Russian Journal of Cardiology 2021;26(7):4238
doi:10.15829/1560-4071-2021-4238
https://russjcardiol.elpub.ru

ORIGINAL ARTICLES
ISSN 1560-4071 (print)
ISSN 2618-7620 (online)

Left ventricular myocardial cellular perfusion against the background of cardiac contractility modulation in patients with heart failure and atrial fibrillation

Amanatova V. A.[1], Safiullina A. A.[1], Uskach T. M.[1,2], Ansheles A. A.[1], Tereshchenko S. N.[1,2], Sergienko V. B.[1]

Aim. To assess the effect of cardiac contractility modulation (CCM) in patients with heart failure (HF) and atrial fibrillation (AF) on left ventricular (LV) myocardial cellular perfusion using perfusion single photon emission computed tomography (SPECT).

Material and methods. ^{99m}Tc-MIBI SPECT gated myocardial perfusion imaging was performed in 60 patients with HF and AF before implantation of CCM device and after 6-months follow-up. All patients received long-term optimal medication therapy for HF.

Results. The results obtained indicate a significant positive effect of CCM use in patients with HF and AF on LV ejection fraction (increase from 22 [18;30] to 25,5 [19;38] (p=0,002)), LV volume (decrease in LV end-systolic volume from 187 [114;238] to 154 [100;201] (p=0,001), end-diastolic volume from 229 [174;290] to 209 [159;259] (p=0,007)), as well as myocardial perfusion values. There is a favorable myocardial perfusion dynamic, which was more pronounced in non-ischemic HF: increase in SRS from 6 [5;9] to 8,0 [6;11] after 6 months (p=0,01)). The extent of impaired perfusion significantly decreases from 12 [9;17] to 9 [6;16] (p=0,04). An indicator reflecting the total impairment of LV myocardial perfusion significantly decreases: total perfusion deficit decreased from 10 [8;14] to 7 [6;14] after 6 months (p=0,02), compared with ischemia-related HF.

Conclusion. Perfusion SPECT makes it possible to assess the myocardial cellular perfusion during CCM therapy in patients with HF of various origin and AF. CCM therapy improves myocardial contractility and perfusion in patients with HF and AF.

Keywords: perfusion single photon emission computed tomography, heart failure, cardiac contractility modulation.

Relationships and Activities: none.

[1]National Medical Research Center of Cardiology, Moscow; [2]Russian Medical Academy of Continuous Professional Education, Moscow, Russia.

Amanatova V. A.* ORCID: 0000-0002-0678-9538, Safiullina A. A. ORCID: 0000-0002-2675-3276, Uskach T. M. ORCID: 0000-0003-4318-0315, Ansheles A. A. ORCID: 0000-0002-2675-3276, Tereshchenko S. N. ORCID: 0000-0001-9234-6129, Sergienko V. B. ORCID 0000-0002-0487-6902.

*Corresponding author: Amanatova.v@yandex.ru

Received: 13.12.2020
Revision Received: 17.02.2021
Accepted: 28.02.2021

For citation: Amanatova V. A., Safiullina A. A., Uskach T. M., Ansheles A. A., Tereshchenko S. N., Sergienko V. B. Left ventricular myocardial cellular perfusion against the background of cardiac contractility modulation in patients with heart failure and atrial fibrillation. *Russian Journal of Cardiology*. 2021;26(7):4238. (In Russ.) doi:10.15829/1560-4071-2021-4238

In developed countries, ~1-2% of the adult population have heart failure (HF), the risk of which increases with population aging; among patients over 70 years of age, it increases by 10% [1]. According to epidemiological studies, the proportion of HF in Russian population is 7%, including severe — 4,5% [2]. Atrial fibrillation (AF) is the most common arrhythmia in clinical practice. In the world, >33 million patients have AF, while every year it develops in more than 5 million people [3].

HF and AF are often combined with each other, having a negative effect on the patient's prognosis [4-7].

Currently, there is growing interest in a novel device-based therapy for HF — cardiac contractility modulation (CCM), indicated primarily to patients with HF and a QRS complex <130 ms [8-12]. The mechanism of CCM therapy is mediated through the cellular electrophysiology by applying a two-phase high voltage pulse to interventricular septum during the absolute refractory period of cardiomyocyte depolarization. MCC therapy is performed using implantable Optimizer system (Impulse Dynamics, Germany) [12].

