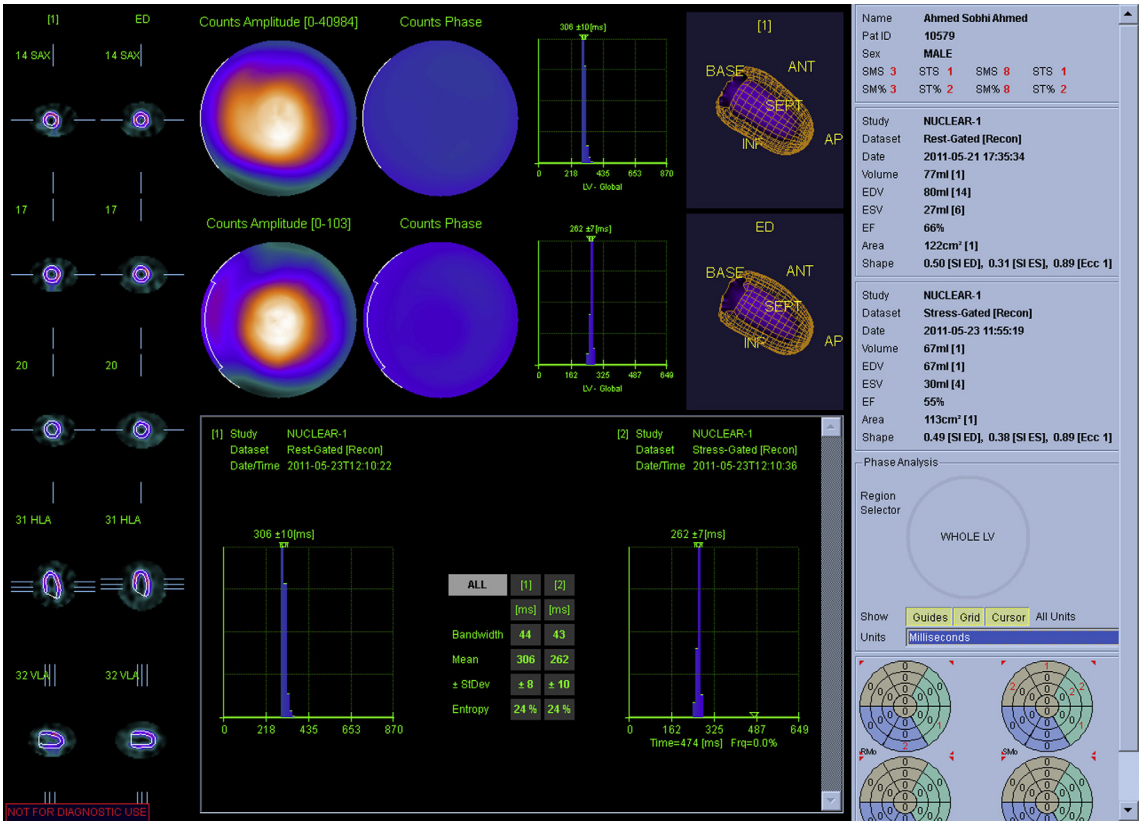

Fig. 7b The gated SPECT study of the control case. The left ventricle ejection fraction is preserved with left ventricle ejection fraction (LVEF) of 55% and there is uniformity in the LV histogram distribution with bandwidth of 44°, standard deviation of ±8° and Entropy of 24%. These values represent synchronous left ventricular contraction.

Several studies on STEMI patients emphasized on the presence of LV dyssynchrony several days after the infarction. Different tools were used including echocardiography and magnetic resonance imaging [4,20,6] however all the imaging studies were performed after the infarction in the first few days which may not reflect the initial actual degree of LV dysfunction (see Figs. 7a and 7b).

The main findings of this study are that LV dyssynchrony occurs during acute STEMI even in the absence of LBBB and its severity is inversely related to LV systolic dysfunction as measured by LVEF. This study does not answer the question of whether the dyssynchrony is the cause or the result of LV dysfunction but it is conceivable that it contributed to the dysfunction. Improvement of LVEF days after acute MI is likely related to relief of stunning and possibly also to improvement of dyssynchrony. Recent studies suggest that dyssynchrony is related to ischemia when assessed by PET imaging [25].

We found in our study a significant increase in bandwidth duration, standard deviation and entropy in cases when compared to controls. In addition there was significant drop in LV systolic function in these patients. LV dysfunction in acute STEMI was demonstrated in a previous study in our center, however the software used at that time couldn't demonstrate the phase imaging parameters mentioned [26,27].

The degree of bandwidth, standard deviation and entropy showed a highly significant reverse correlation with the gated LV ejection fraction which points toward the negative impact of acute LV dyssynchrony on LVEF. Further studies are needed to evaluate the impact of revascularization on this phenomenon.

