Iranian Heart Journal; 2019; 20 (2)

Original Article

Impact of Hypertension on the Phase Analysis Parameters of Gated Single-Photon Emission Computed Tomography Myocardial Perfusion Imaging

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ABSTRACT

Background: We sought to evaluate the association between hypertension (HTN) and left ventricular (LV) mechanical synchrony parameters derived via the phase analysis of gated single-photon emission computed tomography (GSPECT) myocardial perfusion imaging (MPI).

Methods: Ninety-nine patients with no known coronary heart disease (CHD) who underwent GSPECT MPI and had normal resting and post-stress scan with a recent normal echocardiographic examination and a positive history of HTN were recruited. The gated images were analyzed by Cedar–Sinai's quantitative GSPECT. The global and regional LV mechanical synchrony indices—including phase histogram bandwidth (PHB), phase standard deviation (PSD), and entropy—were derived and compared with the results of the control group, which had previously been defined with the same protocol for a group of 100 patients with a low likelihood for CHD.

Results: Comparisons between the study and control groups revealed that neither global nor regional wall-based indices for PHB, PSD, and entropy were significantly different between the 2 groups ($P > 0.05$), whether or not HTN was accompanied by comorbid diabetes. Congruent with the control group, a significant difference was detected between the global LV phase parameters of the 2 genders ($P<0.05$).

Conclusions: HTN does not intrinsically have a significant impact on the mechanical synchrony indices of GSPECT MPI. ***(Iranian Heart Journal 2019; 20(2): 47-55)***

KEYWORDS: Hypertension, SPECT, MPI, Left ventricular dyssynchrony, Phase analysis

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Received: August 26, 2018 **Accepted:** October 18, 2018

Coronary heart disease (CHD) has long been established as a leading cause of morbidity and mortality among adults,[1] and the crucial role of the conventional risk factors in the development of this disease of paramount importance has well been appreciated.[2] Hypertension (HTN) is one of the major independent risk factors, which apart from association with obstructive coronary artery disease could impose significant adverse

effects on the cardiac structure as increased left ventricular (LV) wall thickness and mass, leading to LV hypertrophy and the deterioration of diastolic and systolic functions.[3] On the other hand, some common chronic conditions such as impaired fasting glucose have been estimated to be more prevalent in adults with than in those without HTN.[4] Of note, diabetes mellitus (DM), as a common comorbidity of HTN (and CHD), could itself impose the same adverse effect on the cardiac structure and function.[5]

Gated single-photon emission computed tomography (GSPECT) myocardial perfusion imaging (MPI) is a well-established imaging method for the evaluation of myocardial ischemia as well as for the assessment of other relevant clinical issues in patients with CHD including response to treatment, risk stratification, and myocardial viability.[6] More recently, the application of the evolving technique of LV phase analysis to GSPECT MPI has made it easily applicable to evaluate global and regional LV mechanical dyssynchrony simultaneously with the assessment of the LV myocardial perfusion and function[6, 7] by using different types of automated software algorithms.[7, 8] In addition, compared with other imaging modalities for the assessment of LV mechanical dyssynchrony, the main advantages of the phase analysis of GSPECT MPI are widespread availability, simplicity, repeatability, high reproducibility, and automated quantification.[6, 9-12]

A growing body of literature has investigated different factors which could probably exert an influence on the distribution of the LV phase indices—including the heart rate,[13] the injected dose of the radiotracer, [8] the type of image reconstruction,[14] the acquisition orbit,[15] and the presence or absence of perfusion defects in MPI. [9] Accordingly, the present study was undertaken to determine whether HTN as a common comorbidity in CHD [2] has any appreciable independent impact on the global and regional parameters of phase analysis by comparing the results with those of patients categorized as low risk for CHD.

To the best of our knowledge, this article is the first study to specifically evaluate the impact of HTN on the phase analysis indices of GSPECT MPI.