With the advent of a novel device generation (Optimizer Smart®), which does not require implantation of an atrial lead, it became possible to use CCM in AF [13]. It seems important and relevant to study the effect of this method on left ventricular (LV) myocardial changes in patients with HF and AF.

For a comprehensive assessment of myocardium, a promising method is single-photon emission computed tomography (SPECT) [14]. The advantage of radioisotope diagnostic methods is that they can be used in patients with various implanted devices, as well as with impaired renal function. Perfusion radiopharmaceuticals (RP) based on ^{99m}technetium-methoxy-isobutyl-isonitrile (^{99m}Tc-MIBI) and tetrofosmin (^{99m}Tc-TF) penetrate the sarcolemmal and mitochondrial membranes of cardiomyocytes by passive diffusion with transmembrane electrochemical gradient and are retained in the mitochondria. In this case, it is possible to perform ECG-gated SPECT with estimation of all the necessary parameters of systolic and diastolic myocardial function [15, 16].

Regarding HF of ischemic origin, it is important to highlight such a concept as a hibernating myocardium, which is a viable areas with chronic reduced perfusion, reduced or absent contractility, but preserved metabolism and potential restoration of function with adequate therapy. According to myocardial perfusion SPECT, it is possible to assess the presence and area of hibernating myocardium by comparing perfusion and contractility maps [17]. It can be assumed that CCM will have a favorable effect on areas of such myocardium, thereby improving both perfusion and myocardial contractility.

Considering the above, the aim was to assess the effect of CCM therapy in patients with HF and AF on LV myocardial cell perfusion using perfusion SPECT.

Material and methods

The study included 60 patients. Inclusion criteria were NYHA class II-III HF with reduced ejection fraction (EF) (not <20%) for at least 3 months, paroxysmal or permanent AF, optimal medication therapy for at least 3 months, stable condition >1 month, no left bundle branch block. There were following exclusion criteria: patient's refusal to participate in the study; inclusion in heart transplant waiting list, or after heart transplantation, NYHA class IV HF; acute diseases that, in the researcher's opinion, could adversely affect the safety and/or effectiveness of treatment; reversible HF causes; recent major surgery or trauma; recent cardiac events, including myocardial infarction, percutaneous coronary intervention, or heart surgery within previous 3 months; decompensated HF; acute myocarditis; hypertrophic obstructive cardiomyopathy; class IV angina; mechanical tricuspid valve replacement; impaired vascular access; medical conditions limiting life expectancy to 1 year. The follow-up period lasted 6 months.

All patients signed informed consent to undergo perfusion ^{99m}Tc-MIBI SPECT. The study was limited by contraindications to nuclear diagnostics (pregnancy, lactation, acute fever, acute mental disorders).

Perfusion SPECT was performed using a Phillips BrightView XCT system, which is a combined system equipped with a gamma camera and an X-ray computed tomograph. We used ^{99m}Tc-MIBI (10 mCi). The investigation was carried 30-45 minutes after its intravenous injection. Reconstruction and projection processing was carried out in the Cedar-Sinai AutoSPECT and QPS/QGS software package with iterative Astonish algorithm. Myocardial RP distribution at rest was analyzed by tomoscintigraphiy and polar maps. Perfusion defects were assessed using standard 17-segment model with Summed Rest Score (SRS), Extent, and total perfusion deficit (TPD) parameters. SRS reflects the sum of relative perfusion disorder values — from 0 (normal) to 4 (transmural perfusion defect). The Extent reflects the area (in %) of significant perfusion disorders, and TPD is an integral parameter that takes into account both the area and depth of defects. These parameters are cumulative and do not take into account defect localization. Their high value can correspond to both

Table 1
Clinical and demographic characteristics of patients

Parameter	Value
Age, years	59 [56,0;66,0]
Men/women, %	51 (85%)/9 (15%)
HF etiology Old myocardial infarction DCM	 31 (51,6%) 29 (48,4%)
NYHA HF class	II ФК — 24 (40%)/ III ФК — 36 (60%)
LVEF, %	35,0 [28,0;34,5]
HF duration, months	24 [18,0;48,0]
AF duration, months	24 [12,0;48,0]
Paroxysmal AF	30 (50%)
Permanent AF	30 (50%)
Diabetes mellitus type 2, %	11 (27,5%)
BMI, kg/m^2	30 [27,0;34,5]

Abbreviations: DCM — dilated cardiomyopathy, CAD — coronary artery disease, BMI — body mass index, LVEF — left ventricular ejection fraction, AF — atrial fibrillation, HF — heart failure.