6. Conclusion

LV dyssynchrony may be acquired acutely very early in STEMI and may have a negative impact on LV ejection fraction.

Conflict of interest

None declared.

References

[1] Krumholz HM, Wang Y, Chen J, Drye EE, Spertus JA, Ross JS, Curtis JP, Nallamothu BK, Lichtman JH, Havranek EP, Masoudi FA, Radford MJ, Han LF, Rapp MT, Straube BM, Normand SL. Reduction in acute myocardial infarction mortality in the United States: risk-standardized mortality rates from 1995–2006. JAMA 2009;302(7):767–73.

[2] Guerchicoff A, Brener SJ, Maehara A, Witzenbichler B, Fahy M, Xu K, Gersh BJ, Mehran R, Gibson CM, Stone GW. Impact of delay to reperfusion on reperfusion success, infarct size, and clinical outcomes in patients with ST-segment elevation myocardial infarction: the INFUSE-AMI Trial (INFUSE-Anterior Myocardial Infarction). JACC Cardiovasc. Interv. 2014;7(7):733–40.

[3] Minicucci MF, Farah E, Fusco DR, Cogni AL, Azevedo PS, Okoshi K, Zanati SG, Matsubara BB, Paiva SA, Zornoff LA. Infarct size as predictor of systolic functional recovery after myocardial infarction. Arq. Bras. Cardiol. 2014;102(6):549–56.

[4] Liem M, Bleeker M, van der Hoeven B, van de Veire N, Boersma E, Holman E, van der Wall E, Schalij M, Gorcsan J, Bax J. Left ventricular dyssynchrony acutely after myocardial infarction predicts left ventricular remodeling. J. Am. Coll. Cardiol. 2007;50:1532–40.

[5] Murrow J, Esteves F, Galt J, Chen J, Garcia E, Lin J, Lerakis S, Sher S, Pohlel F, Waller E, Vaughan D, Perin E, Willerson J, Kereiakes D, Preti R, Pecora A, Quyyumi A. Characterization of mechanical dyssynchrony measured by gated single photon emission computed tomography phase analysis after acute ST-elevation myocardial infarction. J. Nucl. Cardiol. 2011;18:912–9.

[6] Zhang Y, Chan AK, Yu CM, Lam WW, Yip GW, Fung WH, So NM, Wang M, Sanderson JE. Left ventricular systolic asynchrony after acute myocardial infarction in patients with narrow QRS complexes. Am. Heart J. 2005;149(3):497–503.

[7] Chen J, Garcia EV, Russell D, Folks BS, Cooke D, Faber L, Lindsey T, Iskandrian A. Onset of left ventricular mechanical contraction as determined by phase analysis of ECG-gated myocardial perfusion SPECT imaging: development of a diagnostic tool for assessment of cardiac mechanical dyssynchrony. J. Nucl. Cardiol. 2005;12:687–95.

[8] Gibbons RJ, Verani MS, Behrenbeck T, Pellika PA, O'Connor JJ, Mahmarian JJ, et al. Feasibility of tomographic 99mTc hexakis 2-methoxy 2-methylpropyl isonitrile imaging for the assessment of myocardial area at risk and the effect of treatment in acute myocardial infarction. Circulation 1989;80:1277–86.

[9] Abdelbary A, Sami W, Tayeh O, Hussien A, Hamed L, Allam A, et al. Acute myocardial perfusion imaging (MPI) – a useful tool for evaluation of therapeutic modalities & a predictor of urgent need for revascularization in acute coronary syndromes (ACS). Egypt. Heart J. 2012;64:165–70.

[10] Abdelbary A, AbdelAal A, Battah A, et al. Thrombolysis or acute PCI in STEMI. A dilemma solved by acute myocardial perfusion imaging. Egypt. Heart J. 2009;61:40–3.

[11] Abdelbary A, AbdelAal A, Abdelfattah A, et al. Can successful mechanical reperfusion achieve comparable myocardial salvage to successful thrombolysis in acute STEMI? A question answered by acute myocardial perfusion Tc99m SestaMIBI imaging. Acute Cardiac Care 2008;10(3):162.

[12] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HDJoint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Katus HA, Lindahl B, Morrow DA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasché P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S. Third universal definition of myocardial infarction. Circulation 2012;126(16):2020–35.

[13] Hesse B, Lindhardt TB, Acampa W, Anagnostopoulos C, Ballinger J, Bax JJ, Edenbrandt L, Flotats A, Germano G, Stopar TG, Franken P, Kelion A, Kjaer A, Le Guludec D, Ljungberg M, Maenhout AF, Marcassa C, Marving J, McKiddie F, Schaefer WM, Stegger L, Underwood R. EANM/ESC guidelines for radionuclide imaging of cardiac function. Eur. J. Nucl. Med. Mol. Imag. 2008;35(4):851–85.