METHODS

Patients and Study Protocol

A group of consecutive patients with no known CHD who had been referred to our department on the basis of the cardiologists' clinical judgment underwent MPI. The study inclusion criteria were coexistence of a positive history of HTN in the presence of normal resting and post-stress MPI in addition to a recent (within 2 months) normal echocardiography indices including a normal global left ventricular ejection fraction (LVEF≥ 50%)[16] in particular and without any appreciable evidence of wall motion abnormality or valvular heart disease. A normal MPI was defined as the absence of any significant perfusion defect read by an expert nuclear medicine specialist in agreement with a summed stress score <4 and the absence of an elevated lung-to-heart uptake ratio (LHR>0.4) or transient LV dilation (>1.1 for the exercise test and >1.15 for the dipyridamole stress test). A normal gated functional study was described as a global LVEF≥50% with a summed motion score and a summed thickening score of zero.[17] Ultimately, a total of 99 subjects met the criteria.

A positive history of HTN as well as DM was defined on the basis of the patients' medical records and documents; all the patients were under medical treatment and reasonably controlled.

The control group was composed of 100 subjects with a low pretest likelihood for CHD who had previously been evaluated for the determination of the normal ranges of global and regional phase indices provided by Malek et al.[17]

Image Acquisition and Processing

Gated SPECT MPI was acquired according to the predefined 2-day stress (exercise or pharmacological with dipyridamole)/ rest protocol using 10–15 mCi of Tc99m-sestamibi in each phase of the study.[18] Imaging was started 15–20 minutes following exercise and 45–60 minutes after resting injections or pharmacological stress tests. The acquisition was performed in the supine position using a dual-headed SPECT-CT camera (Symbia T2, Siemens Medical Systems) with low-energy high-resolution collimators, a window of 20% around the 140-keV Tc99m photopeak, step and shoot mode, 180° right anterior oblique to left posterior oblique arc, noncircular body-contoured orbit with 64 projections, 25 seconds per projection, 16 frames per ECG R-R cycle, and fixed temporal resolution forward-backward gating mode using a fixed acceptance window of 30%. The data were stored in a 64 × 64 matrix.

All the images were initially reviewed for quality assurance and the exclusion of those distorted by any kind of interfering factors including extracardiac or excessive sub-diaphragmatic radiotracer activity and motion artifacts.[19-21] Then reconstruction was done by filtered back projection using Butterworth filtering (cutoff: 0.4, order: 5), followed by data processing with the commercially available Cedar-Sinai's quantitative gated SPECT (QGS) software to derive LV phase indices—including phase histogram bandwidth (PHB) (the width of histogram which includes 95% of the elements in the phase distribution), phase standard deviation (PSD) (standard deviation of the phase distribution), and entropy (defined by summation of $[f_i*\log(f_i)]/\mathrm{Log}(n)]$, in which f and n are representing frequency in the i^{th} bin and number of bins, respectively) based on the 2 modes of global whole LV and regional wall-based model, composed of 5 main ventricular walls: apex, septum, anterior, inferior, and lateral walls.[7,17,22]

Statistical Analysis

The fitness of the interval data to a normal distribution was assessed using the one-sample Kolmogorov–Smirnov test.

The data were described as mean ± standard deviation (SD) for the interval variables and count (%) for the categorical variables. Comparisons of the measured indices between the study groups were performed via the independent *t*-test (for 2 groups) and one-way analysis of variance (ANOVA), followed by the Bonferroni post-hoc test (for 3 groups).

A *P* value≤ 0.05 was considered to be statistically significant. The statistical analyses were conducted with IBM SPSS Statistics 22 for Windows (IBM Inc, Armonk, NY).

RESULTS

Patients

Of the total 99 patients who were enrolled in the study from October 2017 to March 2018, 66 (66.6%) were male. The patients were divided into 2 groups, consisting of patients suffering from only HTN (66.7%) and those with a positive history of HTN in conjunction with DM (33.3%). The mean duration of HTN was 6.1±6.4 years; all the patients were under medical treatment and controlled.