Table 2
Changes of standard contractility parameters according to myocardial SPECT at rest

Parameter	Baseline	After 6 months	p
Contractility parameters			
LVEF	22 [18;30]	25,5 [19;38]	0,002
LV EDV	229 [174;290]	209 [159;259]	0,007
LV ESV	187 [114;238]	154 [100;201]	0,001
CO	3,5 [3,02;4,2]	3,9 [2,9;4,9]	0,5

Abbreviations: LV EDV — left ventricular end diastolic volume, LV ESV — left ventricular end systolic volume, CO — cardiac output, LVEF — left ventricular ejection fraction.

focal scarring and multiple diffuse defects caused by other causes [14]. In addition, the intensity of PR accumulation in each pixel receives its own shade and value as a percentage, which provides a visual assessment of perfusion distribution. This makes it possible to assess the relative perfusion for each segment of blood supply. Apical perfusion defects were considered on a case-by-case basis. since they are considered as a norm [15]. During ECG-gated SPECT, data were collected in 8 frames within the R-R interval and standard parameters of LV contractile function were analyzed: EF, end diastolic volume (EDV), end systolic volume (ESV) of LV [16].

Statistical analysis was carried out using the Excel 2010 and STATISTICA 10 software (StatSoft Inc., USA). Qualitative variables are presented as absolute values and percentages. The following statistical methods were used: two-sided Fisher's exact test, Mann-Whitney U-test. Correlation analysis was carried out using Spearman's rank correlation coefficient. The sample parameters shown in the table are presented as M (sd) and Me [Lq;Uq], where M is the mean, sd — standard deviation, Me — median, Lq;Uq — interquartile range. Differences were considered significant at $p<0,05$.

Results and discussion

The clinical characteristics of patients are presented in Table 1.

Of 60 patients included in the study, 85% were men and 15% were women (age, 59 [56;66] years). There were 40% of all patients with class II HF, 60% — class III HF. The study included patients with paroxysmal (n=30) and permanent (n=30) AF. The median LVEF at inclusion in the study according to echocardiography was 35 [28,0;34,5]%.

Repeated myocardial SPECT was performed in patients 6 months after implantation of CCM.

Changes in standard parameters of contractility and perfusion according to myocardial SPECT is presented in Table 2.

It should be noted that ejection fraction is estimated with echocardiography using a special equation after measuring the LV linear parameters (end diastolic and systolic dimensions), while its correctness depends on accuracy of determining these indicators [17]. With SPECT, LV volumetric parameters are initially obtained (EDV and ESV), and the LVEF is estimated automatically. In addition, when calculating EDV and ESV, the average cardiac cycle is used, which is the sum of all cardiac beats (except for premature contractions) recorded (10 min) under ECG guidance [18-21]. Due to the different methods of estimating LVEF with these two research methods, its values may differ, and according to SPECT, LVEF is usually on average 7-10% lower than with echocardiography.

After 6 months, all patients (n=60) with HF and AF had a significant increase in LVEF according to SPECT from 22 [18;30] to 25,5 [19;38] (p=0,002). There is a significant decrease in both LV ESV from 187 [114;238] to 154 [100;201] (p=0,001) and EDV from 229 [174;290] to 209 [159;259] (p=0,007). A decrease in perfusion disorder indicators such as SRS, Extent, TPD was obtained.

According to generally accepted technique, CCM leads are implanted into the interventricular septum in right ventricle. CCM stimuli directly act on myocardium with an area of 4×7 cm due to spread along the peripheral conduction system.