[14] Boogers M, Van Kriekinge S, Henneman M, Ypenburg C, Van Bommel R, Boersma E, Schneider P, Stokkel M, Schalij M, Berman D, Germano G, Bax J. Quantitative gated SPECT–derived phase analysis on gated myocardial perfusion SPECT detects left ventricular dyssynchrony and predicts response to cardiac resynchronization therapy. J. Nucl. Med. 2009;50:718–25.

[15] Ferreiraa M, Silvab R, Cabanelasc N, Cunhab M, Ramosc D, Albuquerqueb A, Teixeirac R, Moreirab A, Costab G, Limab J,

Providênciac L. Left ventricular mechanical dyssynchrony in patients with impaired left ventricular function undergoing gated SPECT myocardial perfusion imaging. Rev. Port. Cardiol. 2013;32(5):387–94.

[16] Germano G, Kiat H, Kavanagh P, Moniel M, Mazzanti M, Su H, Van Train K, Berman D. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. J. Nucl. Med. 1995;36:2138–47.

[17] Hesse B, Tägil K, Cuocolo A, Anagnostopoulos C, Bardiés M, Bax J, Bengel F, Busemann Sokole E, Davies G, Dondi M, Edenbrandt L, Franken P, Kjaer A, Knuuti J, Lassmann M, Ljungberg M, Marcassa C, Marie PY, McKiddie F, O'Connor M, Prvulovich E, Underwood R, van Eck-Smit BEANM/ESC Group. EANM/ESC procedural guidelines for myocardial perfusion imaging in nuclear cardiology. Eur. J. Nucl. Med. Mol. Imag. 2005;32(7):855–97.

[18] Wassenaar R, O'Connor D, Dej B, Ruddy T, Birnie D. Optimization and validation of radionuclide angiography phase analysis parameters for quantification of mechanical dyssynchrony. J. Nucl. Cardiol. 2009;16:895–903.

[19] Lin X, Xu H, Zhao X, Folks RD, Garcia E, Soman S, Chen J. Repeatability of left ventricular dyssynchrony and function parameters in serial gated myocardial perfusion SPECT studies. J. Nucl. Cardiol. 2010;17:811–6.

[20] Samad Z, Atchley A, Trimble M, Sun J, Shaw L, Pagnanelli R, Chen J, Garcia E, Iskandrian A, Velazquez E, Borges-Neto S. Prevalence and predictors of mechanical dyssynchrony as defined by phase analysis in patients with left ventricular dysfunction undergoing gated SPECT myocardial perfusion imaging. J. Nucl. Cardiol. 2011;18:24–30.

[21] Chen J, Henneman M, Trimble M, Bax J, Borges-Neto J, Iskandrian A, Nichols K, Garcia E. Assessment of left ventricular mechanical dyssynchrony by phase analysis of ECG-gated SPECT myocardial perfusion imaging. J. Nucl. Cardiol. 2008;15:127–36.

[22] Chen J, Garcia E, Bax J, Iskandrian A, Borges-Neto S, Soman P. SPECT myocardial perfusion imaging for the assessment of left ventricular mechanical dyssynchrony. J. Nucl. Cardiol. 2011;18:685–94.

[23] Lucas Gutiérrez, Fernand A Peñafort, Italo B Seretti, Raúl E. New diagnostic tools in heart failure: gated-spect phase analysis for left ventricular dyssynchrony assessment. Ortego. Rev. Fed. Arg. Cardiol. 2013.

[24] Trimble M, Borges-Neto S, Honeycutt E, Shaw L, Pagnanelli R, Chen J, Iskandrian A, Garcia E, Velazquez E. Evaluation of mechanical dyssynchrony and myocardial perfusion using phase analysis of gated SPECT imaging in patients with left ventricular dysfunction. J. Nucl. Cardiol. 2008;15:663–70.

[25] Van Tosh A, Votaw JR, Cooke CD, Reichek N, Palestro CJ, Nichols KJ. Relationships between left ventricular asynchrony and myocardial blood flow. J. Nucl. Cardiol. 2015.

[26] Abdelbary A, Kamal HS, El-Aassar H, El-Naggar A, Abdelfattah A. Improvement in left ventricular functional parameters before and after primary PCI in acute STEMI and its relation to angiographic parameters: gated single photon emission computed tomography (GSPECT) study. JNC 2009;16(4):669.

[27] Kamal HS, Abdelfattah A, Abdelbary A, Al-Aassar H, El-Naggar A. Assessment of left ventricular stunning and its relation to myocardial perfusion before and after primary PCI. A gated SPECT myocardial perfusion study. Acute Cardiac Care 2010;12 (Suppl. 12) (abs).