The demographic and baseline GSPECT data of the whole study group as well as those of the control group are summarized in Table 1.

The LV phase indices (PHB, PSD, and entropy) were derived based on global whole ventricle and regional wall-based synchrony at resting and post-stress conditions.

Global Parameters

As is presented in the tables, the derived values for PHB, PSD, and entropy in neither of the patient groups were significantly different from those in the control group, neither at rest (Table 2) nor at the post-stress phase (*P*>0.05) (Table 3).

Regional Parameters

In the same manner, the regional wall-based synchrony parameters disclosed no significant

difference in PHB, PSD, and entropy between the 2 groups of patients and the control group in either of the rest or post-stress phase (Table 4 and Table 5, respectively).

Sex Differences

In agreement with the control group, all of the 3 calculated synchrony parameters were significantly different between the 2 genders of the whole study group (Table 6).

Stress Test

As is shown in Table 7, a comparison of the 2 types of the stress test revealed no statistically significant difference between any of the synchrony indices.

Table 1. Demographic and baseline GSPECT data of the study population and the control group

Demographic and LV Function Parameters	Patients LLK (N=100)	Patients With HTN+/-DM (N=99)
Male	56(56%)	49(49.5%)
BW (kg)	83.32±17.00	79.21±14.31
Height (cm)	167.15±9.29	164.51±11.03
BMI (Kg/m^2)	29.74±5.2	29.06±4.15
Age (y)	48.47±9.76	59.84±8.93
EDV (mL)	66.3±18.9	65.24±18.49
ESV (mL)	20.5±15.4	16.59±10.04
LVEF	0.74±0.87	0.76±0.09
Exercise stress	19(19%)	49(49.5%)

BW, Body weight; BMI, Body mass index; EDV, End-diastolic volume; ESV, End-systolic volume; LVEF, Left ventricular ejection fraction

Table 2. Comparison of the global whole LV synchrony phase parameters at resting state between the control and the 2 study groups

Global Whole LV Phase Parameters (Rest)	Control Group (N=100)	HTN (N=66)	Patients With DM & HTN (N=33)	*P* value
PHB	29.12±10.40	27.91±10.65	26.55±9.25	.434
PSD	7.07±3.17	6.68±2.78	6.42±2.85	.497
Entropy	0.33±0.75	0.32±0.08	0.32±0.08	.722

Data are presented as mean ± standard deviation, PHB and PSD in degrees, and entropy in percentages. LV, Left ventricle; PHB, Phase histogram bandwidth; PSD, Phase standard deviation

Table 3. Comparison of the global whole LV synchrony phase parameters at the post-stress phase between the control and the 2 study groups

Global Whole LV Phase Parameters (Stress)	Control Group (N=100)	HTN (N=66)	Patients With DM & HTN (N=33)	*P* value
PHB	24.54±9.14	24.36±8.47	25.45±8.62	.837
PSD	5.78±2.55	5.84±2.20	6.19±2.50	.697
Entropy	.29±.07	.29±.080	.31±.07	.598

Data are presented as mean ± standard deviation, PHB and PSD in degrees, and entropy in percentages. LV, Left ventricle; PHB, Phase histogram bandwidth; PSD, Phase standard deviation

Table 4. Comparison of regional wall-based LV synchrony phase parameters at resting state between the control and the 2 study groups