Table 3

Changes of LV contractility parameters depending on HF origin according to C-SPECT

Parameters	Ischemic HF (n=31)		p	Non-ischemic HF (n=29)		p
	Baseline	After 6 months		Baseline	After 6 months	
LVEF	21 [17,5;26,0]	25 [18;25]	0,01	23 [18;30]	37,5 [20;41]	0,009
LV EDV	255 [221;290]	221 [209;262]	0,09	226 [165;290]	162 [135;250]	0,03
LV ESV	192 [171;226]	166 [155;220]	0,08	170 [107;240]	102 [86;164]	0,005
CO	3,4 [2,9;3,8]	3,7 [3,0;4,5]	0,2	3,8 [3,1;4,3]	4,2 [2,7;4,9]	0,5

Abbreviations: LV EDV — left ventricular end diastolic volume, LV ESV — left ventricular end systolic volume, CO — cardiac output, LVEF — left ventricular ejection fraction, HF — heart failure.

Table 4

LV myocardial perfusion parameters depending on HF origin according to myocardial C-SPECT

Parameters	Ischemic HF (n=31)		p	Non-ischemic HF (n=29)		p
	Baseline	After 6 months		Baseline	After 6 months	
SRS	24 [17;34]	23,5 [17;30,5]	0,2	8,0 [6;11]	6 [5;9]	0,01
Extent	44 [29,5;52]	42 [31;51]	0,9	12 [9;17]	9 [6;16]	0,04
TPD	36,5 [23;52]	39 [23;46]	0,8	10 [8;14]	7 [6;14]	0,02

Abbreviations: SRS — summed rest score, TPD — total perfusion deficit.

The effect on activity of key regulatory proteins (phospholamban) is immediately obtained [22]. This quick response helps to restore cell function and increase the contraction strength. Further, local changes lead to a decrease in stress in distant myocardial areas and, over time, to normalization of gene expression. The electrical communication between cells is improved and direct effect of stimuli is increased. Over the months, a significant stress reduction can be observed, which disrupts the remodeling cascade, which promotes reverse remodeling. Studies containing a biopsy examination confirm the development of effect after 3 months [23].

In addition to myocardial perfusion, cardiac SPECT allows to assess its contractility. In this study, it was possible to determine HF nature, since perfusion in ischemic and non-ischemic genesis have precise quantitative parameters. To assess the parameters of perfusion and contractility depending on HF etiology, patients were divided into 2 groups: ischemic (n=31) and non-ischemic (n=29) HF origin.

Standard contractility parameters according to SPECT are presented in Table 3. In the group of patients with ischemic HF origin, there is a significant increase in LVEF from 21 [17,5;26,0] to 25 [18;25] (p=0,01). There is a decrease in LV volumes, however, it does not reach significance at the moment. An insignificant increase in cardiac output is also recorded. In the group of patients with non-ischemic HF origin, LVEF significantly increases from 23 [18;30] to 37,5 [20;41] (p=0,009). LV volumes decreased: EDV — from 226 [165;290] to 162 [135;250] (p=0,03), ESV –from 170 [107;240] to 102 [86;164] (p=0,005). Cardiac output increased, but not significant.

Table 4 shows the standard myocardial perfusion parameters in groups of patients with different HF origin.

SRS is the summed index of deep perfusion defects in all segments of perfusion map at rest. This indicator allows to draw a clear boundary between patients with heart failure of ischemic and non-ischemic origin. So, for patients with significant myocardial scarring, SRS ⩾15 is characteristic. At the same time, in patients with non-ischemic HF origin, SRS, as a rule, vary in the range from 0 to 15.

In the group of patients with ischemic HF origin, no significant perfusion changes were revealed with CCM therapy, which is due to irreversible perfusion defects, and also partly due to chronic impairment of myocardial blood supply (for example, due to chronic coronary total occlusions). Figures 1 and 2 show an example of myocardial SPECT of the patient with ischemic HF origin.

The patient had prior myocardial infarction, as a result of which a large anterior-apical-lateral perfusion defect developed. The SRS amounted to 36, Extent — 51%, TPD — 46%. Initially, there was a sharply reduced systolic wall thickening, decreased LVEF, and significant dilatation of cardiac cavities.

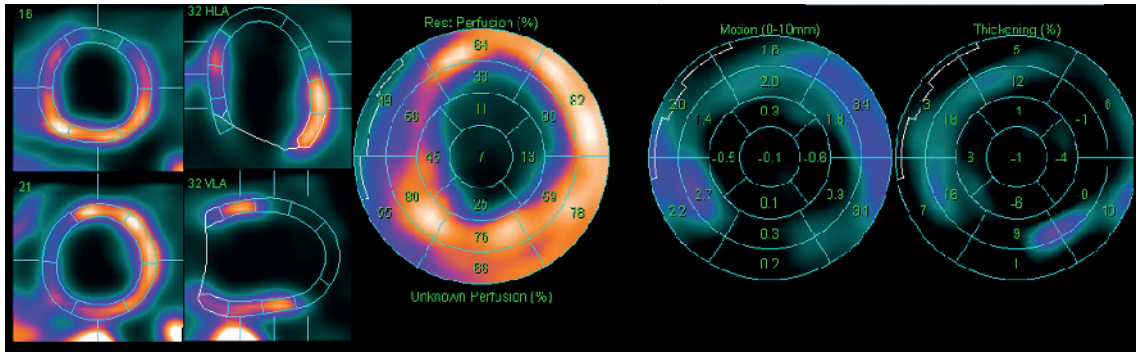

Figure 1. Initial myocardial perfusion SPECT in the patient with ischemic HF. **A.** Perfusion scintigrams. **B.** Polar map of LV perfusion. Uneven RP distribution. A large-focal perfusion defect (transmural old myocardial infarction) of the apex, apical and middle segments of the anterior, anterolateral walls with spread to the apical and partially middle segments of the anterior septal wall and apical segments of LV inferior wall with a total area of about 40% of LV is visualized. **C.** Polar map of systolic LV wall motion. LV dilatation, diffuse hypo(a) kinesis, dyskinesis of the apex, apical segments of the lateral, septal walls of LV (signs of fibromuscular aneurysm, EDV of 411 ml, ESV of 378 ml, stroke volume of 33 ml, LVEF of 8% (N>50%) with heart rate of 84 bpm, cardiac output of 2,7 l/min). **D.** Polar map of LV systolic wall thickening. Systolic thickening of all LV walls is sharply reduced.

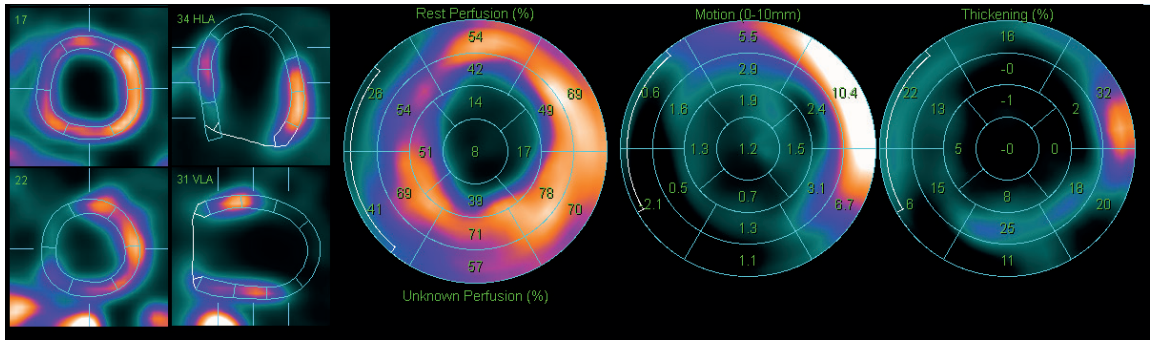

Figure 2. Myocardial perfusion SPECT of the patient with ischemic HF after CCM device implantation.
A. Perfusion scintigrams. **B.** Polar map of LV perfusion. No worsening. Anterior-apical-lateral perfusion defect persists with the development of an aneurysm with an area of 35%. **C.** Polar map of systolic LV wall motion. LV dilatation, diffuse hypo(a)kinesis, dyskinesis of the apex, apical segments of the lateral, septal walls of LV (signs of fibromuscular aneurysm), EDV of 361 ml, ESV of 299 ml, LVEF of 17% (N>50). **D.** Polar map of LV systolic wall thickening. Systolic thickening is moderately restored in the inferolateral and anterolateral LV segments.