Regional Wall-Based Phase Parameters (Rest)		Control Group (N=100)	Patients With HTN (N=66)	Patients With DM & HTN (N=33)	*P* value
Apex	PHB	13.14±4.06	12.00±4.07	13.27±4.68	.176
	PSD	2.65±1.13	2.41±1.26	2.70±1.41	.403
	Entropy	0.14±0.07	0.13±0.07	0.14±0.08	.353
Lateral	PHB	25.80±12.43	24.27±12.06	21.45±7.35	.174
	PSD	7.09±5.08	6.01±3.38	5.24±2.41	.060
	Entropy	0.29±0.10	0.28±0.08	0.26±0.08	.157
Inferior	PHB	23.27±9.60	24.09±9.26	22.36±8.25	.672
	PSD	5.84±3.28	5.78±2.80	5.36±2.33	.721
	Entropy	0.27±0.91	0.28±0.09	0.27±0.08	.747
Septum	PHB	22.5±11.06	21.00±11.73	20.72±17.35	.594
	PSD	5.64±3.44	5.16±3.35	4.78±2.56	.371
	Entropy	0.26±0.09	0.24±0.12	0.24±0.10	.317
Anterior	PHB	25.22±10.28	23.90±10.33	23.09±14.70	.571
	PSD	6.29±3.23	5.68±2.79	5.84±4.89	.505
	Entropy	0.29±0.10	0.28±0.10	0.26±0.08	.328

Data are presented as mean ± standard deviation, PHB and PSD in degrees, and entropy in percentages.
LV, Left ventricle; PHB, Phase histogram bandwidth; PSD, Phase standard deviation

Table 5. Comparison of regional wall-based LV synchrony phase parameters at the post-stress phase between the control and the 2 study groups

Regional Wall-Based Phase Parameters (Stress)		Control Group	Patients With HTN (N=66)	Patients With DM &/or HTN	*P* value
Apex	PHB	11.28±3.93	11.09±3.68	10.54±3.01	.616
	PSD	2.04±1.22	2.08±1.31	1.91±1.06	.806
	Entropy	0.10±0.07	0.11±0.07	0.09±0.06	.681
Lateral	PHB	22.74±12.15	22.09±10.53	22.54±9.00	.935
	PSD	5.63±3.64	5.39±3.10	5.71±2.85	.871
	Entropy	0.26±0.09	0.26±0.09	0.27±0.07	.905
Inferior	PHB	19.88±10.59	20.72±8.69	22.72±9.80	.358
	PSD	4.75±3.06	4.83±2.43	5.67±3.21	.273
	Entropy	0.24±0.08	0.24±0.08	0.27±0.10	.225
Septum	PHB	18.24±7.76	19.27±9.14	20.36±10.81	.452
	PSD	4.23±2.39	4.81±2.84	4.84±2.96	.293
	Entropy	0.22±0.08	0.23±0.09	0.23±0.11	.539
Anterior	PHB	20.88±7.83	20.81±7.45	19.63±5.25	.684
	PSD	5.00±2.35	5.02±2.16	4.70±1.48	.761
	Entropy	0.25±0.08	0.25±0.08	0.25±0.07	.969

Data are presented as mean ± standard deviation, PHB and PSD in degrees, and entropy in percentages.
LV, Left ventricle; PHB, Phase histogram bandwidth; PSD, Phase standard deviation

Table 6. Gender-specific global synchrony parameters in the whole study population

Global Whole LV Phase Parameters(Rest)	Female (N=50)	Male (N=49)	*P* value
PHB	24.96±9.26	30.00±10.53	0.013
PSD	5.88±2.43	7.33±2.97	0.010
Entropy	0.30±0.07	0.34±0.08	0.009

Data are presented as mean ± standard deviation, PHB and PSD in degrees, and entropy in percentages.
LV, Left ventricle; PHB, Phase histogram bandwidth; PSD, Phase standard deviation

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Table 7. Comparison of the global LV synchrony parameters at the post-stress phase between the exercise and pharmacological tests

Global Whole LV Phase Parameters		Pharmacologic Stress Test (N=50)	Exercise Test (N=49)	*P* value
PHB	Stress	23.88±7.42	25.59±9.46	0.319
	Rest	26.40±9.99	28.53±10.35	0.300
PSD	Stress	5.77±2.01	6.15±2.56	0.403
	Rest	6.16±2.66	7.04±2.87	0.119
Entropy	Stress	0.30±0.07	0.30±0.08	0.956
	Rest	0.31±0.08	0.34±0.07	0.072