With repeated SPECT 6 months after CCM device implantation, there is an increase in LVEF and a decrease in LV volumes. Perfusion defect parameters also show a favorable trend: SRS decreases to 32, Extent — 49%, TPD — 44%. However, in patients with ischemic HF origin, a significant perfusion improvement did not occur due to stable perfusion defect after myocardial infarction.

In the group of patients with non-ischemic HF etiology, there was a significant decrease in deep perfusion defects — SRS after 6 months of 6 [5;9] compared with the initial SRS of 8 [6;11] (p=0,01). The Extent significantly decreases from 12 [9;17] to 9 [6;16] (p=0,04), while TPD decreases from 10 [8;14] to 7 [6;14] (p=0,02).

Non-ischemic HF is characterized by dilatation of cardiac cavities and, as a consequence, relative coronary insufficiency with unchanged or slightly altered coronary arteries. Pathological examination in such patients reveals microvasculature impairment, in particular, disorganization and atrophy of basement membranes of supplying vessels and a ruffled endothelial lining with pinocytic activity. In addition, there is a high detection rate of microthrombi, prestasis and stasis of blood corpuscles [24]. In this case, CCM stimuli lead to an increase in intracellular calcium content and, as a consequence, to an increase in cardiomyocyte contractile force due to the phosphorylation of phospholamban, which is responsible for the activity of

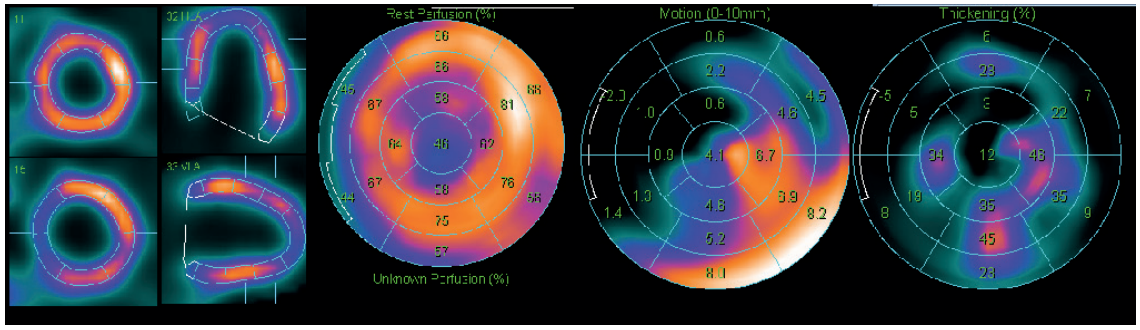

Figure 3. Initial myocardial perfusion SPECT in the patient with non-ischemic HF.
A. Perfusion scintigrams. **B.** Polar map of LV perfusion. There is a diffuse uneven RP distribution, no reliable focal defects. Signs of small focal perfusion defects in the septal and inferolateral LV segments. **C.** Polar map of systolic LV wall motion. LV dilatation, diffuse hypo(a) kinesis of all LV walls, except for the inferolateral, up to dyskinesis of the anterior and septal LV segments. EDV of 139 ml, ESV of 97 ml, stroke volume of 42 ml, LVEF of 30% (N>50%) with heart rate of 117 bpm, cardiac output of 4,7 l/min. **D.** Polar map of LV systolic wall thickening. Systolic thickening of all LV walls is sharply reduced.