Data are presented as mean ± standard deviation, PHB and PSD in degrees, and entropy in percentages.
LV, Left ventricle; PHB, Phase histogram bandwidth; PSD, Phase standard deviation

DISCUSSION

To the best of our knowledge, this article is the first study to specifically evaluate the impact of HTN on the phase analysis indices (PBH, PSD, and entropy) of GSPECT MPI. Compared with the control group, composed of subjects categorized as a low pretest likelihood for CHD with normal ECG, normal LVEF, and negative MPI,[17] we found no significant differences between the mechanical synchrony parameters in the study group, composed of patients suffering from HTN alone or HTN and DM together.

Gated SPECT MPI, which is widely used for the evaluation of CHD, is a validated accurate method to assess mechanical dyssynchrony in conjunction with the assessment of myocardial perfusion and the LV function in a single study.[23] A considerable body of literature has addressed the influence of various technical issues on the relationship between certain preclinical states and the phase analysis parameters of GSPECT MPI. Among the technical factors, the method of image reconstruction and the type of camera represented no influence on the calculated parameters, while the total accumulated count or noise has shown significant effects on the indices in question.[23,24] On the other hand, investigations on the administered dose of the radiotracer on the phase analysis results are still controversial.[8,9] In terms of the patients' demographic data and clinical status, gender as well as the post-stress and resting state of the patients during image acquisition has shown a significant impact on the phase analysis indices; whereas, age and the pattern of perfusion abnormality have demonstrated no influence on mechanical dyssynchrony parameters.[9,23]

HTN, as a major conventional risk factor and a common comorbidity of CHD, is well known for its adverse effects not only on coronary arteries and myocardial perfusion but also on the cardiac structure and function, which may lead to LV hypertrophy and heart failure.[3,5] It may also induce subendocardial ischemia[25,26] and could be hypothesized as a potentially influential factor on LV mechanical dyssynchrony and on the indices derived by GSPECT MPI.[9] In addition, DM has been introduced as a common comorbidity for either CHD or HTN with similar adverse effects on the cardiac structure, perfusion, and function [5] with the same potential impact on LV mechanical dyssynchrony.

Precedent for our study, Hämäläinen et al [27] reported a normal range of phase analysis parameters in a group of subjects wherein hypertensive patients without any history of cardiovascular problems were enrolled and then subanalyzed. In terms of LV phase analysis indices, no statistically significant difference was noted between the subjects without and the patients with risk factors in their subanalysis.

In keeping with this observation, Samad et al[28] provided information about dyssynchrony in patients with LV dysfunction in which patients with a positive history of DM and HTN were analyzed as subgroups. The study revealed an association between HTN and an increase in PSD by a univariant model, even though it was not confirmed by a multivariant analysis. DM, nevertheless, manifested no appreciable influence on the phase analysis parameters in comparison with those of the others without this comorbid condition. Guillermo et al [22] also found no significant association in their pilot study subanalysis between cardiovascular risk factors and LV phase indices.

We provided data which might rule out the association between HTN and mechanical dyssynchrony. Our study also confirmed that the LV phase parameters are significantly influenced by gender. It could also be stated that the different methods of the stress test (ie, exercise and dipyridamole tests) do not have a significant impact on the phase indices derived from GSPECT MPI, which was in contrast with the results of the control group.

Limitations

The present study has all the same limitations of a single tertiary center study with a limited number of patients. Our study should be considered a hypothesis-generating study. We did not classify the hypertensive patients based on the duration or severity of their disease or the type of medical treatment; as a result, a larger study population of patients suffering from HTN having different degrees of adverse impact on the cardiac structure and function might be needed to confirm the results.

Moreover, for ethical reasons, the control group was not recruited from normal volunteer subjects.

New Knowledge Gained

There seems to be no direct association between HTN and LV mechanical synchrony.