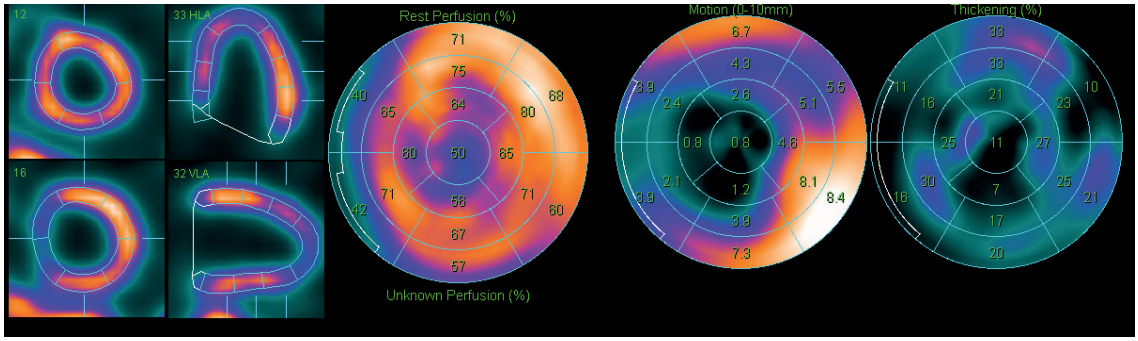

Figure 4. Myocardial perfusion SPECT of the patient with non-ischemic HF after CCM device implantation.
A. Perfusion scintigrams. **B.** Polar map of LV perfusion. No worsening. **C.** Polar map of systolic LV wall motion. Reduction of LV cavity, restoration of systolic motion almost to normokinesis along all LV walls, except for the septal one. EDV of 125 ml, ESV of 79 ml, stroke volume of 46 ml, LVEF of 37% (N>50%) with heart rate of 86 bpm, cardiac output of 3,9 l/min. **D.** Polar map of LV systolic wall thickening. Reduction of LV systolic wall thickening persists.

sarco/endoplasmic reticulum Ca^{2+} adenosine triphosphatase-2a (SERCA2a). In the early CCM therapy stages, there is a local effect, then a change in SERCA2a expression in other parts of ventricular myocardium occurs. Thus, CCM therapy has a positive inotropic effect without increasing myocardial oxygen demand [25]. The positive inotropic effect of CCM therapy is probably a stimulus to reverse myocardial remodeling activation, including improving the state of capillary endothelium, and, consequently, improving microcirculation and cell perfusion in patients with non-ischemic HF.

As an illustration of changes of contractility and perfusion parameters according to myocardial SPECT at rest, a patient with non-ischemic HF is shown as an example in Figures 3 and 4.

At baseline, this patient had SRS of 7, Extent score of 11%, and TPD score of 8%. There is a sharply reduced systolic wall thickening, decreased LVEF, and significant dilatation of cardiac cavities.

Six months after implantation of CCM device, there is an increase in LVEF up to 37% and a decrease in LV volumes. Perfusion defect parameters also show favorable dynamics: SRS decreases to 6 points, Extent — 8%, TPD — 7%

Conclusion

It should be noted that in none of the previous studies in patients with CCM therapy, the assessment of myocardial cell perfusion using SPECT was carried out. Thus, the results of our work for the first time show the effect of CCM therapy on myocardial contractility and cellular perfusion in patients with HF with reduced EF and AF. Taking into account the data obtained, CCM therapy is able to improve perfusion and myocardial contractility according to SPECT in patients with HF of non-ischemic

origin. In patients with ischemic HF, there was no significant improvement in perfusion, which is most likely due to irreversible myocardial scarring. In such patients, it is necessary to study other ways for improving contractile function, one of which is a decrease in hibernating myocardium extent.

Summarizing the above, it should be noted that SPECT is a promising and relevant method for assessing myocardial cell perfusion in patients with implanted devices, including CCM.

Relationships and Activities: none.