CONCLUSIONS

HTN does not intrinsically have a significant impact on the mechanical synchrony indices of GSPECT MPI. It could be concluded that in the presence of this cardinal risk factor, whether or not accompanied by DM, the phase analysis data of the patients with or suspected of CHD could independently be interpreted as the direct effect of the coronary epicardial disease not influenced by this comorbid state.

Conflict of Interest: None.

REFERENCES

1. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998;97(18):1837-47.
2. Khot UN, Khot MB, Bajzer CT, Sapp SK, Ohman EM, Brener SJ, et al. Prevalence of conventional risk factors in patients with coronary heart disease. Jama. 2003;290(7):898-904.
3. Santos M, Shah AM. Alterations in cardiac structure and function in hypertension. Current hypertension reports. 2014;16(5):428.
4. Noh J, Kim HC, Shin A, Yeom H, Jang S-Y, Lee JH, et al. Prevalence of Comorbidity among People with Hypertension: The Korea National Health and Nutrition Examination Survey 2007-2013. Korean circulation journal. 2016;46(5):672-80.
5. Devereux RB, Roman MJ, Paranicas M, O'grady MJ, Lee ET, Welty TK, et al. Impact of diabetes on cardiac structure and function: the strong heart study. Circulation. 2000;101(19):2271-6.
6. Chen J, Garcia EV, Bax JJ, Iskandrian AE, Borges-Neto S, Soman P. SPECT myocardial perfusion imaging for the assessment of left ventricular mechanical dyssynchrony. Journal of Nuclear Cardiology. 2011;18(4):685-94.

7. Van Kriekinge SD, Nishina H, Ohba M, Berman DS, Germano G. Automatic global and regional phase analysis from gated myocardial perfusion SPECT imaging: application to the characterization of ventricular contraction in patients with left bundle branch block. The Journal of Nuclear Medicine. 2008;49(11):1790.

8. AlJaroudi W, Jaber WA, Cerqueira MD. Effect of tracer dose on left ventricular mechanical dyssynchrony indices by phase analysis of gated single photon emission computed tomography myocardial perfusion imaging. Journal of Nuclear Cardiology. 2012;19(1):63-72.

9. AlJaroudi W, Koneru J, Heo J, Iskandrian AE. Impact of ischemia on left ventricular dyssynchrony by phase analysis of gated single photon emission computed tomography myocardial perfusion imaging. Journal of Nuclear Cardiology. 2011;18(1):36-42.

10. Trimble MA, Velazquez EJ, Adams GL, Honeycutt EF, Pagnanelli RA, Barnhart HX, et al. Repeatability and reproducibility of phase analysis of gated single-photon emission computed tomography myocardial perfusion imaging used to quantify cardiac dyssynchrony. Nuclear medicine communications. 2008;29(4):374.

11. Lin X, Xu H, Zhao X, Folks RD, Garcia EV, Soman P, et al. Repeatability of left ventricular dyssynchrony and function parameters in serial gated myocardial perfusion SPECT studies. Journal of nuclear cardiology. 2010;17(5):811-6.

12. Yaghoobi N, Malek H. The age of reason for gated SPECT MPI to deal with cardiac dyssynchrony. Research in cardiovascular medicine. 2015;4(1).

13. Al-Jaroudi W, Iqbal F, Heo J, Iskandrian AE. Relation between heart rate and left ventricular mechanical dyssynchrony in patients with end-stage renal disease. American Journal of Cardiology. 2011;107(8):1235-40.

14. Li D, Zhou Y, Feng J, Yuan D, Cao K, Garcia EV, et al. Impact of image reconstruction on phase analysis of ECG-gated myocardial perfusion SPECT studies. Nuclear medicine communications. 2009;30(9):700.

15. Misaka T, Hosono M, Kudo T, Ito T, Syomura T, Uemura M, et al. Influence of acquisition orbit on phase analysis of gated single photon emission computed tomography myocardial perfusion imaging for assessment of left ventricular mechanical dyssynchrony. Annals of nuclear medicine. 2017;31(3):235-44.