References

1. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Rev Esp Cardiol (Engl Ed). 2016;69(12):1167. doi:10.1016/j.rec.2016.11.005.
2. Ageev FT, Belenkov UN, Fomin IV, et al. Prevalence of chronic heart failure in the European part of the Russian Federation data from EPOCH-CHF. Chronic Heart Failure. 2006;7(1):112-5. (In Russ.)
3. Chugh S, Havmoeller R, Narayanan K. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. Circulation. 2014;129:837-47.
4. Wang T, Larson M, Levy D. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. Circulation. 2003;107:2920-5.
5. Maisel W, Stevenson L. Atrial fibrillation in heart failure: epidemiology, pathophysiology and rationale for therapy. Am J Cardiol. 2003;91(6A):2D-8D.
6. The SOLVD Investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. N Engl J Med. 1992;327:685-91.
7. Zhirov IV, Romanova NV, Tereshchenko SN, Osmolovskaya YuF. Epidemiology and management of heart failure patients with atrial fibrillation. Kardiologiia. 2015;55(3):91-6. (In Russ.) doi:10.18565/cardio.2015.3.91-96.
8. McMurray JJV, Adamopoulos S, Anker SD, et al. Erratum: ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Eur. J. Heart Fail. 2013;15(3):361-2.
9. Russian Society of Cardiology (RSC). 2020 Clinical practice guidelines for Chronic heart failure. Russian Journal of Cardiology. 2020;25(11):4083. (In Russ.) doi:10.15829/1560-4071-2020-4083.
10. Packer DL, Prutkin JM, Hellkamp AS, et al. Impact of implantable cardioverter-defibrillator, amiodarone, and placebo on the mode of death in stable patients with heart failure: Analysis from the sudden cardiac death in heart failure trial. Circulation. 2009;120(22):2170-6. doi:10.1161/CIRCULATIONAHA.109.853689.
11. Cleland JGF, Daubert J-C, Erdmann E, et al. Longer-term effects of cardiac resynchronization therapy on mortality in heart failure [the CArdiac REsynchronizationHeart Failure (CARE-HF) trial extension phase]. Eur. Heart J. 2006;27(16):1928-32. doi:10.1093/eurheartj/ehl099.
12. Pappone C, Vicedomini G, Salvati A, et al. Electrical modulation of cardiac contractility: clinical aspects in congestive heart failure. Heart Failure Reviews. 2001;6(1):55-60.
13. Kloppe A, Boesche L, Aweimer A, et al. Acute and short-term safety and feasibility of the new OPTIMIZER SMART-system: Is it reasonable to avoid an atrial lead? EP Europace. 2018;20(suppl_1):i48. doi:10.1093/europace/euy015.128.
14. Verberne HJ, Acampa W, Anagnostopoulos C, et al. EANM procedural guidelines for radionuclide myocardial perfusion imaging with SPECT and SPECT/CT: 2015 revision. Eur J Nucl Med Mol Imaging. 2015;42(12):1929-40. doi:10.1007/s00259-015-3139-x.
15. Ansheles AA, Sergienko VB. Interpretation of myocardial perfusion SPECT with attenuation correction. Part 2. Bulletin of Radiology and Radiology. 2020;101(1):6-18. (In Russ). doi:10.20862/0042-4676-2020-101-1-6-18.
16. Braunwald's heart disease: a textbook of cardiovascular medicine, Peter Libby, et al., 8th ed. Volume 1: Moscow: Logosphere, 2015. 624 p. (In Russ.) ISBN 978-5-98657-048-8.
17. Trufanov GE. Myocardial perfusion scintigraphy. ELBI-SPb Russia. 2012. 80 p. (In Russ.)
18. Rahimtoola SH. The hibernating myocardium. Am Heart J. 1989;117(1):211-21. doi:10.1016/0002-8703(89)90685-6-14.
19. Practical echocardiography: A guide to echocardiographic diagnostics. Eds. Flakskampf FA, Sandrikova VA. 2 Ed. M.: MEDpress-inform, 2019. 872 p. (In Russ.)
20. Ansheles AA. Specific features of interpretation of myocardial perfusion single-photon emission computed tomography with computed tomographic absorption correction. Journal of radiology and nuclear medicine. 2014;(2):5-20. (In Russ.) doi:10.20862/0042-4676-2014-0-2-5-20.
21. Bugri ME, Satlykova DF, Mareev VYu, Sergienko VB. D-tomoventriculography — a novel method in diagnostics of contractile function of the heart. Cardiology. 2009;49(6):54-60. (In Russ.)
22. Butter C, Rastogi S, Minden H-H, et al. Cardiac Contractility Modulation Electrical Signals Improve Myocardial Gene Expression in Patients With Heart Failure. JACC. 2008;51(18):1784-9. doi:10.1016/j.jacc.2008.01.036.
23. Imai M, Sabbah HN. Therapy with Cardiac Contractility Modulation Electrical Signals Improves Left Ventricular Function and Remodeling in Dogs with Chronic Heart Failure. JACC. 2007;49(21):2120-8.
24. Amosova EN. Cardiomyopathy. Kiev. Book plus. 1999. 182 p. (In Russ.)
25. Mareev YuV. Modulation of cardiac contractility in the treatment of patients with chronic heart failure. Circulatory pathology and cardiac surgery. 2014;18(4):158-63. (In Russ.)