16. Vasan RS, Larson MG, Benjamin EJ, Evans JC, Reiss CK, Levy D. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population-based cohort. Journal of the American College of Cardiology. 1999;33(7):1948-55.

17. Malek H, Rayegan F, Firoozabadi H, Rastgoo F, Haghjoo M, Bakhshandeh H, et al. Determination of normal ranges of regional and global phase parameters using gated myocardial perfusion imaging with Cedars-Sinai's QGS software. Iranian Journal of Nuclear Medicine. 2018;26(1):16-21.

18. Henzlova MJ, Duvall WL, Einstein AJ, Travin MI, Verberne HJ. ASNC imaging guidelines for SPECT nuclear cardiology procedures: Stress, protocols, and tracers. Journal of Nuclear Cardiology. 2016;23(3):606-39.

19. Malek H, Ghaedian T, Yaghoobi N, Rastgou F, Bitarafan-Rajabi A, Firoozabadi H. Focal breast uptake of 99mTc-sestamibi in a man with spindle cell lipoma. Journal of Nuclear Cardiology. 2012;19(3):618-20.

20. Malek H, Yaghoobi N, Hedayati R. Artifacts in Quantitative analysis of myocardial perfusion SPECT, using Cedars-Sinai QPS Software. Journal of Nuclear Cardiology. 2017;24(2):534-42.

21. Malek H, Hedayati R, Yaghoobi N, Bitarafan-Rajabi A, Firoozabadi SH, Rastgou F. The effect of milk, water and lemon juice on various subdiaphragmatic activity-related artifacts in myocardial perfusion imaging. Research in cardiovascular medicine. 2015;4(4).

22. Romero-Farina G, Aguadé-Bruix S, Candell-Riera J, Pizzi MN, García-Dorado D. Cut-off values of myocardial perfusion gated-SPECT phase analysis parameters of normal subjects, and conduction and mechanical cardiac diseases.

Journal of Nuclear Cardiology. 2015;22(6):1247-58.

23. Singh H, Patel CD, Sharma P, Naik N, Singh S, Narang R. Does perfusion pattern influence stress-induced changes in left ventricular mechanical dyssynchrony on thallium-201-gated SPECT myocardial perfusion imaging? Journal of Nuclear Cardiology. 2015;22(1):36-43.

24. Pazhenkottil AP, Buechel RR, Herzog BA, Nkoulou RN, Valenta I, Fehlmann U, et al. Ultrafast assessment of left ventricular dyssynchrony from nuclear myocardial perfusion imaging on a new high-speed gamma camera. European journal of nuclear medicine and molecular imaging. 2010;37(11):2086-92.

25. McLaughlin MG, Danias PG. Transient ischemic dilation: a powerful diagnostic and prognostic finding of stress myocardial perfusion imaging. Journal of nuclear cardiology. 2002;9(6):663-7.

26. Emmett L, Van Gaal WJ, Magee M, Bass S, Ali O, Freedman SB, et al. Prospective evaluation of the impact of diabetes and left ventricular hypertrophy on the relationship between ischemia and transient ischemic dilation of the left ventricle on single-day adenosine Tc-99m myocardial perfusion imaging. Journal of nuclear cardiology. 2008;15(5):638-43.

27. Hämäläinen H, Hedman M, Laitinen T, Hedman A, Kivelä A, Laitinen T. Reference values for left ventricular systolic synchrony according to phase analysis of ECG-gated myocardial perfusion SPECT. Clinical physiology and functional imaging. 2018;38(1):38-45.

28. Samad Z, Atchley AE, Trimble MA, Sun J-L, Shaw LK, Pagnanelli R, et al. Prevalence and predictors of mechanical dyssynchrony as defined by phase analysis in patients with left ventricular dysfunction undergoing gated SPECT myocardial perfusion imaging. Journal of Nuclear Cardiology. 2011;18(1):24-30.